ARE LONELINESS AND SOCIAL ISOLATION RISK FACTORS FOR ILL HEALTH?

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Abstract

Introduction: Social relationships are increasingly being acknowledged as determinants of wellbeing and health in later life. We know that people who feel lonely – i.e. who are unhappy about their relationships – or who are socially isolated – i.e. have few ties or contacts with others – are more likely to experience early death. Whether they are at greater risk of morbidity is unclear.

Aim: This thesis examines whether loneliness and social isolation are risk factors for developing ill health, with a primary focus on incident cardiovascular disease (CVD). The aim is to gauge the potential health gain from tackling loneliness and social isolation.

Methods: Four pieces of empirical research make up the main body of my thesis. First, I designed a novel framework for distinguishing between measures of loneliness and social isolation. I then systematically reviewed the evidence from longitudinal observational studies on loneliness, social isolation and incident CVD. I studied changes in loneliness and social isolation over time in the English Longitudinal Study of Ageing (ELSA), a cohort of adults aged over 50 years old. Finally, I investigated associations between loneliness and social isolation over time, and incident CVD.

Results: My systematic review found that loneliness and social isolation were associated with a 29% increase in risk of incident coronary heart disease (relative risk: 1.29, 95% CI 1.04 to 1.59) and a 32% increase in risk of stroke (relative risk: 1.32, 95% CI 1.04 to 1.68). Among ELSA participants, patterns of social relationships varied substantially over time, both within and between individuals. In survival analyses of ELSA data, loneliness but not social isolation was identified as a risk factor for incident CVD.

Conclusions: Weaker social relationships are risk factors for developing CVD. Intervening to tackle loneliness and social isolation has the potential to improve health outcomes in later life.

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Author's declaration

I declare that this thesis is a presentation of original work and I am the sole author. This work has not previously been presented for an award at this, or any other, University. All sources are acknowledged as References.

Parts of this thesis have been disseminated in the following formats:

- Articles in peer-reviewed journals:

Valtorta, NK, Kanaan, M, Gilbody, SM & Hanratty, B, 2016, 'Loneliness, social isolation and social relationships: what are we measuring? A novel framework for classifying and comparing tools', *BMJ Open*, vol. 6, 4, 10.1136/bmjopen-2015-010799 (Chapter 4)

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Valtorta, NK, 2016, 'Loneliness and isolation: how the « problem » is being tackled in the United Kingdom', *Gérontologie et Société*, vol. 38, 1, pp.41-53 (Chapters 1 & 8)

- Invited article:

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- Conference abstracts:

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Valtorta, NK, Kanaan, M, Gilbody, SM & Hanratty, B, 2016, 'Changes in loneliness and social isolation over time in adults aged over 50: the English Longitudinal Study of Ageing', Poster presentation, *Journal of Epidemiology & Community Health*, vol. 70, Suppl. 1, A70 (Chapter 6)

Valtorta, NK, Gilbody, SM, Kanaan, M & Hanratty, B, 2015, 'A framework for classifying and comparing measures of social relationships used in epidemiological studies', Oral presentation, British Society of Gerontology Annual Conference, Newcastle upon Tyne (Chapter 4)

Valtorta, NK, Kanaan, M, Gilbody, SM & Hanratty, B, 2015, ‘Are loneliness and social isolation predictors of ill health? A systematic review of longitudinal observational studies set in high-income countries’, Oral presentation, International Association of Gerontology & Geriatrics Annual Conference, Dublin (Chapter 5)

Valtorta, NK, Kanaan, M, Gilbody, SM & Hanratty, B, 2015, ‘Loneliness and social isolation as determinants of health: a systematic review of longitudinal observational studies set in high-income countries’, Poster presentation, European Public Health Association Early Career Research Workshop, Glasgow (Chapter 5)

- Invited talks:

Valtorta, NK, Kanaan, M, Gilbody, SM & Hanratty, B, 2016, ‘A public health perspective on loneliness and social isolation’, University College London Social Connections, Cohesion and Health Meeting, London (Chapters 1 to 8)

Valtorta, NK, Kanaan, M, Gilbody, SM & Hanratty, B, 2016, ‘Loneliness, social isolation and health: findings from a three-year project’, Campaign to End Loneliness Research and Policy Forum, York (Chapters 1 to 8)

Valtorta, NK & Hanratty, B 2016, ‘Loneliness and social isolation: a public health challenge?’, Fuse Quarterly Research Meeting, Newcastle upon Tyne (Chapters 1 to 8)

- Media:

National press, including *The Guardian, The Times, The Telegraph* (Chapter 5)

International press: *CNN, TIME Magazine, New York Times, Huffington Post, Forbes, El Mundo*, *ScienceDaily, STAT* (Chapter 5)

Radio: BBC Radio4 World at One, BBC Radio Scotland, RTÉ Radio 1, Doctor Radio (US), talkRADIO (Chapters 5 & 7)

Chapter 1. Introduction

Chapter summary: This first chapter traces the thinking behind the subject and design of my doctoral project. After an introductory section in which I define the overarching concept of social relationships and touch on their relevance for health (1.1.), I critically review the literature that links them to morbidity and mortality (1.2.). Having surveyed the epidemiological evidence and identified gaps in our knowledge, I argue for the need to clarify how specific dimensions of social relationships might influence health, to inform prevention strategies; and I explain how the work presented in the remainder of this thesis sets out to reduce uncertainty in the field (1.3.).

1.1. Social relationships, and their relevance for (public) health

1.1.1. Defining social relationships

A social relationship 'exists between two people when each person influences the other's thoughts, feelings, and or behavior. In other words, a relationship exists when people are at least minimally interdependent' (Clark, 2001, p.14423). According to this definition, the common ground of all social relationships is that they involve two individuals; that they are premised on mutual influence; and that they are characterised by interdependence. Beyond these shared criteria, social relationships can take on a range of forms. They can be of varying strength and length, with changes in people's circumstances across the life course likely to affect the nature and intensity of their exchanges with others. They can connect a variety of individuals, from family members and friends to colleagues and members of the wider community. Depending on situational (e.g. family size) or characterological (e.g. personality traits) factors, someone might engage in many social relationships or be connected to one or two other individuals only. Independently of the number and range of relationships in which a person is involved, their quality is likely to vary, with different relationships fulfilling different functions and meeting different needs, such as the need for a confidant or for someone with whom to participate in a social activity.

1.1.2. Social relationships and health

Research evidence accumulated over the past forty years suggests that social relationships influence health.

1.1.2.1. Social relationships and mortality

In the 1970s and 1980s, investigators conducted a series of observational studies in which poor social relationships were consistently associated with an increased risk of premature mortality (see reviews by Berkman, 1995 and House et al., 1988). This association was observed across different measures of relationships, including marital status, number of close of friends and relatives, or involvement in group activities – a finding confirmed by a recent meta-analysis of longitudinal studies published between 1900 and 2007. According to this meta-analysis of 148 studies, which covered 308,849 adults averaging 63.9 years of age at initial evaluation and followed for a mean duration of 7.5 years, participants with stronger social relationships had a 50% increased likelihood of survival across age, sex, initial health status, cause of death, and follow-up period (Holt-Lunstad et al., 2010).

1.1.2.2. Social relationships and morbidity

The first investigators to put forward a link between social relationships and disease risk were Cassel (1976) and Cobb (1976). Drawing on evidence from animal and human research, the physician and epidemiologist John Cassel identified the ‘presence of other members of the same species’ as a factor contributing to the susceptibility of hosts to environmental disease agents (1976, p.108). Cassel argued that intervening to improve and strengthen individuals’ social supports had the potential to significantly prevent disease. The psychiatrist Sidney Cobb, similarly to Cassel, emphasised the stress-buffering effects of social relationships – i.e. the health-related role of social relationships among people who are under stress (Cohen et al., 2000a; Cohen and Wills, 1985). Focusing on the concept of social support defined as ‘information leading the subject to believe that he or she is loved, esteemed, and belongs to a network of mutual obligation’ (1976, p. 300), Cobb reviewed studies showing its protective effect against the health consequences of various life stresses. This evidence suggested that social support had the potential to provide protection from pathological states, reduce the amount of medication required to treat someone, accelerate recovery, and promote compliance with prescribed medical regimens (Cobb, 1976).

More recently, results from prospective epidemiological studies indicate that social relationships are linked to both physical and mental health outcomes. Evidence from a systematic review of studies on coronary heart disease (CHD) published up until 2001 supports an association between social relationships and CHD: six of the nine studies on disease incidence reported an association between relationships and risk of CHD, and two thirds of the twenty-one prognostic studies found a link between stronger relationships and better prognosis among people with a diagnosis of CHD (Kuper et al., 2005). In a systematic review of 19 longitudinal cohort studies investigating the association between a variety of social relationship dimensions and incident dementia in the general population, low social participation, less frequent social contact and greater loneliness were respectively associated with a 41%, 57% and 58% increase in risk of dementia (Kuiper et al., 2015). Beyond CHD and dementia, social relationships have been linked to other major causes of disease burden world-wide, including stroke (Nagayoshi et al., 2014b), diabetes (Hilding et al., 2015) and disability (Lund et al., 2010).

1.1.2.3. Social relationships as a public health challenge

The health implications of social relationships have recently begun to attract the attention of policymakers in the UK, with a predominant focus on relationships in older age. In the 2012 Care and Support White Paper, loneliness and social isolation were identified as 'a huge problem that society has failed to tackle. […] Social isolation and persistent loneliness, particularly in later life, have a huge impact on people's health and wellbeing. […] We must work together to tackle social isolation.' (Department of Health, 2012). 'Helping older people most at risk of longer-term loneliness and social isolation to remain active' was one of the objectives outlined in the 2010 to 2015 government policy paper on older people (Department for Work and Pensions, 2013). As part of this endeavour, a £1 million fund was provided to fund local initiatives and recruit 'Active at 60 Community Agents' whose role was to foster connections between people within their local communities (Department for Work and Pensions, 2012).

Recognising the societal challenge posed by poor social relationships is a first step in tackling the issue – the next stage is to determine what the potential health gain from intervention might be, and to identify the best strategy for tackling poor social relationships and their health effects. To date, a variety of initiatives have been developed, ranging from group interventions such as educational programmes and social activities, to one-to-one interactions including befriending and cognitive behavioural therapy. The effectiveness of these interventions is unclear, in great part due to heterogeneity in both the approaches to, and the quality of, evaluations (Cattan et al., 2005; Dickens et al., 2011). Whether such interventions have a beneficial effect on participants' health, as well as their social relationships, is unknown.

In order to develop and implement effective intervention strategies, we need a solid understanding of how and in what circumstances poor social relationships affect health. In the following section, I highlight what we do and do not know from the research evidence and what this means for the design of effective interventions.

1.2. Previous research and gaps in the literature

The following section outlines the evidence and gaps in our knowledge about the health implications of social relationships.

1.2.1. Different dimensions of social relationships, and their influence on health

Researchers have used a variety of concepts to study social relationships and their effects on health, ranging from social networks, social interaction and social isolation to social integration, social support, and loneliness. The use of different terminology partly reflects the recognition that social relationships are multi-faceted, and that different dimensions of relationships may have implications for health. For example, Hilding investigated whether the *size* of a personal social network predicted incident diabetes among middle-aged individuals living in Sweden, reporting evidence of a greater risk among men with fewer social relationships (adjusted odds ratio (OR): 1.93, 95% confidence interval (CI): 1.03 to 3.60), but not women (adjusted OR: 0.50, 95% CI: 0.22 to 1.16) (Hilding et al., 2015). Focusing on a different aspect of relationships, Cohen hypothesized that it was the *diversity* of a person's ties with friends, family, work, and community members that was associated with susceptibility to the common cold (Cohen et al., 1997). Based on US data from 276 quarantined healthy volunteers, the study found that among participants who reported three or fewer types of relationships (e.g. with a spouse, with friends or fellow volunteers), the odds of getting a cold after experimental exposure were 4.2 times the odds among people involved in 6 or more types of relationships (adjusted OR: 4.2, 95% CI, 1.34 to 13.29). Other investigators have looked into how the *perceived quality and quantity* of social relationships affect health. In a US population-based sample of 229 participants aged between 50 and 68 years old, Hawkley found that loneliness, defined as 'the distressing feeling that accompanies discrepancies between one's desired and actual social relationships' (2010, p.132), predicted systolic blood pressure increase over 5 years (unstandardized linear regression coefficient $B = 0.152$, $SE = 0.091$, $p < 0.05$, one-tailed).

It is unclear whether some aspects of relationships are more important for health than others. Evidence on the independent, relative, and synergistic effects of different social relationship dimensions is limited. The vast majority of studies include only one measure of social relationships, precluding direct comparisons. The few studies that do examine more than one dimension report conflicting results, with some researchers finding that perceptions of relationships are more influential and others reporting stronger effects for more objective measures of isolation. In relation to mortality risk, US researchers studying a representative sample of 2,101 adults aged 50+ found that over a follow-up period of 6 years, lonely individuals were at increased risk of premature mortality (OR adjusted for socio-demographic characteristics: 1.13, 95% CI: 1.05 to 1.22). There was no evidence to suggest that the availability of friends and family living nearby was associated with mortality risk (friends living nearby: OR: 0.86, 95% CI: 0.66 to 1.11; relatives living nearby: OR: 0.92, 95% CI: 0.72 to 1.17) (Luo et al., 2012). In a prospective cohort study of 4,004 adults aged between 65 and 84 living in the Netherlands, loneliness predicted premature mortality risk over 10 years, but only among men (adjusted hazard ratio (HR), men: 1.30, 95% CI: 1.04 to 1.63; adjusted HR, women: 1.04, 95% CI: 0.90 to 1.24); no higher risk of mortality was found in relation to social isolation, operationalized as either living alone, not/no longer being married or lacking social support (Holwerda et al., 2012). Evidence from the UK, meanwhile, suggests that objective characteristics rather than subjective appraisals of relationships (loneliness), are what matter most when predicting mortality. In a sample of 6,500 men and women aged 52 and older who took part in the English Longitudinal Study of Ageing in 2004-2005 and were followed up for a mean of 7.25 years, social isolation was significantly associated with mortality (adjusted HR: 1.26, 95% CI: 1.08 to 1.48) but loneliness was not (adjusted HR: 0.92, 95% CI: 0.78 to 1.09) (Steptoe et al., 2013b).

Evidence of the comparative effects of different social relationships is further limited by inconsistent use of terminology and operationalization, making it difficult to compare findings across studies. In the absence of a comprehensive framework, investigators from a range of disciplines including sociology, psychology, demography, and epidemiology have suggested definitions of concepts that are not always compatible. For example, House and Khan proposed to distinguish between two dimensions of social relationships: social network and social support (House and Khan, 1985). They defined social network as the structural dimension of social relationships, encompassing aspects such as the density, duration, dispersion, reciprocity and homogeneity of relationships. Meanwhile, social support was defined as the functional aspect of relationships (i.e. covering aspects such as the provision or receipt of information, instrumental help, emotional support or advice). In a different definition, O’Reilly suggested instead that social network be used as the main concept, with social support as a subsidiary concept covering the qualitative and behavioural aspects of the social network (O'Reilly, 1988). Approaches to measurement are even less consistent. Among studies on social relationships and cardiovascular disease (CVD), for example, social support has been assessed using a range of variables, from questions gauging a person’s relationship with work colleagues (Piros et al., 2000) to the availability of confiding, emotional, practical and negative support (Roberts et al., 1995) or the Berkman-Syme Social Network Index, which covers marital status, the number and frequency of contacts with family and close friends, and membership in church and community organizations (Berkman and Breslow, 1983; Sykes et al., 2002).

Faced with conceptual and operational confusion in the literature, researchers seeking to review the evidence have tended to subsume a range of variables under one overarching concept. In a systematic review of observational studies on psychosocial factors and coronary heart disease, Kuper (2005) included a range of variables under the concept of 'social support', from 'high love and support from wife' to 'social network index' and 'social isolation'. More often than not, reviews identify too few studies using a particular type of measure to conduct analyses comparing results based on different social relationship variables. In a review of studies on incident coronary heart disease, the literature on structural characteristics of social relationships (e.g. size of the social network, frequency of contact with others) was analysed separately from studies on the functional aspects of social support (e.g. provision or receipt of material help, the availability of a confiding relationship) (Barth et al., 2010). Evidence was mixed, with the small number of studies limiting its strength: of the three studies that measured functional social support, one reported evidence of an effect on CHD incidence, while another reported evidence of an effect among women only; the two studies on structural social support reported no evidence of association with disease incidence.

1.2.2. Are social relationships primarily a prognostic factor?

Evidence linking social relationships and health has grown steadily since the mid 1970s, when Cassel (1976) and Cobb (1976) first suggested that what they termed 'social support' might be important for health (see section 1.1.2.2. above for the definitions they used). Two characteristics of this evidence testify to its strength: the size of the evidence base collectively indicative of an association (e.g. the near 150 studies on social relationships and mortality risk included in Holt-Lunstad's 2010 review); and the range of health outcomes linked to weaker social relationships, which includes physical and mental health outcomes, and both non-communicable and communicable diseases (Berkman and Krishna, 2014).

The health-related outcome for which there is most evidence of an association with social relationships is mortality. Holt-Lunstad identified 148 studies for inclusion in a meta-analysis and found that isolated individuals were at greater risk of premature mortality (OR for isolation: 1.50, 95% CI: 1.42 to 1.59) (Holt-Lunstad et al., 2010). This finding was consistent across age, sex, initial health status, cause of death, and length of follow-up. As further evidence of the importance of social relationships, the review authors compared their results with the effects of other well-known risk factors for premature mortality, reporting that their protective effect exceeds the benefits of abstaining from alcohol and is comparable with smoking cessation. A more recent meta-analysis focusing on loneliness and social isolation suggests that the magnitude of the association with mortality may not be quite so large: in this analysis, likelihood of premature mortality was 29% greater among socially isolated individuals (adjusted

OR across 14 studies: 1.29, 95% CI: 1.06 to 1.56), and 26% higher among lonely participants (adjusted OR across 13 studies: 1.26, 95% CI: 1.04 to 1.53) (Holt-Lunstad et al., 2015). Unlike the 2010 review, the aggregated estimates from the 2015 meta-analysis were based on fully adjusted data, i.e. using models in which several possible confounders, importantly including socio-economic status, were statistically controlled for. What this suggests is that social relationships influence mortality *independently* of other socio-demographic and psychosocial risk factors. The magnitude of the association, while not as important as the relationship identified in the 2010 review, is still comparable with that of physical inactivity (OR, comparing the physically inactive with the active: 1.25, 95% CI: 1.22 to 1.28) and high Body Mass Index (OR: 1.23, 95% CI: 1.18 to 1.29) (Katzmarzyk et al., 2003).

Studies on mortality do not tell us where, on the disease pathway, social relationships are most important – i.e. whether they influence disease incidence, recovery, and/or case-fatality. So what do we know about the links between social relationships and morbidity? Evidence from individual studies, and reviews of evidence on specific disease outcomes, suggests that social relationships predict prognosis across a range of health conditions. In relation to depression for instance, an Australian study of 164 individuals found that participants with two or more past episodes of depression reported less satisfactory social support in their lives, compared to those with only one or no past episode of depression (Wilhelm et al., 1999). In the literature on CVD outcomes, investigators have repeatedly identified social relationships as a prognostic factor. Lower social support at baseline was associated with a 10% increased risk of recurrent cardiac events at 9 months (OR comparing higher to lower social support: 0.90; 95% CI: 0.84 to 0.97) in a Danish sample of patients who had experienced a first myocardial infarction (Pedersen et al., 2004). A US study of 194 individuals hospitalized following a myocardial infarction found that participants who reported no emotional support were nearly three times more likely to die within six months compared with subjects who reported at least one source of support (OR = 2.9, 95% CI: 1.2 to 6.9) (Berkman et al., 1992). Among US patients undergoing coronary bypass surgery or aortic valve replacement, the risk of death in the six months post surgery was three times higher for those who did not belong to a voluntary organization, compared to those who did (Oxman et al., 1995).

It is less clear whether social relationships are related to the development and onset of ill physical health. While some studies have identified social integration and support as protective against coronary heart disease incidence (Orth-Gomer et al., 1993), several other studies have reported no evidence of an association (Kawachi et al., 1996; Vogt et al., 1992). It is likely that the disparity in effect estimates reflects differences in study characteristics, including how social relationships were measured, the social, demographic and health-related characteristics of the study sample, which potential confounders were controlled for, and length of follow-up. The implications of such differences have yet to be explored formally in evidence syntheses.

1.2.3. Disentangling the influence of social relationships on health, and vice-versa

Whilst a substantial body of research supports a link between social relationships and health, our understanding of the direction of this association is limited by the nature of the evidence. Many of the studies conducted in the past 40 years are cross-sectional. In a scoping review of the more recent evidence published between 2000 and 2013 on social isolation, loneliness and health in older age, 61% (66/109) of observational studies measured social relationships and health at the same point in time (Courtin and Knapp, 2015). Without data collected over time, cross-sectional studies are unable to shed light on the direction of the association between social relationships and health. This is an important limitation, given the potential for reverse causality: what evidence we do have from longitudinal studies and qualitative research suggests that poor social relationships can be risk factors for, as well as consequences of, ill health. In relation to cancer for example, being isolated before diagnosis has been linked to a two-fold increase in risk of breast cancer mortality (HR: 2.14, 95% CI: 1.11 to 4.12) (Kroenke et al., 2006). A meta-analysis of qualitative studies, meanwhile, points to the feelings of loneliness experienced by cancer patients following the intrusion of illness into family life and routines, and its restriction of their activities (Andreassen et al., 2007).

Evidence of the effects of relationships on health, and vice versa, hints at the potentially circular and self-reinforcing influence of weak social relationships and poor health (Cohen et al., 2000a). If we are to isolate the implications of social relationships for health, studies based on longitudinal data are required, to examine the temporal association between a person's social ties and patterns of health and wellbeing over time.

1.2.4. Social relationships and health over time

We know that patterns of social relationships are not uniform across the life course: individuals may become lonely or isolated in old age, be lifelong isolates, or experience isolation as a result of a triggering event. Widowhood, for instance, has been consistently linked to loneliness and social isolation, across different cultures and contexts (Samuelsson and Hagberg, 1998; Van Baarsen et al., 1999; Lichtenstein et al., 1996). Life experiences such as migration, retirement, and entry into care have all been associated with a decrease in the quality and/or quantity of a person's social relationships (Tijhuis et al., 1999; Wu and Penning, 2015; McWhirter, 1990). For many people, intense feelings of loneliness or total isolation are short-lived; for others, isolation is a persistent aspect of daily life. According to recent data from the UK Office for National Statistics, 14.8% of working age adults (i.e. aged 16 to 64) and 14.5% of adults aged

65 to 79 report high levels of loneliness; this increases to 29.2% among individuals aged 80 and above (Thomas, 2015).

Little is known about how changes in social relationships affect health. Very few longitudinal studies investigating the health implications of relationships have considered the latter as a time-varying factor, relying instead on a measure of social relationships at one point in time. This is the case, for example, in a study of participants in the 1958 British Birth Cohort, which found that having fewer than five friends at age 45 predicted poorer psychological wellbeing at 50 (Cable et al., 2013). From such a study, we cannot tell whether the size of a person's social network at the age of 45 reflects the size of their network in previous or subsequent years. Nor can these studies shed light on whether prolonged exposure to poor social relationships is more detrimental than transient experiences, or whether recent changes to one's social network are more problematic.

Alongside reliance on single time point measurement, another factor limiting our knowledge of how changes in social relationships affect health is that much of the evidence focuses on older populations (e.g. the mean age of participants at baseline included in the 2010 Holt-Lunstad meta-analysis was 63.9). The resulting lack of life course perspective limits our insight into how health in later life is shaped by earlier patterns of social relationships. What we know from studies on childhood experiences is that isolation in early life predicts isolation in adolescence and adulthood (Caspi et al., 2006) and that it is associated with smoking, obesity and psychological distress in adulthood (Lacey et al., 2014). How dynamics of social relationships in adults of working age are linked to health in later life is unknown.

1.2.5. Pathways linking social relationships to health

Investigators have identified three main pathways through which social relationships affect health: behavioural, psychological and physiological mechanisms (see sections 1.2.5.1. to 1.2.5.3. below). These pathways are not mutually exclusive, with physiological pathways likely to be mediated via behavioural pathways for example. Nor are these pathways unidirectional: some of them are likely to explain reverse causality, such as when negative perceptions of relationships reinforce low self-esteem and self-confidence. To clarify possible connections between pathways and how they might lead to ill health, researchers have developed two models: the main effects model and the stress-buffering model, introduced below (sections 1.2.5.4. and 1.2.5.5.).

1.2.5.1. Behavioural pathways

Behaviours associated with poor social relationships include physical inactivity, smoking, and multiple health-risk behaviours (Shankar et al., 2011). For example, analyses of data from the US National Health and Nutrition Examination Survey showed that older Americans with a larger circle of friends were more likely to be physically active (Watt et al., 2014). As well as predicting specific health-related behaviours, poor social relationships have been linked to multiple risk behaviour. In a study of US adults aged 30 to 69, Berkman identified a steady gradient between increasing levels of social disconnection and the cumulative prevalence of behaviours including smoking, alcohol consumption and physical inactivity (Berkman and Glass, 2000, pp.149-50).

1.2.5.2. Psychological pathways

Social relationships have been linked to a range of psychological processes. One of the pathways for which there is most evidence is between social relationships and self-efficacy, i.e. the degree of confidence which people have in their ability to engage in certain behaviours – a factor associated with a variety of health-related outcomes (McAuley, 1993; Mendes de Leon et al., 1996; Seeman et al., 1993; Tinetti and Powell, 1993). Lower levels of social network contact predict decline in the health and safety domains of self-efficacy (McAvay et al., 1996), and the association between social networks and health-enhancing behaviours such as physical activity has been shown to be mediated through self-efficacy (Duncan and McAuley, 1993). Besides self-efficacy, deficiencies in social relationships have been associated with other psychological processes, including lower self-esteem and limited use of active coping methods (Steptoe et al., 2004), lack of control over success and failure, and greater negative affect (Ernst and Cacioppo, 1999).

1.2.5.3. Physiological pathways

There is growing evidence that social relationships influence health through physiological mechanisms, including hormonal influences on gene transcription and cellular immunity (Hawkley et al., 2010). Access to stronger social relationships is associated with better endocrine and immune functioning, and greater cardiovascular reactivity (Uchino et al., 1996). Feelings of loneliness, meanwhile, have been found to predict higher blood pressure in a community based study of US middle-aged and older adults followed-up for 5 years (Hawkley et al., 2010).

*

Little is known about the relative contributions of the behavioural, psychological and physiological pathways linking social relationships to health, and how they interact. In an attempt to clarify how these pathways might be interconnected and lead to ill health, researchers have proposed two, non-mutually exclusive, frameworks: the main effects model, and the stress-buffering model.

1.2.5.4. The main effects model

The main effects model proposes that social relationships are beneficial for people's health irrespective of whether they are under stress or not (Cohen et al., 2000a). Figure 1.1 presents the ways in which, according to this model, social relationships affect physical and mental health. Social relationships shape the normative context within which individuals make decisions (social influence), provide access to resources such as health care services and information, and contribute to a person's psychological state. Through these mechanisms, social relationships influence health-related behaviours, which in turn have biological consequences that can lead to physical ill health. Psychiatric disease, meanwhile, is primarily understood as the result of poor psychological states and increased neuroendocrine response.

Figure 1.1 Main effects model

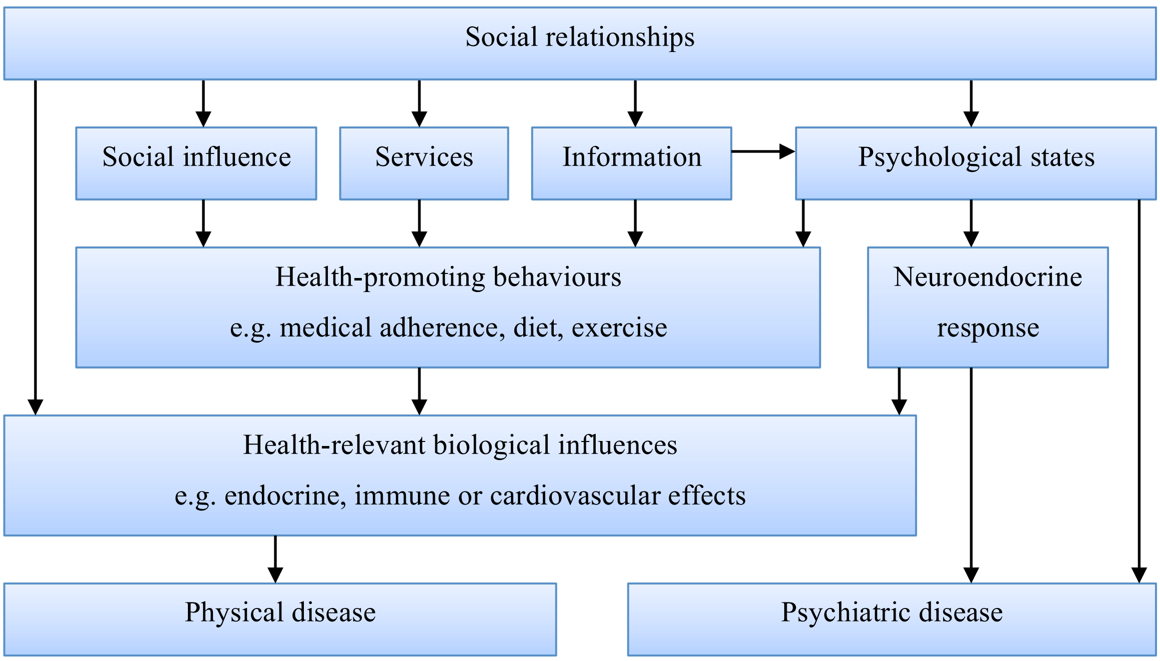


Figure reproduced from Cohen, 2000, p.12.

1.2.5.5. The stress-buffering model

The hypothesis underlying the stress-buffering model is that social relationships primarily or exclusively affect health among people who are under stress (Cohen et al., 2000a). According to this model, the importance of social relationships lies in their ability to prevent responses to stressful events that are detrimental to health. Figure 1.2 shows the different stages at which social relationships can play a role in the pathway linking stressors to disease. First, the perceived availability of support from others can affect a situation's harmful potential, by enhancing a person's appraisal of their ability to cope with a stressful event. Secondly, access to social relationships, and perceptions of relationships, may limit the affective impact of a stressful situation. Finally, the perceived quality of someone's relationships can buffer physiologic and/or behavioural reactions to a stressful event.

Figure 1.2 The stress-buffering model

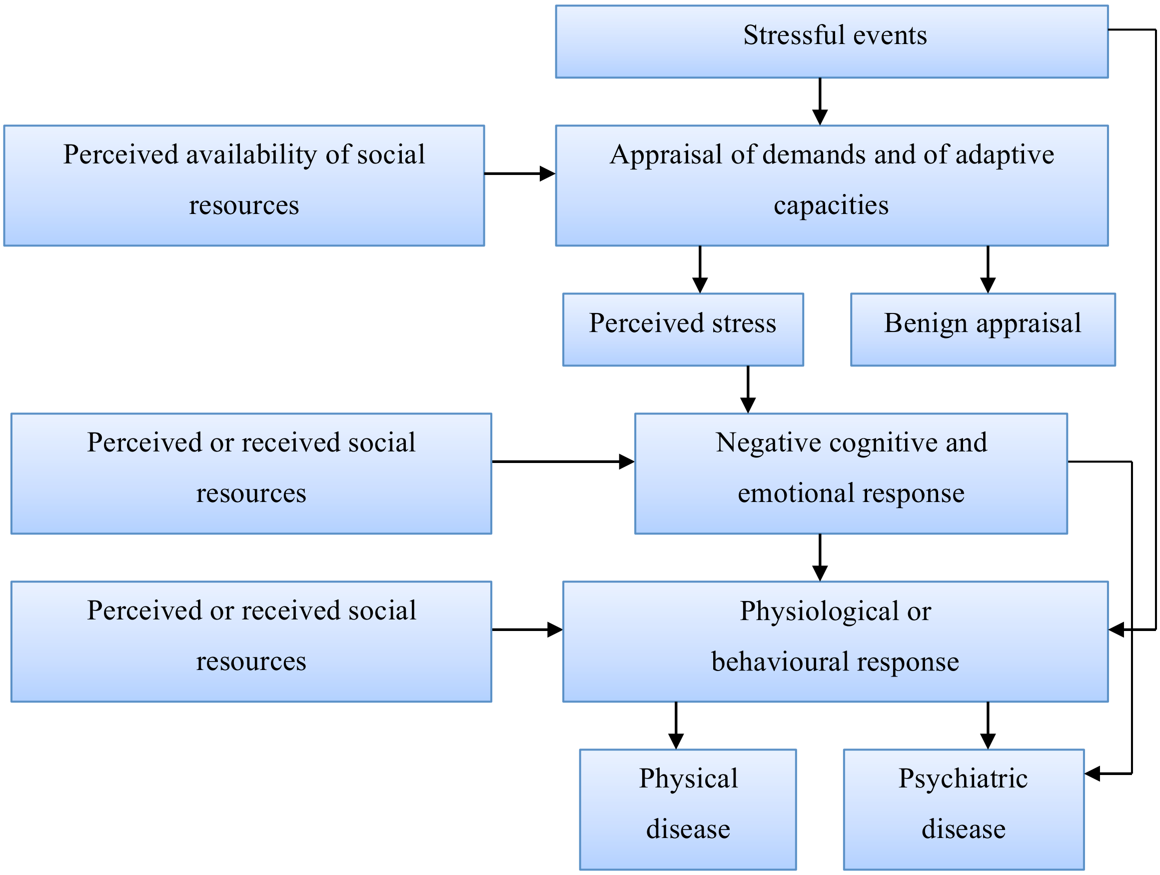


Figure reproduced from Cohen, 2000, p.13.

In the absence of studies empirically testing the assumptions underlying the direct and stress-buffering models, much remains to be clarified. Do the objective and perceived availability of social relationships affect health through different combinations of mechanisms? And what of the role of potential effect modifiers? The stress-buffering model suggests that certain populations, under heightened stress (e.g. economically disadvantaged groups, or frail individuals), may be at increased risk of experiencing the health-damaging effects of poor social relationships – but this hypothesis has yet to be tested.

1.2.6. The evidence on interventions

A range of interventions targeting poor social relationships have been developed, from group initiatives (e.g. educational programmes, social activities) to one-to-one approaches including befriending and cognitive behavioural therapy (Windle et al., 2011). Systematic literature reviews have identified the general characteristics of promising interventions for strengthening social relationships, such as the presence of an underpinning theoretical framework, participant involvement in the design of the intervention and group delivery (Dickens et al., 2011). However, the relative paucity of evaluative studies and heterogeneity in approaches to evaluation mean that no single type of intervention (e.g. cognitive behavioural therapy, or group activity) has yet been shown to successfully strengthen relationships (Cattan et al., 2005; Dickens et al., 2011; Findlay, 2003).

Importantly, it is not known whether interventions aimed at bettering social relationships can prevent decline in the health and wellbeing of participants. It may be that, instead of focusing on secondary prevention – i.e. aiming to improve the social relationships of people who have been identified as isolated or lonely, and through this prevent subsequent ill health – primary prevention strategies offer greater opportunities for intervention. As yet, such strategies, including the promotion of social networks or developing resilience early in the life course, have attracted limited attention in the literature.

1.2.7. Summarising the gaps in the evidence base

The research literature strongly suggests that addressing deficiencies in people's relationships with others has the potential to benefit public health and wellbeing. It is less clear how this might be done effectively. To inform the design of intervention strategies and their evaluation a number of important questions need answering:

- Which aspects of social relationships (e.g. objective versus perceived availability; chronicity versus change) are associated with health outcomes?

- Are social relationships risk factors for developing disease?

- Are certain population groups at greater risk of experiencing adverse health following deficiencies in social relationships?

In the remainder of this chapter, I outline how these questions drive the focus and design of my doctoral project.

1.3. Aims and study design of this doctoral project

Figure 1.3 summarises *why* I undertook the study (aims), *what* I did (objectives) and *how* my work will further knowledge (impact, outcomes and output).

1.3.1. Overall study aim

The overall aim of this study is to further our understanding of the prospective link between social relationships and the health of adults, so as to inform the design of effective intervention strategies.

1.3.2. Specific aims

The study has three specific aims:

1. To clarify the epidemiological literature on social relationships;

2. To investigate the link between loneliness, social isolation and incident CVD;

3. To identify subgroups at greater risk of incident CVD following chronic experiences of loneliness or social isolation.

Figure 1.3 Study aims and objectives

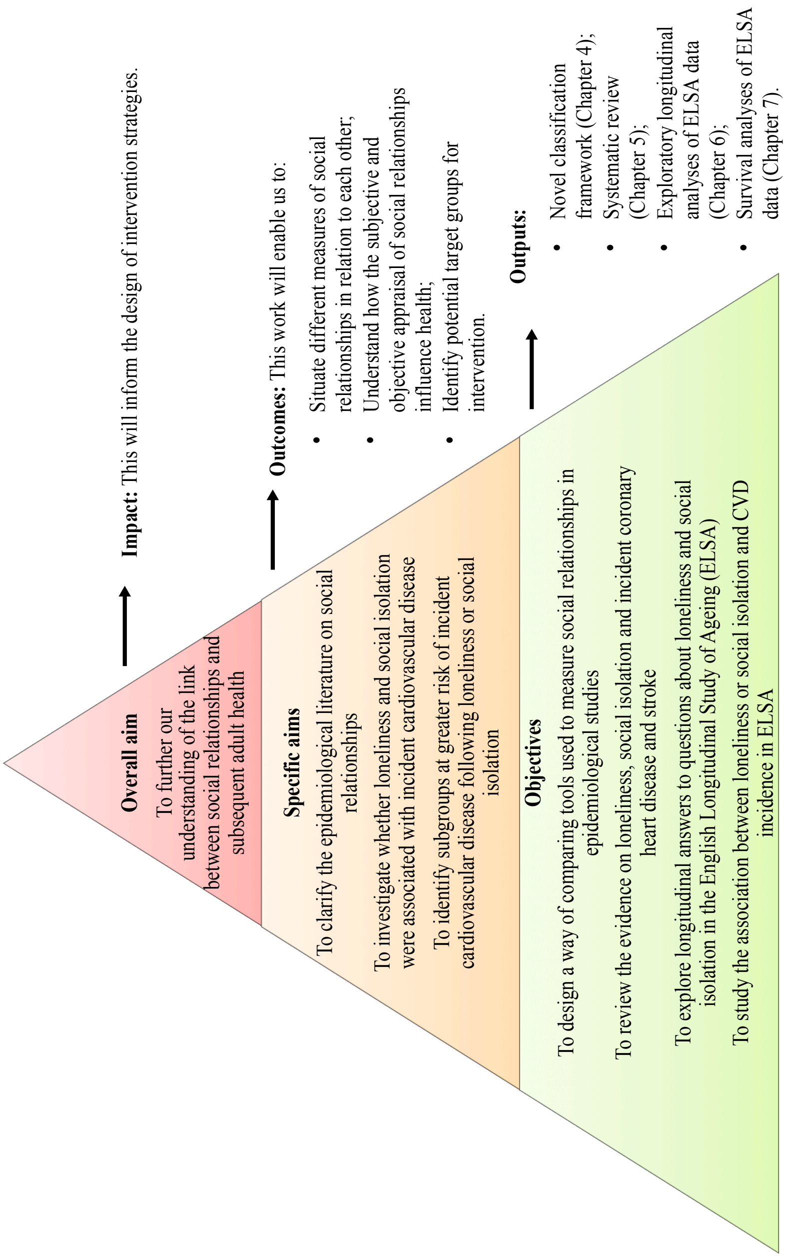


Figure based on the planning triangle developed by the Charities Evaluation Services (CES, 2015).

1.3.3. Study design

1.3.3.1. Study focus: social isolation, loneliness and CVD

One of the guiding principles underlying the design of this project is that using clearly defined concepts holds the key to furthering our understanding of the health implications of social relationships. The two concepts upon which I have decided to focus are 1) social isolation and 2) loneliness. Social isolation is commonly understood by researchers to be an objective measure of the absence of relationships, ties or contacts with other people (de Jong Gierveld et al., 2006). Loneliness, meanwhile, designates the negative feeling associated with someone's perception that their relationships with others are deficient (de Jong Gierveld et al., 2006; Cattan et al., 2005; Perlman and Peplau, 1981). Studying these two concepts alongside each other allows us to gain an insight into the relative contributions of the objective and perceived availability of social relationships.

To investigate the health implications of loneliness and social isolation, I chose to situate my study within a social epidemiological framework. In Chapters 2 and 3, I discuss the theoretical and methodological implications of this choice, and how the framework shaped the design of my empirical work. One of the major implications is that, whilst I focus on CVD – the greatest cause of disease burden worldwide, and an outcome for which there is robust aetiological evidence –, the findings from my project are expected to be of relevance to health and wellbeing outcomes beyond cardiovascular health.

1.3.3.2. Components of the study

To meet the study aims, the project is divided into the following objectives:

- The first step involves clarifying the literature on social relationships, using a novel framework to classify measurement tools used in epidemiological studies (Chapter 4);

- A systematic review was then conducted to characterise the size of the association between loneliness or social isolation and incident coronary heart disease and stroke (Chapter 5);

- To investigate how loneliness and social isolation change over time, I conducted an exploratory study of response patterns to items about social relationships in the first six waves of the English Longitudinal Study of Ageing (Chapter 6);

- To shed light on the relationship between loneliness, isolation and incident CVD over time, and to identify at-risk groups, I undertook survival analyses of data from the English Longitudinal Study of Ageing (Chapter 7);

The findings from the work presented in this thesis are brought together in a final chapter, where I reflect on their implications for the design of interventions, and for future research, practice and policy (Chapter 8).

Chapter 2. Conceptual framework

Chapter summary: Having articulated the rationale for my doctoral project in the introductory chapter, I now turn to describing its conceptual framework. In Chapter 1, we saw that a range of concepts have been used to study social relationships in the epidemiological literature. This thesis focuses on two specific dimensions, loneliness and social isolation (2.1.). After explaining why I chose to study these two aspects of relationships in relation to health (2.2.), I describe where loneliness and social isolation fit within a broader conceptual framework of how social factors influence morbidity and mortality (2.3.). This framework allows me to link social relationships to their social and cultural context, and to clarify how loneliness and social isolation differ from other concepts used in the literature.

2.1. Introduction

The literature on social relationships and their health implications covers a range of concepts, including – but not restricted to – social integration, social networks, isolation, social support and loneliness (see section 1.2.1. in Chapter 1 for examples of the different terms used). Each of these has been defined in more than one way. To add to the confusion this creates, terms have been used loosely and interchangeably. One of the first challenges for any investigator approaching the field of social relationships and health is to ascertain which concept(s) is/are most relevant for their work and why. In the remainder of this section, I define the two dimensions upon which I have chosen to focus in my doctoral project, social isolation and loneliness, and explain the reasons behind this choice.

2.2. Social isolation versus loneliness

2.2.1. Definitions

The two concepts on which my project focuses are: 1) social isolation and 2) loneliness.

2.2.1.1. Social isolation

In this thesis, as in much of the literature on social relationships, social isolation is understood to be an objective concept capturing the absence of relationships, ties or contacts with other people (de Jong Gierveld et al., 2006). Investigators who focus on social isolation are concerned with the extent to which an individual does, or rather does not, interact or exchange with other people. Whilst not necessarily implied in its definition, social isolation has more often than not been approached by researchers as a relative, rather than an absolute situation: a continuum is drawn, running from social isolation at the lower end, to social connectedness and participation at the more active and involved end of the spectrum (see for example Townsend, 1973). Individuals with a comparatively small amount of relationships, ties or contacts are deemed to be socially isolated (de Jong Gierveld et al., 2006).

In theory, there are no limits to the types of relationships (e.g. kin, non-kin, neighbour) that may determine the extent of a person's social isolation. Nor does the definition of social isolation specify whether gauging the presence or absence of ties or contacts extends to assessing interaction with groups of people (e.g. a charitable organisation, or a church group), i.e. beyond individuals. In practice, researchers have tended to investigate the extent of a person's engagement with others by focusing on three types of relationships: family members, friends, and the local community (neighbours and/or activity groups) – see for example the Berkman-Syme Social Network Index (Berkman and Breslow, 1983), the Lubben Social Network Scale (Lubben, 1988) and Wenger's Support Network typology (Wenger, 1991).

2.2.1.2. Loneliness

The concept of loneliness is used by researchers to describe the negative feeling associated with someone's perception that their relationships with others are deficient (Cattan et al., 2005; de Jong Gierveld et al., 2006; Perlman and Peplau, 1981). The main characteristic that sets loneliness apart from social isolation is that it is defined as a subjective experience. As such, it is likely to take on many forms, depending on personal as well as contextual determinants.

A range of theories have been proposed to explain how experiences of loneliness are shaped. The four principal ones are: the 'social needs' perspective, cognitive discrepancy theory, the 'skills and personality deficit' viewpoint, and the evolutionary perspective (Cacioppo and Hawkley, 2009). According to the 'social needs' perspective, individuals experience loneliness when their social needs (for intimacy or companionship, for example) are insufficiently or not met (Weiss, 1973; Dykstra and Fokkema, 2007). The cognitive or cognitive discrepancy approach, meanwhile, argues that loneliness is the result of a mismatch between a person's evaluation of their social relationships and their relationship standards (Perlman and Peplau, 1981). These standards are understood to be shaped by individual-level factors such as personality, and wider determinants including culture and socio-economic context (Perlman and Peplau, 1981, pp.8-10). A third conceptual approach focuses on deficits in social skills and personality traits that interfere with a person's ability to form and maintain social relationships, making them likely to experience loneliness (Marangoni and Ickes, 1989). And a fourth viewpoint has been to study loneliness from an evolutionary perspective, where feeling lonely is seen as an undesirable condition similar to hunger or thirst that signals a rupture in social relationships and thereby motivates their repair or replacement (Cacioppo et al., 2006a). According to this last perspective, loneliness becomes an issue of concern when its persistence creates a self-reinforcing cycle of negative thoughts, feelings and behaviours (Cacioppo and Patrick, 2008).

Across the theoretical orientations taken to study loneliness, researchers have acknowledged two main ways in which experiences might differ: firstly, according to the type of relationship an individual feels unhappy about; and secondly, the frequency of loneliness feelings experienced by an individual. After observing that perceptions of certain types of relationships could give rise to different experiences of loneliness, Weiss proposed to distinguish between emotional loneliness, stemming from the perceived 'absence of a close emotional attachment', and social loneliness, associated with the perceived 'absence of an engaging social network' (Weiss, 1973, pp.18-19). Some of the tools developed to measure loneliness, such as the de Jong Gierveld Loneliness Scale, have purposefully been designed to capture both forms of loneliness (de Jong Gierveld and van Tilburg, 2006). In epidemiological research, the type of loneliness experienced has attracted less attention than the frequency with which people feel lonely. Acknowledging that loneliness can be transient or chronic, and wary of stigmatising or medicalising an experience which most people are likely to experience at some point in their life, researchers interested in the health implications of loneliness have tended to focus on the detrimental effects of persistent loneliness (see for e.g. Patterson, 2010).

2.2.1.3. The relationship between social isolation and loneliness

Social isolation and loneliness are distinct concepts. The distinction between the two terms has sometimes been framed as opposing the *quantity* versus the *quality* of relationships (Roberts, 2015). Both loneliness and social isolation, however, can encompass aspects of relationship quantity as well as quality. Loneliness may be triggered by individuals perceiving that either the quantity (e.g. number of people in one's social network), and/or the quality (e.g. availability of someone who can be trusted) of their relationships is deficient. In so far as social isolation refers to an absence of relationships, and one of the defining characteristics of relationships is that they '[exist] between two people when each person influences the other's thoughts, feelings, and or behavior' (Clark, 2011 – see definition provided in Chapter 1, section 1.1.1.), social isolation need not be restricted to a purely quantitative dimension.

A more accurate way of describing the distinction between social isolation and loneliness is that the former refers to the *objective* situation of an individual, whereas the latter seeks to capture a person's *subjective* experience. As summarised by Townsend, 'to be socially isolated is to have few contacts with family and community; to be lonely is to have an unwelcome feeling of lack or loss of companionship. The one is objective, the other subjective, and, as we shall see, the two do not coincide.' (Townsend, 1973, p.175). It is worth bearing in mind that in practice, when seeking to measure social isolation, social scientists have primarily resorted to self-report questionnaires to gather information on the amount of contact and exchange between people – i.e., whilst the aim is to get at an objective picture of a person's social relationship network, this is often mediated via the person themselves. Measures of social isolation may not therefore be quite as objective as the definition of the concept implies.[1]

Loneliness and social isolation do not always come hand in hand. Individuals can be socially isolated without feeling lonely. This was illustrated in the 203 interviews carried out in Townsend's study of older adults living in East London, where individuals who were socially isolated did not necessarily report feeling lonely (Townsend, 1973, p.181). Nor is the availability of relationships a guarantee against experiencing loneliness: people may feel lonely without being socially isolated. In relation to marriage, for example, Weiss warned against equating the existence of a spouse with emotional attachment: 'It is not marriage that is critical in fending off the loneliness of emotional isolation but rather the availability of emotional attachment, of a relationship with another person such that the mere proximity of the other person can promote feelings of security and wellbeing. There are empty shell marriages, marriages without attachment, that provide no defense against loneliness. Indeed, marriages of this sort may seem to the participants to be the chief cause of their loneliness, since they prevent the formation of genuine attachments' (Weiss, 1973, pp.90-91).

While loneliness and social isolation do not necessarily coincide, they can be experienced simultaneously. The objective characteristics of a social network can increase or decrease a person's likelihood of feeling lonely. In a meta-analysis investigating risk factors for loneliness in later life, marital status was protective against loneliness (weighted mean effect size across 109 studies: -0.45, 95% confidence interval (CI): -0.49 to -0.41), as was having a larger social network (weighted mean effect size across 263 studies: -0.40, 95% CI: -0.44 to -0.36) (Pinquart and Sorensen, 2003). It is important to remember that loneliness is only one of the possible outcomes where someone evaluates the number of relationships they have. Whether a person perceives their relationships to be deficient will depend on a range of factors, including the extent to which they have control over the quantity and quality of their relationships, and their relationship standards. While some people with a small social network might feel lonely, others might feel satisfactorily embedded – particularly where this reflects a choice, as in the case of someone who might prefer to be alone and opt for privacy as a means of avoiding unwanted

[1] In Chapter 4, I take a closer look at the way questions are phrased in tools used to assess social relationships, and the degrees of subjectivity they involve.

social contacts and relationships (de Jong Gierveld et al., 2006).

2.2.2. Justification for studying loneliness and social isolation in relation to health

My decision to focus on the concepts of social isolation and loneliness to further our understanding of how social relationships affect health was motivated by four criteria: what I knew of the research evidence; data availability; relevance to the public discourse on poor social relationships and health; and opportunities for intervention.

2.2.2.1. The relevance of social isolation and loneliness for health

Both social isolation and loneliness have been linked to adverse health outcomes. In a meta-analysis of 14 studies including an objective measure of social isolation, the odds of dying among isolated individuals were 1.29 times that among non-isolated persons (95% CI: 1.06 to 1.56); and aggregated data from thirteen prospective studies on loneliness showed that the odds of dying among lonely individuals were 1.26 times that among individuals who did not feel lonely (95% CI: 1.04 to 1.53) (Holt-Lunstad et al., 2015). Subjective as well as objective isolation have been linked to a range of physical and mental health outcomes, including increased blood pressure (Hawkley et al., 2010), depressive symptoms (Cacioppo et al., 2006b; Kawachi and Berkman, 2001) and dementia onset (Kuiper et al., 2015).

The comparative effects of social isolation and loneliness on health have, to date, received little attention in the epidemiological literature. Because researchers have not tended to include more than one measure of isolation in their studies, the independent, relative, and synergistic effects of social isolation and loneliness are unclear (Holt-Lunstad et al., 2015). To address this gap in the literature, I decided to include both concepts in my doctoral project, with the aim of exploring differences and similarities in their potential effects on health.

2.2.2.2. Data availability

I was aware that one of the reasons why researchers to date might not have simultaneously considered loneliness and social isolation in their studies was the (un)availability of data. Investigators have often had to rely on secondary data analyses of datasets designed with other foci in mind, e.g. health-related behaviours or biological/physiological risk factors, with a limited choice of variables on social relationships (Berkman, 1985). Recently however, a number of cohorts with comprehensive measures of relationships have been developed, including the Health and Retirement Study, the English Longitudinal Study of Ageing and the Irish Longitudinal Stduy of Ageing. These datasets offer the opportunity to study the subjective feeling of loneliness and the experience of social isolation in the same population, as well as to explore their relationships over time. An explanation of why I selected the English Longitudinal Study of Ageing for my study is provided in section 3.2.4 below.

2.2.2.3. Relevance to public concern about the health and wellbeing implications of social relationships

The importance of loneliness and social isolation for health and wellbeing has been a recurring feature in public discourse in the UK in recent years, with the media regularly reporting on new research and initiatives to tackle deficiencies in social relationships (Knapton, 2015; BBC Radio 4, 2016; Hafner, 2016; Wood, 2016). Understanding why this is a particularly topical issue is an aspect of contextualisation which I have frequently returned to while conducting my doctoral project. Using Bacci's 'What is the problem represented to be?' approach, I have argued elsewhere that the 'popularity' of loneliness and social isolation needs to be understood within the broader context of societal concern about caring for older people (Valtorta et al., 2016b). The names and targets of national campaigns set up in Europe in the last decade (e.g. 'Coalitie Erbij, de nationale coalitie tegen eenzaamheid' – Netherlands, 'The Campaign to End Loneliness' – England, 'La Mobilisation Nationale contre l'Isolement des Agés' – France) are indicative of what is seen to be problematic: the campaigns publicly focus on loneliness or social isolation – rather than social capital, social support or social participation, for instance – and explicitly target older adults as being particularly at risk of experiencing these situations. This is not to say that when loneliness and social isolation are used in these contexts, they are clearly defined; but it suggests that these are the concepts that non-academics are preoccupied with and where research would be helpful.

I chose to focus on loneliness and social isolation to maximise the relevance of my work beyond the realm of research, believing that sharing the language of campaigners and policy-makers would make it easier to engage with them. Being aware that policy and campaigning discourses are often contexts in which definitions are absent or blurred, I was keen not to replicate this and made conceptual clarity one of the bases of my project. I was also intent on not taking as a given some of the assumptions that commonly underpin the public discourse on loneliness and social isolation, such as its perceived association with older age or its modifiable effects on health (Valtorta et al., 2016b). In summary, I saw the use of shared terminology as a means of facilitating dissemination, as well as an opportunity to challenge common assumptions about how loneliness and social isolation might be tackled from a societal perspective.

2.2.2.4. Opportunities for intervention

The overarching aim of my doctoral project was to inform the design of intervention strategies to tackle the health implications of social relationships. From the evaluative literature, I knew that having a robust theoretical framework was one of the criteria for which there was evidence of success (Cattan et al., 2005; Dickens et al., 2011); I was also aware that appropriate strategies for tackling more objective domains such as the number of people in a person's social network might not have an effect on people's feelings about their relationships (Fokkema and van Tilburg, 2007). My rationale for studying both loneliness and social isolation, using clearly defined concepts, was that this would make my work of relevance to at least two types of initiatives: those aimed at increasing the quantity and quality of someone's relationships; and actions designed to influence people's perceptions of their relationships (de Jong Gierveld et al., 2006).

*

Having clarified what is meant by loneliness and social isolation in this project and why I chose to focus on these two dimensions of social relationships, I now turn to describing the overarching framework within which loneliness and social isolation are hypothesised to influence health.

2.3. Loneliness, social isolation and their health implications in context: a social epidemiological framework

The framework I used to study loneliness, social isolation and their health implications is based on the conceptual model developed by Berkman (Figure 2.1) (Berkman and Krishna, 2014). This model is rooted in social epidemiology and its assumption that the distribution of health and disease in a society reflects the distribution of social advantages and disadvantages (Honjo, 2004). Bringing together two theoretical trends in social epidemiology – psychosocial theory, which focuses on endogenous biological responses to human interaction, and the 'social production of disease' theory, which explicitly addresses economic and political determinants of health (Krieger, 2001) – Berkman embeds the psychosocial and biological concomitants of social relationships within a larger social and cultural context. The health implications of relationships are interpreted as part of a cascading process operating at three different levels: social-structural conditions (macro), social relationships (mezzo) and psychosocial mechanisms (micro). In the following section, I describe each level and explain how I have adapted the model for my project (changes are marked in red on the diagram in Figure 2.1). Note that while the focus of my doctorate is on the mezzo level, it is nonetheless useful here to contextualise this within the macro and micro levels, and situate loneliness and social isolation in relation to other frequently encountered terms in social epidemiology.

2.3.1. Macro level

At the macro level, socio-cultural, socio-economic, political and social conditions shape the form and content of people's social relationships, as well as their perceptions of relationships. Understanding how resources are distributed at a community and societal level offers insight into how social relationships are patterned. Researchers have found that the risk of social isolation in the working-age population is contingent upon cultural patterns of household structure and local sociability (Gallie et al., 2003). Empirical studies focusing on older populations, meanwhile, have highlighted the importance of structural factors to understand experiences of severe loneliness (Nyqvist and Forsman, 2015; Scharf et al., 2002). These structural factors include social capital – i.e. the norms, networks and social trust that facilitate coordination and cooperation for mutual benefit (Putnam, 2000) – and social exclusion – understood as a process of progressive social rupture preventing individuals from participating in society (Silver, 2007). In countries characterised by greater income inequality, older adults report feeling more discrimated against (Vauclair, 2015). Thomese (2003) has shown that in areas where older adults share a feeling of community embeddedness and are concerned for the wellbeing of their neighbours, fewer people report feeling lonely.

The role of the wider social context is key to interpreting findings about mezzo and micro level processes, and for understanding their relevance for policy and practice. The success of interventions is likely to depend on careful consideration of how social relationships are lodged within larger societal and cultural contexts; and understanding this context is critical for developing robust theories of change and identifying lever points for action.

2.3.2. Mezzo level

The mezzo level covers objective and subjective dimensions of social relationships, including social isolation and loneliness. In the Berkman model, the mezzo level focuses on the 'extent, shape and nature of social networks' but does not include perceptions of relationships; these are instead seen as operating at the micro level, i.e. primarily shaped by the more objective characteristics of a person's social network. Yet studies have identified limited overlap between social isolation and loneliness (Victor et al., 2009; Shankar et al., 2011) and it is likely that loneliness plays a role beyond that of mediating the association between objective characteristics of a person's social network and wellbeing (Cohen et al., 2000a). To reflect this hypothesis – i.e. that loneliness has implications for health *independently* of social isolation – I have modified the Berkman model, incorporating perceptions of social relationships at the mezzo level. In the rest of my project, I primarily consider loneliness and social isolation as independent factors – though never losing sight that loneliness and social isolation might be

Figure 2.1 Conceptual model of how loneliness and social isolation influence health

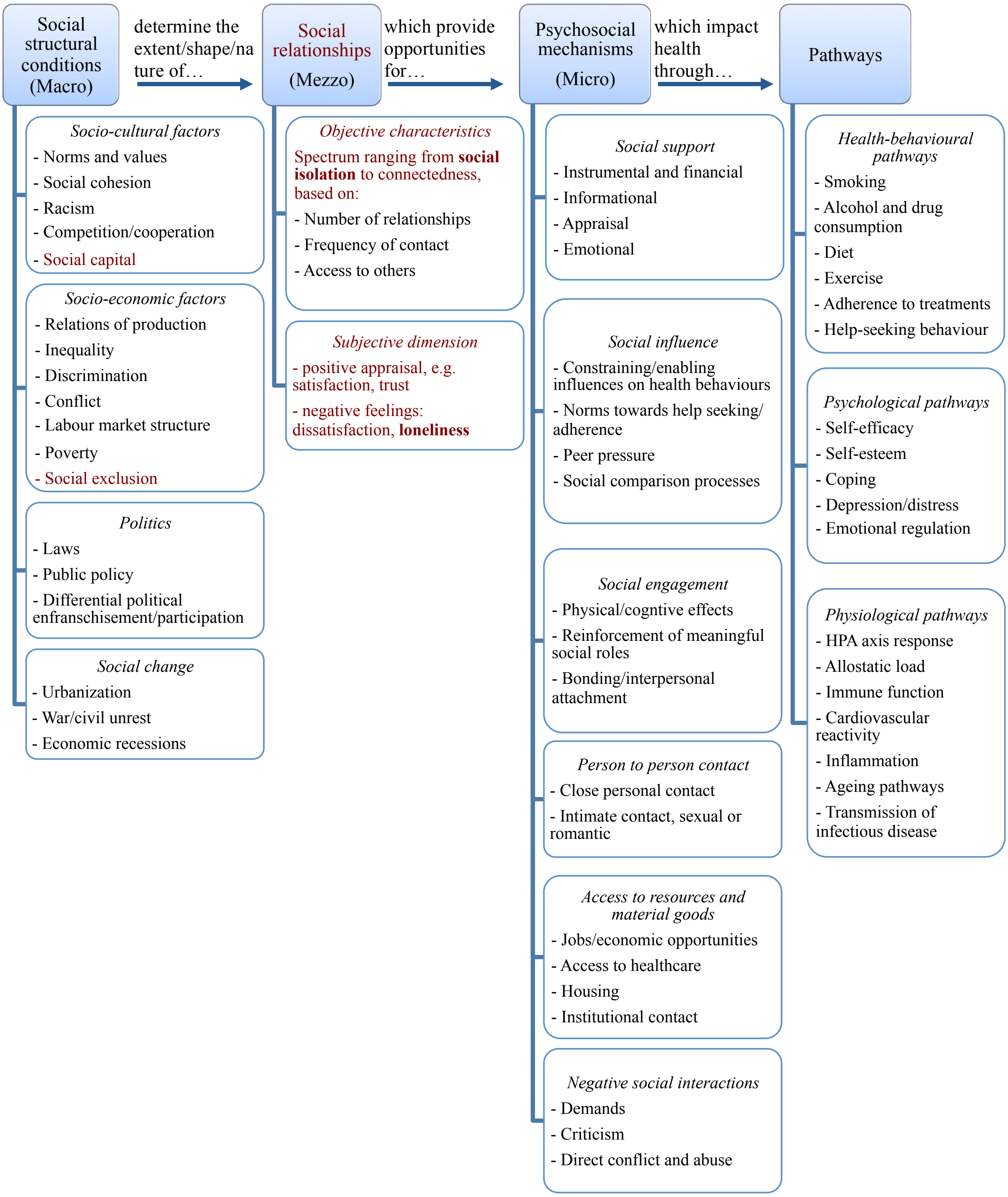


Diagram based on Berkman and Krishna, 2014, p.242.

mediators or moderators of each other's effects. Where possible, I have investigated this, e.g. through controlling for loneliness in social isolation analyses and vice-versa in longitudinal analyses of data from the English Longitudinal Study of Ageing (ELSA), or testing for interaction effects (see Chapter 7).

2.3.3. Micro level

Access to, and perceptions of, social relationships shape and provide opportunities for a range of psychosocial mechanisms. These can broadly be divided into six categories: social support, social influence, social engagement, person-to-person contact, access to resources and material goods and negative social interactions. The purpose of my doctorate is not to test whether any of these mechanisms are particularly relevant for my main outcome of interest, incident cardiovascular disease (CVD). Rather, I present them here as explanations for why loneliness and social isolation might plausibly be hypothesized to influence morbidity, and how.

2.3.3.1. Social support

People who feel lonely or are isolated may have reduced access to social support, either because they have few or no relationships to turn to, or because they do not feel that they can rely on the relationships they have (Perlman and Peplau, 1981). Social support is one of the main mechanisms through which social relationships have been hypothesised to influence health in the epidemiological literature and refers to the resources provided by others in a person's social network (Cohen et al., 2000a). It has typically been divided into subtypes, the more common ones being: emotional support; instrumental or tangible support; informational support; and appraisal support (House, 1981). Emotional support encompasses the availability of 'love and caring, sympathy and understanding and/or esteem or value […] from others' (Thoits, 1995). Most often, this type of support is provided by a close relationship or confidant. Instrumental or tangible support describes help received in kind, money or labour, to assist with tasks such as grocery shopping, transport, cooking or housework. Informational support relates to the provision of information or advice, while appraisal support refers to help with decision-making and the provision of feedback. Different types of social support can be difficult to disaggregate and are frequently combined in measures of either received or provided social support, with less attention devoted to aspects of reciprocity.

2.3.3.2. Social influence

A second way in which social relationships can affect health is via social influence. Social influence covers a range of ways in which 'people obtain normative guidance by comparing their attitudes with those of a reference group of similar others. Attitudes are confirmed and reinforced when they are shared with the comparison group but altered when they are discrepant.' (Marsden and Friedkin, 1994, p.5). Examples of social influence include shared norms around health behaviours such as the consumption of alcohol, smoking, healthcare use, dietary patterns and treatment adherence (Higgs and Thomas, 2016; Rosenquist et al., 2010; Christakis and Fowler, 2008; Cialdini and Trost, 1998). On the one hand, socially isolated individuals may be protected from the negative influence of peers; conversely, they may not have access to health promoting messages and influences, in the same way that severely lonely individuals might not be inclined to positively engage with health-improving advice and activities (Seeman, 2000).

2.3.3.3. Social engagement

Another way in which social relationships are seen to influence psychosocial processes is by providing (or in the case of isolation and loneliness, denying) opportunities for social engagement, in the form of group recreation, getting together with friends, attending community events or going to church for example. Participation in a meaningful social context helps to define and strengthen social roles such as parental, familial and community roles, in turn fostering shared values and a sense of belonging or attachment. This is commonly referred to in the Scandinavian literature as 'social anchorage', understood as the 'degree [to which] the individual belongs to and is anchored within formal and informal groups, and in a more qualitative sense his feeling of membership in these groups' (Hanson, 1988). Examples of beneficial effects linked to social engagement include better cognitive functioning in later life and the ability to cope with minor life stresses (Kuiper et al., 2016; Thoits, 1995).

2.3.3.4. Person-to-person contact

The fourth micro-level mechanism through which social relationships influence psychosocial mechanisms is through person-to-person contact. This channel is primarily important where infectious diseases are transmitted from person to person. On the one hand, the reduced opportunity for human contact stemming from social isolation is likely to mean that isolated individuals are less likely to be exposed to infectious disease transmission. Lonely individuals, however, may not be immune to the diffusion of socially patterned disease. When the perceived need for human contact exceeds health-protecting advice, they might be particularly at risk of disease transmission, for example through unprotected sexual activity (Martin and Knox, 1997).

2.3.3.5. Access to material resources

A fifth mechanism through which social relationships can influence wellbeing and health is through access to material resources. Sociologists have shown how the remit and spread of a person's social network shapes their access to life-opportunities, with Granovetter's now influential study identifying 'weak ties' (i.e. ties lacking in intimacy) as the means through which influence and information travels around networks, and through which opportunities for mobility are accessed (Granovetter, 1973). Isolated or lonely individuals may not be as likely to benefit from such ties, either because they simply do not exist (in the case of absolute isolation) or because the negative feelings associated with loneliness preclude individuals from seizing potential opportunities.

2.3.3.6. Negative social interactions

A last mechanism linking social relationships to health is via negative social interactions, such as criticism, demands or direct conflict (Tun et al., 2013). Experiences of neglect and abuse in early childhood have been linked to a range of long-term physical and mental health sequalae in adulthood, including fatigue, psychological distress, depression and CVD (Batten et al., 2004; Cho et al., 2012; Lacey et al., 2014). In adulthood, experimental studies conducted in laboratories have shown that conflict and demands directly influence physiological reactions, fuelling heightened inflammatory activity and increases in cortisol levels (Chiang et al., 2012; Friedman et al., 2012).

*

The micro-level mechanisms outlined above – social support, social influence, social engagement, person-to-person contact, access to resources and material goods, and negative social interactions – are presented separately for simplicity; but it is important to remember that they need not be mutually exclusive and that different mechanisms can operate simultaneously. Similarly, the pathways linking these mechanisms to health are complex, and likely to be intertwined. Three main pathways have been identified: health-related behaviours, psychological mechanisms and physiological outcomes. Since they have already been introduced in Chapter 1 (see section 1.2.5. for an overview of each pathway), I will focus here on the pathways of particular relevance to the primary outcome of interest in my doctorate, CVD.

2.3.4. Pathways to health outcomes

2.3.4.1. Health-related behaviours

Social relationships influence patterns of health-promoting or risk-generating behaviours; they provide opportunities for people to share behaviours and norms around these behaviours, as well as being a potential source of support for behaviour-related decisions. In a series of papers based on the Framingham Heart Study, researchers uncovered the network dynamics of smoking, alcohol consumption and obesity. Using longitudinal data from 1971 to 2003, Christakis and Fowler (2008) found that people who had a close relationship with a smoker (through family, friends or work-related contact) had a 61% greater risk of smoking than individuals whose close ties did not smoke. Over the same study-period, clusters of participants gave up smoking, suggesting that smoking cessation was a collective rather than individual phenomenon. Similarly, changes in the alcohol consumption among a person's social network predicted subsequent alcohol consumption for that individual (Rosenquist et al., 2010). A participant's chance of becoming obese increased by 57% when they had a friend who became obese, and where one spouse became obese, the likelihood of the other spouse becoming obese increased by 37% (Christakis and Fowler, 2007).

2.3.4.2. Psychological pathways

Perhaps more so than for any of the other pathways covered in Figure 2.1, disentangling the effects of social relationships on mental health and vice-versa has been problematic for researchers. A first challenge has been determining whether perceptions of social relationships, including loneliness, are conceptually and functionally distinct from psychological distress and depressive symptomatology (Cacioppo et al., 2006b). Theorists have argued that there is an important distinction between loneliness and depression, centred around the observation that 'In loneliness there is a drive to rid oneself of one's distress by integrating a new relationship; in depression there is instead a surrender to it' (Weiss, 1973, p.15). In practice, the consistent evidence of association between loneliness and depressive symptoms across different studies and populations, with correlation coefficients typically falling between 0.40 and 0.65, has prompted debate about whether loneliness should be considered separately from depression (Mezuk et al., 2016; Cacioppo et al., 2006b; Tiikkainen and Heikkinen, 2005). In one of the tools most commonly used to assess depressive symptomatology, the CES-D Scale, loneliness is included amongst the 20 questionnaire items, illustrating how it is understood by some researchers to be part of rather than separate from depressive symptoms (Radloff, 1977). More recently, empirical findings based on samples of young adults and adults aged between 50 and 68 have supported the distinction between loneliness and depressive symptoms. In a study of

2,525 young American adults, factor analyses of the UCLA Loneliness Scale and the Beck Depression Inventory indicated that the loadings of loneliness items on the depressive symptoms factor were less than 0.10 and that the loadings of depressive symptoms items on the loneliness factors were similarly low (0.19; Cacioppo, 2006b). Similar analyses of the answers from a population-based sample of 229 US adults found that the loneliness items on the UCLA Scale and the depressive symptoms items in the CES-D Scale (minus the loneliness item) loaded on distinct factors (Cacioppo et al., 2010).

As well as the potential for conceptual overlap, another challenge for researchers has been the potential for reverse-causality and self-reinforcement (Kawachi and Berkman, 2001). Loneliness and social isolation have both been identified as risk factors for, and consequences of, mental illness and psychological distress in later life (AARP Foundation, 2012; Victor et al., 2005b; Jaremka et al., 2014). Investigators have therefore had to rely on longitudinal study designs to uncover the potential consequences of exposure to loneliness or social isolation. In a recent meta-analysis of longitudinal cohort studies, a small but significant effect of social isolation and negative perceptions of social relationships was found in relation to risk of cognitive decline (for social isolation, pooled odds ratio (OR): 1.08, 95% CI: 1.05 to 1.11; for negative perceptions of relationships, pooled OR: 1.15, 95% CI: 1.00 to 1.32). With regards to affective states, more positive perceptions of emotional and instrumental support and access to large or diverse social networks have been associated with a lower likelihood of depressive symptoms (Santini et al., 2015). Loneliness has been linked to lower self-esteem and limited use of active coping methods (Steptoe et al., 2004), while social isolation has been associated with a decline in self-efficacy (McAvay et al., 1996).

2.3.4.3. Physiological pathways

Social relationships have been linked to some of the major biological risk factors for CVD. A five-year study of Americans aged 50 to 68 found that higher levels of loneliness at baseline were associated with increased blood pressure at follow-up, independently of age, gender, ethnicity, recognized cardiovascular risk factors and other psychosocial mechanisms (Hawkley et al., 2010). Similarly, in a nationally representative sample of adults aged over 50 living in England, social isolation was associated with higher blood pressure, as well as with greater levels of inflammatory markers (Shankar et al., 2011).

The physiological implications of social relationships suggest that isolation and loneliness may affect health by accelerating the process of aging, acting like a chronic stressor on the organism (Berkman and Krishna, 2014). With this hypothesis in mind, epidemiologists have recently begun to take a lifecourse approach to the study of social relationships and health, extending their analyses beyond later life experiences. In my doctoral project, I applied no age-related criteria when reviewing the literature, since I was aware of the possible implications of social relationships earlier in life for health in older age. My analyses of ELSA were however necessarily restricted to adults aged 50, because no younger participants were included. ELSA offered opportunities that are described in detail in Chapter 6 and explain why I chose it for my analyses. However, the lifecourse pattern of social relationships will be of relevance for interpreting my findings, and needs to be kept in mind when thinking about possible intervention strategies.

*

The evidence from empirical studies on the psychosocial, behavioural and physiological mechanisms linking social relationships to health suggests that loneliness and social isolation may influence the risk of developing CVD, and that addressing them would benefit public health and wellbeing. In this chapter, I have presented the overarching framework within which I set out to test this hypothesis. In the following chapter, I turn to considering the methodological approach I chose, social epidemiology, and discuss the implications of applying an epidemiological lens to the study of loneliness, social isolation and health.

Chapter 3. Methodological considerations

Chapter summary: In Chapter 2, I presented the theoretical framework underpinning my study of the link between loneliness, social isolation and cardiovascular disease incidence. This framework is rooted in social epidemiology, a discipline that encompasses a range of methods for researching the social determinants of health in a population (3.1.). In this third chapter, I explain which methods I chose, and why (3.2.). Acknowledging the assumptions of my investigative approach, I reflect on how this shaped the design of my project (3.3.).

3.1. Introduction

There is no single 'correct' philosophy of research (Guba, 1990). The approach chosen by an investigator depends on multiple factors, ranging from broader social and historical influences to personal attributes (e.g. education and training background) and the nature of the topic researched (Smith, 1998). In public health as in many other research fields, once an issue has been identified, the first task is to turn the 'problem' into (an) answerable question(s) (Pencheon et al., 2006). The researcher then determine(s) which methods are most appropriate for studying the issue. In this chapter I explain how I came to adopt a socio-epidemiological approach to study social relationships and health, and discuss the methodological implications of this choice.

3.2. Rationale for my choice of methods

The main question underpinning my doctoral project was 'Are loneliness and social isolation associated with an increased risk of ill health?'. As a public health researcher interested in quantifying the potential burden of disease associated with loneliness and social isolation, I arrived at this question using deductive reasoning: based on the theoretical framework presented in Chapter 2, I hypothesised that loneliness and social isolation might influence disease risk. The investigative angle I chose is grounded in social epidemiology, the branch of epidemiology concerned with how social factors affect health (Honjo, 2004).

Rather than corresponding to a particular set of methods, social epidemiology is best understood as an 'intellectually eclectic' approach to enquiry that draws on a range of traditions – e.g. the natural and social sciences, the humanities, policy analysis, political science – to identify determinants of health at the population level (Popay, 2003). It offers a range of methods from which investigators can choose from, depending on their ontological (what is reality?), epistemological (how do you know something?) and methodological (how do you go about finding something out?) perspectives (Guba, 1990). In the following section (section 3.2.1.), I explain why I chose to use both qualitative and quantitative methods; I then go on to detail each method and why I selected it in favour of others (sections 3.2.2. to 3.2.5).

3.2.1. A realist perspective on social epidemiology

Epidemiology's emphasis on populations rather than individuals explains that it has traditionally been dominated by a positivist outlook (Bruce et al., 2013). Positivism aims to uncover the general laws governing human behaviour at the population level, using methods akin to those of scientists who study the laws of the physical world such as experiments, measuring instruments or surveys (Smith, 1998). Yet whilst it has customarily relied on quantitative techniques, social epidemiology need not be restricted to purely numerical analyses (Hajat, 2011). Popay has argued for the importance of qualitative enquiry in studying social factors and health, based on the insights it offers into the complex lives of individuals and why they act in the way that they do (Popay, 2003). Qualitative methods include document analysis, interviews or ethnographic observation – i.e. methods dependent upon conceptual rather than numerical analysis (Green and Thorogood, 2014).

For my doctoral project, I used both quantitative and qualitative methods, considering them to be complementary rather than incompatible. This position reflects the realist view of the world[2] underpinning my investigative approach. According to realism, there are multiple different ways of perceiving a single, mind-independent reality (Bhaskar, 1975). Reality is a concept extending beyond consciousness or the self; it is not wholly discoverable or knowable, which explains differences between reality and people's perceptions of reality (Bisman, 2002). Within a realist framework, both quantitative and qualitative methods are seen as appropriate for researching different perceptions of reality and the causes and mechanisms underlying actions and events (Clark, 2008).

To answer my research question, I first classified measures of social relationships using a qualitative, conceptual approach (Chapter 4). I then went on to study the link between loneliness or social isolation and incident disease using quantitative analyses – specifically, meta-analysis (Chapter 5) and secondary analysis of longitudinal observational data (Chapters 6 and 7). Because three of the four empirical chapters in my thesis were devoted to using quantitative methods, it might seem as though I primarily saw the qualitative part as enhancing the understanding arrived at using quantitative methods. Such an approach implies an unequal 'handmaiden' role for qualitative analysis (Popay, 2003). The alternative view I adopted was to conceive of qualitative methods as allowing me to get at a different kind of knowledge. This

[2] Alternatively known as critical realism (Hunt, 1991), postpositivism (Denzin & Lincoln, 1994; Guba & Lincoln, 1994) or neopostpositivism (Manicas & Secord, 1982).

approach, known as the ‘epistemological model’, suggests that conceptual research is equal, if different from, numerical research. The differences between the enhancement and epistemological models are summarised in Table 3.1.

Table 3.1 Two contrasting models of the relationships between qualitative and quantitative research in social epidemiology

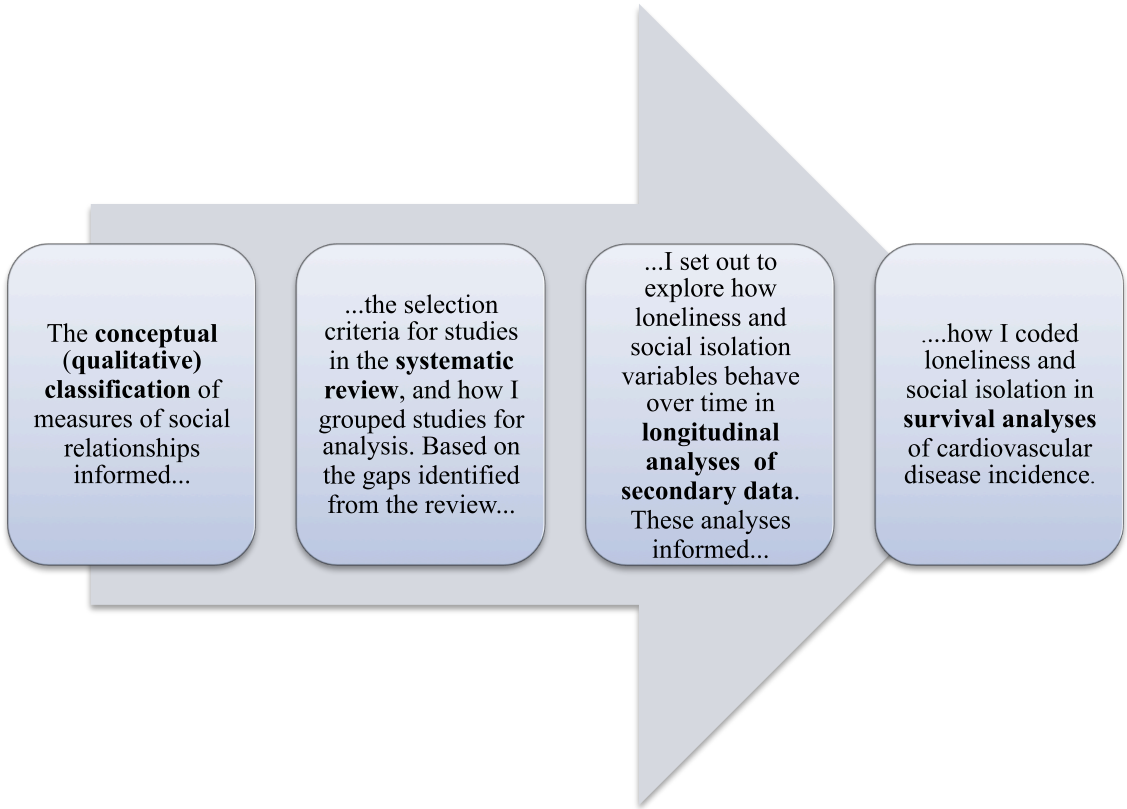
Model 1: The enhancement model. Qualitative research can enhance the work of epidemiologists by:
1) Generating hypotheses for quantitative epidemiological research to ‘test’ 2) Helping to construct more sophisticated measures of social phenomena 3) Explaining unexpected results
Model 2: The epistemological model. Qualitative research can contribute to epidemiological understanding by:
1) Researching the parts other methods do not reach by addressing different kinds of questions 2) Thickening understanding by adding conceptual and theoretical depth to knowledge 3) Shifting the balance between the researcher and the researched 4) Challenging traditional epidemiological ways of knowing

Table based on Popay, 2003, p.60.

‘Thickening understanding by adding conceptual and theoretical depth to knowledge’ (see Point 2 under the epistemological model heading in Table 3.1) was a key reason for using qualitative methods. Without a clearer conceptual understanding of how social relationships had been measured in the past, I could not embark on informed empirical quantitative analyses of my own. Figure 3.1 summarises the linear process through which the qualitative stage informed the quantitative analyses in my study.

In the next section of this chapter, I describe in more detail how each stage informed the next phase of my project, and explain why I chose the specific methods that I did.

Figure 3.1 Flow diagram illustrating how each method used in my thesis informed the next stage of the study



3.2.2. Systematic classification of social relationship measures

Before conducting quantitative analyses to test whether loneliness and social isolation were associated with incident cardiovascular disease (CVD), I was aware of the need to clarify a) which measures of social relationships qualified as capturing these two concepts and b) where they fitted in relation to other measures of social relationships. From working in the field of social relationships and health research prior to my doctorate, I knew that many different instruments existed; and that it was not always clear from terminology alone what each tool set out to measure (see Chapter 4 for examples of questionnaire items and of how differences in terminology generate confusion). I set about classifying existing measurement tools, grouping them based on similarities and differences (Bailey, 1994). This approach had three main advantages. First, it allowed me to transcend instrument labels and boundaries. After observing that the names of questionnaires offered limited insight into how questions were phrased, and noting that the formulation of questions could vary quite markedly within tools themselves, I developed a classification based on characteristics identified at the item rather than questionnaire level. This approach allowed me to account for diversity within as well as between questionnaires. Secondly, by identifying a manageable number of dimensions according to which the items of questionnaires differed or resembled each other, I could simplify a complex reality and thereby improve our understanding of it. Thirdly, once all of the tools identified from my searches were mapped within one framework, I anticipated that it would be much easier to compare them and to situate specific instruments in relation to the wider pool of available measures.

The classification I produced was a qualitative classification. I arrived at it without statistical analyses or quantification, unlike clustering methods (Bailey, 1994). The principal reason for not using cluster analysis was that the latter seeks to group a sample of objects into homogeneous classes (Everitt, 1995), making it ill-suited for classifying objects where clear groupings are not easily distinguishable. The qualitative approach I chose was able to accommodate overlap across tools as well as across the dimensions used to define the classification. A second reason for preferring a qualitative perspective here was that the classification was primarily intended as an (i.e. one) example of how we might make sense of the literature – rather than as a definitive take on how to classify measures. It was designed to bring *conceptual* clarity to the literature, as well as to generate discussion and debate about how social relationships are measured in epidemiological studies. Because it was not intended as a static and comprehensive typology of the measurement tools available to researchers, I did not think it necessary (or suitable) to formally test its validity and reliability. My approach was no less scientific for this omission: I developed the classification using a systematic and rigorous process of grouping items according to similarities and differences in how they were formulated, describing each stage in Chapter 4 so that whoever might wish to reproduce and repeat it could do so.

3.2.3. Systematic review and meta-analysis of longitudinal observational data

Once I had designed a way of comparing measures of social relationships, I was in a position to systematically review the literature on loneliness, social isolation and risk of CVD. As with any systematic literature review, my rationale was that there were many studies on social relationships and CVD, and that it was not clear what the overall message from their findings was. Systematically reviewing the evidence would allow me to appraise and condense the evidence into an informative summary for researchers, practitioners, policy-makers and any other stakeholder (e.g. third sector organisations, service providers) (Centre for Reviews and Dissemination, 2009). Traditional reviews have been criticised for being haphazard and biased, subject to the idiosyncrasies of the individual reviewer (Mulrow, 1987). Using a systematic, transparent approach to identify, assess and interpret all the relevant information offered a way for me to minimize, as well as to explore, systematic errors of bias (Oxman and Guyatt, 1988). Systematically reviewing past studies would also help to refine my research hypothesis and study design (Mulrow, 1994). The review would be used to identify not only what had already been done and therefore need not be duplicated, but also the pitfalls of previous work and how I could avoid them in my own analyses of longitudinal observational data.

I chose to review quantitative rather than qualitative evidence, because what I was interested in was not *why* loneliness and social isolation might be associated with incident CVD, but *whether* there was an association. Had I intended to further develop the theory around why social relationships influence health, qualitative data would have been a useful source of information. Instead, I decided to concentrate on improving our knowledge of the size of the effect on health – anticipating that, were I to identify a sizeable effect, this could provide the basis for future qualitative work around underlying mechanisms and potential intervention points.

My research question was a temporal one: I wished to know whether people developed disease *following* experiences of loneliness and social isolation. I therefore selected longitudinal data as the most appropriate evidence for answering this question. I combined these data in a meta-analysis, because this offered a further set of advantages: meta-analyses increase power, i.e. the chance of detecting a real effect as being statistically significant if it exists; they improve precision, since estimates are derived from a larger sample of participants; and they can be used to formally assess the degree of conflict across studies, and reasons for this, using statistics (Higgins and Green, 2011).

The alternative would have been to synthesise the evidence in a narrative review. Had the evidence been of especially poor quality, or where serious publication or reporting bias had been identified, narrative synthesis would have been an appropriate approach. This was not the case of the evidence in my review. The studies were heterogeneous, and this could have been an argument for ruling out meta-analysis; on the other hand, meta-analysis offered the opportunity to formally explore this heterogeneity and its impact on findings, rather than un-informatively discarding it as a limitation of the evidence. The decision to pool studies that used different measures of social relationships was supported by the findings from the classification I elaborated to inform the review: rather than being clearly distinguishable from one another, tools overlapped in their content and remit.

3.2.4. Secondary analysis of longitudinal data

Systematically reviewing the quantitative evidence on loneliness, social isolation and incident CVD allowed me to identify gaps in the epidemiological literature (these are detailed in Chapter 5). To address these gaps, I decided to conduct secondary analyses of data collected as part of the English Longitudinal Study of Ageing (ELSA) (Steptoe et al., 2013a). My rationale for using data that had already been collected rather than generating a new set of data for my study was that within the timeframe of a three-year doctoral project it was not possible to design and conduct an observational primary study large enough and over a sufficiently long period of time (multiple years) to answer my research question (Arber, 2001; Smith, 2008). In theory, I could have designed an experimental study with an intervention designed to tackle loneliness and social isolation, and evaluated it. In practice, our limited knowledge of which interventions work to tackle these experiences (Cattan et al., 2005; Dickens et al., 2011) means that it would have required more than the restricted time and resources I had to carefully plan, design and implement an intervention strategy worth evaluating. ELSA offered the opportunity of using a large dataset for which information was rigorously collected every two years from 2002 onwards. I knew that by the time I began my doctorate, six waves of data would be available for analysis. Even if it had been possible to generate data of my own, the ready availability of good quality data in ELSA meant that collecting more data would have been questionable ethically. Not only would my data be, in all likelihood, less informative (due to the necessarily limited scale of a doctoral primary study), but it would also mean needlessly imposing on participants and using up resources for recruitment, data collection, inputting and data cleaning that could be more efficiently directed elsewhere (Kiecolt and Nathan, 1985).

I was aware of the limitations of secondary data analysis, in particular the potential for a mismatch between primary and secondary research objectives (Dale et al., 1988). Surveys often do not contain all the variables of interest to the secondary researcher. Even when they do, there may be too few indicators of a concept for reliable measurement. Before selecting ELSA as the dataset I would use, I familiarised myself with its variables. I compared these with the variables used in the studies included in my systematic review, to check whether ELSA included similar variables to those used in existing research. I also drew up a list of all the independent and dependent variables I might be interested in including in my analyses, based on my theoretical framework of how social relationships affected health, and listed it and how these were operationalized in ELSA. This process confirmed that ELSA contained all the variables necessary (or at least the variables from which I could derive the ones I wanted) for my analyses.

An important part of the familiarization process was gauging not only the content, but also the format of the data collection process in ELSA. The context and sequence of survey items can influence responses (Kiecolt and Nathan, 1985) and so can the medium through which questions are asked, such as via self-report completion of a questionnaire, in face-to-face interviews or via third party assessment (e.g. blood pressure or cholesterol levels). All three of these methods are used in ELSA (Steptoe et al., 2013a). A number of studies have documented that interviewer characteristics, especially race, sex and age, have an effect on responses to survey questions (Schuman and Converse, 1971; Martin, 1983). As a secondary analyst, I could not influence these parameters; but I analysed and interpreted the data with these limitations in mind (e.g. acknowledging stigma or reluctance to share information with interviewers as a potential explanation for differences in the prevalence of loneliness depending on whether data were collected in person or via self-report questionnaires).

ELSA was not the only longitudinal dataset I could have selected. In the UK, studies with measures of both loneliness and social isolation include Understanding Society (Buck and McFall, 2012), Whitehall II (Marmot and Brunner, 2005) and the Newcastle 85+ Study (Collerton et al., 2009). The reason I chose ELSA was that it allowed me to look at a nationally representative sample of adults aged 50 and over – a less restricted sample, in terms of age and generalizability, than the Whitehall II (focusing on civil servants) or the Newcastle 85+ (covering adults aged 85 and over). Unlike Understanding Society, where loneliness is measured at every other wave (Yu et al., 2015), ELSA includes measures of social relationships in consecutive waves, making it a better fit for the type of discrete-time survival analysis I planned to conduct (see section 3.2.5. below for details on this analysis). Because ELSA only covers adults aged 50+, this meant that my analyses would necessarily exclude experiences of social relationships at younger ages – a limitation which it will be helpful to bear in mind when interpreting my findings. Still, ELSA offered a number of advantages compared with other datasets, including the availability of robust social and biological indicators, and multiple measures of loneliness and social isolation (Steptoe et al., 2013a). This latter strength meant that I could test the sensitivity of my analyses to the use of different measures, a non-negligible advantage in an area of research where the validity and reliability of measures is often unclear (Bowling, 2005).

Although I focused on ELSA, the approach I took to study loneliness, social isolation and incident CVD was intended as an example of how similar analyses might be performed on other datasets. Outside of the UK, the Irish Longitudinal Study of Ageing (Kearney et al., 2011), France's Gazel Cohort (Goldberg et al., 2007) and the US Health and Retirement Survey (Sonnega et al., 2014) are all potential datasets in which trends in social relationships over time can be explored, and where links with a range of health outcomes can be studied. In Chapters 6 and 7, I describe the methods I used in detail so that researchers wishing to replicate my analyses can do so on other datasets. I provide annotated Stata 'do files' (see Appendices 6.2 and 7.1), which contain all the commands I used and which can be adapted by any Stata software user for their dataset of interest. Future cross-data and cross-national comparative studies will provide insight into how the relationship between loneliness, social isolation and health varies across populations, contexts and time.

3.2.5. Survival analyses

I used ELSA data to answer two main questions: a) how do people's answers to questions about loneliness and social isolation change over time and b) are loneliness and social isolation associated with risk of incident CVD? The descriptive analyses I conducted to answer the first question highlighted that loneliness and social isolation varied substantially over time (see Chapter 6). This finding prompted me to look for statistical methods that could take this variability into account when looking at the association with CVD incidence. I chose survival analysis because it accommodates time-varying variables (Mills, 2011). This meant that I could incorporate changes in social relationships into my epidemiological analyses, an aspect which I knew not to have been studied before. Survival analysis also enabled me to take into account censored data, i.e. cases for which information about survival time is incomplete (Bruce et al., 2013). In summary, survival analysis allowed me to make maximum use of the data available in ELSA.

3.3. Acknowledging the assumptions underlying my choice of methods

The methods I used in my doctoral project entail assumptions about what we can and cannot learn from them. In particular, reliance on standardised questionnaires to assess loneliness and social isolation implies that these concepts can be empirically measured; and my focus on association rather than causality is grounded in the premise that causal relationships cannot automatically be inferred from observational data. In the remainder of this chapter, I reflect on how these two assumptions shaped the design of my project, and what this means for interpreting its results.

3.3.1. Loneliness and social isolation as measurable entities

The way in which experiences of loneliness and social isolation are 'captured' throughout this thesis, both in the literature reviewed and in my longitudinal analyses, is through questionnaires. These are sets of questions designed to collect information from respondents on a topic which the researcher is interested in (McLean, 2006). Questionnaires allow researchers to quantify individuals' experiences, and the use of a fixed set of questions enables repeatability, reproducibility and comparability of findings across studies that use the same tool (Ackroyd, 1992). Where they are administered by a person rather than on paper or via the Internet, standardisation can help to minimise the interviewer's influence on responses. Another advantage is efficiency, since ready-available questionnaires can be used without each investigator having to design their own (Oppenheim, 1992).

It is important to acknowledge that using questionnaires to capture loneliness and social isolation implies that these entities can be objectively defined and described, and that it is possible to measure them empirically. This is one of the ways in which to approach the study of social relationships, but it is not the only one. Critics of standardised measurement tools have emphasised the inherent subjectivity of loneliness and social isolation, stressing that these experiences are mediated through the gaze of a particular individual, at a particular time and within a specific socio-environmental context (Victor et al., 2009). According to this argument, questionnaires offer limited insight into what are understood to be fundamentally personal and relativist experiences.

For my doctoral project, I sought to reconcile questionnaire use with the recognition that experiences of loneliness and social isolation are complex by minimising assumptions about what it is exactly that these tools 'measure'. For instance, I did not assume that direct single-item questions to assess loneliness (e.g. 'Do you often feel lonely?) were less appropriate than multi-item tools where loneliness is not explicitly mentioned to avoid under-reporting due to stigmatisation (de Jong Gierveld and van Tilburg, 2006). Instead, I saw them as complementary: direct questions rely on *participants' interpretation* of 'lonely' or 'loneliness', while multiple-item indirect questionnaires tell us about loneliness and social isolation *as defined by the researcher*. In the latter case, regardless of whether the participant feels or would report feeling lonely if asked directly, the set of answers they provide to the questions put together by researchers determines whether or not they are classed as 'lonely'. Another assumption I avoided was to interpret the answers of ELSA participants at each wave as reflecting experiences across the two-year interval between study waves. Being aware of the potential fluctuation between data collection points, I approached answers at each wave as snapshots instead. Throughout my analyses and interpretation, I bore in mind that what tools captured was potentially a 'socially acceptable' picture, i.e. that participants might have chosen to report only what they felt comfortable and willing to share (Victor et al., 2009). In Chapter 8, I return to this issue of public versus private accounts, and what this means for interpreting and deriving implications from my work.

3.3.2. Association versus causation

Establishing causal links between variables is a challenge for epidemiologists (Susser, 1973). Epidemiological data are rarely gathered within a closed system where, according to positivists, it is possible to identify a simple causal relationship between a small number of observable entities without taking into account external complexity (Smith, 1998). In my doctoral project, the participants in the studies that contributed to my systematic review and in ELSA were not restricted to a particular setting or context; there is no clear limit to the variables that might have affected exposure to risk factors for ill health, or health outcomes. One of the consequences of this is that 'interference' from external factors cannot be avoided (McNamee, 2003), which complicates the interpretation of findings: statistical associations may be the result of confounding, i.e. the presence of an extraneous factor associated both with the exposure and the outcome (Last, 2001).

To minimise risk of confounding in the survival analyses I undertook using ELSA data, I included three key variables in my statistical models: age, gender and socio-economic status. These variables were selected because the literature suggested that they were factors correlated with exposure and predictive of outcome, but not on the causal pathway. Age, gender and socio-economic status are recognised risk factors for CVD (Hippisley-Cox et al., 2008). A meta-analysis of risk factors for loneliness among adults over 60 years old found that being older, female, educated at a lower level and earning a smaller income predicted higher levels of loneliness (Pinquart and Sorensen, 2003). In relation to social isolation, previous analyses of ELSA showed that being older, male and less wealthy was associated with an increased risk of lacking social relationships (Shankar et al., 2011; Steptoe et al., 2013b; Beach and Bamford, 2016).

As an acknowledgement that potential confounding by unmeasured factors cannot be excluded when using observational data, throughout my thesis I refer to *association*, rather than causation, to qualify the findings from my systematic review and analyses of ELSA. When I use the term 'risk factor', I understand it to mean an 'attribute or exposure that is associated with an increased probability of a specified outcome, such as the occurrence of a disease. *Not necessarily a causal factor* [my emphasis]: it may be a risk marker.' (Porta, 2008). This is not to say that I think it impossible for observational data to provide information about causality. Rather, I adopt the common viewpoint among epidemiologists that a set of criteria need to be applied to a body of evidence before claims are made about a causal relationship – i.e. a causal relationship cannot be inferred based on one observational study alone (Gordis and Forgione, 2014). The goal of chapters 5, 6 and 7 is to investigate whether there is any evidence of association; in chapter 8, I discuss whether the findings from my doctoral project as a whole, in the context of the existing literature, support causal inference based on the guidelines suggested by Gordis (see Table 3.2; Gordis, 2014, p.250).

Table 3.2 Gordis guidelines for assessing evidence of causation

Guidelines for assessing causation	
1. Temporal relationship	The hypothesised causal factor has to be observed before the outcome.
2. Strength of the association	The stronger the association, the more likely the causal link.
3. Dose-response relationship	Evidence of a dose-response effect where the greater the exposure, the more likely people are to experience the outcome, is suggestive of causality.
4. Replication of the findings	Replication of findings across populations and contexts increases the likelihood of causality.
5. Biologic plausibility	Being able to hypothesise plausible underlying mechanisms for the association strengthens causality inference.
6. Consideration of alternate explanations	Ruling out alternate explanations increases the likelihood of causality.
7. Cessation of exposure	If a factor is causal, we would expect the risk of disease to decline when exposure to the factor is reduced.
8. Consistency with other knowledge	Consistency with the findings from other studies is more likely to suggest causality.
9. Specificity of the association	Causation is more likely when an association is observed among a specific population and disease – though association between a risk factor and multiple health outcomes need not weaken the likelihood of causation.

*

The aim of this third chapter was to clarify the assumptions underlying the approach and methods I used in my doctorate. Having presented the rationale for the focus and design of my project (Chapter 1), outlined its theoretical framework (Chapter 2) and explained the philosophy underpinning my choice of methods (Chapter 3), I now turn to reporting on the first objective of my project: the design of a novel way to compare tools used to measure social relationships in epidemiological studies (Chapter 4).

Chapter 4. Classification of social relationship measures[3]

Chapter summary: In this chapter I present a novel way of classifying tools used to measure social relationships in epidemiological studies. The aim of this classification was to inform the selection criteria and analytical approach I would apply in my systematic review of the literature on loneliness, social isolation and incident cardiovascular disease (see Chapter 5). After illustrating how loose and interchangeable terminology can lead to confusion (4.1.), I describe the steps I took to clarify the literature, elaborating a classification based on how investigators have operationalized social relationships (4.2.). I explain the two dimensions that make up the classification – a) structure versus function, and b) degree of subjectivity – and demonstrate how this new way of looking at measurement tools allows us to compare instruments across theoretical and disciplinary boundaries (4.3.). I conclude with a discussion of the classification's strengths and limitations, outlining its potential to inform future research (4.4.).

4.1. Introduction: the limits of using concepts to map the literature

In Chapter 2, I defined loneliness and social isolation, drawing on the work of previous researchers to clarify the remit of each concept and situate them in relation to other dimensions of social relationships. While these definitions provide a solid conceptual basis for my thesis, they cannot mask the terminological inconsistency encountered in the literature. In the absence of a comprehensive framework, investigators from a range of disciplines, including sociology, psychology, demography and epidemiology, have tended to define concepts in silos. One of the consequences of this disjointed approach is that different concepts have developed in parallel and it is not always clear how they relate to one another. For instance, is the 'social disconnectedness' defined by Cornwell as 'a lack of social relationships and low levels of participation in social activities' the same as de Jong Gierveld's 'social isolation' (Cornwell and Waite, 2009; de Jong Gierveld et al., 2006)? Or how do the two subjective feelings of perceived social support and loneliness compare (de Jong Gierveld and van Tilburg, 2006; Russell et al., 1978)?

Recognising that the coexistence of different definitions and disciplinary perspectives hinders coherence across the literatures, researchers have proposed ways of integrating concepts within an overarching framework. Due developed a framework with social relations as the main concept and the structure and the function of social relations as subconcepts (see Figure 4.1). In this model, the structure of social relations is defined as referring to the individuals with whom

[3] A shorter version of this chapter was published in *BMJ Open* (Valtorta et al., 2016 – see Appendix 8.1).

one has an interpersonal relationship, and the linkages between these individuals. The function of social relations, meanwhile, is understood as the qualitative and behavioural aspects of social relations, including social support, social anchorage and relational strain (Due et al., 1999).

Figure 4.1 Conceptual framework

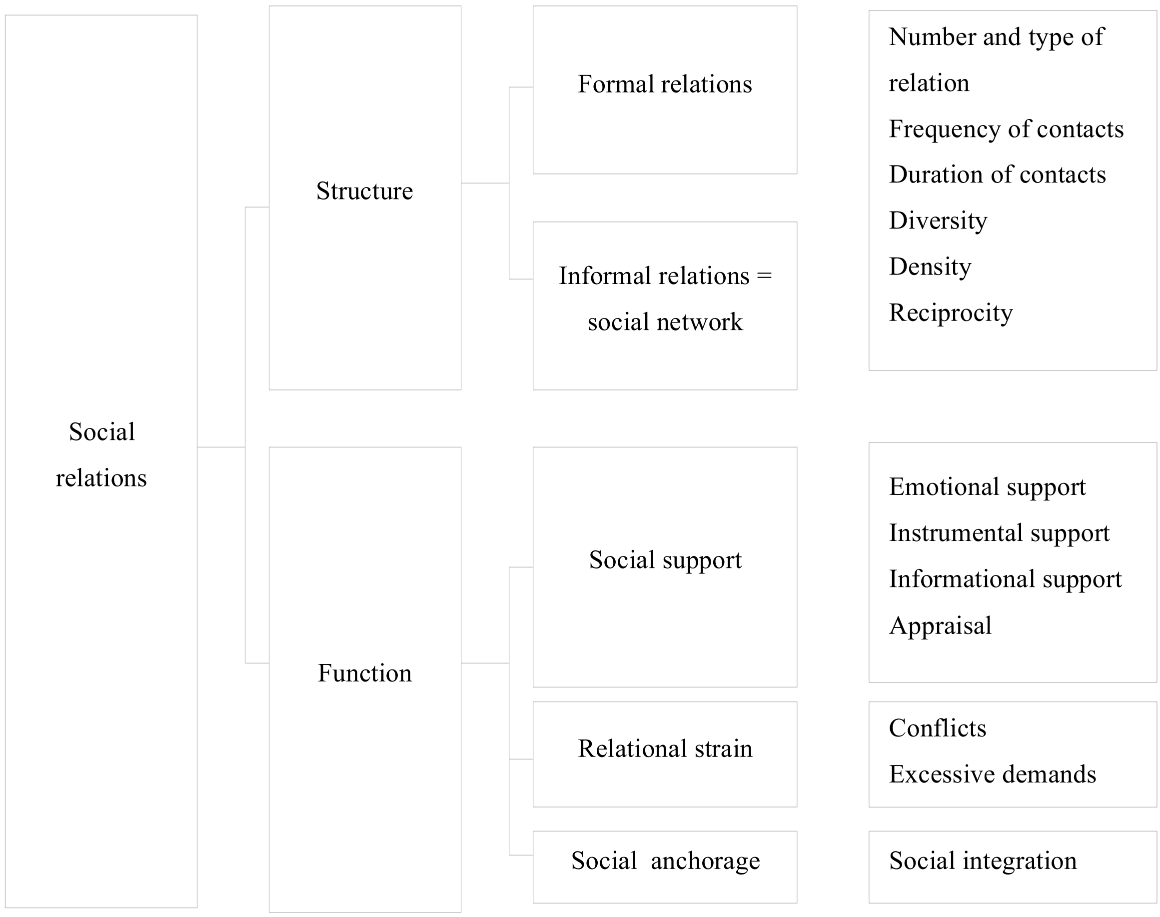


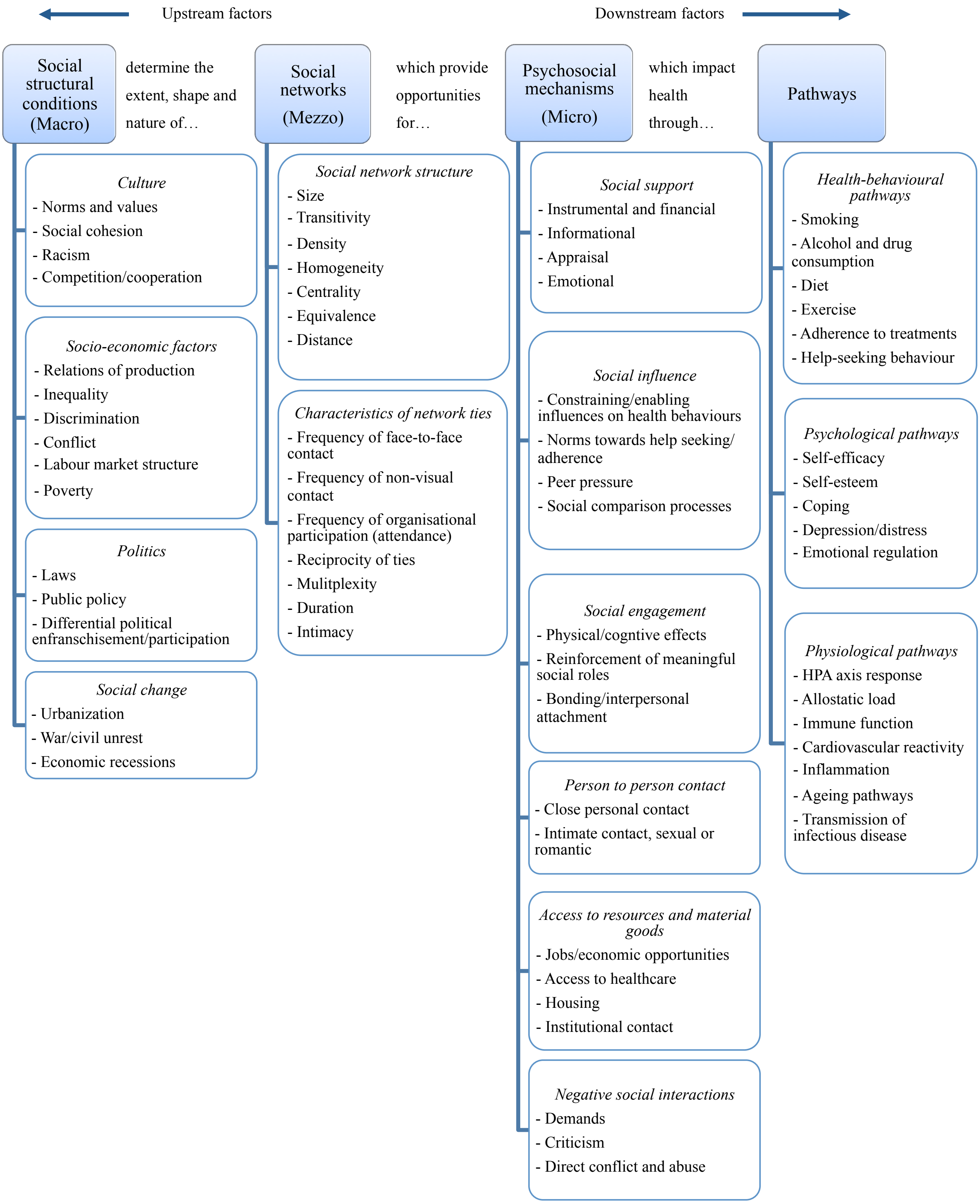
Figure reproduced from Due et al., 1999, p.662.

Figure 4.2 illustrates an alternative model, proposed by Berkman (Berkman et al., 2000).[4] This model distinguishes between 'social networks', i.e. the structure and related characteristics of social relationships; and the mechanisms through which these might impact health, including social support, social influence, social engagement, person-to-person contact, access to resources and material goods and negative social interactions.

There are two main limitations to how both Due and Berkman's frameworks can help us make

[4] This is the model that I adapted and used as the theoretical framework for studying social relationships and health – see Chapter 2. Here I focus on its distinction between 'social networks' and 'psychosocial mechanisms' – a distinction which is conceptually useful for informing future investigations, but which does not address terminological and operational inconsistency in studies that have already been published.

Figure 4.2 Berkman's model



Reproduced from Berkman and Krishna, 2014, p.242.

sense of the literature. First, both frameworks cover concepts – they do not touch upon the measures used by researchers to capture the dimensions they describe. While we might reasonably expect measures to map onto concepts, this is regrettably often not the case, in great part because of a second limitation: inconsistency in the terminology. As an example, in a study of psychosocial risk factors for heart disease in France and Northern Ireland (Sykes et al., 2002), one of the variables measured was labelled as social support. Yet when we look at the tool used to capture this variable, the Berkman-Syme Social Network Index was chosen – which is confusing, given the distinction between social support and social structure or network promoted by Due and Berkman (see the definitions presented above). As another example of loose terminology, in a systematic review of observational studies on psychosocial factors and coronary heart disease, 'social support' was understood to encompass a range of situations and measurement tools, including 'high love and support from wife', 'social network index' and 'social isolation' (Kuper et al., 2002). This raises the question of how comparable these measures are and whether, as researchers, we should be more precise about what we set out to measure.

An important reason for bringing clarity to the literature is that different domains of social relationships might have different implications for health. Unfortunately, most epidemiological studies focus on only one measure of social relationships, precluding direct comparisons. Evidence from the few studies that do include measures of objective as well as subjective aspects of social relationships suggests that the two dimensions are weakly correlated, and that they have independent effects on health-related outcomes (Cacioppo et al., 2006b; Hawkley et al., 2003; Hughes et al., 2004). A single approach to measuring social relationships is therefore unlikely to be appropriate for all purposes and investigators need to choose measurement tools carefully, basing their choice on clear hypotheses of how and why social relationships might influence particular health outcomes (Berkman and Krishna, 2014).

To overcome the lack of conceptual clarity in the literature, I set about classifying the instruments used in epidemiological studies in a way that allowed comparison across disciplinary boundaries. The classification I developed builds upon a distinction frequently referred to in the literature, the difference between functional (qualitative) and structural (quantitative) aspects of social relationships (House and Khan, 1985) and takes into account a second, important, dimension: the way in which questionnaire items are phrased, which informs us about the degree of subjectivity asked of respondents.

4.2. Methods used to develop the classification

The classification was developed in two stages. First, I used a systematic search strategy which I had previously designed to identify studies on the association between social relationships and health and social care service use among adults aged 65 and over (Valtorta et al., 2016a). Searches were tailored to eight electronic databases (MEDLINE, EMBASE, Scopus, Web of Science, CINAHL Plus, the Cochrane Library, the Centre for Reviews and Disseminations database and PsycINFO), using a combination of index headings (e.g. 'Loneliness', 'Social isolation', 'Social support') and free text terms (see Figure 4.3 for the search strategy used in MEDLINE) and were last updated in October 2015. The 32,205 records identified were screened by two researchers (Danni Collingridge Moore and myself) who selected studies that included a measure of the quantity and/or quality of individuals' social relationships. No study design, language, publication type or date restrictions were applied. The reference lists of relevant studies were screened for further eligible records. Once all the studies with a measure of individuals' social relationships had been identified, I retrieved the content of the measurement tool(s) used in each study and grouped the questions used according to how they were formulated. Through this process, I identified two ways in which questions differed: 1) whether they were asking about the structure or the function of social relationships and 2) whether respondents were being asked to report on: past and present contact with others; the availability of relationships as they perceive it; the adequacy of their relationships; or feelings relating to social relationships.

In a second phase, I tested whether the framework, based on the two dimensions identified, could be used to classify the measures used in studies on social relationships and incident cardiovascular disease (CVD). To find these studies, sixteen electronic databases (MEDLINE, EMBASE, CINAHL Plus, PsycINFO, ASSIA, Web of Science, Cochrane Library, Social Policy and Practice, National Database of Ageing Research, Open Grey, HMIC, ETHOS, NDLTD, NHS Evidence, SCIE, and NICE) using a combination of thesaurus and free text terms including loneliness, social isolation, social relationships, social support, social network (search last updated in May 2015; for an example of the full electronic strategy used to search MEDLINE, see Figure 5.1 in Chapter 5). The titles and abstracts of the 35, 925 records identified were screened by two researchers (Barbara Hanratty and myself), who selected eligible studies based on whether they included a measure of the quality and/or quantity of individuals' social relationships.

Figure 4.3 MEDLINE search strategy

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Searched online 03.04.13

Search Strategy:
----

1. Loneliness/
2. Social isolation/
3. Social distance/
4. Exp Social Environment/
5. lonely.mp.
6. solitude.mp.

7. exp Health Services/
8. exp Patient Care/
9. Home Care Agencies/
10. Home Care Services/
11. Home Health Aides/
12. "social service".mp.
13. "social care".mp.
14. utili?ation.mp.

15. 1 or 2 or 3 or 4 or 5 or 6
16. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
17. 15 and 16
18. limit 17 to "all aged (65 and over)"

4.3. Results

The systematic searches identified 54 instruments (see Appendix 4.1 for a full list, including references to the studies in which each tool was used and references to the original article or report in which the tool was described). The number of questions in each tool ranged from one to thirty-two. Taking each question at a time, I considered its content and the way in which it was formulated. This allowed me to develop a classification based on a) whether the question was about the function or structure of social relationships and b) the degree of subjectivity which it required from respondents.

4.3.1. The classification explained

In this section, I describe the two dimensions that make up my framework and provide examples of questions for each of their subdivisions.

4.3.1.1. First dimension: structure versus function

One way in which social relationships can be divided up is by distinguishing between their structure and their function. Questions that touch on the structure of social relationships seek to find out who people share an interpersonal relationship with and to assess the linkages between these individuals (Due et al., 1999). Structural characteristics of social relationships cover the number and type of people with whom a person interacts, the diversity and the density of a person's social network, and frequency and duration of contact between individuals. Examples of questions concerned with structure include: 'Have you ever been married? If so, are you now married, separated, divorced or widowed?' (Berkman-Syme Social Network Index – see Berkman and Breslow, 1983), or 'How many relatives do you see or hear from at least once a month?' (Lubben Social Network Scale – see Lubben , 1988).

Questions on the functional aspects of social relationships target the qualitative and behavioural characteristics of interactions and exchanges between people (Due et al., 1999). These questions are about the purpose and nature of relationships, with much of the literature focusing on their beneficial functions, in particular receiving and providing social support. This can take the form of emotional help (e.g. expressions of love and caring), tangible aid (e.g. transport), information or companionship (Cohen et al., 2000a). In the Interpersonal Support Evaluation List (ISEL) for example, people are asked to react to statements including 'If I needed a ride to the airport very early in the morning, I would have a hard time finding someone to take me' or 'I feel that there is no one I can share my most private worries and fears with' (possible answers: definitely true, probably true, probably false or definitely false) (Cohen et al., 1985). While the epidemiological literature has focused on social support as the main mechanism through which social relationships affect health, other functions are likely to affect health too, notably social influence and engagement, and opportunities for person-to-person contact (Berkman and Krishna, 2014). Examples of questions to do with function include: 'At present, do you have someone you can share your most private feelings with (confide in) or not?' (Interview Schedule for Social Interaction – see Duncan-Jones, 1981) and 'We are interested in how you feel about the following statement: I can count on my friends when things go wrong' (Zimet et al., 1988).

4.3.1.2. Second dimension: the degree of subjectivity asked of respondents

All answers to self-report questionnaires involve a degree of subjectivity, since answers are mediated via the perceptions and interpretations of individuals (Holt-Lunstad et al., 2010). Nevertheless, when comparing questions on social relationships, I found that the degree of subjectivity expected of respondents varied, based on the way in which items were formulated.

In the following section, I describe each of the four different formulations identified, starting with the more objective questions and progressively moving towards greater subjectivity.

a) Items assessing respondents' involvement in social relationships

A first type of question aims to capture people's involvement in social relationships using a relatively objective approach. These questions often, but not always, ask individuals to quantify their social relationships and require a numerical answer. For example: 'How many relatives do you see or hear from at least once a month?' (possible answers: 0, 1, 2, 3 or 4, 5 to 8, or 9+, Lubben Social Network Scale, Lubben, 1988). Such questions attempt to gauge the size and range of social relationships in which a person is involved, most often by trying to capture frequency of contact or social interaction.

b) Items assessing the availability of social relationships as perceived by respondents

Answers to the questions described above, i.e. questions about involvement in social relationships, could be telling us more about needs rather than access to relationships – i.e. people might not have engaged in certain interactions or social relationships because they did not feel the need to, rather than because they could not do so (Cohen et al., 2000b). One way to get at the availability of social relationships is to ask people whether such relationships are available to them. For example, in a 4-item measure of social isolation used in the Japan Public Health Center-based Prospective Study II, participants were asked: 'Do you have someone who is supportive of your opinions and actions?' (Ikeda et al., 2008). Questions are often phrased hypothetically, for example: 'Is there someone who would give you any help at all if you were sick or disabled, for example, your husband/wife, a member of your family, or a friend?' (OARS Social Resource Scale, Fillenbaum, 1988). These questions do not tell us about whether social relationships are actually available to individuals; they are a measure of availability as perceived by respondents.

c) Items assessing the adequacy of social relationships from respondents' perspective

A third type of question asks respondents to report on whether they are satisfied with the quality and/or quantity of their interaction with others. Examples of such items include: How satisfied are you with the kinds of relationships you have with your family and friends? (possible answers: very dissatisfied, somewhat dissatisfied, satisfied; 11-item Duke Social Support Index (Powers et al., 2004)); and 'I find my circle of friends and acquaintances too limited.' (possible answers: 'yes!', 'yes', 'more or less', 'no', and 'no!' or 'yes', 'more or less', and 'no' (de Jong Gierveld and van Tilburg, 2006)). Answering such questions requires participants to appraise their social relationships against their expectations.

d) Items where respondents are asked about their feelings relating to social relationships

A last type of question focuses on feelings associated with social relationships. Questions can cover both positive and negative feelings that relate to how people feel about the quality as well as the quantity of their relationships. Whilst in the third type of question described above, people are simply expected to report on whether they are satisfied with relationships, the ‘feelings’ question goes beyond by attempting to capture whether the state of their relationships generates positive or negative feelings. For example, in the UCLA Loneliness Scale, respondents are asked whether they ‘feel isolated from others’, ‘feel left out’, or ‘feel completely alone’ (Russell, 1996). The UCLA Loneliness scale’s 20 items cover aspects relating to the frequency and intensity of negative feelings (e.g. ‘How often do you feel alone?’), without reference to a specific timeframe. Feelings about social relationships are assessed via 9 positive and 11 negative items, with each item rated from 1 (never) to 4 (often). The total score obtained can range from 20 to 80, with higher scores suggesting greater loneliness. Another commonly used tool to assess feelings of loneliness is the de Jong Gierveld Loneliness Scale (de Jong Gierveld and van Tilburg, 2006). This scale covers both social and emotional aspects of loneliness and encompasses such issues as people’s sense of emptiness, missing having people around and the availability of people to rely on, trust and feel close to. Five items are positively phrased (e.g. ‘I can call on my friends whenever I need them’) and six are negatively phrased (e.g. ‘I miss having a really close friend’). This 11-item scale (and the shorter 6-item version) is scored on a 5 point Likert scale from 1 (strongly disagree) to 5 (strongly agree). A score of 0 means complete social embeddedness and the absence of loneliness; a score of 11 refers to severe loneliness.

Another way of gauging people’s feelings is by directly asking, e.g. asking respondents to report how much they agree with the statement ‘I often felt lonely’. Some studies have found single item approaches to be strongly related to the overall score obtained from multi-item loneliness scales (de Jong Gierveld and van Tilburg, 1999; Russell et al., 1978; Di Tommaso and Spinner, 1993). Nonetheless, individuals might be reluctant to share their negative feelings of loneliness and/or may have differing understandings of what is meant by ‘loneliness’. Because of the potential for under-reporting and inconsistency, using a single question is not generally considered to be as robust an approach as using multi-item questionnaires, where loneliness is gauged indirectly (Weiss, 1982).

4.3.2. Uses of the classification

The classification I developed has two main applications: first, it allows us to clarify what each questionnaire (and their questions) is/are asking; secondly, it provides a framework for comparing measurement tools according to their content.

4.3.2.1. Using the classification to clarify what each questionnaire is asking

In the process of developing the classification, it became apparent that whilst the majority of questionnaires were designed with a total score in mind (i.e. no subscales), they often included more than one type of question. In Table 4.1, I list each of the instruments identified from the systematic searches and the dimensions they cover. An 'X' in a cell indicates that at least one of the questions in the multi-item questionnaire covered this dimension/sub-division of the dimension. As well as offering an insight into the contents of each tool, the table illustrates the multi-dimensionality of many instruments: sixteen of the fifty-four measures included questions on the structure as well as the function of social relationships; and twenty questionnaires contained items requiring varying degrees of subjectivity from respondents.

Table 4.1 Classification of social relationship measures, listed alphabetically

Tool used	Number of items	Dimension 1: function v. structure		Dimension 2: degree of subjectivity			
		Structure	Function	Involvement in relationships	Perceived availability	Perceived	Feelings/ Emotions
Berkman-Syme Social Network Index*	4	X	X	X			
11-item de Jong Gierveld Loneliness Scale*	11		X		X	X	X
35-item Duke Social Support Index	32	X	X	X	X	X	
11-item Duke Social Support Index	11	X	X	X	X	X	
4-item Duke Social Support Index	4	X	X	X	X		
Duke-UNC Functional Social Support Questionnaire	11	X	X			X	
ENRICHD Social Support Inventory (ESSI)	7	X	X	X	X	X	
Gijón Scale for the elderly's social-family assessment, family and social relationships subscales	10	X		X			
12-item Interpersonal Support Evaluation List (ISEL)	12		X		X		
Interview Measure of Social Relationships	Data not found	X	X	X	X	X	
Litwin Support Network Types	7	X		X			
10-item Lubben Social Network Scale	10	X	X	X	X		
6-item Lubben Social Network Scale	6	X	X	X	X		
Medical Outcomes	20		X		X		

Study (MOS) Social Support Survey							
Multidimensional Scale of Perceived Social Support (MSPSS)	12		X		X		
Negative Affect Scale	5		X				X
Nottingham Health Profile Social Isolation subscale	5		X		X		X
Older Americans Research and Service Center (OARS) Social Resource Scale	7	X	X	X	X	X	X
Oslo-3 Social Support Scale	3		X		X		
Personal Resource Questionnaire (PRQ2000)	15		X		X	X	X
University of California, Los Angeles (UCLA) Loneliness Scale	20		X		X	X	X
Wenger Support Network Typology	8	X		X			
A measure of social isolation (LaVeist 1997)	2	X		X			
A measure of social network (Mechakra-Tahiri 2011)	4	X		X			
A measure of social anchorage (Rennemark 2009)	4		X				X
Questionnaire on social network (Rodriguez-Artalejo 2006)	4	X		X			
Question about the number of sources of support (Tennstedt 1993)	1	X	X	X			
An index of social support (Lai 2006)	5	X	X	X	X		
A measure of living arrangements and informal	2	X		X			

care (Crets 1996)							
A measure of satisfaction with social support (Feld 1994)	6		X		X	X	
A measure of social integration (Orth-Gomer 1996)	6	X	X	X	X		
A measure of social isolation (Cloutier-Fischer 2009)	2	X	X	X	X		
A measure of social network (Reed 1983)	9	X		X			
A measure of social network (Reed 1984)	4	X		X			
A measure of social support (Tran 1997)	5	X		X			
A measure of social support (André-Petersson 2006)	13		X		X	X	X
A measure of social support (Ikeda 2008)	4	X	X	X	X		
A measure of social support (Kuper 2006)	6	X		X	X		
An social network index (Rutledge 2008)	12	X		X			
Social network type (Coe 1984)	2	X		X		X	
Social network type - family (Coe 1985)	2	X		X		X	
Multi-item measures combining questions about frequency of contact with others and participation in activities	2 or more	X		X			
Question(s) about frequency of face to face and/or phone contact with family and/or friends and/or neighbours, e.g.: 'How many times during the past week did you spend some time	1 or more	X		X			

with someone who does not live with you? ' (Hyduk 1996)							
Question(s) about the geographical proximity of family and friends	1	X		X			
Question(s) about the number of close friends or relatives, e.g. asking respondents for the 'number of friends [they] feel close to' (Lee 2008)	1 or more	X	X	X			
Question(s) about participation in social activities such as going to the cinema, sport events, church attendance or volunteering, e.g. 'In the past two weeks, did you go to a show or movie, sports event, club meeting, classes or other group event?' (The Longitudinal Study of Aging, 1992)	1 or more	X		X			
Question(s) about the perceived availability of emotional, tangible, informational and/or other support, e.g. 'Is there someone who would give you any help at all if you were sick or disabled, for example your husband/wife, a member of your family, or a friend?' (Barresi, 1987)	1 or more		X		X		
Question(s) about received support, e.g. asking participants whether they	1 or more		X	X			

received assistance during the past month with 7 tasks, including shopping, housework or going to the doctor							
Question(s) about satisfaction with social relationships and/or participation, e.g. asking participants whether they believe their present level of social activities to be adequate	4		X			X	
Question(s) about the size of a person's network, e.g. number of friends and relatives outside the household	1 or more	X		X			
Question about time spent alone	1	X		X			
Single-item question about feeling lonely, e.g.: 'How often in the last 12 months have you been bothered by loneliness?'	1		X				X

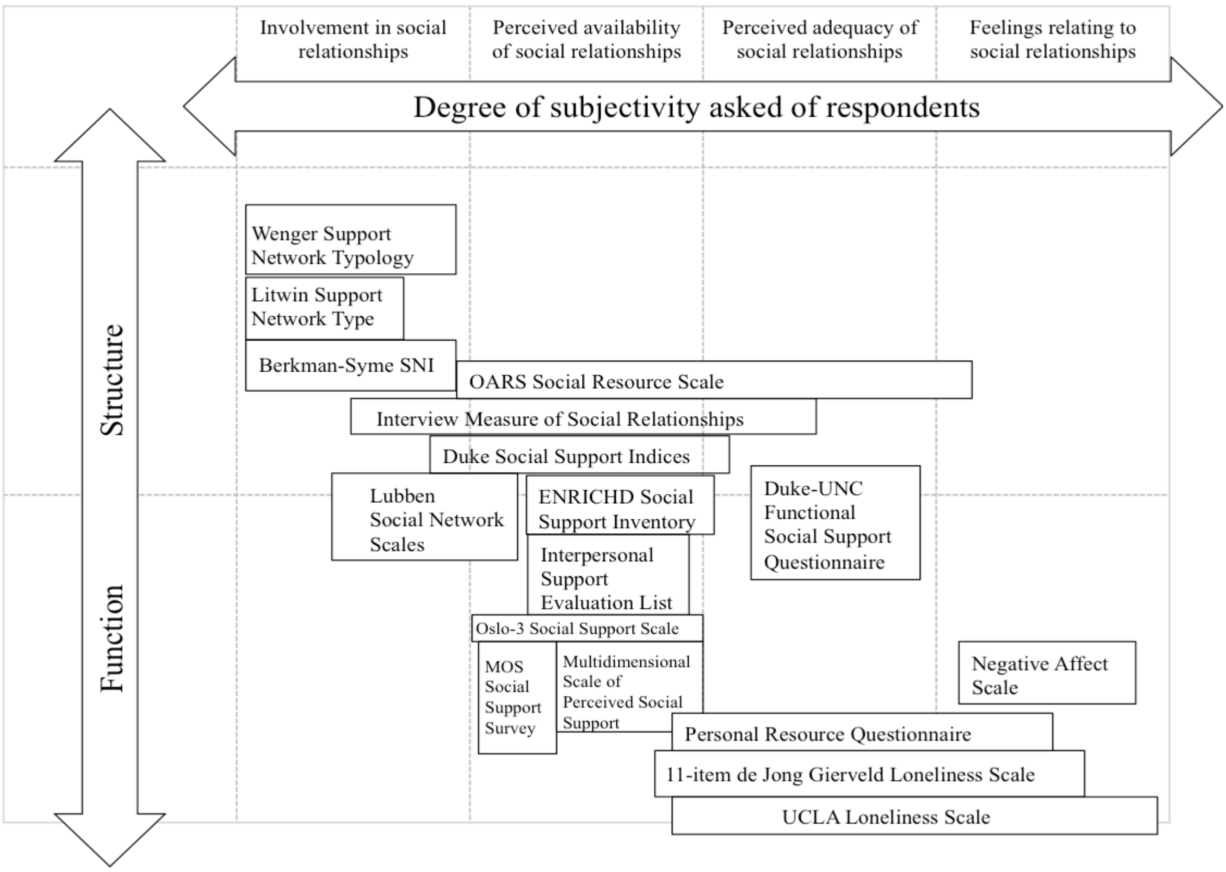
* Asterisks indicate that subscales are available for this questionnaire.

4.3.2.1. Using the classification to compare measures

Making clear what each instrument covers allows us to situate tools in relation to other available measures. In Figure 4.4, I mapped the multi-item questionnaires developed as stand-alone tools onto a two-dimensional diagram. Questionnaires were placed on the diagram according to whether they contained questions focusing on the structural, functional or both aspects of relationships (vertical axis); and according to the degree of subjectivity asked of respondents (horizontal axis). Where questionnaires contained more than one type of question, they were mapped accordingly. For example, in the Duke Social Support Indices participants are asked about their involvement in relationships, as well as to report on the perceived availability and adequacy of relationships; this is reflected in the diagram by the tool spanning across the three types of questions. Similarly, where questionnaires included questions about structural as well as functional aspects, they were placed so as to straddle both areas of the diagram (see for example the Lubben Social Network Scales, the ENRICH Social Support Inventory or the Duke-UNC Functional Social Support Questionnaire). For the purpose of clarity, I did not include single-item tools and tools that were developed for specific studies or datasets in the diagram.

Figure 4.4 is a useful visual tool for comparing and contrasting instruments. For example, it shows that whilst they both explicitly target social support, the ENRICHD Social Support Inventory includes questions on the function as well as the structure of relationships, whereas the MOS Social Support Survey focuses on functional aspects only. The diagram also enables us to identify tools with similar foci and questionnaires that might complement each other. As might be expected, tools explicitly designed for measuring loneliness (e.g. the UCLA Loneliness Scale and the de Jong Gierveld Loneliness Scale) tend to be based on more subjective questions, whereas social network indices primarily use more objective measures. Perhaps less intuitively given that loneliness is commonly defined as referring to the negative feeling associated with people perceiving the *quantity and quality* of their relationships to be deficient (Perlman and Peplau, 1981), we note that tools explicitly designed to measure loneliness tend to focus exclusively on the functional aspects of relationships.

Figure 4.4 Multi-item questionnaires mapped onto a two-dimensional diagram



Overall, the diagram shows that, underlying the differences in labels – i.e. the explicit focus of instruments – there is significant overlap across questionnaires. The OARS Social Resources Scale, the Interview Measure of Social Relationships and the Duke Social Support Indices are an example of how three tools appearing to target different concepts – social resources, social relationships and social support – contain similarly phrased questions on the same aspect of social relationships, their function. This overlap is important because it suggests that even though, conceptually, studies might be claiming to focus on different aspects of relationships, in practice it may be that these same studies are measuring relationships in a similar way, or using overlapping questions.

4.4. Discussion

The classification described in this chapter was designed to help researchers to interpret the existing literature on loneliness and isolation, as well as to help inform future epidemiological studies on social relationships. Rather than a comprehensive review of instruments, it was intended as an example upon which future work could build. As well as helping to clarify a heterogeneous literature, the aim was to generate discussion and debate about how epidemiologists measure social relationships, and what that means for our knowledge of their influence on health. In particular, the multi-dimensionality of many instruments raises the question of what exactly it is that we are seeking to measure. One the one-hand, surveying different aspects of social relationships using one tool can be seen as a positive way of taking into account the complexity of social relationships; but if a tool includes questions about perceptions of relationships, frequency of contact and access to help from others, what does this mean for drawing inferences about potential mechanisms? One of the limitations of using complex tools is that they do not shed light on which specific aspects of social relationships influence health outcomes, making it difficult to identify the dimensions upon which to focus for intervention.

4.4.1. Strengths and limitations of my classification approach

The framework I developed transcends disciplinary and conceptual boundaries, allowing researchers to compare measures that have been developed from different theoretical perspectives. In bringing clarity to a complex literature, the classification can help to clarify the health implications of different social relationships dimensions, and the potential health gain from intervention.

My aim was not to produce a comprehensive classification of all the tools used to measure social relationships in the epidemiological literature and beyond. Rather, it was to create a framework that other researchers could in turn use to compare measures, which they have identified through their own scoping searches. While the classification allows researchers to compare different tools and clarify the remit of each instrument, it does not offer guidance on the psychometric properties of each measure; nor does it provide advice as to which tool might be best suited for the population, setting and/or outcome of interest. Decisions as to the appropriateness of tools for future studies cannot therefore rely solely on the classification, but will require careful assessment of instrument validity, reliability and pertinence given the hypothesized link with the health outcome studied. It will be useful to have the perspective of other researchers on the ease of use, reliability and validity of the classification, as well as its suitability for classifying tools designed to measure negative social interactions – a dimension which was not captured in my search strategies and was therefore absent from my review.

4.4.2. Implications for research in the area of social relationships and health

One of the main ways in which the framework can be employed is by researchers who intend to review the literature, and who need to clarify which dimensions of social relationships they are interested in. Rather than rely on inconsistent conceptual terminology, they can use the classification to define the remit of their review (e.g. focus on functional or structural dimensions) and identify which measurement tools do and do not meet their criteria. Conceptual inconsistency has meant that systematic reviews relying on labels such as 'social support' have, in the past, ended up synthesizing evidence based on measures with limited, if any, overlap (see for example the review by Kuper et al., 2002, where measures included 'high love and support from wife', scores on a 'social network index' and assessment of 'social isolation'). Conversely, reviews focusing only on studies where the social relationship domain of interest is explicitly referred to – e.g. loneliness – may exclude potentially relevant measures that capture negative feelings associated with perceiving that one's social relationships are deficient. The classification I developed offers a means of focusing systematic reviews on meaningful domains of social relationships, without being unnecessarily reductive.

As well as informing inclusion criteria for systematic reviews, this classification can be useful in the analytical and synthesis stages of a systematic review. When choosing which studies to group together in preliminary analyses, researchers can turn to the classification to assess whether there is any overlap in the tools used, which could justify grouping them together. In meta-analyses, it may be pertinent to pool the results of studies that use similar, or overlapping, measures of social relationships.

*

In this chapter, I have presented a novel classification framework that helps to navigate the epidemiological literature on social relationships. One of these literatures is the evidence on loneliness, social isolation and incident CVD risk. In the next chapter, I systematically review this evidence, using the classification framework discussed here to inform inclusion criteria and data synthesis.

Chapter 5. Loneliness and social isolation as risk factors for coronary heart disease and stroke in high-income settings – a systematic review of longitudinal observational studies[5]

Chapter summary: To find out whether feeling lonely or being socially isolated are risk factors for developing cardiovascular disease, I systematically reviewed the evidence linking loneliness and social isolation to incident coronary heart disease and stroke among individuals living in high-income countries. This fifth chapter reports how I approached and conducted the study. After introducing the background to, and the rationale for, the review (5.1.), I describe the strategy used to retrieve and analyse the available data (5.2.). The results of two meta-analyses on coronary heart disease and stroke are then presented separately (5.3.), followed by a discussion in which I situate my findings in relation to the literature, summarize the strengths and limitations of the study and discuss implications for policy, practice and research (5.4).

5.1. Background and rationale

We know that the risk of non-suicide and non-accident related mortality is on average 26% greater among lonely adults and 29% higher among those who are socially isolated (Holt-Lunstad et al., 2015). The influence of social isolation and loneliness is comparable with well-established risk factors, including physical activity and obesity (Holt-Lunstad et al., 2010). Compared with our understanding of these recognised risk factors, however, we know much less about the implications of relationship quantity and quality for disease aetiology. In the following section I outline the gaps in our knowledge and how I set about addressing them.

5.1.1. What we do not know, and why this is problematic

Studies on mortality do not tell us whether loneliness and isolation are prognostic factors only – i.e. they affect chances of recovery once a person is ill – or whether they are also an aetiological factor, associated with an increased risk of becoming ill. This gap in our knowledge means that we do not know whether intervening to promote social relationships could prevent disease occurrence. Being able to quantify the potential benefits of intervention is an important step in determining the extent of the challenge posed to public health and society, and in being able to compare the influence of social relationships with other recognised risk factors for ill health. Only once we have an idea of the size of the health burden associated with deficiencies in social

[5] A shorter version of this chapter was published in *Heart* (Valtorta et al., 2016 – see Appendix 8.1).

relationships can we make informed decisions about prioritising them as a public health issue and allocate the appropriate resources for intervention.

The leading cause of disease burden in the UK and across high-income countries as defined by the World Bank (World Bank, 2014) is cardiovascular disease (CVD). In 2012, CVD accounted for 16.1% (2,875,000) of Disability-Adjusted Life Years (DALYs) in the UK, and 18.4% (61,609,000) of DALYs across high-income countries. The evidence on behavioural, psychological and physiological pathways linking social relationships to ill health suggests a plausible link between loneliness or social isolation and incident CVD. Behaviours associated with loneliness and social isolation include physical inactivity, smoking, and multiple health-risk behaviours (Shankar et al., 2011). Loneliness has been linked to lower self-esteem and limited use of active coping methods (Steptoe et al., 2004), and researchers have found that social isolation predicts decline in the health and safety domains of self-efficacy (McAvay et al., 1996). Feeling lonely or being socially isolated is associated with defective immune functioning and higher blood pressure (Grant et al., 2009; Hawkley et al., 2010). This evidence suggests that loneliness and social isolation may be important risk factors[6] for developing CVD, and that addressing them would benefit public health and wellbeing.

5.1.2. Research questions

I set out to systematically review the evidence from longitudinal observational studies on the association between loneliness or social isolation and incident coronary heart disease (CHD) and stroke in high-income settings. The primary question driving my review was: are loneliness and social isolation associated with developing coronary heart disease and stroke in high-income countries?

Secondary objectives included:

- exploring whether loneliness or social isolation were differentially associated with incident CHD and stroke;

- investigating whether the association between social relationships and disease incidence varied according to age, gender, marital status, socio-economic position, ethnicity and health.

[6] As mentioned in Chapter 3 (section 3.3.2) the term risk factor is understood in my thesis to mean ‘An attribute or exposure that is associated with an increased probability of a specified outcome, such as the occurrence of a disease. Not necessarily a causal factor: it may be a risk marker’ (Porta, 2008).

5.2. Methods

This study followed the Centre for Reviews and Dissemination's Guidance for undertaking reviews in healthcare (Centre for Reviews and Dissemination, 2009). The methods to be used in the review were set out in a protocol registered with the International Prospective Register of Systematic Reviews, registration number: CRD42014010225 (PROSPERO, 2014). The full study protocol can be consulted here:
http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014010225.

5.2.1. Study selection criteria

Below I list the criteria that were used to select the studies for my review.

5.2.1.1. Population

All populations were eligible for inclusion (e.g. community-based participants, patients in a health care setting). There was no age cut-off for including or excluding studies.

5.2.1.2. Timeframe

The review did not exclude studies based on date of data collection. While recognising that strategies for CHD and stroke prevention have changed over the past decades, I did not feel that these changes justified excluding older evidence, since it could still shed light on the association between social relationships and disease incidence. Much of what we know concerning heart disease, for example, is based on the Framingham Heart Study, which began in 1948 (Tsao and Vasan, 2015).

5.2.1.3. Setting

Studies were included if they were set in high-income countries as listed by the World Bank in 2014 (World Bank, 2014). The decision to exclude studies set in low and middle-income countries was based on the recognition that the burden of disease in these settings differs from that in high-income countries (World Health Organization, 2013) and that findings would therefore be of limited relevance for the UK context.

5.2.1.4. Exposure

Studies were eligible for inclusion if they included at least one measure of loneliness or social isolation. Since there is no comprehensive list of what constitutes an accepted measure of loneliness or social isolation, and since terminology is inconsistent, the search strategy intentionally included many terms encountered in the literature to allow for the variety in terminology. Thanks to the classification of social relationships developed in Chapter 4, I was able to consider studies where the focus was not explicitly on loneliness or social isolation, but where the tools used to assess relationships nonetheless qualified them for inclusion (i.e. they did qualify as measures of loneliness or social isolation). Measures at the more objective end of the spectrum (asking participants to quantify their social involvement or to report on the availability of social relationships) were considered to capture social isolation, while measures including questions about individuals' (negative) feelings qualified as measures of loneliness.

Decisions were based on the following criteria:

a) Loneliness

The measure had to be consistent with the definition of loneliness as a subjective negative feeling associated with someone's perception that their relationships with others are quantitatively and/or qualitatively deficient. Two examples of such tools are the de Jong Gierveld Loneliness Scale (de Jong Gierveld and van Tilburg, 2006) and the UCLA Loneliness Scale (Russell et al., 1978).

Tools where loneliness was not explicitly identified as the concept being measured, but which nonetheless fitted the above definition of loneliness, were eligible for inclusion. The Multidimensional Scale of Perceived Social Support is an example of such a tool (Zimet et al., 1988).

Studies in which loneliness was measured using a single item measurement tool (e.g. where participants are asked how often they feel lonely – as used in Stessman, 2014) were also eligible for inclusion. Such tools raise the following question: how do we know what is being measured? Regardless of what researchers have in mind when designing and/or administering such questions, participants' understanding of the concept may be different. Some researchers have also suggested that, given the stigma associated with loneliness, a direct single question is not appropriate for capturing people's feelings of loneliness (de Jong Gierveld and van Tilburg, 2006). Based on findings from a comparison of responses to a direct single-item question and a multiple-item tool, which show that the tools perform very similarly in terms of identifying the never lonely and the significantly lonely (Victor et al., 2005a), it was decided that studies using a single-item question should not be excluded from this review; and that the implications of using different tools to measure loneliness would be explored in subgroup analyses.

b) Social isolation

To be eligible for inclusion, measures had to be consistent with the definition of social isolation as an objective measure of the absence of relationships, ties or contacts with other people. The Berkman-Syme Social Network Index is one example of such a tool (Berkman and Breslow, 1983).

Based on my previous experience of searching the literature on social relationships and service use (see Chapter 4), I anticipated that few tools would explicitly be labelled as measuring social isolation. To capture relevant tools, a variety of terms relating to interpersonal contact, ties and interaction were all included in the search strategy included (see section 3.2.2.1.b. for details of the terms used in the database searches).

Studies that only used questions focusing on the presence or absence of a specific relationship (e.g. marital status) were excluded, since the hypothesis underlying my systematic review was that the absence of relationships in general, rather than the absence of a specific type of social relationship, was problematic for health.

c) Loneliness and social isolation

Some tools combine items relating to loneliness and some items relating to social isolation, as in the case of the Older Americans Resources and Services Social Resource Scale, for example (Fillenbaum and Smyer, 1981). Studies that used such tools were included in the review, with plans to perform subgroup analyses and explore whether studies using such measures reported different results.

d) Reliability and validity of the measures

Studies were not excluded based on the reliability and validity of the tools used to measure loneliness or social isolation. Instead, it was decided to explore the relationship between the reliability and validity of measurements tools, and the effects reported, via subgroup analyses.

e) Type of measure

The types of measures used were expected to vary and to include dichotomous (e.g. lonely v. not lonely) and continuous (e.g. score on loneliness scale) measures. The type of measure used did not constitute a criterion for exclusion.

5.2.1.5. Outcome

To meet inclusion criteria, studies had to investigate new diagnosis of CHD and/or stroke at the individual level as a function of loneliness and/or social isolation. Studies were excluded if CHD or stroke diagnosis was not the first instance of diagnosis among participants – except where analyses controlled for previous events.

a) CHD

CHD was defined as encompassing the diagnoses listed under codes I20-I25 of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), i.e. including angina pectoris, acute myocardial infarction and related complications (World Health Organisation, 1992).

b) Stroke

Stroke was defined as encompassing the diagnoses listed under ICD-10 codes I60–69, i.e. including ischaemic and haemorrhagic strokes (World Health Organisation, 1992).

c) Type of measure

The types of outcome measures used were expected to include dichotomous and time-to-event measures. The type of measure used did not constitute a criterion for exclusion.

5.2.1.6. Study design

To be eligible for inclusion, studies had to follow a longitudinal observational design. While randomized controlled trials have been used to look at the effect of loneliness on thoughts, moods, self-regulation and personal characteristics in the moment, inducing persistent feelings of loneliness or confining participants to social isolation would be highly unethical (Cacioppo and Patrick, 2008). In theory, it would be possible to design trials where all participants were either persistently lonely or isolated, and evaluate whether decreasing loneliness or isolation led to improvements in health outcomes. In practice, from previous systematic reviews of the literature, we know that evidence of interventions successfully strengthening social relationships is scarce; and that intervention studies rarely include repeated measures of health outcomes and/or changes in social relationships (Dickens et al., 2011; Cattan et al., 2005; Findlay, 2003). Observational longitudinal research is an alternative that can provide information on the temporal relationship between loneliness or social isolation on the one hand,

and ill health on the other.[7]

Cross-sectional studies were excluded. Without data collected over time, such studies are unable to shed light on the direction of the association between social relationships and health. This is an important limitation because of the potential for reverse causality: poor social relationships can be risk factors for, as well as consequences of, ill health.

Studies had to include quantitative analyses in which loneliness and/or social isolation was treated as an independent variable and incident CHD and/or was the dependent variable.

5.2.1.7. Language

Studies published in any language were included. Where a source was not in a language understood by myself or any of the review team members, translation was to be sought. In practice, this was not required – among the studies identified via our electronic searches, no non-English language studies met our inclusion criteria.

5.2.1.8. Publication type or status

Studies were not excluded on the basis of publication type or status, in order to minimise publication bias (Centre for Reviews and Dissemination, 2009). To ensure that peer-reviewed work was included where available, the authors of conference abstracts and theses were contacted and asked whether their work was available in other published formats.

5.2.1.9. Publication date

Studies were not excluded on the basis of publication date, since it was felt that studies could contribute valuable information regardless of when they were published (see above, section 5.2.1.2.).

5.2.1.10. Methodological quality

In line with recommendations in the Centre for Reviews and Dissemination guidance and the *Cochrane handbook for systematic reviews of interventions*, studies were not excluded on the basis of their methodological quality (Centre for Reviews and Dissemination, 2009; Higgins and Green, 2011). Instead, the implications of study quality were to be explored via subgroups

[7] Note that repeated cross-sectional studies were excluded from this review, as they are designed to permit analysis of change at the population rather than at the individual or micro level.

(see section 5.2.5. below).

5.2.2. Search strategy

The search strategy for this review combined four approaches: after performing an electronic search, the reference lists of eligible studies were screened, papers citing the identified studies were searched and experts were contacted.

5.2.2.1. Electronic databases

An electronic search strategy was designed with the assistance of Rocio Rodriguez-Lopez, an information specialist working at the centre for Reviews and Dissemination at the University of York. It was constructed to be highly sensitive, so as to retrieve as many potentially relevant studies as possible. Details of the search are provided below.

a) Sources

Sixteen databases were searched up until June 2014, with searches rerun in May 2015 to identify any additional material of relevance published in the interval. The following eight databases were accessed via the University of York Library's webpages,
http://subjectguides.york.ac.uk/healthsciences/searchingliterature:

- MEDLINE (Ovid SP), 1946 – current;
- Embase (Ovid SP), 1974 – current;
- Cumulative Index to Nursing and Allied Health Literature Plus (CINAHL Plus) (EBSCO), 1937 – current;
- PsycINFO (Ovid SP), 1887 – current;
- Applied Social Sciences Index and Abstracts (ASSIA) (ProQuest), 1987 – current;
- Web of Science, 1898 – current,
- Cochrane Library (Wiley), 1898 - current;[8]
- Social Policy & Practice (Ovid SP), 1981 – current;

A ninth database was accessed via the Centre for Policy and Ageing's database:

- National Database of Ageing Research, 1955 – current.

[8] Excluding the Cochrane Central Register of Controlled Trials (CENTRAL), since it exclusively covers experimental study designs,and these were excluded from this review.

Grey literature was identified via the following seven databases:

- Open Grey, http://www.opengrey.eu;
- The Health Management Information Consortium (HMIC);
- The British Library electronic theses database (ETHOS), http://ethos.bl.uk/Home.do;
- The Networked Digital Library of Theses and Dissertations (NDLTD), http://www.ndltd.org;
- NHS Evidence;
- Social Care Institute for Excellence;
- National Institute for Health and Social Care (NICE).

b) Search terms

Since the review did not initially focus on specific health outcomes, no terms relating to health were included in the search strategy. After discussion with information specialists at the University of York, it was decided that this approach was more appropriate than the alternative strategy of combining a necessarily non-exhaustive list of generic and specific health-related terms. While the decision to include no health terms in the strategy limited the specificity of the search, it maximised its sensitivity.

The following subject headings, words and variations were incorporated into a search strategy tailored to each database:

- Terms related to exposure – i.e. loneliness or social isolation:

    - Subject headings: Loneliness; Social Distance; Social Isolation; Interpersonal Relations; Social Environment (encompasses Community Networks and Social Support)

    - Free text: free text terms relating to social relationships are listed in Table 5.1.

Table 5.1 Free text terms relating to social relationships

Search terms chosen…	…to pick up the following words and phrases
lonel(truncation)	lonely, loneliness
solit(truncation)	solitude, solitary
social(truncation) isolat(truncation)	social isolation, socially isolated, perception of social isolation, perceived social isolation
perceived isolation	perceived isolation
social alienat(truncation)	social alienation, socially alienated, alienated
social(truncation) integrat(truncation)	social integration, socially integrated
social(truncation) distan(truncation)	social distance, socially distant
social(truncation) detach(truncation)	social detachment, socially detached
social relation(truncation);	social relation(s), social relationship(s)
personal relation(truncation) – to pick up personal relationship and plurals;	personal relation(s), personal relationship(s)
Interpersonal	interpersonal relation(s), interpersonal relationship(s)
societ(truncation)	societal isolation, societal alienation, alienated from society, isolated from society
social contact	social contact(s)
personal contact	(inter)personal contact(s)
social link	social link(s)
personal link	(inter)personal link(s)
social tie	social ties(s)
personal tie	(inter)personal tie(s)
social(truncated) support(truncated)	social support(s), socially supported
informal support	informal support(s)
personal support	(inter)personal support(s)
perce(truncation) (within 3 words of) support	perceived support, perception of (the) support
social network	social network(s)
discussion network	discussion network(s)
social participation	social participation
social(truncation) activit(truncation)	social activity, social activities, socially active
active socially	active socially
social(truncation) engage(truncation)	social engagement, socially engaged
social(truncation) connect(truncation)	social connection(s), connectedness, socially connected
social(truncation) disconnect(truncation)	social disconnectedness, socially disconnected
social(truncation) cohes(truncation)	social cohesion, socially cohesive
social(truncation) embedded(truncation)	social embeddedness, socially embedded
social(truncation) vulnerab(truncation)	social vulnerability, socially vulnerable
social interaction	social interaction(s)
personal interaction	(inter)personal interaction(s)
relationship (within 3 words of) satisfaction	relationship satisfaction, satisfaction with (a) relationship(s)
quality (within 3 words of) relation	quality of (a) relation(ship)(s)
quantity (within 3 words of) relation	quality of (a) relation(ship)(s)
social capital	social capital
social health	social health
social wellbeing	social wellbeing
Intimacy	intimacy

- Terms referring to study design: longitudinal; observational; epidemiological; cohort; case-control; prospective retrospective. Study design search filters were tailored to each database, based on the filters suggested by the InterTASC Information Specialists' Sub-Group (InterTASC Information Specialists' Sub-Group, 2014).

Different combinations of terms were tried in MEDLINE, to gauge the specificity and sensitivity of different searches. We initially attempted, for example to include terms relating to specific measurement tools used to assess loneliness or social isolation. Screening of the first 2,000 studies identified via this approach showed that this strategy was not sensitive enough, and I therefore decided that terms relating to measurement tools should be dropped from the electronic search strategy.

Figure 5.1 MEDLINE search strategy

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Searched online 10/06/14
Strategy saved as: Loneliness_Medline
Search Strategy:
----
1 loneliness/ (2206)
2 social isolation/ (10940)
3 social alienation/ (1309)
4 social support/ (51329)
5 community networks/ (5430)
6 social distance/ (1444)
7 interpersonal relations/ (55367)
8 Friends/ (2680)
9 psychosocial deprivation/ (1817)
10 Social Participation/ (545)
11 (lonely or loneliness or solitude).ti,ab. (3910)
12 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (19533)
13 (social wellbeing or social health or social capital).ti. (1205)
14 or/1-13 (134819)
15 exp cohort studies/ (1353453)
16 cohort$.tw. (280225)
17 controlled clinical trial.pt. (88473)
18 epidemiologic methods/ (29786)
19 exp case-control studies/ (662637)
20 (case$ and control$).tw. (331312)
21 or/15-20 (1913522)
22 and/14,21 (15308)

For an example of the search strategy used in MEDLINE, see Figure 5.1. Details of the electronic searches tailored to each database alongside the numbers of studies identified can be found in Appendices 5.2 and 5.3.

5.2.2.2. Reference lists

Bibliographies and reference lists of papers meeting the inclusion criteria were manually searched to locate articles not otherwise identified in the database searches, and to identify research centres and individuals who had published three or more articles on the topic.

5.2.2.3. Citation searching

Papers identified for inclusion in the review were entered into Scopus (selected here because it is the largest database of abstracts and citations) to search for articles that had cited these papers and could be eligible for inclusion.

5.2.2.4. Contacting experts

The intention was to contact individuals who had published three or more relevant articles on the topic, to ask whether they knew of further evidence which our searches might not have identified. Because no researchers meeting this criterion were identified via our database and reference searches, I resolved to contact investigators who had recently undertaken searches of the literature on social relationships and health, identified through the Campaign to End Loneliness' Research Hub (Campaign to End Loneliness) – asking them to check the list of included studies for any missing evidence, published or unpublished, which they might know of.

5.2.2.5. Documenting the search

A search log was kept to record:

- the sources searched;
- the date(s) when sources were searched;
- the key words and subject headings used (for electronic databases);
- the results of the searches.

5.2.2.6. Managing references

All references identified via the search strategy were saved in a single library file using Endnote version X7.1 (McCracken, 2013). Duplicate articles were removed based on title, authors, year and journal title.

5.2.3. Study selection

The study selection process is summarised below.

5.2.3.1. Decision to retrieve full texts

Two people (Nicole Valtorta and Barbara Hanratty) independently screened titles and abstracts for studies of relevance (e.g. mentioning social relationships and disease). Disagreements were resolved through discussion.

The search strategy was intended to capture all disease outcomes. After this first screening stage, 1,173 references were identified as potentially meeting inclusion criteria. Table 5.2 provides a breakdown of these records according to disease outcome.

Due to resource constraints, the decision was taken to proceed by focusing on a specific health outcome: CVD. This outcome was selected as it is the greatest source of burden of disease in high income countries (World Health Organization, 2013) and enough is known about its aetiology to hypothesise that social relationships may be an important cardiovascular risk factor (Berkman and Krishna, 2014). The full reports of articles on CVD that mentioned social relationships or disease aetiology were obtained.

Table 5.2 Number of studies eligible for full text screening, listed according to health outcome, from the least to the most common outcome researched

Mental health/wellbeing	703
General health	304
CVD	95
Dementia and Alzheimer's Disease	30
Cancer	11
Diabetes	7
Sleep problems	6
Obesity	5
Musculoskeletal disorder	5
Neuropathologies	3
Fatigue	3
Hearing difficulties	1

5.2.3.2. Selection of studies for inclusion in the review

Two researchers (Nicole Valtorta and Barbara Hanratty) independently examined the full papers retrieved and decided which studies met the inclusion criteria, using a screening sheet (reproduced in Appendix 5.1). In cases where further information was needed to make a decision on inclusion, I contacted authors (three, i.e. 60% of authors contacted, responded). When authors did not reply, I searched for additional information from related publications to inform our decision.

5.2.4. Data extraction

Data were extracted from the studies identified for inclusion using a standardised form (see Appendix 5.1).

The data extraction form was piloted on 10% of studies, to allow for refining its content and format. Once the data extraction form had been piloted and necessary changes had been made, one person (Nicole Valtorta) extracted data from all studies identified for inclusion and a second person (Sara Ronzi) checked extraction forms against the original papers. If data were missing or additional data were needed, authors of primary studies were contacted.

5.2.5. Validity assessment

In line with the practice recommended by the Cochrane collaboration, I a) focused on 'risk of bias' rather than 'study quality' to assess the validity of included studies (Higgins and Green, 2011, Section 8.2.2) and b) used a domain-based evaluation approach to study assessment (Higgins and Green, 2011, Section 8.2.2). A focus on risk of bias rather than quality clarifies that what is of interest here is the extent to which the design and conduct of a study are likely to have affected results, rather than focusing on quality per se or on the quality of study reporting (though it does not dispense us from having to rely on these reports to critically appraise the research) (Higgins and Green, 2011; Olivo et al., 2008). Taking a domain-based approach to assessment, unlike scales, has the advantage of transparency for users of reviews – since each domain of the tool is assessed separately, rather than an overall score calculated across domains – and allows the reviewer to explore the implications of each validity domain in subgroup analyses (Higgins and Green, 2011, Section 8.3.1).

Initially, study validity was to be assessed using the questions included in the risk of bias tool for observational studies developed by Petticrew and Roberts (2006) . After piloting this tool on 5 studies, it was felt that an approach more tailored to cohort studies was needed. Two commonly used checklists, the Newcastle-Ottawa Scale (Wells et al., 2014) and the Effective Public Health Practice Project Quality Assessment tool (Thomas et al., 2004) were considered as alternatives – but since not all aspects of relevance to the studies in my review were covered by these tools (e.g. potential for differential loss to follow-up, measurement error at exposure), I developed a tool based on the Agency for Healthcare Research and Quality framework and taxonomy of threats to validity (Viswanathan et al., 2013). Drawing on this framework, the following domains were selected for assessment: sampling bias, nonresponse bias, missing data, differential loss to follow-up, information error with regards to exposure and outcome measure, detection bias and confounding.

5.2.5.1. External study validity

The external validity of a study refers to the extent to which its findings can be generalised to the target population. In the case of the association between social relationships and health, it may be that loneliness and social isolation have a particularly detrimental effect on the health of specific population groups, e.g. individuals experiencing greater stress or who are already at increased risk of developing disease (Cohen et al., 2000a). The extent to which each study sample was representative of the target population was assessed by investigating three potential sources of bias (see Table 5.3 for criteria):

- Sampling bias: sampling bias relates to how the study sample was selected, and whether the methods used (e.g. random selection, recruitment based on voluntary interest) ensured that it was representative of the target population.

- Nonresponse bias: risk of non-response bias refers to the likelihood of bias introduced by systematic differences between respondents and non-respondents in ways likely to have increased risk of bias.

- Missing data: bias might be introduced due to missing data where subjects with full data differ from subjects with missing data in ways likely to modify the association between poor social relationships and health.

5.2.5.2. Internal study validity

Internal validity refers to the rigour of a study and the extent to which the effects observed are true for the people in this study. If less rigorous studies are biased towards over-estimating the effect of an exposure, this can lead to false positive results – i.e. concluding that the effect of an intervention/exposure is greater than it really is. Conversely, if less rigorous studies are biased towards under-estimating the effect of an intervention/exposure, this can lead to false negative results – i.e. underestimating the effect. Internal study validity was investigated in this review by assessing the likelihood of differential loss to follow-up, information error, detection bias and confounding:

- Differential loss to follow-up was evaluated by looking at whether subjects lost to follow-up differed from subjects who remained in the study in ways likely to have increased risk of bias (e.g. participants in worse health dropping out at faster rates than individuals in better health).

- Information error: with regards to the exposure, emphasis was placed on whether the tools used to measure loneliness and/or social isolation on each study had been validated and/or shown to be reliable; methods for ascertaining disease outcome were likewise appraised to distinguish between more or less robust techniques.

- Detection bias: studies were assessed based on whether outcome assessors were blinded to the exposure status of individuals. While recognising that the large cohort studies from which many of the studies were derived meant that outcome assessors were unlikely to be involved in or aware of exposure, this criteria was still felt to be of relevance for smaller studies.

- Confounding: confounding refers to 'a distortion of the estimated effect of an exposure on an outcome, caused by the presence of an extraneous factor associated both with the exposure and the outcome, that is, confounding is caused by a variable that is a risk factor for the outcome among non-exposed persons and is associated with the exposure of interest, but is not an intermediate step in the control pathway between exposure and outcome' (Last, 2001). Confounding factors have the potential to introduce significant bias; they can lead to overestimation or underestimation of an effect, depending on the direction of the associations between the confounding factor and exposure and disease (Zaccai, 2004). Based on a survey of the literature on the association between poor social relationships and incident disease, the following potential confounding factors – i.e. factors correlated with exposure, predictive of outcome but not on the causal pathway – were identified as being particularly relevant for this review: age, gender and socio-economic status (Pinquart and Sorensen, 2003; Hippisley-Cox et al., 2008; Shankar et al., 2011; Steptoe et al., 2013b; Beach and Bamford, 2016). The studies included in our review were consequently assessed to check whether they used appropriate techniques to minimise the risk of confounding bias, e.g. by adjusting for potential confounders in statistical analyses or by stratifying analyses so as to evaluate the association between social relationships and incident disease within homogeneous categories or strata of the potentially confounding variables.

Table 5.3 Criteria used to assess external study validity

Domain	Lower risk of bias	Higher risk of bias	Unclear risk of bias
Sampling bias	Random sample or method not likely to introduce a high risk of bias.	Sampling method unlikely to ensure representativeness of sample; explicit differences in relevant characteristics between sample and target population.	No information available.
Non-response bias	Non-respondents did not significantly differ from respondent with regards to risk factors for loneliness or social isolation, and to CVD risk factors.	Non-respondents significantly differed from respondent with regards to risk factors for loneliness or social isolation, and to CVD risk factors.	No information available.
Missing data	Subjects lost to follow-up did not significantly differ from the rest of the sample.	There were significant differences between the baseline data reported for the whole sample and the baseline data of subjects lost to follow-up.	No information available.

The criteria for assessing internal study validity are presented in Table 5.4. Using a standardized form (see Appendix 5.1), risk of bias and precision was assessed for each outcome reported. One person (Nicole Valtorta) appraised the quality of all included studies. A second reviewer (Sara Ronzi) checked the assessment forms against the original papers.

No studies were excluded on the basis of quality; instead, subgroup and sensitivity analyses were performed, to explore differences and test the stability of findings according to internal study validity.

Table 5.4 Criteria used to assess internal study validity

Domain	Lower risk of bias	Higher risk of bias	Unclear risk of bias
Differential loss to follow-up	Subjects lost to follow-up did not significantly differ from the rest of the sample.	There were significant differences in characteristics likely to increase risk of bias between the baseline data reported for the whole sample and the baseline data of subjects lost to follow-up.	No information available
Measurement error – exposure	Available data suggest that the tool used to measure loneliness and/or social isolation was comparatively valid and reliable.	Loneliness and/or social isolation were assessed using a tool that was of limited validity and/or reliability.	No information available
Measurement error – outcome	Measure based on information from medical records, registers and/or death certificates.	Reliance on self-report of diagnosis.	No information available
Detection bias	Assessors were blinded to exposure.	Assessors were not blinded to exposure.	No information available
Confounding	Studies controlled for CVD risk factors correlated with loneliness/social isolation, i.e. gender (in mixed samples), age, socio-economic status. Note that measures relating to health (e.g. diabetes, health-behaviours) are not included in this list because of them potentially being on the causal pathway.	Studies did not control for age, gender and socio-economic status.	No information available

5.2.6. Threats to precision

Precision is generally no longer considered to be part of risk of bias assessment, since it relates to the absence of random error whereas risk of bias refers to systematic error (Viswanathan et al., 2013). It was nevertheless felt that threats to precision in this review might be of interest, given that studies were likely to be at risk of over-fitting due to the relatively large sample sizes required for the statistical methods and models commonly used in these studies. Over-fitting occurs when a model is excessively complex, such as having too many parameters relative to the number of observations. The consequence is that a statistical model describes random error or noise instead of the underlying relationship between variables (Everitt, 2002). To assess risk of over-fitting, I recorded the size of each study and the number of events per predictor variable.

5.2.7. Data synthesis

The approach to synthesis taken in this review drew on the four stages outlined in the Centre for Reviews and Dissemination guidance (Centre for Reviews and Dissemination, 2009). First, it was hypothesized that poor social relationships might have different effects on CHD and stroke disease incidence, and that these effects might be modified by individual and social factors.

In a second stage, studies were grouped according to their measure of social relationships and study characteristics and results were summarized in a table. This stage revealed that the majority of papers reported the relative hazard of new diagnosis comparing people with higher versus lower levels of loneliness or social isolation. Three papers reported odds ratios and two reported relative risk. Since incidence of disease was low (<10%) in the studies reporting odds ratios, these estimates can be approximated to the relative risk (Zhang and Yu, 1998). Where the lonely or isolated group was used as the reference, results were transformed to allow comparison across all studies.

In a third stage, patterns emerging from the data during the preliminary synthesis were investigated to identify factors that might explain variations in the size and direction of effects. Only papers for which an effect estimate and standard error or confidence interval were available, or could be calculated, contributed to this stage of the analysis. Where several papers reported results drawing on data from the same cohort, the result for the longest follow-up time was privileged, to avoid violating the assumption of independence of samples. If a study included multiple measures of exposure and/or outcome, the result relating to the most comprehensive measure was selected (e.g. if a study reported results for total coronary heart disease as well as separately for fatal and non-fatal events, the estimates for total heart disease were retrieved). Where a study used statistical controls to calculate an effect size, data were extracted from the most complex model, to minimize risk of confounding. All effect sizes were transformed to the natural log for analyses. Using Revman version 5.3 (The Cochrane Collaboration, 2014), CHD and stroke effect estimates were plotted in separate forest plots and heterogeneity between studies was assessed using the I^2 statistic.

Following confirmation of heterogeneity, potential sources of variation were explored through pre-specified subgroup analyses for which more than one study per subgroup was available. Because of the limited number of studies, meta-regression (which would require at least 10 studies per covariate of interest) was not performed. Instead, it was possible to perform subgroup analyses comparing results according to exposure to loneliness versus social isolation (CHD studies only), gender, and internal validity components. The effect of age, marital status, socio-economic position, ethnicity and health could not be investigated due to lack of data and heterogeneity in analyses that did not allow for creating distinct groups of studies for each of these variables. Since heterogeneity could not be explained and removed based on our subgroup analyses, but studies were deemed sufficiently similar to warrant aggregation of results, results relating to CHD, and results relating to stroke, were pooled quantitatively in two separate meta-analyses using random effects models. Random-effects models were chosen because they allow for between-study variation, an approach consistent with the review's underlying assumption: that the effects estimated in the different studies would not be identical since they are derived from different populations and investigate different domains of social relationships.

The decision to pool results across studies measuring loneliness and social isolation was taken based on the way in which social relationships were assessed in the included studies. Initially, because I was aware that loneliness and social isolation were different experiences, I anticipated considering them separately. However, what the classification developed in Chapter 4 showed (and the data extraction process for this review confirmed) was that the tools used to measure social isolation commonly included items tapping into a more subjective appraisal of relationships. For example, the Lubben Social Network Index asks participants about how many relatives and friends they feel close to; and whether they have someone to talk to when they have an important decision to make (Lubben, 1988). In other words, there was overlap between the dimensions of social relationships captured in the included studies. I therefore decided to pool results from studies across the different measures of social relationships, to answer the broader question of whether deficiencies in social relationships are associated with disease incidence. I then used subgroup analyses to explore differences in results according to whether the dimension captured in each study was primarily loneliness or social isolation, or both.

In the final analytical stage of the review, the robustness of the synthesis was assessed by performing sensitivity analyses, to test whether internal study validity and small-study effects affected the overall results. The possibility of publication bias was explored by evaluating contour-enhanced funnel plots for asymmetry, drawn using STATA version 12 (StataCorp, 2011). In line with the Cochrane recommendations, it was decided that the limited number and the heterogeneity of studies included in the review did not meet criteria for reliably using tests for funnel plot asymmetry (Higgins and Green, 2011).

5.3. Results

The results of my analyses are presented below.

5.3.1. Overview of included studies

After a two-stage process, a total of 23 studies based on 16 cohorts were identified for inclusion in the review.. First, the titles and abstracts of the 35,925 records retrieved after de-duplication were screened for studies on social relationships and health. The records thus identified (n=1,173) were then screened for studies on incident CHD and/or stroke (see section 5.2.1.5 for inclusion criteria) and 95 studies met eligibility criteria for full text screening. Seventy-two studies were excluded, based on study design (n=28), measure of social relationships (n=26), outcome measure (n=12), no analysis linking social relationships to disease incidence (n=5) or duplication (n=1). Eleven studies on CHD and 8 studies on stroke met inclusion criteria for the quantitative syntheses (i.e. these studies were based on independent samples reporting data from which the natural log of the estimate and its standard error could derived). See Figure 5.2 for a flow diagram of the study selection process.

An overview of study characteristics is presented in Table 5.5. The 23 prospective studies included in the review drew on data from 16 longitudinal datasets, for a total of 181,006 participants aged 18+. Thirty-eight per cent of subjects were from Europe, 33% from North America, 25% from Asia (Japan and Asian Russia) and 5% from Australia. Nine papers reported data on men only (Andre-Petersson et al., 2006; Eng et al., 2002; Hedblad et al., 1992; Kawachi et al., 1996; Orth-Gomer et al., 1993; Reed et al., 1984; Reed et al., 1983; Rosengren et al., 2004; Sykes et al., 2002), 6 articles focused on women (Eaker et al., 1992; Gafarov et al., 2013; Kuper et al., 2006; Rutledge et al., 2008; Strodl and Kenardy, 2008; Strodl et al., 2003) and the remainder included a mixed sample (Avendano et al., 2006; Barefoot et al., 2005; Colantonio et al., 1992; Ikeda et al., 2008; Player et al., 2007; Nagayoshi et al., 2014a; Thurston and Kubzansky, 2009; Vogt et al., 1992). Of the 23 records included, twenty were based on community samples and 3 focused on at risk individuals (Hedblad et al., 1992; Player et al., 2007; Rutledge et al., 2008). Studies included between 98 and 47,713 subjects and baseline data collection years ranged from 1965 to 1996. Prevalence of loneliness or social isolation varied widely, between 2.8% (Nagayoshi et al., 2014a) and 77.2% (Gafarov et al., 2013). A total of 4,628 CHD and 3,002 stroke events were recorded, over follow-up periods ranging from 3 to 21 years. Table 5.6 provides further details of individual study characteristics.

Figure 5.2 PRISMA flow chart of included studies

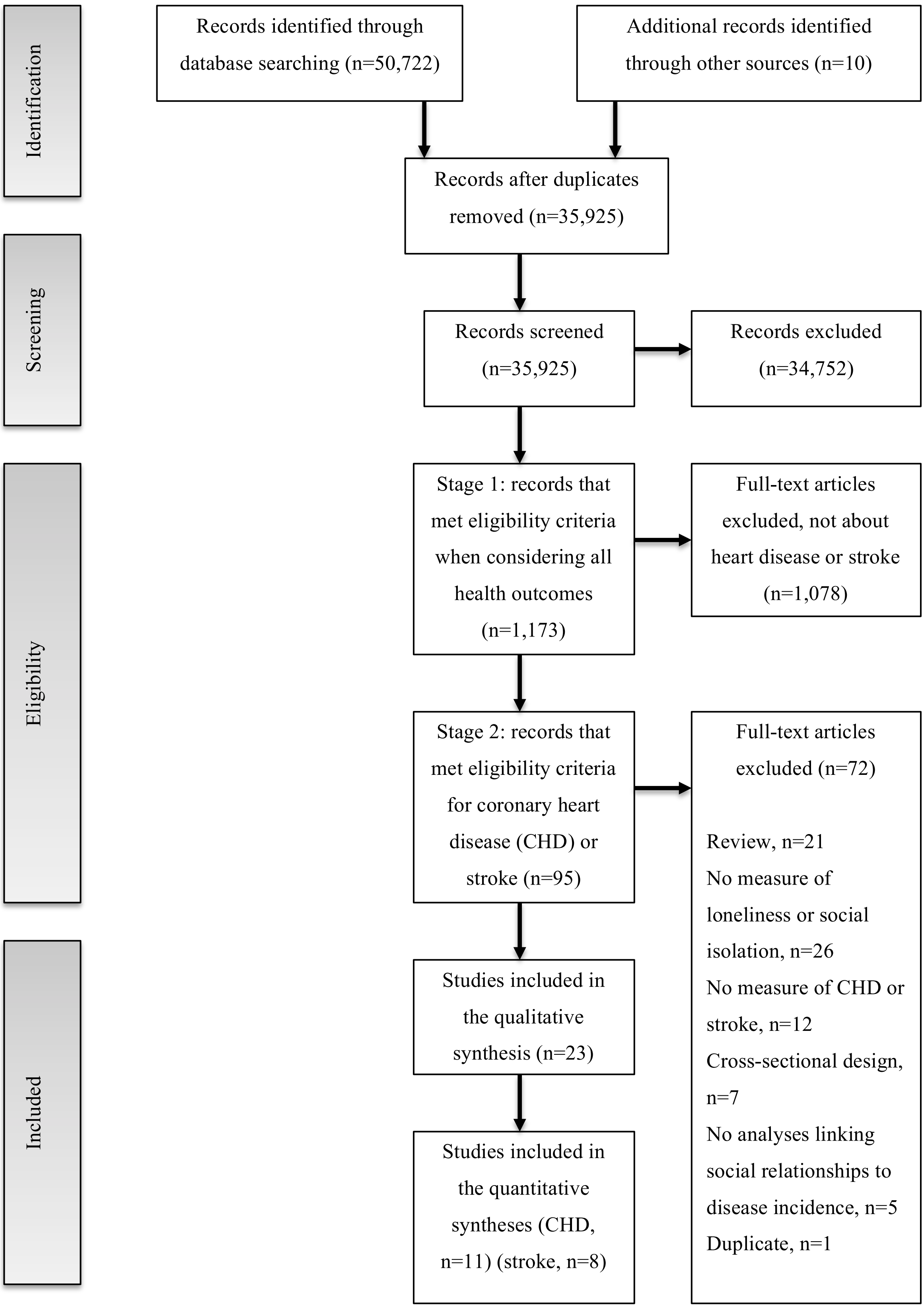


Table 5.5 Overview of included study characteristics

Population characteristics across the included studies	
Total number of participants	181,006
Age of participants	Aged 18 and over
Breakdown of the population according to world region	- Europe: 38% of participants - North America: 33% of participants - Asia (Japan and Asian Russia): 25% of participants - Australia: 5% of participants
Study characteristics	
Baseline data collection years, range	1965 to 1996
Length of follow-up, range	3 to 21 years
Size, range	Between 98 and 47,713 subjects
Gender	- All-male sample in 9 papers (Andre-Petersson et al., 2006; Eng et al., 2002; Hedblad et al., 1992; Kawachi et al., 1996; Orth-Gomer et al., 1993; Reed et al., 1984; Reed et al., 1983; Rosengren et al., 2004; Sykes et al., 2002) - All-female sample in 6 papers (Eaker et al., 1992; Gafarov et al., 2013; Kuper et al., 2006; Rutledge et al., 2008; Strodl and Kenardy, 2008; Strodl et al., 2003) - Mixed sample in 8 papers (Avendano et al., 2006; Barefoot et al., 2005; Colantonio et al., 1992; Ikeda et al., 2008; Player et al., 2007; Nagayoshi et al., 2014a; Thurston and Kubzansky, 2009; Vogt et al., 1992)

Table 5.6 Individual study characteristics

NB: Studies are grouped according to the dimension of social relationships they investigated (loneliness, social isolation or a combination of both); the measure of social relationships used (e.g. studies using the Berkman-Syme Social Network Index are grouped together); and the datasets used (i.e. studies reporting data from the same dataset e.g. the Established Populations for the Epidemiologic Studies of the Elderly Study are grouped together).

First author & year published	Data source & country	Data collect-ion dates	Population group (number of participants)	Age of study subjects at baseline	Follow-up period - mean, median and/or range	Outcome measure	Number of events	Covariates adjusted for	Main results for my review
Studies with a measure of loneliness									
André-Petersson, 2006	Men Born in 1914 Study, Sweden	1982-1983 to 1996	Men born in 1914 and living in Malmö in 1982/3, who showed adaptive behaviour in a stressful situation (n=208)	67-68	Mean: 10.3 years	Myocardial infarction (MI), fatal or non-fatal; register based	43	Prevalent coronary heart disease (CHD) (previous experience of MI or angina pectoris), use of antihypertensive drugs, socio-economic status (SES), s-triglycerides	Cox proportional hazards model. Comparing subjects with unsatisfactory (lonely) versus (v.) satisfactory social support (not lonely), hazard ratio (HR): 1.19, 95% confidence interval (CI): 0.64 to 2.22
Eaker, 1992	Framingham Heart Study, USA	1965-1967 to 1987	Female homemakers living in Framingham, Massachusetts in 1948 and who completed a 300-item psychosocial questionnaire (n=353)	45 to 64	Study length: 20 years	MI or coronary death, both sudden and not sudden; medical records	30	Age, systolic blood pressure, ratio of serum total cholesterol to high-density lipoprotein cholesterol, diabetes, cigarettes, body mass index (BMI)	Cox proportional hazards model. Comparing lonely v. not lonely subjects, HR: 4.0, 95% CI: 1.8 to 9.2
Thurston, 2009	National Health and Nutrition Survey, USA	1971-1975 to 1992	Civilian non-institutionalized men (44%) and women (56%) who were administered the Center for Epidemiological Studies-Depression Scale (CESD) at baseline (n=2,616)	Mean: 44.8 years; range: 25-74	Mean (SD): 14.9 years (5.1); range: 0-18.9 years	CHD, ICD-9 codes 410 to 414; home discharge reports and death certificates	357	Age, race, education, income, marital status, hypertension, diabetes, cholesterol, physical activity, smoking, alcohol use, systolic and diastolic blood pressures, BMI, depressive symptoms	Cox proportional hazards model. Whole sample: comparing subjects with high v. low levels of loneliness, HR: 1.53, 95% CI: 1.07 to 2.21. Men: comparing subjects with high v. low levels of loneliness, HR: 0.88, 95% CI: 0.43 to 1.78. Women: comparing subjects with high v. low levels of loneliness, HR: 1.81, 95% CI: 1.20 to 2.94

Studies with a measure of social isolation									
Avendano, 2006	Established Populations for the Epidemiologic Studies of the Elderly Study (EPESE, New Haven sample), USA	1982 to 1994	Men and women living in New Haven, Connecticut, in 1982, in one of 3 housing strata: 1) public elderly housing that is age and income restricted, 2) private elderly housing that is age restricted, and 3) private community housing and apartments. (n=2,250)	65+	Study length: 12 years	Stroke, fatal or non-fatal; self-report of diagnosis, obituaries, surveillance of hospital admissions and annual interviews with next of kin. Records were matched to the National Death Index and death certificates	270	Age, sex, race, education, income	Cox proportional hazards model. Aged 65-74: comparing people who scored 1 or less v. scoring higher on the social network index, HR: 2.03, 95% CI: 0.96 to 4.28. Aged 75+: comparing people who scored 1 or less v. scoring higher on the social network index, HR: 1.36, 95% CI: 0.48 to 3.81
Colantonio, 1992	EPESE Study (New Haven sample), USA	1982 to 1988	Men (41%) and women (59%) aged 65 and over, living in New Haven, Connecticut, in 1982, in one of 3 housing strata: 1) public elderly housing that is age and income restricted, 2) private elderly housing that is age restricted, and 3) private community housing and apartments. (n=2,604)	Mean: 74	Study length: 7 years	Stroke; hospital admission records, death certificates, Health Care Financing Administration data, self-reported strokes from annual contacts - verified against hospital records, using ICD-9 codes 431, 432.9, 433.0-434.9 and 436-437.1	167	Age, sex, housing stratum, hypertension, diabetes, physical function, smoking	Cox proportional hazards model. When the social network variable was added to the multivariate model, X^2= 0.15, df=1, p-value=0.6995
Eng, 2002	Health Professionals Follow-up Study, USA	1988 to 1998	Male health professionals aged 40 to 75 in 1986 (n=28,369)	Mean: 55.2 years; range: 42-77	Study length: 10 years	4 outcomes: nonfatal MI, fatal MI, sudden cardiac death, combined measure of total CHD (i.e. all incident first events of nonfatal myocardial infarction, fatal coronary heart disease, sudden cardiac death, coronary artery bypass graft surgery and angioplasty); medical records, death certificates, interviews with next of kin	1,816 incident cases of total CHD, including: 618 cases of nonfatal MI, 142 cases of fatal CHD (excluding sudden cardiac death), and 97 sudden cardiac deaths	Age (5-year categories), time period (1988-1990, 1990-1992, 1992-1994, 1994-1996, 1996-1998), occupation in 1986, smoking history (never, past, and current in categories of 1-14, 15-24, and ≥25 cigarettes/day), daily alcohol intake (0, 0.01-9.9, 10-19.9, 20-29.9, and ≥30 g/day), quintiles of BMI, quintiles of physical activity, routine physical examination in the last 2 years (yes/no), ability to climb several flights of stairs (yes/no), ability to do heavy housework (yes/no), employment status (full time, part-time, retired, disabled), history of hypertension, diabetes, high serum cholesterol, history of myocardial infarction in a parent aged <60 years (yes/no) in 1986, quintiles of energy-adjusted intakes of total fat, saturated fat, folate, and fibre, multivitamin and vitamin E supplement use (yes/no)	Cox proportional hazards model. Nonfatal MI: comparing subjects with a low v. high level of social network, HR: 1.11, 95% CI: 0.80 to 1.53. Fatal CHD: comparing subjects with a low v. high level of social network, HR: 1.82, 95% CI: 1.02 to 3.23. Sudden cardiac death: comparing subjects with a low v. high level of social network, HR: 0.71, 95% CI: 0.28 to 1.81. Total CHD: comparing subjects with a low v. high level of social network, HR: 0.99, 95% CI: 0.81 to 1.20

Kawachi, 1996	Health Professionals Follow-up Study, USA	1988 to 1992	Male health professionals aged 40 to 75 in 1986 (n=32,624)	Range: 42-77	Study length: 4 years	8 outcomes: total stroke, fatal stroke, nonfatal stroke, total CHD, fatal CHD, nonfatal CHD, sudden cardiac death, non-sudden cardiac death; medical records supplemented by correspondence and telephone interviews	104 incident cases of stroke (91 non-fatal, 13 fatal) and 403 cases of incident CHD (275 non-fatal MI, 128 cases of fatal CHD)	Age, time-period, smoking status, history of hypertension, diabetes mellitus, hypercholesterolemia, diagnosis of angina pectoris, deciles of BMI, parental history of MI before age 60, daily alcohol intake, tertiles of physical activity	Cox proportional hazards model. Total stroke: comparing subjects with a low v. high level of social network, HR: 2.02, 95% CI: 1.00 to 4.08. Fatal stroke: age-adjusted model only, comparing subjects with a low v. high level of social network, HR: 3.64, 95% CI: 0.78 to 16.9. Nonfatal stroke: comparing subjects with a low v. high level of social network, HR: 1.86, 95% CI: 0.85 to 4.06. Total CHD: comparing subjects with a low v. high level of social network, HR: 1.14, 95% CI: 0.74 to 1.73. Fatal CHD: comparing subjects with a low v. high level of social network, HR: 1.42, 95% CI: 0.72 to 2.81. Nonfatal CHD: comparing subjects with a low v. high level of social network, HR: 1.00, 95% CI: 0.58 to 1.71. Sudden cardiac death: comparing subjects with a low v. high level of social network, HR: 0.68, 95% CI: 0.16 to 2.96. Non-sudden cardiac death: comparing subjects with a low v. high level of social network, HR: 1.89, 95% CI: 0.87 to 4.13
Gafarov, 2013	Multinational Monitoring of Trends and Determinants in Cardio-vascular Disease (MONICA) - Psychosocial Study, Russia	1994 to 2010	Women aged 25-64 in 1994 living in one of the Novosibirsk districts, Western Siberia (n=870)	Range: 25-64	Study length: 16 years	2 outcomes: MI, stroke; register, medical records and death certificates	MI: 15; stroke: 35	None reported	Cox proportional hazards model. Across the whole sample, MI: comparing subjects with low v. higher levels of social network, HR: 2.92, 95% CI: 1.040 to 8.208. Stroke: comparing subjects with low v. higher levels of social network, HR: 2.72, 95% CI: 1.094 to 6.763. In the 55-64 age group, MI: comparing subjects with low v. higher levels of social network, HR: 5.9, 95% CI: 1.534 to 22.947 Focus on close contacts: MI: comparing subjects with low v. higher levels of close social network, HR: 4.9, 95% CI: 1.108 to 21.762. Stroke: comparing subjects with low v. higher levels of social network, HR: 4.1, 95% CI: 1.193 to 14.055
Sykes, 2002	Prospective Epidemiological Study of Myocardial Infarction (PRIME) Study, Northern Ireland and France	1991 to 1994	Men aged 50 to 59 in 1991-1994 and initially free from any cardiovascular disease (n=9,758)	Range: 50-59	Study length: 5 years	2 outcomes: 'hard CHD' (i.e. subjects who had died from CHD or had at least one non-fatal MI), total AP (i.e. angina pectoris or unstable angina); postal questionnaire followed-up by hospital or general practitioner notes, and death	Hard CHD: 163; total AP: 154.	Hostility, competitiveness, depression, impatience	Logistic regression. Hard CHD, full model: $X^2 = 7.389$, df = 5, p-value>0.05. Total AP, full model: $X^2 = 16.242$, df = 5, p-value = 0.006. The authors report that only depression and hostility contributed to the effect

Nagayoshi 2014	Atherosclerosis Risk in Communities Study, USA	1990-2 to 2010	Men (44%) and women (56%) aged 45-64 in 1987-1989, living in one of 4 communities: Washington County, MD; suburban Minneapolis, MN; Forsyth County, NC; and Jackson, MS (n=13,686)	Mean: 57; range: 46-69	Median: 18.6 years; maximum: 20.9 years	2 outcomes: stroke, ischemic stroke only; phone calls, surveillance of hospital discharges, death certificates - checked against medical records	905 incident strokes, of which ischemic: 804	Age, sex and race, socio-economic status (education attainment, income, occupation), marital status, behavioural risk factors (smoking status, alcohol drinking, physical activity), major stroke risk factors (hypertension, diabetes mellitus, low-density lipoprotein, high-density lipoprotein, lipid-lowering medication use, BMI)	Cox proportional hazards model. Stroke: comparing subjects with small v. larger network, HR: 1.44, 95% CI: 1.02 to 2.04. Ischemic stroke only: comparing subjects with small v. large social networks, HR: 1.41, 95% CI: 0.98 to 2.03
Player, 2007	Atherosclerosis Risk in Communities Study, USA	1990-2 to 1996-8	Men (48.3%) and women (51.7%) aged 45-64 in 1987-1989, living in one of 4 US communities and with blood pressures in the prehypertension range (120 to 139 mmHg systolic or 80	Range: 48-67; 50.4% sample were aged 48-57, 49.5% aged 58-67 years	Range: 4-8 years	Progression from pre-hypertension to CHD or CHD death; hospital discharge summaries, death certificates, supplemented with information from interviews with next of kin and coroners' or medical examiners' reports for out-of-hospital causes and dates of death	262	None	X^2 analysis. P-value associated with $\chi 2$ in bivariate analysis re. social networks = 0.220
Rosengren, 2004	Men born in 1933 Study, Sweden	1983 to 1998	Men born in 1933 in Gothenborg (n=741)	49-50	Study length: 15 years	CHD (MI; coronary revascularization; acute hospitalization with discharge diagnosis of angina); hospital registers	92	Smoking, physical activity, serum cholesterol, serum triglyceride, systolic blood pressure, BMI, diabetes, family history of CHD	Cox proportional hazards modelling. Comparing subjects with high v. low levels of integration, HR: 0.45, 95% CI: 0.24 to 0.84
Orth-Gomer, 1993	Men born in 1933 Study, Sweden	1983 to 1988-9	Men born in 1933 in Gothenborg (n=736)	49-50	Study length: 6 years	CHD, including fatal and non-fatal MI and sudden and non-sudden coronary death; hospital records, death certificates, national cause-specific death register	25	Serum cholesterol, BMI, smoking, treatment for hypertension, diabetes, physical activity	Multiple logistic regression. Comparing subjects in the lower v. upper quartiles of social integration, odds ratio (OR): 3.8, 95% CI: 1.1 to 13.9; regression coefficient = -0.656, standard error (SE) = 0.327, p-value=0.04

Kuper, 2006	Women's Lifestyle and Health Cohort Study, Sweden	1991-1992 to 2002	Women aged 30-50 residing in the Uppsala health care region (n=47,713)	Mean (SD): 40.3 years (5.8); range: 30-50	Mean: 135 months, i.e. 11 years and 3 months	Fatal and non-fatal MI; national hospital discharge and death registers	210	Age, cigarette smoking, exercise, alcohol consumption, weight, height, diabetes, high blood pressure	Cox proportional hazards modelling. Comparing subjects with the highest v. lowest social support, HR: 1.3, 95% CI: 0.9 to 1.8
Ikeda, 2008	Second cohort of the Public Health Center-Based Prospective Study, Japan	1993-1994 to 2004	Men (47.5%) and women (52.5%) aged 40 to 69 years in 1993-1994 and living in one of 13 administrative districts (n=44,152)	Mean: 53.6; range: 40-69	Mean: 10.7 years	4 outcomes: nonfatal MI, fatal MI, nonfatal stroke, fatal stroke; medical records, letter and telephone follow-up, death certificates	Nonfatal MI: 301; fatal MI: 191, nonfatal stroke: 1,057; fatal stroke: 327	Age (years), smoking status (never, former, or current), ethanol intake (non-drinkers and former drinkers, less than weekly, <150 g/wk, or ≥150 g/wk), BMI (kg/m2 in quartiles), leisure time sports activity (<1 day/mo, 1 to 3 days/mo, or ≥1cday/wk), perceived stress (less, moderate, or high), occupation	Cox proportional hazards model. Nonfatal MI: comparing subjects with low v. very high levels of support, HR: 0.90, 95% CI: 0.60 to 1.35; comparing men with low v. very high levels of support, HR: 1.06, 95% CI: 0.68 to 1.67; comparing women with low v. very high levels of support, HR: 0.55, 95% CI: 0.19 to 1.57. Fatal MI: comparing subjects with low v. very high levels of support, HR: 1.00, 95% CI: 0.61 to 1.63; comparing men with low v. very high levels of support, HR: 1.12, 95% CI: 0.65 to 1.94; comparing women with low v. very high levels of support, HR: 0.58, 95% CI: 0.17 to 1.99. Nonfatal stroke: comparing subjects with low v. very high level of support, HR: 1.11, 95% CI: 0.89 to 1.37; comparing men with low v. very high level of support, HR: 1.09, 95% CI: 0.84 to 1.43; comparing women with low v. very high level of support, HR: 1.22, 95% CI: 0.85 to 1.74. Fatal stroke: comparing subjects with low v. very high level of support, HR: 1.45, 95% CI: 1.00 to 2.10; comparing men with low v. very high level of support, HR: 1.59, 95% CI: 1.01 to 2.51; comparing women with low v. very high level of support, HR: 1.25, 95% CI: 0.63 to 2.46
Reed, 1984	Honolulu Heart Program Study, USA	1971 to 1979	Men of Japanese ancestry born between 1900 and 1919 and living in Oahu, Hawaii, in 1965 (n=4,251)	Range: 51-72	1971 to 1979	2 outcomes: CHD (MI and CHD deaths), stroke; hospital and medical records, post-mortem data	CHD: 155; stroke: 98	Age	Multiple logistic regression analysis. CHD: comparing subjects with low v. high networks, p-value ≤0.05. Stroke: comparing subjects with low v. high networks, p-value >0.05
Reed, 1983	Honolulu Heart Program Study, USA	1971 to 1979	Men of Japanese ancestry born between 1900 and 1919 and living in Oahu, Hawaii, in 1965 (n=4,389)	Range: 51-72	1971 to 1979	4 outcomes: nonfatal MI, fatal MI, angina, and total CHD (MI+angina); hospital discharge and mortality records	Total CHD: 218; nonfatal MI: 95; fatal MI: 76; angina: 47	Age, systolic blood pressure, serum cholesterol, serum glucose, serum uric acid, forced vital capacity, BMI, physical activity index, cigarettes/day, alcohol consumption, complex carbohydrate, socio-economic status	Multiple logistic regression: coefficients associated with social network scores, CHD: beta = -0.0836, p-value > 0.05; nonfatal MI: beta = -0 0576, p-value > 0.05; fatal MI: beta = -0 0505, p-value > 0.05; angina: beta = -0.1348, p-value > 0.05

Rutledge, 2008	Women's Ischemia Syndrome Evaluation (WISE) Study, USA	1996 to 2005	Women referred for a coronary angiogram to evaluate suspected myocardial ischemia (n=629)	Median (SD): 59.6 (11.6); aged 18+	Mean: 5.9 years	Stroke; inquiry by nurse or physician, death certificates	32	Age, education history, ethnicity, Beck Depression Inventory scores, diabetes, smoking, dyslipidaemia and hypertension histories, waist-circumference, coronary artery disease severity score	Cox proportional hazards modelling. Comparing subjects with low v. high social network index scores, HR: 2.7, 95% CI: 1.1 to 6.5
Vogt, 1992	Health maintenance organization, USA	1970-1971 to 1986	Men (46.1%) and women (53.9%) enrolled for at least two years with a managed care health maintenance organization in Portland, Oregon (n=2,396)	15.5% aged 18-29; 30.25 aged 30-44; 36.8% aged 45-64; 17.5% aged 65+	Length of study: 15 years	2 outcomes: CHD, stroke; medical care and mortality records	NR	Age, sex, socio-economic status, current and former smoking, subjective health status	Cox proportional hazards modelling. CHD: comparing subjects in the low v. high tertiles of social network size, HR: 1.2, 95% CI: 0.9 to 1.6, p-value = 0.26. Stroke: comparing subjects in the low v. high tertiles of social network size, HR: 0.9, 95% CI: 0.6 to 1.3, p-value = 0.58
Barefoot, 2005	Copenhagen City Heart Study, Denmark	1991–1994 to 1997	Men (44.3%) and women (55.7%) living in Copenhagen (n=9,460)	Mean: 57.5; range: 21-93	Mean: 5.7 years; maximum: 7.2 years	CHD; national health and hospital discharge registers	427	Age, gender, education, BMI, family history of coronary disease, systolic blood pressure, glucose, high density lipoprotein cholesterol, total cholesterol, smoking, alcohol consumption, physical activity, self-rated health	Cox proportional hazards modelling. Comparing people with 6-7 contacts to 0-1 contacts, HR: 0.67, 95% CI: 0.33 to 1.39. Comparing people with 5 intimate contacts to no contact, HR: 0.39, 95% CI: 0.14 to 1.06
Hedblad, 1992	Men Born in 1914 Study, Sweden	1982-1983 to 1987	Men born in 1914 and living in Malmö in 1982/3 who participated in a long-term ECG recording and had at least one episode of ST segment	67-68	Mean: 53.1 months i.e. just over 4 years and 5 months	CHD; infarct and mortality registers	17	Previous IHD, hypertension, hyperlipidaemia, obesity, high alcohol consumption, current smoking and low to moderate physical activity, social support and social influence indices, marital status	Multiple logistic regression. Comparing subjects with low v. high contact frequency, relative risk (RR): 1.2, 95% CI: 0.3 to 4.9; regression coefficient = 0.193, SE = 0.713

Studies with a measure combining loneliness and social isolation									
Strodl, 2003	Australian Longitudinal Study on Women's Health, Australia	1993 to 1996	Women aged 70-75 identified via national Medicare database (n=6,994)	Range: 70-75	Study length: 3 years	CHD; self-report	503	None	Logistic regression. Comparing subjects with low to fair v. very high social support, OR: 1.41, 95% CI 1.11 to 1.79, p-value ≤ .01
Strodl, 2008	Australian Longitudinal Study on Women's Health, Australia	1993 to 1996	Women aged 70-75 identified via national Medicare database (n=8,907)	Range: 70-75	Study length: 3 years	Stroke; self-report	174	None	Logistic regression. Comparing subjects with low to fair v. very high social support, OR: 0.88, 95% CI: 0.62 to 1.25

5.3.2. *Assessment of loneliness and social isolation*

Three papers measured loneliness (Andre-Petersson et al., 2006; Eaker et al., 1992; Thurston and Kubzansky, 2009), 18 measured social isolation (Avendano et al., 2006; Barefoot et al., 2005; Colantonio et al., 1992; Eng et al., 2002; Gafarov et al., 2013; Hedblad et al., 1992; Ikeda et al., 2008; Kawachi et al., 1996; Kuper et al., 2006; Orth-Gomer et al., 1993; Nagayoshi et al., 2014a; Player et al., 2007; Reed et al., 1984; Reed et al., 1983; Rosengren et al., 2004; Rutledge et al., 2008; Sykes et al., 2002; Vogt et al., 1992) and two papers used a measure that combined loneliness and social isolation (Strodl and Kenardy, 2008; Strodl et al., 2003).

5.3.2.1. Loneliness

Among the loneliness studies, two used a direct single item, asking about loneliness feelings in the day (Eaker et al., 1992) or in the past week (Thurston and Kubzansky, 2009). A third study used a thirteen-item tool that captured three relationship domains (perceived availability, adequacy or access), with subjects classed as having unsatisfactory relationships if they scored low in at least one of these three areas (Andre-Petersson et al., 2006).

5.3.2.2. Social isolation

Across the 18 studies with a measure of social isolation, 11 tools were used. Six studies used the Berkman-Syme Social Network Index, a composite measure of four domains of social connection: marital status, number and frequency of contacts with children, close relatives, and close friends, church group membership and membership in other community organizations (Berkman and Breslow, 1983). Two studies used the 10-item Lubben Social Network Scale, covering relationships with family, friends, a confidant, helping others and living arrangements (Lubben, 1988). The nine other tools used were multi-item questionnaires about the availability and/or frequency of contact across a range of social relationships.

5.3.2.3. Loneliness and social isolation – combined measure

One cohort study used a combined measure of social isolation and loneliness, the 11-item Duke Social Support Index, which asks about frequency of interaction and satisfaction with social relationships (Goodger et al., 1999).

5.3.2.4. Type of variable – categorical versus continuous

Loneliness and social isolation were predominantly treated as a categorical variable, with studies allowing for 2, 3, 4 or 6 categories. Two studies included data based on analysing loneliness or social isolation as a continuous variable (Sykes et al., 2002; Thurston and Kubzansky, 2009). Where researchers relied on the same tool, they did not necessarily use the same analytical approach. For example, half of the studies that used the Berkman-Syme Social Network Index categorized individuals into four levels of social connection, from socially isolated to socially integrated (Eng et al., 2002; Gafarov et al., 2013; Kawachi et al., 1996). Two studies dichotomised the index score based on the mean score (Colantonio et al., 1992) or comparing those who score 1 or less to those who scored higher (Avendano et al., 2006), and a further study treated the score as a continuous variable (Sykes et al., 2002). Out of the 23 articles included in the review, only one study reported data based on measuring social relationships more than once (Thurston and Kubzansky, 2009).

5.3.3. Ascertainment of CHD and stroke

Eighteen studies included a measure of CHD and 10 studies measured stroke incidence (five studies reported on both outcomes, explaining why the total exceeds 23 i.e. the number of included articles). New diagnosis of CHD or stroke was ascertained from medical records, death certificates or national registers in all but 4 cohort studies. In the Australian Longitudinal Study on Women's Health, information about new diagnosis was collected based on self-report only (Strodl and Kenardy, 2008; Strodl et al., 2003) and in the Women's Ischemia Syndrome Evaluation Study incidence of stroke was investigated via telephone interviews with a nurse or physician (Rutledge et al., 2008). A further two cohort studies (the Established Populations for Epidemiologic Studies of the Elderly Study and the Prospective Epidemiological Study of Myocardial Infarction) verified self-report of events against medical records (Avendano et al., 2006; Colantonio et al., 1992; Sykes et al., 2002). The majority of studies with a measure of CHD focused on MI and/or CHD death (11/18). Four studies included angina pectoris within their measure of CHD and a further two studies presented results for angina separately. In the case of one study, the remit of the CHD measure was unclear (Vogt et al., 1992).

5.3.4. Study validity

Table 5.7 summarises risk of bias across the studies included in our review (see section 5.2.5. for details of criteria). For many of the instruments assessing social relationships, there was limited information on reliability and validity. Fourteen studies used tools for which there were data suggestive of comparative validity and reliability, but in most instances information was based on other study samples and may therefore be of limited generalizability (see Appendix 5.4 for detailed information on the validity and reliability of tools, presented alongside associated effect estimates to allow visual comparison of results across tools). No data were found on the reliability and validity of the tools used in 7 studies and for 2 studies data indicated low validity (Andre-Petersson et al., 2006) or reliability (Vogt et al., 1992). Four cohorts (6 articles) relied on subjects reporting new diagnosis for all or part of the outcomes measured and were consequently deemed at greater risk of misclassification (see Table 5.6 for details of outcome assessment). Limited information on attrition and blinding of outcome assessment meant that susceptibility to differential loss to follow-up and detection bias was often unclear. In larger studies, given the many risk factors investigated and the relatively long follow-up periods, outcome assessment is less likely to have been influenced by knowledge of baseline information on loneliness and social isolation.

The results reported in 12 papers were at lower risk of confounding, i.e. analyses controlled or accounted for age, gender and socio-economic status (Andre-Petersson et al., 2006; Avendano et al., 2006; Barefoot et al., 2005; Eaker et al., 1992; Eng et al., 2002; Ikeda et al., 2008; Reed et al., 1983; Nagayoshi et al., 2014a; Rosengren et al., 2004; Rutledge et al., 2008; Thurston and Kubzansky, 2009; Vogt et al., 1992). Four studies presented results from univariate analyses (Gafarov et al., 2013; Player et al., 2007; Strodl and Kenardy, 2008; Strodl et al., 2003), with a further study adjusting for age only (Reed et al., 1984). The remaining 8 reports did not control for socio-economic status. In the case of the Health Professionals Follow-up Study the relative socio-economic homogeneity of the sample may limit the impact of this omission (Eng et al., 2002; Kawachi et al., 1996).

Table 5.7 Internal validity

First author and year published	Threats to internal study validity				
	Differential loss to follow-up	Information bias		Detection bias	Confounding
		Measurement error – exposure	Measurement error – outcome		
Studies with a measure of loneliness					
Andre-Petersson, 2006					
Eaker, 1992					
Thurston, 2009					
Studies with a measure of social isolation					
Avendano, 2006					
Colantonio, 1992					
Eng, 2002					
Gafarov, 2013					
Kawachi, 1996					
Sykes, 2002					
Nagayoshi, 2014					
Player, 2007					
Orth-Gomer, 1993					
Rosengren, 2004					
Kuper, 2006					
Ikeda, 2008					
Reed, 1983					
Reed, 1984					
Rutledge, 2008					
Vogt, 1992					
Barefoot, 2005					
Hedblad, 1992					
Studies with a combined measure of loneliness and social isolation					
Strodl, 2003				NA (self-report)	
Strodl, 2008				NA (self-report)	

Key

Lower risk of bias: white

Higher risk of bias: black

Unclear risk of bias: grey

5.3.5. Loneliness, social isolation and CHD

The results from the random effects meta-analysis for the association between loneliness or social isolation and incident CHD are shown in Figure 5.3. Across 11 studies (3,794 events; one study did not report numbers) based on independent samples, the average relative risk (RR) of new CHD when comparing high versus low loneliness or social isolation was 1.29 (95% confidence interval (CI): 1.04 to 1.59). There was strong evidence of heterogeneity within this comparison (I^2=66%, χ^2=29.16, df=10, p=0.001), and I undertook subgroup analyses to explore whether this could be explained by social relationship domain (loneliness v. social isolation), gender, risk of confounding and higher risk of bias due to exposure measurement error. As indicated by the overlapping confidence intervals and the tests relative to subgroup analyses, there was no evidence that effects differed according to each subgroup (see Figures 5.4 a,b,c and d). Due to limited information and study numbers, it was not possible to formally explore other potential sources of heterogeneity – such as participant characteristics other than gender, availability and access to care, use of different measures to assess social relationships or differences in follow-up time.

Figure 5.3 Forest plot of studies investigating the association between deficiencies in social relationships and incident CHD

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Loneliness				
André-Petersson 2006	0.17395331	0.3173003	6.7%	1.19 [0.64, 2.22]
Eaker 1992	1.38629436	0.4161854	4.7%	4.00 [1.77, 9.04]
Thurston 2009	0.42526774	0.1825	11.2%	1.53 [1.07, 2.19]
Social isolation				
Barefoot 2005	0.39877612	0.3666054	5.6%	1.49 [0.73, 3.06]
Eng 2002	-0.01005034	0.1002678	14.5%	0.99 [0.81, 1.20]
Gafarov 2013	1.07158362	0.5270221	3.3%	2.92 [1.04, 8.20]
Ikeda 2008	-0.10536052	0.2069	10.2%	0.90 [0.60, 1.35]
Kuper 2006	-0.26136476	0.1745385	11.5%	0.77 [0.55, 1.08]
Rosengren 2004	0.69314718	0.3511146	6.0%	2.00 [1.00, 3.98]
Vogt 1992	0.18232156	0.1467793	12.6%	1.20 [0.90, 1.60]
Combined				
Strodl 2003	0.3435897	0.1219042	13.6%	1.41 [1.11, 1.79]
Total (95% CI)			**100.0%**	**1.29 [1.04, 1.59]**

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 29.16$, df = 10 (P = 0.001); $I^2 = 66\%$
Test for overall effect: Z = 2.35 (P = 0.02)

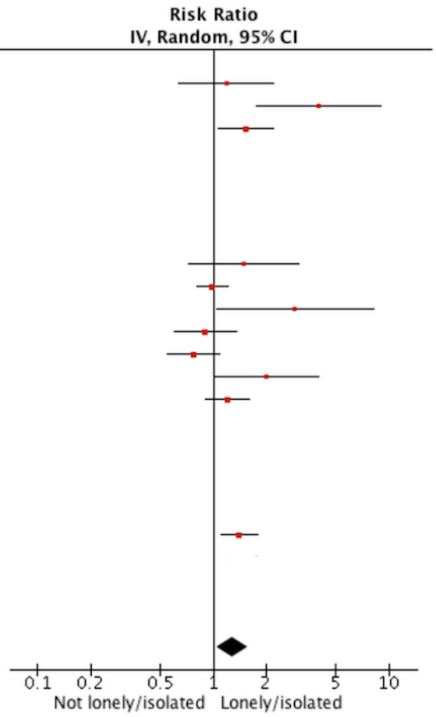
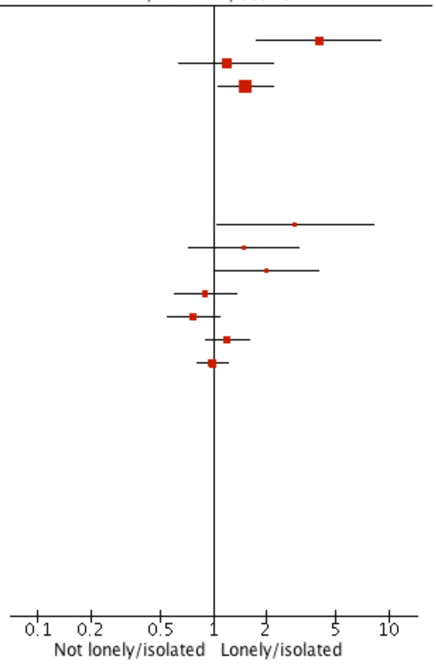


Figure 5.4 a, b, c and d Subgroup analyses of results from CHD studies

a) According to social relationship domain (loneliness v. social isolation)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Loneliness				
Eaker 1992	1.38629436	0.4161854	25.1%	4.00 [1.77, 9.04]
André-Petersson 2006	0.17395331	0.3173003	32.0%	1.19 [0.64, 2.22]
Thurston 2009	0.42526774	0.1825	43.0%	1.53 [1.07, 2.19]
Social isolation				
Gafarov 2013	1.07158362	0.5270221	4.2%	2.92 [1.04, 8.20]
Barefoot 2005	0.39877612	0.3666054	7.6%	1.49 [0.73, 3.06]
Rosengren 2004	0.69314718	0.3511146	8.1%	2.00 [1.00, 3.98]
Ikeda 2008	-0.10536052	0.2069	15.7%	0.90 [0.60, 1.35]
Kuper 2006	-0.26136476	0.1745385	18.3%	0.77 [0.55, 1.08]
Vogt 1992	0.18232156	0.1467793	20.8%	1.20 [0.90, 1.60]
Eng 2002	-0.01005034	0.1002678	25.3%	0.99 [0.81, 1.20]

Risk Ratio IV, Random, 95% CI

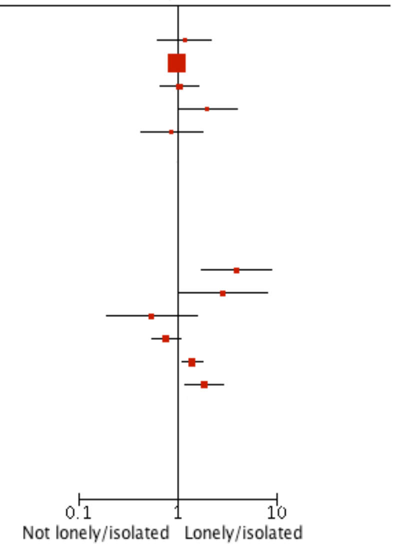


Test for subgroup differences: $Chi^2 = 2.39$, $df = 1$ ($P = 0.12$), $I^2 = 58.1\%$

b) According to gender

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Men				
André-Petersson 2006	0.17395331	0.3173003	7.5%	1.19 [0.64, 2.22]
Eng 2002	-0.01005034	0.1002678	66.4%	0.99 [0.81, 1.20]
Ikeda 2008	0.05826891	0.2292099	14.2%	1.06 [0.68, 1.66]
Rosengren 2004	0.69314718	0.3511146	6.1%	2.00 [1.00, 3.98]
Thurston 2009	-0.12783337	0.3624004	5.8%	0.88 [0.43, 1.79]
Women				
Eaker 1992	1.38629436	0.4161854	13.8%	4.00 [1.77, 9.04]
Gafarov 2013	1.07158362	0.5270221	10.9%	2.92 [1.04, 8.20]
Ikeda 2008	-0.597837	0.5387361	10.7%	0.55 [0.19, 1.58]
Kuper 2006	-0.26136476	0.1745385	21.6%	0.77 [0.55, 1.08]
Strodl 2003	0.3435897	0.1219042	23.1%	1.41 [1.11, 1.79]
Thurston 2009	0.62593843	0.2285981	19.9%	1.87 [1.19, 2.93]

Risk Ratio

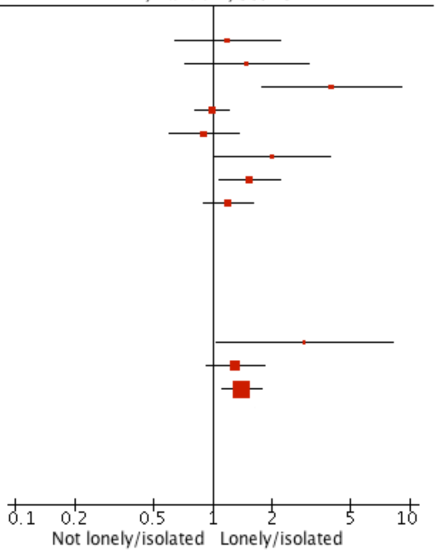


Test for subgroup differences: $Chi^2 = 1.88$, $df = 1$ ($P = 0.17$), $I^2 = 46.9\%$

c) According to risk of confounding

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Lower risk				
André-Petersson 2006	0.17395331	0.3173003	9.3%	1.19 [0.64, 2.22]
Barefoot 2005	0.39877612	0.3666054	7.7%	1.49 [0.73, 3.06]
Eaker 1992	1.38629436	0.4161854	6.5%	4.00 [1.77, 9.04]
Eng 2002	-0.01005034	0.1002678	20.6%	0.99 [0.81, 1.20]
Ikeda 2008	-0.10536052	0.2069	14.3%	0.90 [0.60, 1.35]
Rosengren 2004	0.69314718	0.3511146	8.2%	2.00 [1.00, 3.98]
Thurston 2009	0.42526774	0.1825	15.7%	1.53 [1.07, 2.19]
Vogt 1992	0.18232156	0.1467793	17.8%	1.20 [0.90, 1.60]
Higher risk				
Gafarov 2013	1.07158362	0.5270221	3.9%	2.92 [1.04, 8.20]
Kuper 2006	0.26136476	0.1745385	33.2%	1.30 [0.92, 1.83]
Strodl 2003	0.3435897	0.1219042	62.9%	1.41 [1.11, 1.79]

Risk Ratio
IV, Random, 95% CI

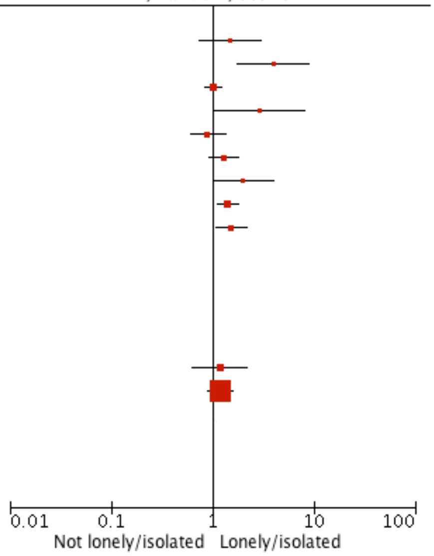


Test for subgroup differences: $Chi^2 = 0.18$, $df = 1$ ($P = 0.67$), $I^2 = 0\%$

d) According to risk of bias due to measurement error – exposure

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Lower risk				
Barefoot 2005	0.39877612	0.3666054	6.8%	1.49 [0.73, 3.06]
Eaker 1992	1.38629436	0.4161854	5.7%	4.00 [1.77, 9.04]
Eng 2002	0.01005034	0.1002678	18.3%	1.01 [0.83, 1.23]
Gafarov 2013	1.07158362	0.5270221	3.9%	2.92 [1.04, 8.20]
Ikeda 2008	-0.10536052	0.2069	12.7%	0.90 [0.60, 1.35]
Kuper 2006	0.26136476	0.1745385	14.3%	1.30 [0.92, 1.83]
Rosengren 2004	0.69314718	0.3511146	7.2%	2.00 [1.00, 3.98]
Strodl 2003	0.3435897	0.1219042	17.2%	1.41 [1.11, 1.79]
Thurston 2009	0.42526774	0.1825	13.9%	1.53 [1.07, 2.19]
Higher risk				
André-Petersson 2006	0.17395331	0.3173003	17.6%	1.19 [0.64, 2.22]
Vogt 1992	0.18232156	0.1467793	82.4%	1.20 [0.90, 1.60]

Risk Ratio
IV, Random, 95% CI



Test for subgroup differences: $Chi^2 = 0.83$, $df = 1$ ($P = 0.36$), $I^2 = 0\%$

5.3.6. Social isolation and stroke

Figure 5.5 shows the results of the random effects meta-analysis for the association between social relationships and incident stroke (NB: there were no studies with a measure of loneliness only, but one study used a measure combining loneliness and social isolation). Across nine independent study samples (2,577 events; one study did not report numbers), the average relative risk of stroke incidence was 1.32 (95% CI: 1.04 to 1.68). Following confirmation of heterogeneity (I^2=53%, χ^2=17.07 df=8, p=0.03) subgroup analyses were performed according to risk of confounding and risk of bias due to outcome measurement error (there were too few studies to perform any other analyses). There was no evidence of effects differing according to subgroup (see Figures 5.6 a and b); similarly to the evidence on CHD, there was insufficient information to explore other potential sources of heterogeneity.

Figure 5.5 Forest plot of studies investigating the association between deficiencies in social relationships and incident stroke

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Social isolation				
Avendano 2006 a	0.70803579	0.3813272	7.3%	2.03 [0.96, 4.29]
Avendano 2006 b	0.3074847	0.5284787	4.4%	1.36 [0.48, 3.83]
Gafarov 2013	1.00063188	0.464709	5.4%	2.72 [1.09, 6.76]
Ikeda 2008	0.10436002	0.1074	21.1%	1.11 [0.90, 1.37]
Kawachi 1996	0.70309751	0.3587	8.0%	2.02 [1.00, 4.08]
Nagayoshi 2014	0.36464311	0.1768265	16.5%	1.44 [1.02, 2.04]
Rutledge 2008	0.99325177	0.4531951	5.7%	2.70 [1.11, 6.56]
Vogt 1992	−0.10536052	0.1972459	15.2%	0.90 [0.61, 1.32]
Combined				
Strodl 2008	−0.12783337	0.1788756	16.4%	0.88 [0.62, 1.25]
Total (95% CI)			**100.0%**	**1.32 [1.04, 1.68]**

Heterogeneity: Tau² = 0.06; Chi² = 17.07, df = 8 (P = 0.03); I² = 53%
Test for overall effect: Z = 2.26 (P = 0.02)

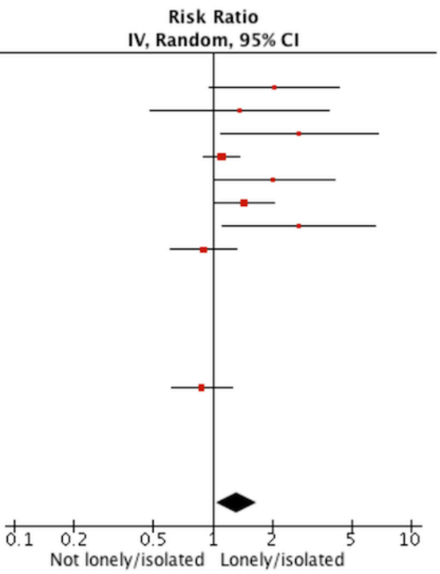
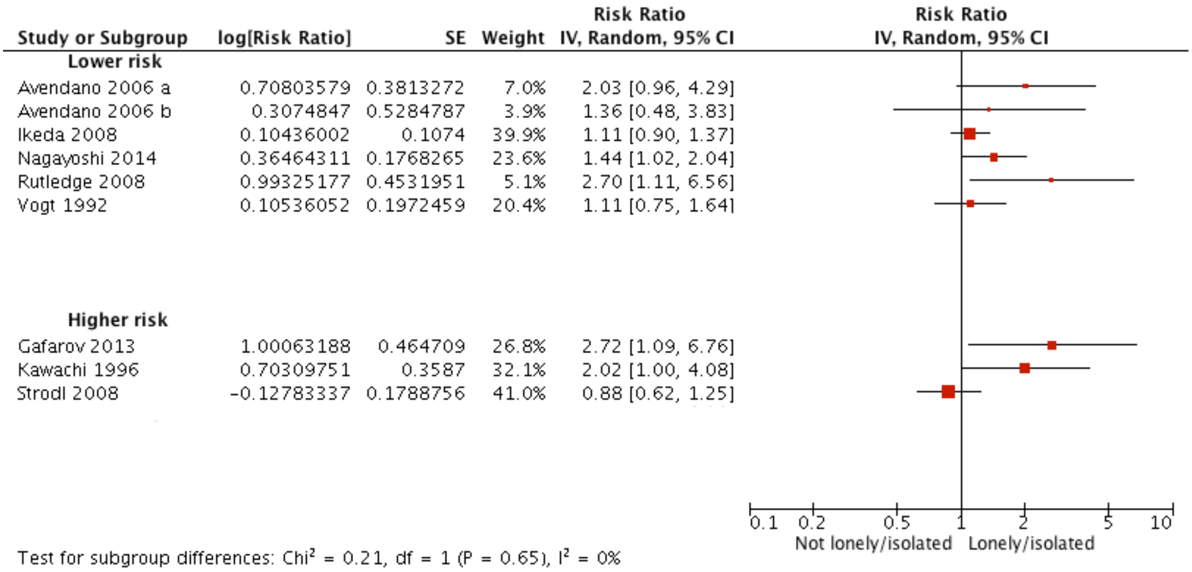


Figure 5.6 a and b Subgroup analysis of stroke studies

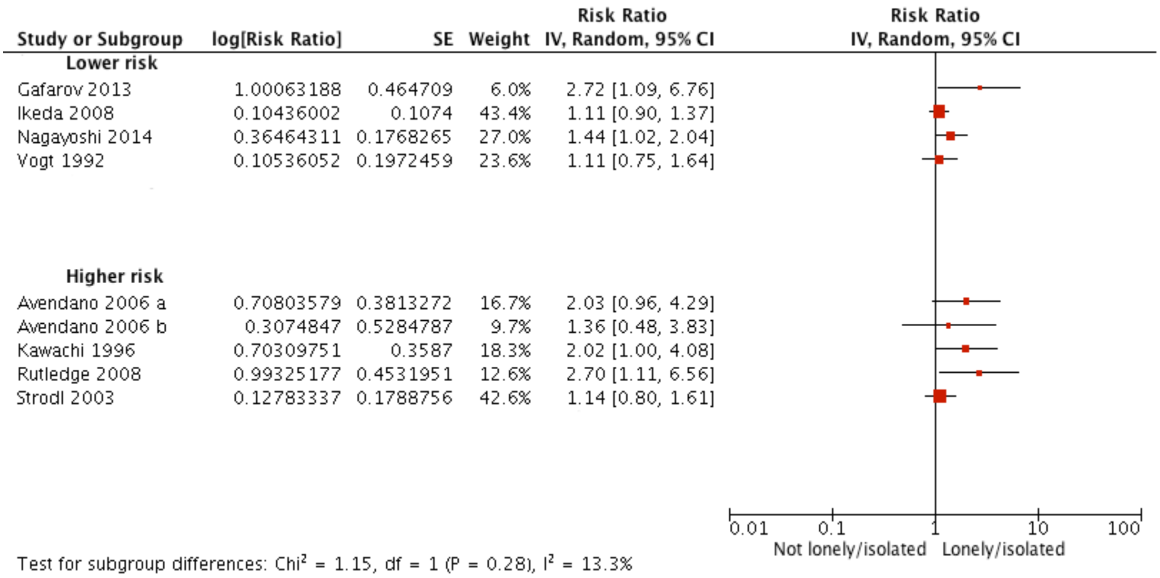
a) According to risk of confounding



Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Lower risk				
Avendano 2006 a	0.70803579	0.3813272	7.0%	2.03 [0.96, 4.29]
Avendano 2006 b	0.3074847	0.5284787	3.9%	1.36 [0.48, 3.83]
Ikeda 2008	0.10436002	0.1074	39.9%	1.11 [0.90, 1.37]
Nagayoshi 2014	0.36464311	0.1768265	23.6%	1.44 [1.02, 2.04]
Rutledge 2008	0.99325177	0.4531951	5.1%	2.70 [1.11, 6.56]
Vogt 1992	0.10536052	0.1972459	20.4%	1.11 [0.75, 1.64]
Higher risk				
Gafarov 2013	1.00063188	0.464709	26.8%	2.72 [1.09, 6.76]
Kawachi 1996	0.70309751	0.3587	32.1%	2.02 [1.00, 4.08]
Strodl 2008	-0.12783337	0.1788756	41.0%	0.88 [0.62, 1.25]

Test for subgroup differences: $Chi^2 = 0.21$, df = 1 (P = 0.65), $I^2 = 0\%$

b) According to risk of bias due to measurement error – outcome



Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Lower risk				
Gafarov 2013	1.00063188	0.464709	6.0%	2.72 [1.09, 6.76]
Ikeda 2008	0.10436002	0.1074	43.4%	1.11 [0.90, 1.37]
Nagayoshi 2014	0.36464311	0.1768265	27.0%	1.44 [1.02, 2.04]
Vogt 1992	0.10536052	0.1972459	23.6%	1.11 [0.75, 1.64]
Higher risk				
Avendano 2006 a	0.70803579	0.3813272	16.7%	2.03 [0.96, 4.29]
Avendano 2006 b	0.3074847	0.5284787	9.7%	1.36 [0.48, 3.83]
Kawachi 1996	0.70309751	0.3587	18.3%	2.02 [1.00, 4.08]
Rutledge 2008	0.99325177	0.4531951	12.6%	2.70 [1.11, 6.56]
Strodl 2003	0.12783337	0.1788756	42.6%	1.14 [0.80, 1.61]

Test for subgroup differences: $Chi^2 = 1.15$, df = 1 (P = 0.28), $I^2 = 13.3\%$

5.3.7. *Risk of bias across studies*

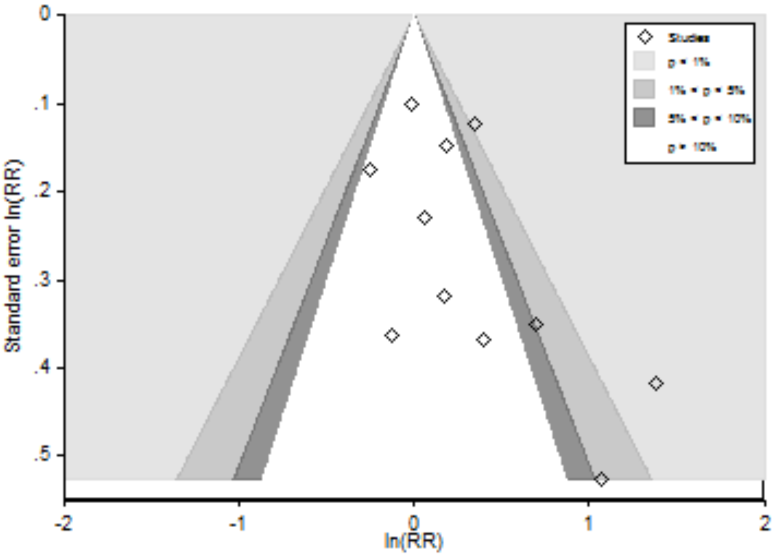
To test whether the review findings were sensitive to internal study validity, results with and without studies at greater risk of bias were compared. Sensitivity analyses did not reveal evidence of a difference in the ratio of the relative risks for CHD and stroke according to study validity (see Table 5.8). Visual assessment of contour enhanced funnel plots suggested that studies might be missing in areas of statistical significance (see Figures 5.7 a and b).

Table 5.8 Sensitivity analyses

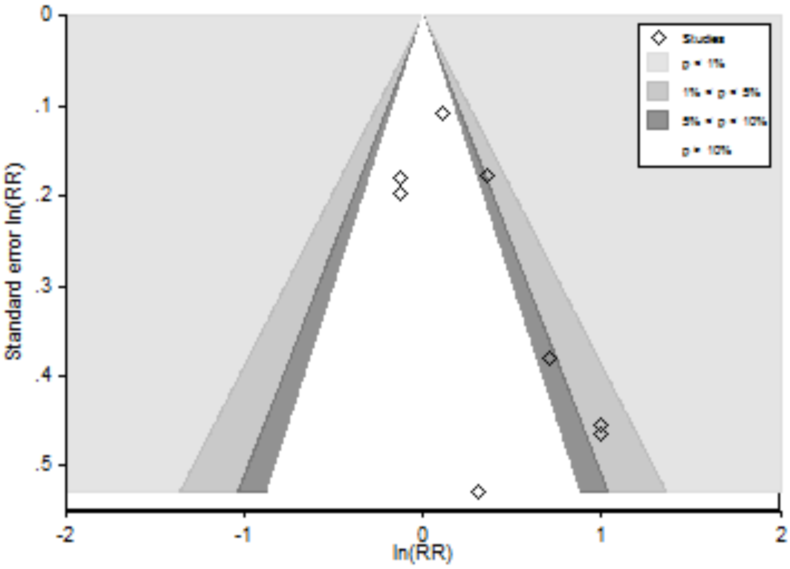
Outcome of interest	Pooled estimate of the relative risk, based on all studies (95% CI) (number of effect estimates)	Without studies at greater risk of information bias (exposure)	Without studies at greater risk of information bias (outcome)	Without studies at greater risk of confounding	Without studies at greater risk of bias in at least one domain
CHD	1.29 (1.04 to 1.59) (n=11)	1.34 (1.03 to 1.74) (n=9)	1.28 (1.01 to 1.63) (n=10)	1.34 (1.03 to 1.76) (n=7)	1.42 (1.00 to 2.01) (n=7)
Stroke	1.32 (1.04 to 1.68) (n=8)	1.42 (1.09 to 1.85) (n=7)	1.30 (0.98 to 1.71) (n=4)	1.34 (1.05 to 1.73) (n=6)	1.30 (0.98 to 1.71) (n=4)

Figure 5.7 a and b Contour enhanced funnel plots to assess risk of publication bias

a) For CHD studies



b) For stroke studies



Comparisons of fixed- and random-effects estimates showed the random-effects estimates to be more beneficial (CHD: RR, random-effects: 1.29, 95% CI: 1.04 to 1.59, compared with RR fixed-effects: 1.18, 95% CI: 1.06 to 1.31; stroke: RR, random-effects: 1.32, 95% CI: 1.04 to 1.68, compared with RR fixed-effects: 1.19, 95% CI: 1.03 to 1.36). This suggests the presence of small-study effects, which could be due to reporting bias. Although subgroup analyses found no evidence that study quality and true heterogeneity explained small-study effects in our review, these, along with chance, remain possible explanations.

5.3.8. Additional studies with insufficient data to contribute to the meta-analyses

Seven papers with a measure of social isolation were excluded from quantitative synthesis since they either did not report data in a format suitable for pooling and/or shared data with other studies (Colantonio et al., 1992; Hedblad et al., 1992; Orth-Gomer et al., 1993; Player et al., 2007; Reed et al., 1984; Reed et al., 1983; Sykes et al., 2002). Of the four papers that did not duplicate data from other studies, two reported results based on the Honolulu Heart Program: social isolation appeared to predict CHD but not stroke in analyses adjusted for age, though the association disappeared in multivariate analysis (Reed et al., 1984; Reed et al., 1983). In a univariate analysis of data from the Atherosclerosis Risk in Communities Study (USA) the Lubben Social Network score did not significantly predict incident CHD among people with prehypertension (Player et al., 2007). A further study found no evidence of an association between social isolation and CHD among men in France and Northern Ireland (Sykes et al., 2002), although it should be noted that this study controlled for depression, one of the possible pathways through which social isolation might lead to disease.

5.4. Discussion

I summarise the main findings from my review below and discuss them in relation to other published studies (section 5.4.1.). I then turn to the strengths and limitations of my review (section 5.4.2.), and consider the implications of its findings for policy, practice and research (section 5.4.3.).

5.4.1. Summary of findings, and comparison with other work

This review found that deficiencies in social relationships are associated with an increased risk of developing CHD and stroke. Poor social relationships were associated with a 29% increase in risk of incident CHD (pooled RR: 1.29, 95% confidence interval: 1.04 to 1.59) and a 32% increase in risk of stroke (pooled RR: 1.32, 95% confidence interval: 1.04 to 1.68).

To my knowledge, this is the first systematic review to focus on the association between loneliness or social isolation and subsequent first occurrence of CHD or stroke. Earlier reviews reported that prognosis for CVD is worse among people with poorer social relationships (Holt-Lunstad et al., 2015; Holt-Lunstad et al., 2010). Two narrative reviews on social support and CHD described an association with prognosis as well as incidence, but in both instances strength of evidence was low (Kuper et al., 2002; Barth et al., 2010). A recent review of seven papers found that loneliness and social isolation were linked to occurrence of CHD (Steptoe and Kivimaki, 2013), but inclusion of studies where fatal events may not have been the first occurrence of disease meant that the effect on prognosis and incidence could not be disentangled.

The size of the association between deficiencies in social relationships and incident CVD identified in this review is comparable to other recognised psychosocial risk factors. A meta-analysis of prospective studies on anxiety and CHD incidence found that anxious individuals had a 26% greater risk of MI (HR: 1.26 95% CI: 1.15 to 1.38 – see Roest et al., 2010) . A recent individual-participant-data meta-analysis reported an age and sex adjusted hazard ratio for job strain relative to no job strain of 1.24 for ischemic stroke (95% CI: 1.05 to 1.47 – see Fransson et al., 2015).

The findings from this review suggest that efforts to reduce the risk of CHD and stroke could benefit from taking both loneliness and social isolation into account. There was no evidence, either within or across studies, to suggest that loneliness was more strongly related to disease incidence than social isolation, or vice-versa. Evidence linking both subjective and objective isolation to increased blood pressure (Grant et al., 2009; Hawkley et al., 2010), a major risk for CHD and the most important risk factor for stroke, further supports targeting both dimensions of social relationship deficiencies.

5.4.2. Strengths and limitations

The focus on longitudinal studies is a strength of this work. Data collected over allow us to comment on the direction of the relationship between deficiencies in social relationships and health. Many studies on this topic are cross sectional and therefore liable to reverse causation – an important limitation of the literature, given that poor social relationships can be risk factors for as well as consequences of ill health.

Several of the included studies were at increased risk of imprecision due to over-fitting; pooling their results improved the precision of the evidence. Results were pooled across measures of different aspects of social relationships (loneliness v. social isolation) because, taken together, they can answer the broader question of whether deficiencies in social relationships are associated with disease incidence. It was anticipated that the studies included in the review would be heterogeneous and I explored this heterogeneity whenever possible. There was no statistical evidence to suggest that components of internal validity (such as measurement error or risk of confounding) were associated with effect estimates. Too few studies used the same measures of social relationships (e.g. the Berkman-Syme Social Network Index or the Lubben Social Network Scale) to conduct formal tests of whether results differed according to the instrument used. Subgroup analyses specified a priori showed no difference between the association of loneliness or social isolation with CHD incidence and there was no evidence across studies of differences between men and women.

The studies included in my review reported insufficient data to explore effect modifiers in depth. Seven of the estimates included in the meta-analyses (5 CHD, 2 stroke) were extracted from studies where participants were of higher socio-economic status and in better health than the target population. Since the effect of deficiencies in social relationships may be greater among individuals under stress (Cohen et al., 2000a), the results from this review may not reflect the extent of their health-related implications among disadvantaged groups. It should also be noted that the review included data collected from 1965 onwards and that more recent strategies for CHD and stroke prevention may have modified the influence of loneliness and social isolation on disease incidence.

In common with other reviews, confounding by unmeasured common causes cannot be excluded; nor can the possibility of reverse causation be eliminated, in situations where deficiencies in social relationships are the result of subclinical disease for example. It is also possible that publication bias accounted for some of the effect found in the review. Conversely, the pooled effects could be a conservative estimate: most of the studies in this review statistically adjusted for factors likely to be on the causal pathway, such as depression or health-related behaviours.

A final limitation concerns my reporting of results as relative, rather than absolute, estimates. To provide estimates of absolute risks, I would have needed to either a) know what the control group risk was across studies or b) provide a range of estimates based on the spectrum of control group risks reported in each study (Higgins and Green, 2011, Section 12.5.4.2). Neither option was possible in the case of the present review, since:

a) The included studies did not report sufficient data to estimate absolute risks across the evidence: five of the eleven studies in the CHD meta-analysis and three of the eight studies in the stroke meta-analysis did not report data on the number of events in the unexposed group and/or total number of participants in the unexposed group. Had a robust 'assumed' control group risk been available elsewhere in the epidemiological literature, I could have used this instead; but I found no such data.

b) Because the pooled results from random effects models describe the average of effects across studies rather than a typical effect it would not be meaningful to use them to derive a range of absolute estimates.

Notwithstanding the review's limitations, its results are based on a comprehensive search for the existing evidence on loneliness, social isolation and incident CVD; and its findings are relevant to policy, practice and future research.

5.4.3. Implications

The implications of my findings for policy, practice and research are discussed in turn below.

5.4.3.1. Implications for policy

The main finding of the review, that isolated individuals are at increased risk of developing CHD and stroke, supports public health concerns over the implications of social relationships for health and wellbeing. As well as potentially reducing mortality, addressing loneliness and social isolation could contribute to the prevention of two of the leading causes of morbidity in high-income countries. Tackling loneliness and isolation may be a valuable addition to CHD and stroke prevention strategies – although the effectiveness of interventions has yet to be determined.

A variety of interventions directed at loneliness and social isolation have been developed, ranging from group initiatives such as educational programmes and social activities to one-to-one approaches including befriending and cognitive behavioural therapy. These interventions have primarily focused on secondary prevention, aiming to improve the social relationships of people who have been identified as isolated or lonely. Whether such interventions can improve weakened relationships and influence the incidence of CVD is an important unanswered question. It may be that more promising opportunities lie in primary prevention strategies, such as promoting social networks or developing resilience – strategies that have, to date, received limited attention. Such strategies could draw on what is known about risk factors for loneliness and social isolation: these range from socio-demographic characteristics including marital status, gender and socio-economic status, to material resources and health status (de Jong Gierveld et al., 2006; Pinquart and Sorensen, 2003). Health-related behaviours may also be important, with lonely and isolated people more likely to engage in health-damaging behaviours such as smoking and physical inactivity (Shankar et al., 2011).

5.4.3.2. Implications for practice

Health practitioners have an important role to play in acknowledging the importance of social relations to their patients. If lonely and isolated patients are requiring treatment more often than others, then health practitioners are well placed to play a key role in identifying those at highest risk. We do not yet know how the individual clinician can best intervene once they have identified isolated or lonely patients in the clinic; but what is clear is that tackling this problem could have benefits for the health system as well as for the affected individuals.

5.4.3.3. Implications for research

The findings of this review are based on studies that controlled for different factors, e.g. socio-economic status, gender, health-related-behaviours, depression and hypertension. Some of these factors are likely to be on the causal pathway (Berkman and Krishna, 2014). Future studies exploring the mechanisms and pathways through which social relationships can lead to developing disease will help improve our understanding of the role played by social relationships in disease aetiology, and how they might interact with other individual and contextual-level factors such as socio-economic status, access to care and exposure to stress. It may be that particular groups of people are at increased risk of experiencing the adverse health consequences of poor relationships – a hypothesis that has yet to be tested in relation to the objective and subjective quality and quantity of relationships and CVD incidence. Future research will also need to consider the different ways in which to reach people with poor social relationships, so as to inform the appropriate targeting of interventions.

Importantly, all of the results included in my review of the evidence were based on studies where social relationships were measured at one point in time only; and where either loneliness or social isolation was looked at, but not both. Studies that measure social relationships repeatedly and include measures of loneliness as well as social isolation are needed to help clarify how social relationships evolve across the life-course and how the two dimensions of relationships interact and affect health outcomes. This is what I set out to explore in Chapters 6 and 7, using data from the English Longitudinal Study of Ageing to study how feelings of loneliness and situations of social isolation evolve over a ten-year period and what this means for CVD incidence.

Chapter 6. Changes in reported loneliness and social isolation in adults aged over 50: analysis of data from the English Longitudinal Study of Ageing

Chapter summary: We know little about how loneliness and social isolation change over time and the relationship between loneliness and social isolation is poorly understood (6.1). To inform the measurement of loneliness and social isolation in epidemiological studies, I explored how survey responses about social relationships evolve over a 10-year period, using data from the first six waves of the English Longitudinal Study of Ageing (6.2). I drew on five distinct measures of social relationships: three instruments assessing loneliness and two indices of social isolation. In this chapter, I describe changes at the cohort and individual level over time and investigate associations between different measures (6.3). Based on my findings, I consider implications for interventions and for research into the links between loneliness, social isolation and health – including my own epidemiological study, reported in Chapter 7 (6.4).

6.1. Introduction

In this first section of this chapter, I summarise what is known about loneliness and social isolation over time and explain why a longitudinal study is needed to enhance our understanding of these experiences.

6.1.1. Loneliness, social isolation and time

When defining loneliness, investigators commonly distinguish between transient and persistent experiences (Cacioppo and Patrick, 2008; Perlman and Peplau, 1981). Transient or short-lived loneliness is recognized as a feeling which many will experience at some point in their lives. Whilst unpleasant, researchers have argued that it need not cause alarm and that it may in fact serve as a trigger for people to repair or replace social connections where these are fractured (Cacioppo et al., 2006a). Prolonged or chronic experiences of loneliness, by contrast, are not thought to have such positive effects. ‘Loneliness becomes an issue of serious concern […]’, writes Cacioppo, ‘when it settles in long enough to create a persistent self-reinforcing loop of negative thoughts, sensations and behaviours.’ (Cacioppo and Patrick, 2008, p.7). Because of its potentially detrimental consequences for health and wellbeing, persistent rather than transient feelings have been the primary focus of research on loneliness (see for example the development of tools focusing on the frequency of loneliness feelings, such as the UCLA

Loneliness Scale – Russell et al., 1978).

Similarly to loneliness, social isolation is often defined in terms of frequency. The content of the social relationship measures identified and classified in Chapter 4 illustrates how common it is for researchers to use frequency of interaction to distinguish between isolated and less isolated individuals. For example, the Berkman-Syme Social Network Index and the Lubben Social Network Scale enquire about the number of friends and close friends seen or heard from *at least once in the past month* (Berkman and Breslow, 1983; Lubben, 1988). In the Duke Social Support Index and in the Older Americans Resources and Services Social Resources Scale, study participants are asked about the frequency with which they have interacted with family, friends and others in the past week (Fillenbaum, 1988; Powers et al., 2004). The fewer social interactions people have with others, the more isolated they are thought to be (de Jong Gierveld et al., 2006).

Despite the explicit focus of research on persistent situations of loneliness and social isolation, we know relatively little about how these experiences change over time. Few studies to date have included repeated measures of social relationships. Where investigators have assessed loneliness or social isolation more than once, they have relied on small samples with high rates of attrition, raising issues of statistical power and bias. For example, in a Swedish study of rural older adults aged between 67 and 80 years at baseline, levels of reported loneliness remained stable over a 13-year period, but this finding was based on 69 of the 143 participants recruited at baseline (Samuelsson and Hagberg, 1998). In a study of loneliness and social isolation among older people in rural Wales, around half of the participants followed over a period of 20 years reported different levels of loneliness and/or social isolation over time – though again this study was able to rely on data for only 47 of the 500 participants recruited at baseline (Wenger and Burholt, 2004). Because studies to date have focused on either loneliness or social isolation, it is not clear whether these follow similar patterns over time.

Taking advantage of the availability of both loneliness and social isolation measures in the English Longitudinal Study of Ageing (ELSA), a large representative cohort of adults living in England aged 50+ (Steptoe et al., 2013a), I set out to explore changes in answers to questions about social relationships over a 10-year period. The primary rationale for undertaking this exploratory work was that, since only one of the longitudinal studies reviewed in Chapter 5 had measured social relationships more than once (and even then only two time points were used), I wished to gain further insight into how best I might study and code serial measures in my own epidemiological analyses (see Chapter 7, where I present survival analyses on incident non-fatal cardiovascular disease (CVD)). More specifically, there were two questions I wished to address. First, could I assume that loneliness and social isolation were stable over time which could justify relying on baseline measures only in epidemiological analyses? Or did answers vary over time, potentially revealing common trajectories (e.g. decrease, increase, stability at high or low levels)? Secondly, how different were loneliness and social isolation patterns? Could it be that they were so correlated that it would be preferable to only focus on one dimension? As well as informing future epidemiological analyses, I was aware that studying patterns of responses to questions about loneliness and social isolation over time could shed light on trends at both the population and individual levels. From previous work by Victor, I knew that the prevalence of loneliness had remained stability in the last 60 years (Victor, 2011). But what of social isolation? And, if prevalence was stable, was it always the same people reporting weaker social relationships? To help gauge the extent of the potential public health challenge, these are the questions I set out to answer.

6.1.2. Study aim and objectives

The aim of my study was to enhance understanding of how reported loneliness and social isolation change over time. The primary objectives were:

- To describe and compare the prevalence of loneliness and social isolation at each wave;
- To study patterns of reported loneliness and of social isolation across waves;
- To explore the relationship between loneliness and social isolation.

Alongside these primary objectives, the study provided an opportunity to investigate:

- Whether response patterns differed according to the measure of loneliness or social isolation used;
- Whether people who might be particularly at risk of feeling lonely or being isolated – older adults, widows and widowers, participants with a low socio-economic status and people in worse health (Lichtenstein et al., 1996; Petitte et al., 2015; Shankar et al., 2011; Steptoe et al., 2013b) – presented different patterns of social relationships when compared with the rest of the population.

Overall, the aims and objectives of this study were to *describe* patterns of answers to questions about loneliness and social isolation – i.e. the goal was *not* to predict or explain trajectories. This is because, while they are the focus of this chapter, in the wider context of my doctoral project, social relationships are first and foremost considered as an explanatory rather than an outcome variable. I focused on describing patterns of answers over time to understand how the variables behaved in ELSA and how social relationships could best be coded as independent variables when studying their links with health outcomes. In Chapter 7, I put this knowledge into practice, applying what I learned of social relationship patterns over time to study their association with incident CVD.

In the following section, I describe the methods I used to achieve the study aims. I explain how I selected the study sample (section 6.2.1.), how I retrieved and cleaned the data (section 6.2.2), which variables I selected and why (section 6.2.3.) and the statistical tools I used to analyse them (section 6.2.4.).

6.2. Methods

The methods for this study were set out *a priori* in a protocol which included an outline of the rationale for my secondary data analyses, the research questions I formulated, and the methods I anticipated using to answer them. Every effort was made to adhere to the predetermined protocol; when and where amendments were required, these were documented in a protocol addendum. The protocol and addendum are included in Appendix 6.1.

6.2.1. Participants

In the following section I present an overview of ELSA and explain how participants were selected for my study.

6.2.1.1. Sample

a) General overview

ELSA is a panel study of individuals and their partners aged 50+, living in private households in England. Ethical approval for the study was granted by the National Research Ethics Service (Steptoe et al., 2013a). The study began in 2002, drawing its initial sample from individuals who took part in the Health Survey for England (HSE) either in 1998, 1999, or 2001 (Taylor et al., 2007). HSE is an annual cross-sectional survey, designed to monitor the population's general health (Mindell et al., 2012). HSE participants were selected from the Postcode Address File (PAF), generally accepted as having the best coverage for surveys of private households in the UK (Taylor et al., 2007).

A multi-stage stratified probability sampling design was used, in order for every address on the

PAF in England to have an equal chance of inclusion. First, postcode sectors stratified by health authority and the proportion of households in non-manual socio-economic groups were selected with probability proportional to their size. In a second stage, a fixed number of addresses were identified systematically from each postcode sector and households were selected for each address. Up to three households were randomly selected per address. Eligible individuals were asked to participate in a personal interview followed by a nurse visit (Taylor et al., 2007).

The HSE years 1998, 1999 and 2001 were chosen as the sampling frame for ELSA because they were recent and could provide a sufficiently large sample size. Taking these three HSE years together, a total of 31,051 households were sampled. Figure 6.1 summarises the ensuing sample selection process for ELSA's first wave.

Figure 6.1 ELSA sample definition for wave 1

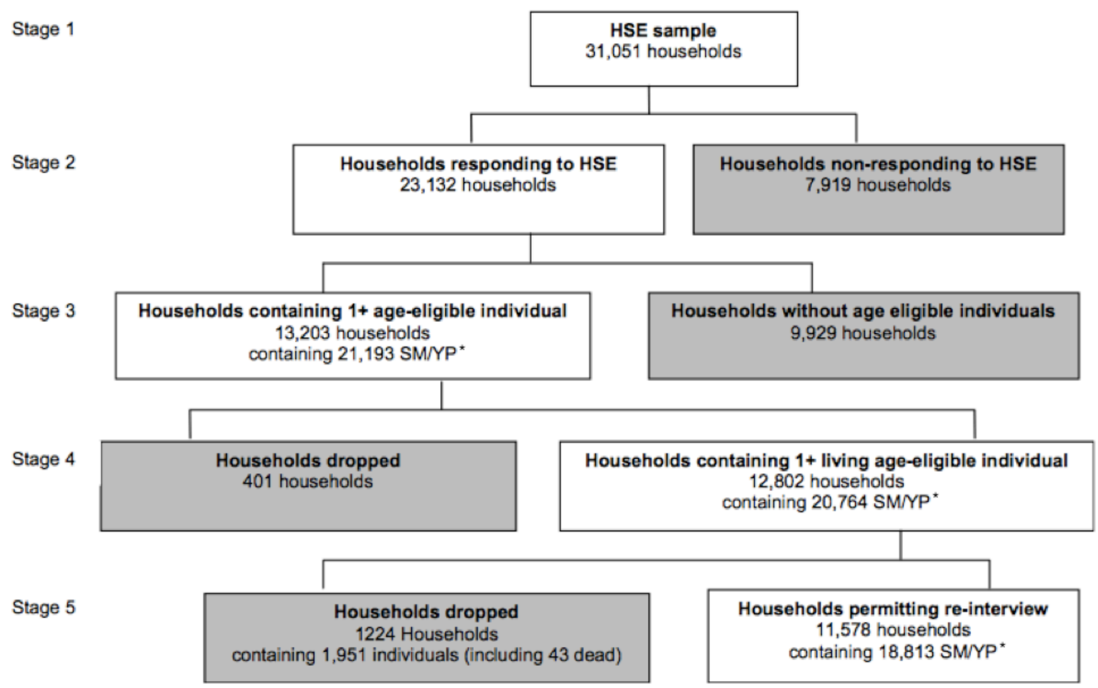


Figure reproduced from Taylor et al., 2007, p.10

* SM/YP: 'SM' stands for 'sample member', i.e. people aged 50+; and 'YP' stands for 'younger partner', i.e. partners of sample members, who were aged under 50.

Only those households that responded to HSE were eligible for inclusion in Wave 1 of ELSA (Stage 2). To be invited to take part in ELSA, these households had to include at least one age-eligible individual (Stage 3) who was alive according to administrative records (Stage 4) and gave permission to be contacted again in future (Stage 5). Alongside the target sample, partners aged under 50 and partners who had joined the household since HSE were invited for interview. As a result of this process, a sample of 11,578 households containing 18,813 core members and partners were eventually issued for ELSA. The Wave 1 fieldwork produced 12,099 productive individual interviews: 11,391 with core members (of which 204 were partial responses and 158 were proxy responses), 636 with younger partners (aged under 50) and 72 with new partners.

Data were collected every 2 years (see Figure 6.2 for a visual summary of the data collection process). Information is collected using computer-assisted personal interviews and self-completion questionnaires, with additional nurse visits every 4 years (at waves 2, 4 and 6) for the assessment of biomarkers. To maintain ELSA's representativeness of all age groups over 50, its sample has been refreshed at three waves of data collection – waves 3, 4 and 6. The Wave 3 refreshment sample included people aged between 50 and 53 years selected from HSE 2001-2004. In Wave 4, a sample of individuals aged 50 to 74 and their partners was added using data from HSE 2006. The Wave 6 refreshment sample included respondents from HSE 2009, 2010 or 2011 aged between 50 and 55 years.

Figure 6.2 Overview of the data collection process in ELSA, waves 1 to 6

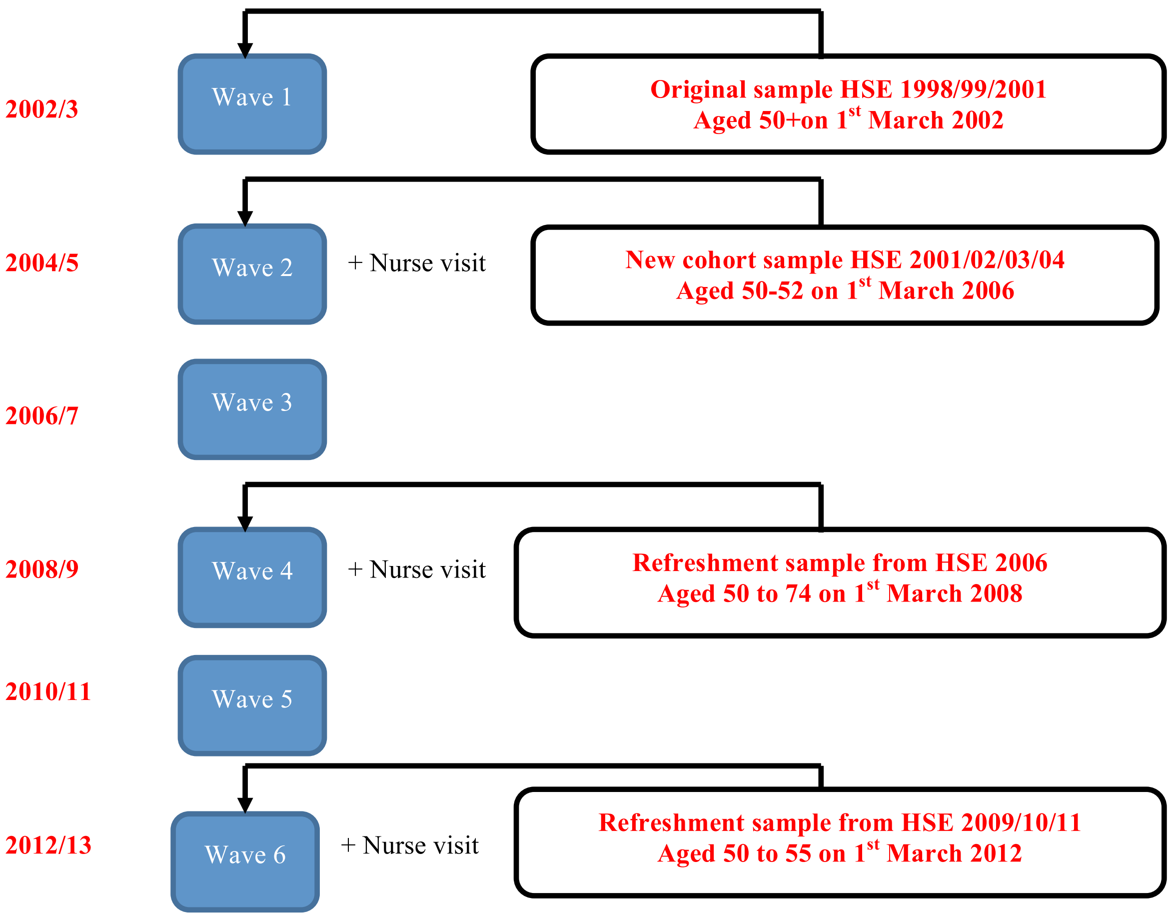


Figure updated from Steptoe et al., 2012, p.1642.

b) Response rates and attrition

Table 6.1 summarises the number of core participants in the first six waves of ELSA and presents interview response rates for those core members who joined the study at Wave 1. Taking into account all core members (i.e. not just those who joined the study in wave 1), cross-sectional response rates were 67% in wave 1, 82% in wave 2, 73% in wave 3, 74% in wave 4, 80% in wave 5 and 68% in wave 6 (Bridges et al., 2015). Of those core members who took part in the first wave, 82% responded in wave 2, 73% in wave 3, 74% in wave 4, 78% in wave 5 and 85% in wave 6.

Table 6.1 ELSA achieved sample numbers and response rates

Wave	1	2	3	4	5	6
Wave 1 sample, number interviewed	11,391	8,780	7,736	6,623	6,242	5,659
Wave 3 refreshment sample, number interviewed	NA	NA	1,275	972	936	888
Wave 4 refreshment sample, number interviewed	NA	NA	NA	2,290	1,912	1,796
Wave 6 refreshment sample, number interviewed	NA	NA	NA	NA	NA	826
Wave 1 sample members who have died (cumulative)	NA	504	1,164	1,620	2,158	2,682
Wave 1 sample members study response rates*	67%	82%	73%	74%	78%	85%

Table updated from Steptoe et al., 2012, p.1643.

* The response rate here is defined as the total number of people who participated in an interview divided by the number of individuals eligible for the wave, where eligibility is conditional on membership of the core sample and being alive or not having moved outside of the UK.

At each wave, between 84% and 91% of core members who were not interviewed by proxy returned a valid self-completion questionnaire (Taylor et al., 2007; Bridges et al., 2015; Scholes et al., 2009; Scholes et al., 2008; Blake et al., 2015; Cheshire et al., 2012). People who completed the questionnaire tended to be younger, white, more educated, more likely to own their house, and to be retired, compared with non-respondents (Bridges et al., 2015).

Table 6.2 Comparison of eligible participants from Cohort 1 who did and did not take part in an interview in wave 5

Participant characteristic, wave 1	Cohort 1 members who took part in wave 5 (n=6,242)	Cohort 1 members who were lost to follow-up (n=3,071)	p-value, difference
Age (years)			
50-59	68%	32%	
60-69	69%	32%	<0.001
70-79	66%	34%	
80+	56%	44%	
Gender			
Women	63%	32%	0.630
Men	67%	33%	
Wealth quintile			
1 (lowest)	57%	44%	
2	64%	37%	
3	67%	33%	<0.001
4	71%	29%	
5 (highest)	74%	26%	
Education			
No qualifications	60%	40%	<0.001
Intermediate	69%	31%	
Higher education	77%	23%	
Limiting long-standing illness			
Yes	64%	36%	<0.001
No	68%	32%	

Table reproduced from Steptoe et al., 2012, p.1643.

In common with other panel studies, loss-to follow up in ELSA is socio-economically patterned. Table 6.2 highlights the differences between those participants from the first cohort who did and did not take part in wave 5.[9] Participants lost to follow-up were more likely to

[9] Data are presented for wave 5 rather than wave 6 so that comparisons focus on people who were known to be alive at wave 5. Wave 6 mortality status was not publicly available in ELSA when this table was designed (last checked: September 2016).

report lower levels of education, be less wealthy, be older and report a limiting long-standing illness.

6.2.1.2. Selection of the analytical sample

ELSA includes partners under the age of 50, but the study designers did not intend for them to be analysed as individuals in their own right. Rather, they were incorporated into ELSA to provide more complete information on sample members and their partnerships (Taylor et al., 2007). For my analyses, I focused on ELSA's main target population (the core sample), i.e. individuals aged 50+ who took part in HSE. I used all of the waves available for analysis in September 2015 (when I started my analyses of ELSA), i.e. waves 1 to 6. Note that some of the variables of interest were not part of the main and/or self-completion questionnaires from wave 1, but were introduced later on (e.g. the three-item UCLA Loneliness Scale was added at wave 3), hence analyses for these variables were necessarily restricted to fewer than six waves (see section 6.2.3.1. below for details about when each question or questionnaire was added to the survey).

6.2.2. Data retrieval and cleaning

ELSA data files and accompanying materials (including dictionaries, user guides and technical reports) are available for download from the Economic and Social Data Service (web address: https://discover.ukdataservice.ac.uk/series/?sn=200011). The data files of relevance for this specific study were the core data files for waves 1, 2, 3, 4, 5 and 6, and the longitudinal harmonised file for waves 1 to 6 (version C). The harmonised file was created as part of the University of South California's Program on Global Aging, Health, and Policy initiative to increase the availability and ease of use of data sets on aging around the world (Phillips et al., 2014). It contains cleaned and processed variables that have been checked for consistency across waves.

Using Stata/SE 14.2 (StataCorp, 2011), I extracted all the variables of interest (see the study protocol in Appendix 6.1 for a list of the variables I had identified using the data dictionaries available from the UK Data Service website) from each wave and collated them into a single, wide format file (i.e. a file where each participant is listed as a separate observation).

Once all of the variables had been retrieved, I cleaned the data following the steps outlined in *The practice of survey research* (Ruel et al., 2016). Data were first checked cross-sectionally for consistency in unique identifiers, cosmetics (labels and formatting) and missing value and skip-pattern coding, before being cleaned for implausible values. The final step involved checking the dataset for consistency in coding and plausibility of patterns across all waves. Once the data cleaning process was complete, I created a long file version of the dataset (i.e. a file where each year of data is listed as a separate observation) to facilitate longitudinal analyses.

6.2.3. Variables

The primary variables of interest were loneliness and social isolation. I also selected a small number of socio-demographic and health-related variables to explore the patterning of social relationships among subgroups. Below, I describe each of the variables I used.

6.2.3.1. Loneliness

ELSA includes three instruments that can be used to assess loneliness as defined in this thesis, i.e. as a negative feeling associated with someone perceiving that their relationships are qualitatively and/or quantitatively deficient (Perlman and Peplau, 1981; Cattan et al., 2005; de Jong Gierveld et al., 2006). These three instruments are: a direct question asking participants how frequently they feel lonely, in general; a direct question asking participants how frequently they felt lonely in the past week; and the three-item UCLA Loneliness Scale, which asks about feelings relating to social relationships in general. The contents of each question and their psychometric properties are summarised in Table 6.3.

Table 6.3 Loneliness measures included in ELSA

Measure of loneliness	Question(s)	Scoring system	Psychometric properties	When and where it was included in ELSA
Direct single-item question about loneliness in general	How often do you feel lonely?	Respondents were given the choice of three answers: often (scored 3); some of the time (scored 2); or hardly ever or never (scored 1).	Some studies have found a correlation between single item approaches and scores on multi-item loneliness scales (de Jong Gierveld and van Tilburg, 1999; Russell et al., 1978; Di Tommaso and Spinner, 1993), which would suggest convergent validity. No data were found re. reliability.	From wave 3 onwards, this question was included in the main self-completion questionnaire, alongside questions on how participants felt about various different aspects of their life.
Direct single-item question about loneliness in the past week (part of the 20-item Centre for Epidemiologic Studies Depression Scale (Radloff, 1977)	Participants were asked whether they would agree or disagree with the following statement: 'Much of the time during the past week, you felt lonely.'	Agreeing was scored as 1, disagreeing was scored as 0.	See above.	From wave 1 onwards, this question was part of the main interview.
The three-item UCLA Loneliness Scale (Hughes et al., 2004)	The scale includes three questions: 1) How often do you feel you lack companionship? 2) How often do you feel left out? 3) How often do you feel isolated from others?	For each question, respondents are offered the following options: Hardly ever or never (score of 1); some of the time (score of 2); or often (score of 3). Answers are summed to provide a total loneliness score ranging from 3 to 9, with a higher score suggesting greater levels of loneliness.	Using data from the US Health and Retirement Study (HRS),and the Chicago Health, Aging, and Social Relations Study, Hughes reported evidence of: satisfactory reliability (alpha coefficient of reliability = 0.72); discriminant validity (loneliness score was associated with greater likelihood of depressive symptoms and higher scores on scale of perceived stress); and convergent validity (correlation between the self-labelling loneliness statement in the CESD depression index and the Three-Item Loneliness Scale was much higher than the correlation between any of the other components of the short CES-D Scale). See Hughes et al., 2004.	From wave 2 onwards, the scale was included as part of the self-completion questionnaire.

As noted in Chapter 5 (see section 5.2.1.4.), there is no consensus in the research literature over which measure of loneliness is most robust or informative. On the one hand, indirect and multiple-item tools are preferred by researchers who argue that participants are likely to under-report a stigmatised feeling when asked directly (Weiss, 1982). These investigators advise using multiple-item tools and/or questions that do not directly refer to loneliness (de Jong Gierveld and van Tilburg, 1999). This indirect, multi-item approach can also help to narrow what it is that is being measured, since 'loneliness' is a word to which respondents are likely to ascribe different meanings and attributes (Victor et al., 2005a). On the other hand, multi-item scales are more susceptible to missing data since they require that several, rather than just the one, questions be answered. Failure to provide valid responses for all the items results in a missing overall score (Ruel et al., 2016). The interpretation of multi-item questionnaires is also less straightforward than answers to a single question. A direct question on the frequency of a person's negative feelings can for example allow us to distinguish between participants who report feeling rarely, sometimes or often lonely. By contrast, scores derived from multiple questions rarely have a natural or obvious cut-off point. In the case of the three-item UCLA Loneliness Scale, researchers have resorted to grouping people who score between 3 and 5 as 'not lonely' and people with score of 6 to 9 as 'lonely' (Steptoe et al., 2013b). Yet a score of 5 on the three-item UCLA Loneliness Scale could be reached by respondents who reply that they often feel isolated from others, hardly ever feel out of tune with others and hardly ever feel that they lack companionship (see Table 6.3 for details of the exact phrasing of the UCLA Loneliness Scale questions). A score of 6, meanwhile, can be reached by answering that one *sometimes* experiences all three feelings, i.e. feeling isolated from others, out of tune with others and lacking companionship. This example raises the question of whether someone who scores 6 can reasonably be classified as feeling more frequently lonely than someone who scores 5 on the UCLA Loneliness Scale; and whether this tool can legitimately be used as a 'scale', since this would imply that an individual's score is a clear indication of the *intensity* of their experience (see Babbie, 2012, p.162).

In addition to the question of whether the UCLA Scale can meaningfully be interpreted as a scale, its suitability for measuring loneliness among older adults has also been challenged (Campaign to End Loneliness, 2015). The tool was initially developed with groups of American college students, whose social networks and expectations are likely to differ from those of older participants (Lubben, 1988). For this reason, gerontologists have tended to promote the use of instruments specifically tailored to older populations, such as the de Jong Gierveld Loneliness Scale (de Jong Gierveld and van Tilburg, 1999). How scores on the UCLA Loneliness Scale and the de Jong Gierveld Scale compare is not known. Using data from the US Health and Retirement Study (HRS) and the Chicago Health, Aging, and Social Relations Study to test the validity and reliability of the 3-item UCLA among older adults, Hughes reported evidence of satisfactory reliability, discriminant validity and convergent validity (see Table 6.3 above for details; Hughes et al., 2004). This suggests that the tool may be suitable for an older population, though we should bear in mind that perceptions among English adults might be different from those of US adults.

Given the paucity of psychometric data and the advantages and disadvantages of both direct and indirect ways of measuring loneliness, I decided to include both types of tool in my analyses. The availability of three different measures of loneliness in ELSA offered the opportunity to explore longitudinal patterns for each measurement tool and to compare them.

6.2.3.2. Social isolation

Throughout this thesis, the term 'social isolation' is employed to describe the absence of contacts, ties or relationships with others (de Jong Gierveld et al., 2006). In Chapter 4, we saw that a variety of tools have been used to measure the presence or absence of relationships across a person's social network. None of the more commonly used instruments, such as the Berkman-Syme Social Network Index (Berkman and Breslow, 1983) or the Lubben Social Network Scale (Lubben, 1988) have been included in ELSA. Differences in how questions were asked in ELSA and in established tools mean that it is not possible to reproduce existing scales using the available variables in ELSA. Instead, researchers interested in individuals' links to others must first put together one, or several, instrument(s), of their own, drawing on the many questions included in the survey which touch upon the availability of network members such as children, other relatives and friends. Shankar and colleagues have developed one such index based on the following items (Shankar et al., 2011; Steptoe et al., 2013b):

- whether the respondent was married or cohabiting with a partner (scored as 1 if unmarried or without a cohabiting partner; 0 otherwise);

- frequency of contact with children (scored as 1 if contact was less than once a month; 0 otherwise);

- frequency of contact with other immediate family members (scored as 1 if contact was less than once a month; 0 otherwise);

- frequency of contact with friends (scored as 1 if contact was less than once a month; 0 otherwise);

- membership of any organizations, religious groups or committees (scored as 1 if the respondent did not report belonging to any organization; 0 otherwise).

While this tool initially appeared adequate for the purpose of this study, two limitations were identified. First, it does not cover contact with non-partners living in the household such as children or other relatives. An exploratory investigation of household size and marital status showed that in wave 1, there were 762 core members living with someone who was neither their partner or spouse. In the Shankar index, these individuals would have scored 0 on the marital status/partnership item, and their contact with other individuals living in the same house would not have been captured by the index. In other words, such individuals would be classed as comparatively isolated when in fact they may have access to social contact within the household.

Secondly, the Shankar index does not take into account access to colleague networks for those currently in employment. Since ELSA includes adults of working age I adapted the index developed by Shankar to produce an Index of Social Contacts (ISC) based on six items:

- size of the household;
- frequency of contact with children;
- frequency of contact with other immediate family members;
- frequency of contact with friends;
- membership of any organizations, religious groups, or committees;
- whether currently in employment.

The purpose of this tool was to capture the presence or absence of relationships rather than to study the size of people's social networks. Each item was therefore dichotomized, so as to distinguish between whether people did or did not have access to the type of contact in question and scored according to the criteria listed in Table 6.4. Scores were combined in an unweighted index, with each item treated equally in the calculation of the measure. Overall scores ranged from 0 to 6, with higher scores indicating greater social isolation.

Table 6.4 Scoring criteria for the Index of Social Contacts (ISC)

Item	Criteria for scoring
Household size	Living alone was scored as 1; scored 0 otherwise.
Frequency of contact with children	A score of 1 was allocated where frequency of contact in person, via phone or in writing was lower than once a month; scored 0 otherwise.
Frequency of contact with other immediate family members	A score of 1 was allocated where frequency of contact in person, via phone or in writing was lower than once a month; scored 0 otherwise.
Frequency of contact with friends	A score of 1 was allocated where frequency of contact in person, via phone or in writing was lower than once a month; scored 0 otherwise.
Membership of any organizations, religious groups, or committees	Membership of no organization, group or committee was scored as 1; scored 0 otherwise.
Employment status	Being currently unemployed or having retired was scored as 1; full and part-time employment were scored as 0.

* Monthly contact was chosen as the cut-off to reflect the threshold most commonly used in tools since the Berkman-Syme Social Network Index (Berkman and Breslow, 1983; Shankar et al., 2011; Steptoe et al., 2013b). Note that where people did not have any family or friends, this was scored as 1 – since having no children, for example, by extension means having no children with whom to interact; and likewise with other family and friends.

As with all other multi-item questionnaires aiming to capture objective characteristics of a person's social relationships, the ISC is based on self-reported items. There are no other data (such as survey questions, qualitative material from participants in the form of interviews or diaries or interviewer observations) in ELSA against which the validity of answers about frequency of contact and social participation can be checked. Nor was it possible to test for the reliability of the ISC: data were collected only once for each participant at each wave, and the two-year gap between collection points was too long to check reliability over time. Because I had no reason to assume interrelatedness between items (e.g. between household size and job status, or between contact with family and social participation), I did not test for internal consistency. The only psychometric criteria I applied in developing and using the ISC was its interpretability, i.e. the degree to which I could assign qualitative meaning to its quantitative scores (Mokkink et al., 2012): a score of 6 meant that the person was 'socially isolated' i.e. did not have access to the social relationships covered in the index; a score of 5 meant that they had access to one of the social relationship measures in the index; a score of 4 meant they reported two of the social relationships covered in the index; and so on, down to the score of 0, interpreted as the participant having access to all 6 of the domains covered in the ISC.[10]

[10] I am aware that the scoring system I chose may seem counter intuitive, and that coding the ISC with 0 as socially isolated through to 6 as not isolated might have been easier to interpret (i.e. 0 = no relationships, versus 6 = plenty of relationships). The reason I chose to use higher scores as indicative of isolation was to be consistent with the

The absence of psychometric data is one of the ISC's main limitations, though it should be noted that in this respect it is no different from the Shankar index or previous tools designed to measure social isolation. When the Berkman-Syme Social Network Index was first developed, Berkman acknowledged that the extent to which respondents' answers reflected their actual relationships was unknown (1977). Forty years later this uncertainty remains, despite the Berkman-Syme Index being one of the more commonly used tools in the epidemiological literature (Berkman and Krishna, 2014). To ascertain the validity of my findings, it will be important to test the psychometric properties of the ISC in future; in the meantime, the paucity of data does not make it less suitable than alternatives such as the Shankar index for which there are no psychometric data either.

Like many of the tools used to quantify social relationships, the ISC tells us little – if anything – about the quality of a person's social relationships or their relative weights, concentrating instead on the frequency of contact and the availability of ties. Yet the definition of social isolation as 'the absence of contacts, ties and/or *relationships*' (Clark, 2001) implies that social isolation also encompasses a qualitative dimension. To complement the ISC, I therefore designed a second tool to capture the reported number of *close* relationships, providing us with an opportunity to explore how this is linked to the quantity of relationships. This tool covers four domains:

- whether the respondent has a close relationship with their spouse or partner;
- the number of children with whom the respondent has a close relationship;
- the number of other family members with whom the respondent has a close relationship;
- the number of friends someone has a close relationship with.

Answers to each of the four items were coded according to the criteria set out in Table 6.5. and were combined in an unweighted index. The total score for this Index of Close Relationships (ICR) amounts to the number of people with whom each individual reports that they have a close relationship.

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cumulative scoring used in the UCLA loneliness scale, where a higher score is indicative of greater loneliness. Because most tools in the literature use this cumulative approach, and in order not to create confusion in my analyses by having tool using different scoring spectra, I too used a cumulative score where higher scores indicate greater isolation for the ISC.

Table 6.5 Scoring of the Index of Close Relationships (ICR)

Item	Scoring
Whether the respondent has a close relationship with their spouse or partner	Yes is scored as 1, no is scored as 0. Where a person has no partner, this is scored as 0.
The number of children with whom the respondent has a close relationship	The number reported is used as the score. E.g. if a participant reports that they have 3 children with whom they have a close relationships, this is scored as 3.
The number of other family members with whom the respondent has a close relationship	The number reported is used as the score. E.g. if a participant reports that they have 5 other family members with whom they have a close relationships, this is scored as 5.
The number of friends someone has a close relationship with	The number reported is used as the score. E.g. if a participant reports that they have 10 friends with whom they have a close relationships, this is scored as 10.

Whilst I used the ICR as a measure of the quantity of meaningful relationships reported by participants, it is important to bear in mind that 'close' was not defined at any point in ELSA. This means that we do not know what participants understood the term to mean. In choosing to use the ICR, I was aware that, as for any instrument seeking to measure perceptions, individuals were likely to have applied different criteria when answering these questions (Weiss, 1982). I was therefore careful to interpret differences in scores with caution in my analyses, in particular where larger numbers of close relationships could be an indication of participants applying less stringent criteria to appraise 'closeness' than others who reported fewer close ties.

6.2.3.3. Socio-demographic and health measures

Data were retrieved for several socio-demographic and health measures to a) describe the population under study and b) explore differences in loneliness and social isolation based on different circumstances.

Demographic characteristics. Data were extracted regarding participants' age, gender, ethnicity and marital status (including widowhood) at each wave. These participant characteristics are collected as part of the main in-person interview (Bridges et al., 2015).

Socio-economic status. ELSA includes many indicators of socio-economic status such as education, job status, income and wealth (Steptoe et al., 2013a). I selected employment to capture individuals' current status, and total household wealth as a more comprehensive measure capturing a person's lifetime living standards (Banks et al., 2003). Employment status was assessed by directly asking participants which of the following descriptors best described their situation: employed, self-employed, unemployed, partly retired, retired, disabled or looking after home or family. Total household wealth is a robust indicator of socio-economic status and living standards in ELSA and includes financial wealth, the value of any home and other property, the value of business assets, physical wealth such as artwork and jewellery, and debt (Phillips et al., 2014; Banks et al., 2003). Employment status was collected during the main interview at all waves. Total household wealth was available for waves 1 to 5.

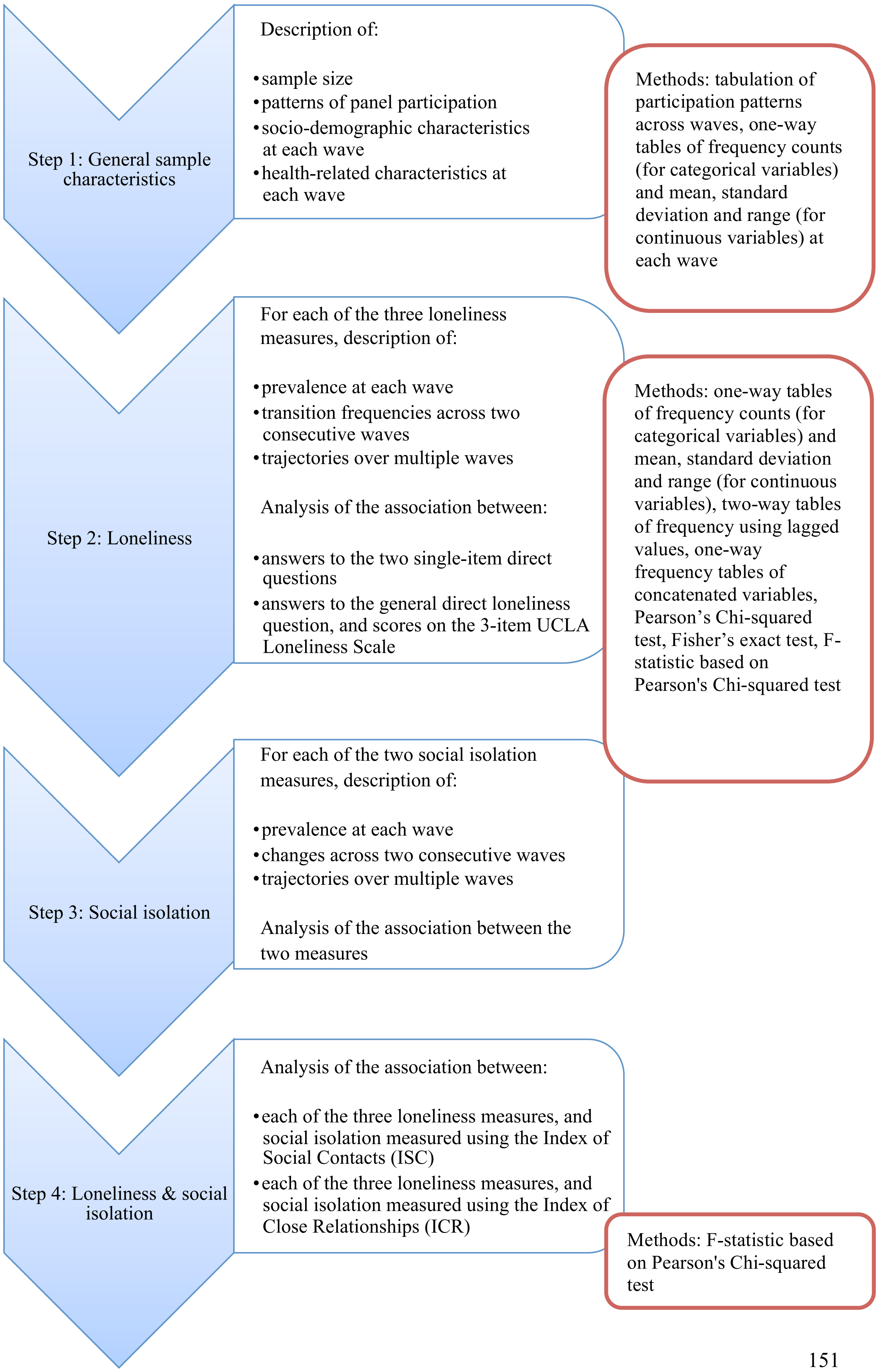
Health status. To gauge general health, two measures were selected: self-rated general health and whether the respondent reported a limiting long-standing illness. Self-reported general health status was recorded using a scale ranging from Excellent to Poor (all waves except for wave 3) or from Very Good to Very Bad (wave 3). The presence of a limiting long-standing was measured by combining answers to two questions: whether participants reported suffering from one or more long-standing illnesses and whether these illnesses limited daily activities.

6.2.4. Statistical analysis

The steps I took to study loneliness and social isolation in ELSA are summarised in Figure 6.3. First, I generated descriptive statistics on the size of the sample at each wave and tabulated the frequency of patterns of participation across all waves to visualise differences and similarities across the sample – e.g. how many individuals took part in all waves, or had missing waves, and what the patterning of this was. Using one-way tables of frequency counts for categorical variables (gender, ethnicity, education, income and wealth quintiles, private health insurance cover, labour force status, self-reported health and limiting long-standing illness) and mean, standard deviation and range for age, I produced summary tables of the sample's socio-demographic and health variables at each wave.

Having familiarised myself with the general characteristics of the sample, I turned to the loneliness variables. All three measures – the direct general question, the direct question about loneliness in the past week and the three-item UCLA Loneliness Scale – were treated as categorical variables.

Figure 6.3 Overview of my analyses of loneliness and social isolation in ELSA



For each of the three measurement tools, I studied: the prevalence of loneliness at each wave, transition frequencies across two consecutive waves and trajectories over multiple waves. Prevalence data were drawn from one-way tables of frequency counts and transition frequencies were examined in two-way tables where answers at one wave were compared with answers in the previous wave (lagged values). To extend my analyses beyond transitions across two waves, I created concatenated variables for each measure of loneliness, summarizing participants' answers throughout the study. For example, for a person who never reported feeling frequently in the past week and took part in all waves, the value of the concatenated variable would be '000000' to reflect no report of loneliness across the six waves. Concatenated values were then tabulated in one-way tables of frequency.

My analyses were aimed at *describing* patterns rather than *explaining* them. This is why I did not formally test whether loneliness at one wave predicted loneliness in the next using regression models, which would have required taking into account a range of potential confounders and explanatory variables. This task was beyond the exploratory scope of my study, the aim of which was to inform subsequent analyses where loneliness would be the explanatory rather than the outcome variable. Nor did I apply formal tests to ascertain risk of bias. Analyses were based on available cases only, i.e. for prevalence at each wave I included all the participants who provided a valid response for that wave; for transition frequencies, anyone with two consecutive waves contributed to the analyses; and for the analyses across multiple waves, I first looked at patterns among those with the maximum amount of data (e.g. six waves if a question had been asked at all six waves, or four waves if the question was only available from waves 3 to 6). Aware that using available cases only might affect the validity of my findings, I compared frequencies and patterns among people who provided valid answers at all waves with those among people who had missing data for one, two or more waves. This allowed me to use data from people who joined the cohort at later waves for the analyses across more than two waves (e.g. at waves 3 or 4).

As a means of assessing heterogeneity and visually gauging the shape of patterns over time, I randomly sampled a small proportion of participants (0.2% or 0.5 % depending on the total number of people with more than two waves of data for the variable of interest) with at least two waves of data for each loneliness measure and plotted their answers across waves. This random selection procedure was intended to avoid bias in the selection process (Viswanathan et al., 2013); by aiming to obtain around 20 patterns each time, the intention was to provide a manageable number of plots from which I could gain a sense of, and demonstrate, how diverse the data were.[11] Due to the large number of observations and the diversity of trajectories,

[11] Note that the exact number of randomly selected participants for each analysis varied, depending on the variables and number of waves under study. E.g. selecting 0.2% of people with valid answers to the direct question about loneliness in the past week did not produce the same number as selecting 0.2% of people with valid answers on the

plotting the data for all participants in a single graph would not have been informative (Diggle and Diggle, 2002).

After observing that there was much heterogeneity in the longitudinal patterns of loneliness, I explored opportunities for identifying clusters of individuals who followed similar progressions over time (Jones and Nagin, 2007). Group-based trajectory modelling, a specialized form of finite mixture modelling, was initially identified as a promising method for identifying distinct groups of participant trajectories; but two considerations led me to drop this approach. First, after piloting it on the direct question about loneliness in the past week (a dichotomous variable), I realised that this method was ill-suited to a situation where there is great heterogeneity in patterns: it identified the optimal number of groups as three, with one group of 'never lonely/isolated', once group of 'always lonely/isolated' and a third group in which participants with very different trajectories of social relationships were all clustered into a 'fluctuating' category. In other words, the numbers of people exhibiting particular patterns were too small to justify creating a category of their own using a group-based trajectory modelling. The second consideration was that group-based trajectory modelling was not a method I could then have gone on to meaningfully use in epidemiological analyses of the association between social relationships and health outcomes in ELSA. Whilst it is becoming a popular method in longitudinal observation studies (Nagin and Odgers, 2010), this method requires that trajectories be modelled over a fixed period of time and that subsequent health outcomes then be looked at. Events that occur during the time period over which the explanatory variable (in my case, loneliness) is measured cannot be taken into account in the analyses. For example, in ELSA, this would have meant studying patterns of loneliness over waves 1 to 4 or 5, and then studying health outcomes at wave 5 and or 6. Since the events I intended to study (incident CVD) were rare, this was unlikely to allow for a sufficiently powered study. Perhaps more crucially, the assumption that patterns of loneliness or social isolation over a 6 or 8 year-period would predict subsequent health outcomes was not one that would allow me to investigate shorter term effects. What if participants' replies in the wave immediately prior to the event was what primarily mattered, for instance?

Instead of group-based trajectory modelling, I performed subgroup analyses to explore whether people with shared characteristics exhibited similar patterns. I looked for homogeneity of answers among widow(er)s, adults from a lower socio-economic background, people aged 80+ and those reporting a long-standing limiting illness. These particular variables were selected because of previous evidence suggesting that they were associated with loneliness and social isolation (Lichtenstein et al., 1996; Petitte et al., 2015; Shankar et al., 2011; Steptoe et al.,

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three-item UCLA Scale, since the numbers of eligible people differed (far more people had valid answers for the direct question than for the composite scale).

2013b). I used Pearson's χ^2 statistic to formally test for association between each of these variables, and frequency of reported loneliness (Conover, 1999). Where the required minimum of 5 counts per cell was not met for Pearson's test, I applied Fisher's exact test instead (Fisher, 1935). Because my aim was not to explain patterns using socio-demographic and health variables, I did not resort to techniques such as generalized linear modelling, latent-response formulation or Markov models – though I acknowledge that these methods could in future be used to better understand why people experience changes in their relationships.

Once I had looked at each loneliness measure separately, I compared answers on different tools. My purpose was to assess correlation between the two direct questions and between the general direct question and scores on the three-item UCLA Loneliness Scale. I wanted to identify whether the values obtained for one variable tended to be higher for higher values of the other variable. As a formal test, I used a statistic based on Pearson's chi-squared statistic which accounts for clustering by panel variable. In recognition of the fact that participants reported several observations and that there answers cannot therefore be considered as independent, Pearson's chi-squared statistic is turned into an F-statistic with non-integer degrees of freedom by using a second-order Rao and Scott correction (Rao and Scott, 1984).

Note that I focused on correlation, rather than studying agreement or prediction. My aim was not to assess the amount of agreement between the values of the two variables, since this would have implied that I was comparing alternative ways of measuring the same feeling. Whilst all three tools come under the umbrella of 'loneliness measure', we have seen in section 6.2.3.1. that in the case of the two direct questions, they had different timeframes (week versus undefined); and that the three-item UCLA Loneliness Scale cannot readily be interpreted as an indicator of loneliness *frequency*, unlike the direct questions. Rather, it combines elements of intensity with frequency, making it difficult to hypothesize valid equivalences as would be necessary for assessing agreement (Bland and Altman, 1986).This is also why I did not look directly at whether the question about loneliness in the past week was correlated with the three-item UCLA Loneliness Scale; there would have been too many differences (in time frame, mode of administration, direct versus indirect questions, frequency versus combined intensity and frequency) to make such a comparison meaningful. Again, because my intent was not to assess the ability of one variable to predict values of the other, I did not formulate predictive models using regression analyses.

After completing my exploration of the loneliness variables, I used the same procedure to look at the two measures of social isolation: the ISC and the ICR. For each index, I studied prevalence at different waves, transition frequencies across consecutive waves and trajectories over multiple waves. I drew one-way tables of frequency counts and examined transition frequencies in two-way tables where answers at one wave were compared with lagged values. Concatenated variables were generated and patterns of answers were compared across the same subgroups as for loneliness – widow(er)s, adults from a lower socio-economic background, people aged 80+ and those reporting a long-standing limiting illness – as well as across participants with different numbers of waves, to check for likelihood of bias due to missing data and/or attrition.

Having looked at the ISC and ICR variables separately, I studied correlation between the two. For this stage of the analysis and for comparison with loneliness, I dichotomized the two indices. The many possible scores on both indices meant that it would not have been manageable to keep them as they were in correlation analyses. Whilst I could have treated the number of close friends as continuous, I was not so much interested in relative isolation, i.e. comparing those with comparatively fewer (but still possibly quite a few) relationships with those who reported comparatively more, as in absolute isolation – people with very few close relationships. I therefore distinguished between people who reported one or fewer close relationships in the ICR – classed as isolated – and those with more relationships. Similarly, to distinguish people with very limited social contact from others, I categorized those who scored 5 or 6 (i.e. who reported none or only one contact) as socially isolated and the rest as not isolated. My rationale for including people with one contact or close relationship in the 'isolated' category was that I considered these people to be more vulnerable to isolation; unlike more 'connected' people, the removal of that single relationship would mean that, unless it was automatically replaced by another new relationship, these people were likely to experience absolute isolation.

As a formal test of correlation between social isolation as measured in the ISC and in the ICR, I used the F statistic with non-integer degrees of freedom described above. This was also the formal test used in the final stage of my analyses, where I assessed correlation between loneliness and social isolation.

Altogether, a total of 29 hypotheses were tested in my analyses. To reduce my overall chances of falsely rejecting each hypothesis using a fixed significance level, rather than letting my chances increase with each additional test, I controlled for multiple-testing using the Bonferroni adjustment (Miller, 1981). This adjustment involves dividing the true critical level by the number of tests run; for my study, this meant dividing the chosen significance level of 0.05 by 29, i.e. the appropriate critical level was 0.002.

All analyses were performed using Stata/SE 14.2 (StataCorp, 2011). An annotated Stata 'do file' listing all stages of the analysis is provided in Appendix 6.2.

6.3. Results

Before turning to the primary focus of this chapter, i.e. patterns of loneliness and social isolation over time, the following section summarises the characteristics of the study sample. To facilitate reading, the number of tables included in the main body of this chapter has been limited to those of relevance for the primary analyses. All other tables have been labelled with an 'A' and are included in the appendix (see Appendix 6.2).

6.3.1. Characteristics of the study sample

The characteristics of the study sample, including size, patterns of panel participation, demographic and health-related profile are described in the following section.

6.3.1.1. Sample size and patterns of panel participation

A total of 15,783 people were interviewed at least once in the course of the six waves of data collection. Table 6.6 provides a breakdown of core respondent numbers at each wave, split according to cohort membership. In the first wave, 11,391 members participated. Of these 11,391individuals, half took part in the sixth wave of data collection; the remainder of respondents at wave 6 pertained to the cohorts introduced at waves 3, 4 and 6.

Table 6.6 Number of core respondents at each ELSA wave, split by cohort

ELSA wave	Number of completed interviews				
	Cohort 1	Cohort 3	Cohort 4	Cohort 6	Total
Wave 1	11,391	NA	NA	NA	11,391
Wave 2	8,780	NA	NA	NA	8,780
Wave 3	7,535	1,275	NA	NA	8,810
Wave 4	6,623	972	2,291	NA	9,886
Wave 5	6,242	936	1,912	NA	9,090
Wave 6	5,659	888	1,796	826	9,169

On average, participants were followed for 5.5 years. The panel was neither balanced nor compact,[12] with 45 different patterns of participation. The most frequent pattern of participation was taking part across all 6 waves, although this only accounted for just over 30% of patterns

[12] A balanced panel has the same number of observations for each participant, while an unbalanced panel has different numbers of time observations for each individual. A compact panel covers only consecutive time periods for each person, i.e. there are no missing waves (Diggle & Diggle, 2002).

(see Table A6.7, in Appendix 6.2, p.324).

6.3.1.2. Socio-demographic characteristics

The socio-demographic characteristics of participants are summarised in Table 6.8. Mean age at wave 1 was 65.2 (SD: 10.2), with a minimum of 50. Maximum age is unclear, since ELSA does not provide birth year information for individuals aged 90 years old or older (e.g. wave 1 respondents born on or before 02/29/1912 were assigned a birth year value of 1912). Patterns of age distribution across the subsequent waves were consistent with the introduction of younger members at waves 3, 4 and 6, which explains why the sample at wave 6 was only two years older than at wave 1 (67.8 years at wave 6 v. 65.2 at wave 1). Women accounted for 55% (plus or minus one percentage point) of participants at each wave and the sample was predominantly white (97%). Total household wealth was positively skewed, ranging from -£1,578,980 to £39,300,000. Negative values for household wealth, which accounted for between 3.4% of respondents at wave 5 and 4.2% at wave 3 were due to this variable incorporating debt (Phillips et al., 2014). Around two thirds of the core members (61% to 79%, depending on the wave) were not in employment – i.e. they were retired, unemployed, out of work due to disability or caring for their home or family.

6.3.1.3. General health characteristics

Just under a third of participants qualified their health as being good, with a further 29% describing it as very good and 12% stating that it was excellent (see Table 6.9). At each wave, 8% of the sample answered that their health was poor. Over a third of participants reported suffering from a limiting long-standing illness.

Table 6.8 Socio-demographic characteristics of the sample

Variable	Wave 1, n	% or mean (SD) & range	Wave 2, n	% or mean (SD) & range	Wave 3, n	% or mean (SD) & range	Wave 4, n	% or mean (SD) & range	Wave 5, n	% or mean (SD) & range	Wave 6, n	% or mean (SD) & range
Age	11,391	65.2 (10.2), 50 to 90	8,780	66.8 (9.8), 52 to 90	8,810*	65.8 (10.6), 50 to 90	9,886	66.2 (9.7), 50 to 90	9,090	67.8 (9.3), 52 to 90	9,169	67.8 (9.7), 50 to 90
Gender	11,391		8,780		8,810		9,886		9,090		9,169	
Female	6,205	54%	4,380	55%	4,869	55%	5,460	55%	5,034	55%	5,096	56%
Male	5,186	46%	3,950	45%	3,941	45%	4,426	45%	4,056	45%	4,073	44%
Ethnicity	11,384		8,779		8,810		9,884		9,090		9,167	
White	11,065	97%	8,586	98%	8,575	97%	9,585	97%	8,811	97%	8,849	97%
Non-white	319	3%	193	2%	235	3%	299	3%	279	3%	318	3%
*Total household wealth**	11,191	203,610 (383,670), -358,550 to 10,400,000	8,661	262,175 (400,027), -111,700 to 9,297227	8,574	295,218 (527,174), -1,578,980 to 20,080,000	9,605	326,777 (698,476), -255,580 to 39,300,000	8,873	331,109 (469,291), -105,000 to 10,600,000	NA**	NA
Lowest quintile		≤16,000		≤40,400		≤52,150		≤66,300		≤77,235	NA	NA
Second quintile		16,001-93,000		40,401-149,000		52,151-168,000		66,301-173,000		77236-185,000	NA	NA
Third quintile		93,001-163,000		149,001-225,870		168,001-251,000		173,001-264,000		185,001-279,800	NA	NA
Fourth quintile		163,001-294,720		225,871-363600		251,001-407,000		264,001-437,000		279,801-455,000	NA	NA
Highest quintile		≥294,721		≥363601		≥407,001		≥437,001		≥455,001	NA	NA
Labour force status	11,336		8,754		8,787		9,876		9,056		9,135	
Employed	2,973	26%	2,049	23%	2,484	28%	2,632	27%	2,018	22%	2,057	23%
Self-employed	634	6%	467	5%	518	6%	621	6%	533	6%	544	6%
Unemployed	118	1%	66	1%	74	1%	112	1%	88	1%	96	1%
Partly retired	78	1%	48	1%	35	0.4%	56	1%	52	1%	40	0.4%
Retired	5,696	50%	4,728	54%	4,482	51%	5,310	54%	5,397	60%	5,539	61%
Disabled	745	7%	499	6%	476	5%	529	5%	451	5%	422	5%
Looking after home or family	1,092	10%	897	10%	718	8%	616	6%	517	6%	437	5%

*At waves 3, 4 and 6 new members joined the cohort – hence why sample numbers do not necessarily decline as would be expected from attrition alone, but are sometimes larger in one wave than in previous ones (e.g. 9,886 participants in wave 4, compared with 8,810 participants in wave 3).

**NA: not available. Total annual income and wealth for Wave 6 have not yet been made available on the Economic and Social Data Service website.

Table 6.9 Self-reported health and limiting long-standing illness

NB: At wave 3, an alternative scale of self-reported general health status (otherwise known as the 'European scale') was used, with the following response options: Very Good, Good, Fair, Bad and Very Bad (Phillips et al., 2014). This explains the differences in distribution at wave 3, compared with all other waves.

Variable	**Wave 1, n**	**%**	**Wave 2, n**	**%**	**Wave 3, n**	**%**	**Wave 4, n**	**%**	**Wave 5, n**	**%**	**Wave 6, n**	**%**
Self-reported health	11,216		8,682		8,639		9,585		8,731		8,779	
Excellent	1,425	13	1,063	12	2,154	25	1,183	12	1,021	12	1,028	12
Very good	3,239	29	2,391	28	3,688	43	2,771	29	2,565	29	2,506	29
Good	3,508	31	2,755	32	2,185	25	3,068	32	2,814	32	2,796	32
Fair	2,187	20	1,794	21	490	6	1,837	19	1,635	19	1,729	20
Poor	857	8	679	8	122	1	726	8	696	8	720	8
Limiting long-standing illness	11,382		8,773		8,803		9,878		9,078		9,164	
Yes	4,041	36	3,193	36	3,082	35	3,481	35	3,295	36	3,346	37
No	7,341	65	5,580	64	5,721	65	6,397	65	5,783	64	5,818	63

6.3.2. *Loneliness and social isolation: cross-sectional and longitudinal patterns*

Descriptions of cross-sectional and longitudinal patterns are provided below for each of the social relationship measures in turn.

6.3.2.1. Loneliness

a) Direct single-item question about loneliness in general, part of the self-completion questionnaire

The direct single-item question was included in ELSA's self-completion questionnaire from wave 3 onwards. Valid answers to the direct loneliness question 'How often do you feel lonely?' were available for 84% to 88% of participants at each wave. From the cross-sectional patterns of response summarised in Table 6.10, two clear characteristics emerge: firstly, a majority of participants did not report feeling lonely often; and secondly, the population prevalence of reported loneliness is remarkably stable across waves. In wave 3, 8% of participants reported feeling often lonely, while 25% reported feeling lonely some of the time and the remaining 67% reported hardly ever or never feeling lonely. In the following three waves, the distribution of answers was nearly identical to that in wave 3, despite the sample being on average 2 years older in wave 6 compared with wave 3 (mean age at wave 3: 65.8 years, compared with mean age at wave 6: 67.8). This finding – i.e. the stability of loneliness at population level – remained true when the younger members introduced at waves 4 and 6 were ignored: in wave 6, 8% of the members who joined in wave 1 or 3 (mean age: 70.3, SD: 9.1, range: 56+) reported feeling often lonely and 25% reported feeling lonely some of the time. In other words, the prevalence of feelings did not increase or decrease with time and/or age.

Table 6.10 Cross-sectional summary of loneliness – direct single-item question about feeling lonely in general

Variable	Wave 3 – n (%)	Wave 4 – n (%)	Wave 5 – n (%)	Wave 6 – n (%)
How often do you feel lonely?	7,410	8,327	8,006	7,845
Often	596 (8)	687 (8)	616 (8)	598 (8)
Some of the time	1,821 (25)	1,964 (24)	1,973 (25)	1,984 (25)
Hardly ever or never	4,993 (67)	5,676 (68)	5,417 (68)	5,263 (67)
Missing	1,400 (16)	1,559 (16)	1,084 (12)	1,324 (14)

To investigate how loneliness reports evolve over time at the individual rather than the population level, we can first look at transitions between two study waves. A total of 9,792 participants provided valid responses for two or more consecutive waves. Overall, the transition frequencies listed in Table 6.11 are indicative of relative stability across waves. From one interview to another, people were more likely to state the same frequency of feelings or move to the adjacent category. For example, 86% of reports where people did not feel often lonely were followed by the same answer of no loneliness in the following wave; 11% switched to answering that they felt lonely some of the time. Few individuals skipped from reporting feeling hardly or never to often lonely, or vice versa (9% and 1% respectively). Reporting feeling rarely lonely was comparatively more stable than reports of occasional or frequent loneliness: reporting feeling sometimes lonely, or often lonely, was repeated at the next wave for around 50% of people, compared with 86% of instances where rare loneliness was reported being followed by that same answer. What this suggests is that, while at the level of the population the prevalence of frequent loneliness was stable across waves, those who report feeling often lonely at one wave are not necessarily the same individuals who reported frequent loneliness feelings in the previous wave; and the same applies to occasional feelings of loneliness.

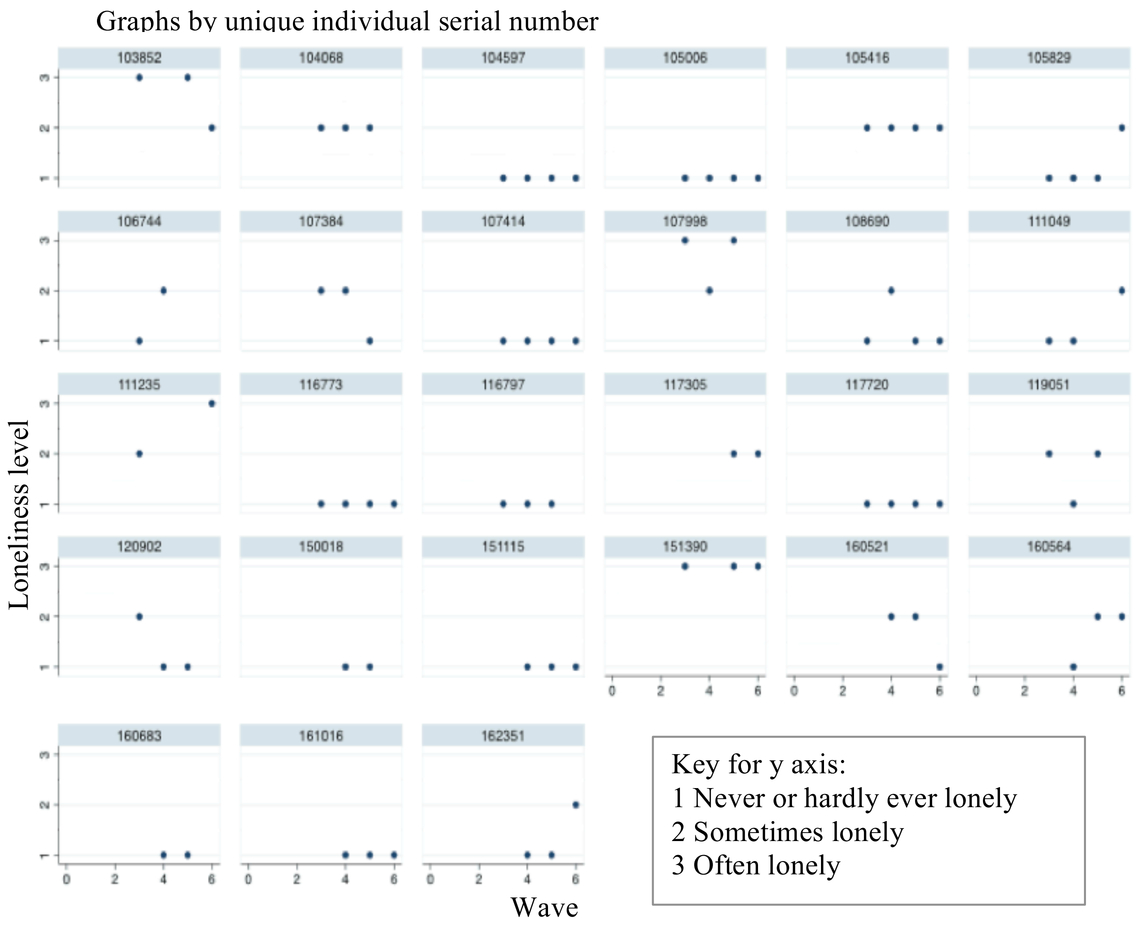
Table 6.11 Transition frequencies across two consecutive waves - direct single-item question about loneliness in general

NB: The number of observations reported in this table refer to 'person-waves', i.e. each person contributes information more than once. For example, where an individual took part in 3 consecutive waves, they contributed information twice: between the first and second wave, and between the second and third.

How often do you feel lonely?	**Answer given at the following wave**		
	Hardly ever or never	**Some of the time**	**Often**
Hardly ever or never (n=13,252)	11,513 (87%)	1,552 (12%)	187 (1%)
Some of the time (n=4,470)	1,515 (34%)	2,469 (55%)	486 (11%)
Often (n=1,383)	119 (9%)	524 (38%)	740 (54%)

What of loneliness reports across multiple waves? There were 4,117 individuals who provided valid answers for the four waves (waves 3 to 6) in which the direct self-completed question was included. Figure 6.4 illustrates some of the different patterns emerging from this large sample, based on a subsample of 27 participants selected randomly. From this subsample alone, we note the variability of patterns across individuals: apart from the 9 individuals who reported never feeling lonely in all of the waves they took part in, no two respondents had the same answers. Some patterns indicated an increase in loneliness feelings (e.g. individuals 105829 and 160564), others a decrease (e.g. individuals 160521 and 107384), with a few individuals experiencing both (e.g. individuals 107998 and 108690). Just over half of the subsample (14 out of 27) reported feeling sometimes lonely at least once and 4 participants reported frequent loneliness in one or more waves.

Figure 6.4 Empirical growth plots for 27 randomly selected individuals, showing responses to the self-report direct loneliness question across waves



The variability of loneliness patterns was confirmed when looking at the whole sample of individuals who provided valid answers for the four waves (n=4,117). A total of seventy-four different sequences of answers were observed, with the most common pattern (53% of the sample, n=2,169) being no loneliness across all four waves (see Tables A6.12 & A6.13, pp.326-27). Given the diversity of the sample in age, gender, socio-economic status and health status, this heterogeneity was not altogether unexpected. Perhaps more surprising was the finding that heterogeneity persisted when patterns of response were explored among subgroups of older adults, widows and widowers, participants in the lowest quintile of socio-economic status and individuals with a limiting long-standing illness (see Table A6.14, p.328).

As well as the diversity of response patterns, another feature clearly emerged from the data: reporting feeling frequently lonely was not as uncommon as cross-sectional prevalence figures (8%, see Table 6.10) might lead us to think. While only 2% of participants reported feeling often lonely at all four waves, a further 12% (n=499) reported frequent loneliness in at least one wave:

- 7% of participants (n=276) reported feeling often lonely in one wave only;

- 3% of participants (n=139) reported feeling often lonely in two waves;

- 2% of participants (n=84) reported feeling often lonely in three waves.

If we add up these proportions, we find that 14% of the sample reported frequent loneliness at least once. To check whether any bias was introduced by only looking at people with valid answers at all four waves, I looked at whether comparable prevalence figures were obtained when looking at people with fewer waves. When people with three waves of data only were considered, a similar proportion (15%) reported frequent loneliness at least once (see Table A6.15, p.328).

To check whether the frequency of reported loneliness was greater among individuals in more vulnerable situations, subgroups were examined separately. As outlined in the methods section of this chapter (see section 6.2.4.), the vulnerable situations referred to here relate to risk factors for loneliness and social isolation previously identified in the literature: older age, widowhood, lower socio-economic status and ill health (Lichtenstein et al., 1996; Pettite et al., 2015; Shankar et al., 2015; Steptoe et al., 2013). The results presented in Table 6.16 show that these individuals consistently reported feeling ‘often lonely’ more frequently. The proportion of participants reporting feeling frequently lonely in at least one wave was twice as high among those who, at wave 3 (i.e. the first wave in which the question about loneliness was asked), were aged 80 and over (27% v. 13%); more than twice as high among participants in the lowest socio-economic quintile (28% v.12%) and among people with a limiting long-standing illness (24% v. 10%); and more than 2.5 times higher among people who had lost their spouse (29% v.11%).

Table 6.16 Frequency of chronic loneliness reports among participants who took part in all four waves of data collection - subgroup analyses

Subgroup (characteristic at wave 3)	**Number of times that the participant reported feeling frequently lonely over the course of the four waves – n (%)**					**Results of Pearson Chi-square tests**
	0	**1**	**2**	**3**	**4**	
Aged 80+ (n=202)	146 (72)	23 (11)	10 (5)	12 (6)	11(5)	$X^2(4) = 44$, p <0.001
Aged <80 (n=3,915)	3,395 (87)	253 (7)	129 (3)	72 (2)	66 (2)	
Widowed (n=521)	357 (69)	54 (10)	45 (9)	28 (6)	37 (7)	X^2 (4) = 202, p <0.001
Not widowed (n=3,596)	3,184 (89)	222 (6)	94 (3)	56 (2)	40 (1)	
Lowest wealth quintile (n=540)	388 (72)	67 (12)	41 (8)	20 (4)	24 (4)	X^2 (4) = 107, p <0.001
Highest four wealth quintiles (n=3,502)	3,088 (88)	203 (6)	96 (3)	62 (2)	53 (2)	
With a limiting long-standing illness (n=1,152)	879 (86)	117 (10)	71 (6)	43 (4)	42 (4)	X^2 (4) =133, p <0.001
Without a limiting long-standing illness (n=2,962)	2,660 (90)	158 (5)	68 (2)	41 (1)	35 (1)	

b) Feelings of loneliness in the past week

I now turn to the measure of loneliness included as part of the CESD 20 item questionnaire, where participants are asked about the frequency of their loneliness feelings *in the past week*. Do loneliness reports based on this measure follow the same patterns as those based on the direct loneliness question included in the self-completion questionnaire?

First, let us look at cross-sectional patterns of response. In each of the six waves in which the question was asked, a minimum of 95% of core members provided a valid answer. From the prevalence figures summarised in Table 6.17 we see that between 12% and 14% of respondents at each wave reported feeling lonely much of the time. This is a little higher than the prevalence of frequent loneliness reported when no timeframe was specified in the question (8%, see Table 6.10). From ELSA, it is not possible to say whether the difference in prevalence is due to differences in experiences of loneliness or to the distinct phrasing and administration of the questions. For instance, the absence of a 'sometimes' option for the question about loneliness in the past week means that some participants who occasionally felt lonely may have opted for stating that they were often lonely, rather than not at all (Victor et al., 2005a).

Table 6.17 Cross-sectional summary of loneliness scores – CESD single-item

Variable	Wave 1 – n (%)	Wave 2 – n (%)	Wave 3 – n (%)	Wave 4 – n (%)	Wave 5 – n (%)	Wave 6 – n (%)
Lonely much of the time during the past week?	11,039	8,615	8,576	9,529	8,669	8,728
Yes	1,527 (14)	1,219 (14)	1,170 (14)	1,251 (13)	1,167 (13)	1,049 (12)
No	9,512 (86)	7,396 (86)	7,406 (86)	8,278 (87)	7,502 (87)	7,679 (88)
Missing	352 (3)	165 (2)	234 (3)	357 (4)	421 (5)	441 (5)

To look at changes over time at the individual level, we can use data from the 12,136 participants who provided valid responses for two or more consecutive waves. Their answers indicate that, similarly to the direct self-completion question, when participants reported not feeling frequently lonely in the last week at one wave they were highly likely to report no loneliness in the following wave (93% of cases, see Table 6.18). Where someone reported feeling frequently lonely, however, this was only repeated 53% of the time in the following wave i.e. reports of frequent loneliness in the past week were less stable.

Table 6.18 Transition frequencies across two consecutive waves

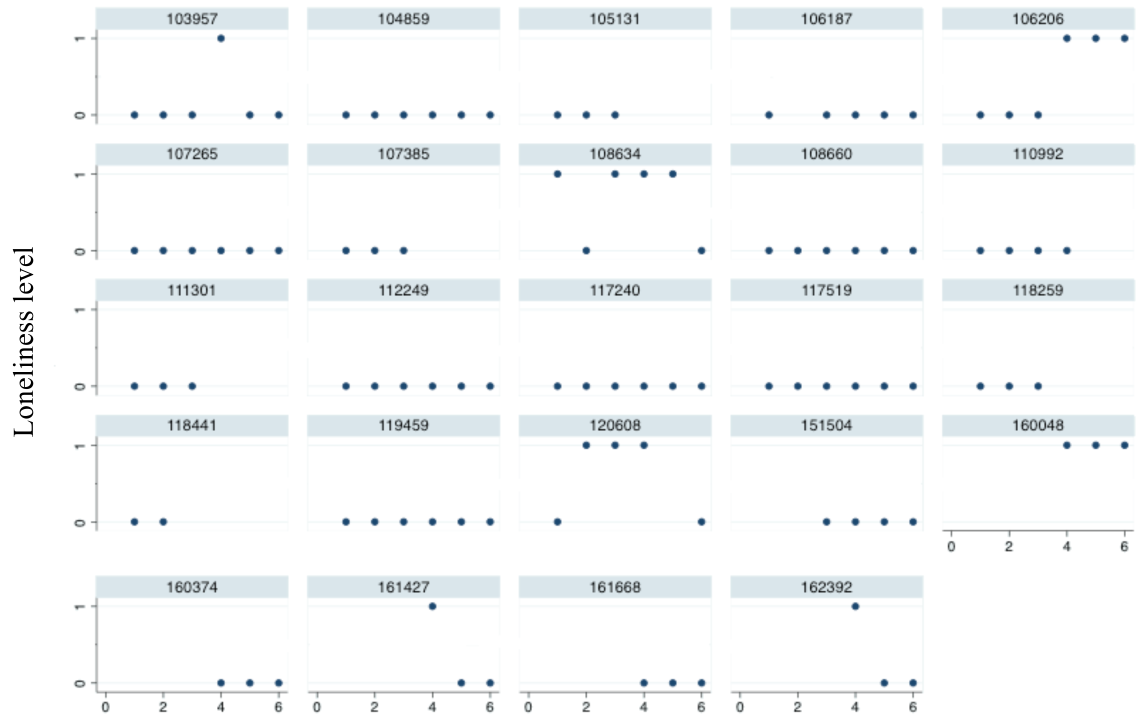
NB: As in Table 6.11 above, the number of observations reported in this table refer to 'person-waves', i.e. each person contributes information more than once. For example, where an individual took part in 3 consecutive waves, they contributed information twice: between the first and second wave, and between the second and third.

'Much of the time during the past week, you felt lonely'	**Answer given at the following wave**	
	No	**Yes**
No (n=33,223)	30,819 (93%)	2,404 (7%)
Yes (n=4,883)	2,286 (47%)	2,597 (53%)

Selecting a random subsample of participants allows us to get a first impression of patterns of answers across more than two waves. The 24 patterns shown below (see Figure 6.5) suggest that the most common pattern of response (17 out of 24) was consistently reporting not feeling frequently lonely in the past week. Among those who replied feeling frequently lonely in the last week at least once, this was repeated in half of the cases (4 out of 7) and was a single occurrence in the other half (3 out of 7).

Figure 6.5 Empirical growth plots for 24 randomly selected individuals, showing responses to the CESD loneliness question across waves

Graphs by unique individual serial number



Wave

Key for y axis:
0 Not lonely much of the time in the past week
1 Lonely much of the time in the past week

Extending these preliminary analyses to the 4,473 individuals who took part in all six waves of data collection, we obtain similar findings. Seventy per cent (n=3,115) of the sample reported not feeling lonely much of the time in the past week across all waves (see Tables A6.19 & A6.20, pp.330-31). By contrast, only 1% of respondents (n=65) reported feeling lonely much of the time in the past week across all waves. The response patterns of the remaining 29% participants indicated substantial variability; they also highlighted that frequent loneliness in the past week was experienced at least once in the course of the study by many:

- 13% of participants (n=581) reported feeling lonely much of the past week in one wave only. This was the most common pattern after consistently reporting not feeling lonely much in the past week across all 6 waves;

- 7% of participants (n=309) reported feeling lonely much of the past week in two waves;

- 4% (n=181) reported feeling lonely much of the past week in three waves;

- 3% (n=119) reported feeling lonely much of the past week in four waves;

- 2% (n=103) reported feeling lonely much of the past week in five waves.

Combined with the 1% of individuals who reported frequent loneliness across all waves this amounts to 30% of the sample experiencing frequent loneliness in the past week at some point in the study. Sensitivity analyses using data from participants who took part in 5, 4 or 3 waves only likewise showed that the proportion of people reporting frequent loneliness at least once over the course of the study was high (36%, 32% and 25% respectively – see Table A6.21, p.331). This is substantially greater than the proportion of people who, at a given point in time, reported experiencing frequent loneliness in the past week (12 to 14%, see Table 6.17 above).

As was the case when loneliness was assessed without specifying a timeframe, frequency of feelings in the past week was greater among individuals in more vulnerable situations (see Table 6.22). The proportion of people reporting frequent loneliness was around twice as high among adults aged 80+, widowed participants, those in the lowest wealth quintile and individuals with a limiting long-standing illness.

Table 6.22 Frequency of loneliness in the past week among participants who took part in all six waves of data collection – subgroup analyses

Subgroup (characteristic at wave 1)	**Number of times that the participant reported feeling frequently lonely over the course of the four waves – n (%)**							
	0	**1**	**2**	**3**	**4**	**5**	**6**	**Results of Pearson Chi square tests**
Aged 80+ (n=125)	57 (46)	24 (19)	12 (10)	11 (9)	7 (6)	8 (6)	6 (5)	$X^2(6) = 47$, p<0.001
Aged <80 (n=4,348)	3,058 (70)	557 (13)	297 (7)	170 (4)	112 (3)	95 (2)	59 (1)	
Widowed (n=582)	238 (41)	95 (16)	77 (13)	48 (8)	50 (9)	45 (8)	29 (5)	$X^2(6) = 385$, p<0.001
Not widowed (n=3,891)	2,877 (74)	486 (13)	232 (6)	133 (3)	69 (2)	58 (1)	36 (1)	
Lowest wealth quintile (n=550)	263 (48)	104 (19)	65 (12)	44 (8)	28 (5)	27 (5)	19 (3)	$X^2(6) = 153$, p<0.001
Highest four wealth quintiles (n=3,847)	2,791 (73)	472 (12)	238 (6)	134 (3)	90 (2)	76 (2)	46 (1)	
With a limiting long-standing illness (n=1,216)	664 (55)	196 (16)	143 (12)	73 (6)	47 (4)	55 (5)	38 (3)	$X^2(6) = 216$, p<0.001
Without a limiting long-standing illness (n=3,256)	2,450 (75)	385 (12)	166 (5)	108 (3)	72 (2)	48 (1)	27 (1)	

The two loneliness questions examined so far produce similar pictures: overall, infrequent loneliness across waves was the more common pattern among participants, whether reported for the past week or for an undefined period of time. While the prevalence of loneliness remained stable at the population level across waves, at the level of individuals feelings fluctuated so that many more participants reported experiencing frequent loneliness than cross-sectional data might have led us to think.

c) Are similarities in findings due to an association between responses to the two loneliness questions?

While the purpose of this study was not to investigate overlap and agreement between the different measures in ELSA, a look at the relationship between responses can help to answer whether the similarity in patterns between the two self-report questions is due to an association between the two measures. Testing for correlation between the two instruments shows that answers to the question about loneliness in the past week were associated with answers to the self-completion question ($F(2, 22{,}865) = 5{,}035$, $p<0.001$, see Table 6.23). The most common combinations of responses involved reporting similar loneliness levels across the two questions. For instance, in 99% of cases where people reported that they did not feel often lonely, this was associated with answering not often feeling lonely in the past week. When people said that they were often lonely, in 71% of cases they reported feeling often lonely in the past week.

Table 6.23 Association between response to the single-item CESD question, and the self-completion question

NB: The number of observations reported in this table corresponds to the number of person-waves, i.e. participants contributed information as many times as the number of waves in which they took part.

'Much of the time during the past week, you felt lonely'	**How often do you feel lonely?**			**Result of F-test**
	Hardly ever or never	**Some of the time**	**Often**	
No (n=27,709)	20,985 (76%)* (99%)**	6,010 (22%) (78%)	714 (3%) (29%)	$F(2, 22{,}865) = 5{,}035$, $p<0.001$
Yes (n=3,773)	310 (8%) (2%)	1,689 (45%) (22%)	1,774 (47%) (71%)	
Total (31,482)	21,295 (68%) (100%)	7,699 (25%) (100%)	2,488 (8%) (100%)	

* Percentages on the first line correspond to row frequency.

** Percentages on the second line correspond to column frequency.

Where respondents reported different levels of loneliness for the two questions, these differences were suggestive of fluctuations in loneliness rather than signalling incompatibility or invalidity of answers. For example, in 45% of cases where participants answered that they often felt lonely in the past week, they reported feeling *sometimes* lonely when no timeframe was specified. In these instances, the past week may have been perceived as a particularly lonely week, a time when the respondent felt lonelier than usual. Conversely, where participants reported feeling often lonely, in 29% of cases they said that they did not often feel lonely in the past week. This suggests that in the past week, respondents had felt less lonely than usual.

*

After comparing answers to the two direct loneliness questions, I now turn to patterns of answers to the three-item UCLA Loneliness Scale.

d) The three-item UCLA Loneliness Scale[13]

The three-item UCLA scale was included in ELSA from wave 2 onwards. Valid cross-sectional data were available for between 83% and 88% of core members at each wave (see Table 6.24). The distribution of scores was positively skewed (reminder: scores ranged from 3 to 9, with lower scores indicating less loneliness). The most frequent score at each wave was 3 (scored by between 50% and 53% of participants) which corresponds to reporting hardly ever or never feeling lonely. The maximum score of 9, meanwhile, was recorded for 2% of the sample at each wave. Taking each of the three questions separately, we see that at each wave the frequency of reporting feeling that one often either lacks companionship, feels left out, or feels isolated from others ranged from 5 to 8% (see Table 6.25).

[13] In my analyses, each score on the three-item UCLA scale is considered separately, i.e. scores were not dichotomized to distinguish between more or less lonely individuals. While the three-item score is often dichotomized in the epidemiological literature – indeed I use it as such for my sensitivity analyses in Chapter 7 – there are currently no clear guidelines on how best to do so. The way in which each question is phrased makes it difficult to gauge whether thresholds distinguish between the frequency or the intensity of feelings (e.g. one might reply feeling frequently lacking in companionship but rarely experiencing either of the two other feelings covered by the tool, scoring 5; and another might report feeling all three emotions 'sometimes', scoring 6 – can we reasonably infer that the latter individual is lonelier than the former?). Hence why here I opted to use all of the information provided by the scale, treating each score separately.

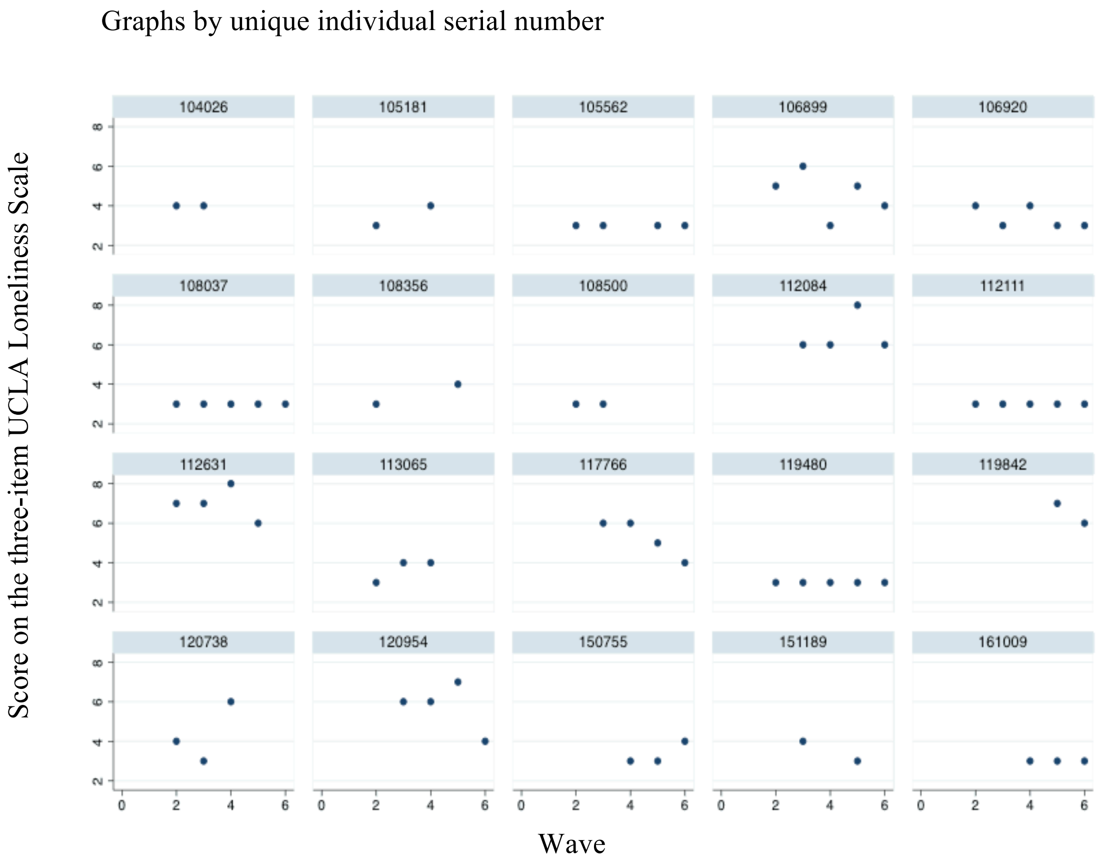
Table 6.24 Cross-sectional summary of loneliness scores –three-item UCLA Loneliness Scale

Three-item UCLA Loneliness Scale (higher scores indicate more frequent and/or intense loneliness)	**Wave 2 – number of participants (%)**	**Wave 3 – number of participants (%)**	**Wave 4 – number of participants (%)**	**Wave 5 – number of participants (%)**	**Wave 6 – number of participants (%)**
3	4,011 (53)	3,664 (50)	4,077 (49)	4,048 (51)	3,903 (50)
4	1,235 (16)	1,196 (16)	1,429 (17)	1,260 (16)	1,239 (16)
5	889 (12)	890 (12)	1,044 (13)	951 (12)	966 (12)
6	818 (11)	907 (12)	902 (11)	955 (12)	962 (12)
7	327(4)	339 (5)	407 (5)	367 (5)	342 (4)
8	146 (2)	175 (2)	215 (3)	183(2)	164 (2)
9	162 (2)	179 (2)	178 (2)	172 (2)	188 (2)
Missing	1,093 (12)	1,460 (17)	1,634 (17)	1,154 (13)	1,405 (15)

Table 6.25 Cross-sectional summary of loneliness scores – three-item UCLA Loneliness Scale questions listed separately

Three-item UCLA Loneliness Scale, individual questions	**Wave 2 – number of participants (%)**	**Wave 3 – number of participants (%)**	**Wave 4 – number of participants (%)**	**Wave 5 – number of participants (%)**	**Wave 6 – number of participants (%)**
Lack of companionship	7,687	7,410	8,314	8,003	7,834
Often	513 (7)	581 (8)	646 (8)	616 (8)	606 (8)
Some of the time	2,069 (27)	2,155 (29)	2,406 (29)	2,303 (29)	2,255 (29)
Hardly ever or never	5,105 (66)	4,674 (63)	5,262 (63)	5,084 (64)	4,973 (63)
Feeling left out	7,648	7,390	8,294	7,987	7,813
Often	363 (5)	378 (5)	418 (5)	385 (5)	365 (5)
Some of the time	2,203 (29)	2,253 (30)	2,396 (29)	2,301 (29)	2,272 (29)
Hardly ever or never	5,082 (66)	4,759 (64)	5,480 (66)	5,301 (66)	5,176 (66)
Feeling isolated from others	7,641	7,389	8,295	7,966	7,808
Often	404 (5)	432 (6)	486 (6)	424 (5)	437 (6)
Some of the time	1,797 (24)	1,913 (26)	2,179 (26)	2,103 (26)	2,138 (27)
Hardly ever or never	5,440 (71)	5,044 (68)	5,630 (68)	5,439 (68)	5,233 (67)

Figure 6.6 Empirical growth plots for 20 randomly selected individuals, showing responses to the three-item UCLA Loneliness Scale across waves



Empirical growth plots for 20 randomly selected individuals illustrate the diversity in response patterns over time (see Figure 6.6). The variability of patterns was confirmed when the whole sample was analysed: across the 3,321 participants who provided data for the five waves in which the three-item UCLA Loneliness Scale was included, there were 1,085 different combinations of scores (e.g. scoring 3-4-4-5-5, or 4-4-4-7-6 over the 5 waves), with the most common pattern being a score of 3 (i.e. hardly or never lonely) in all five waves (n=983, 30%). Only 9 participants consistently scored very highly (i.e. had scores of 8 or 9, which cannot be reached by answering hardly ever or never to any of the three questions) across the five waves.

Subgroup analyses showed that widow(er)s, those in the lowest wealth quintile and participants with a limiting long-standing illness were at least twice more likely to report the highest scores of 8 or 9 at least once during the course of the study (see Table 6.26). While the proportion of adults aged over 80 who reported higher scores was greater than among younger participants, the difference was not statistically significant.

Table 6.26 Frequency of reporting a score of 8 or 9 at least once over the five waves in which the three-item UCLA Loneliness Scale was included

Subgroup (characteristic at wave 2)	Number of times that the participant reported feeling frequently lonely over the course of the four waves – number of participants (%)		
	Never	At least once	Results of Pearson Chi square test
Aged 80+ (n=107)	91 (85)	16 (15)	$X^2(1) = 5$, p=0.026
Aged <80 (n=3,214)	2,934 (91)	280 (9)	
Widowed (n=406)	329 (81)	77 (19)	$X^2(1) = 58$, p<0.001
Not widowed (n=2,915)	2,696 (92)	219 (8)	
Lowest wealth quintile (n=398)	322 (81)	76 (19)	$X^2(1) = 57$, p<0.001
Highest four wealth quintiles (n=2,885)	2,667 (92)	218 (8)	
With a limiting long-standing illness (n=924)	760 (82)	164 (18)	$X^2(1) = 123$, p<0.001
Without a limiting long-standing illness (n=2,395)	2,263 (95)	132 (6)	

e) Are answers to the direct question about loneliness in general and scores on the three-item UCLA Loneliness Scale correlated?[14]

To compare the findings based on the three-item UCLA Loneliness Scale and those from the direct question about loneliness in general was due to correlation, I looked for evidence of an association. Scores on the three-item questionnaire were associated with answers to the direct self-completion question ($F(12, 1.4e+05) = 1{,}961$, $p<0.001$, see Table 6.27). Where respondents scored 3 on the three-item UCLA Loneliness Scale, this was associated with reporting feeling hardly lonely to the direct question in 95% of cases. In 85% of the cases where people scored 9 on the UCLA scale, they reported feeling lonely often when asked directly.

In 31% of instances with a score of 8 and in 45% of cases with a score of 7 – i.e. relatively high scores – respondents reported that they felt lonely only sometimes when asked directly. This could be an indication of participants' reluctance to admit to feelings of loneliness, as could the fact that 30% of those who replied feeling hardly lonely to the direct question scored above 3 on the UCLA scale (which is the score that corresponds to answering hardly or never to all three questions that compose the scale). On the other hand, had respondents felt stigmatized, we might have expected more people who answered feeling hardly lonely or lonely some of the time when asked directly to score highly on the UCLA scale. Yet in only 0.2% of cases where people reported feeling hardly lonely did they score 8 or 9 on the UCLA scale, and in only 4% of cases where participants reported feeling sometimes lonely did they score likewise.

[14] Note that I report here on the association between the direct question relating to loneliness in general and the three-item UCLA Loneliness Scale score, but not with CESD Loneliness question. This is because the many differences between the UCLA Scale and the CESD question – timeframe, self-completion v. interview, frequency v. intensity – mean that I felt that little would be gleaned from studying the association between these two tools.

Table 6.27 Association between responses to the three-item UCLA and the self-completion question

Score on the three-item UCLA Loneliness Scale	How often do you feel lonely? Number of person-waves (%)			Result from the F test
	Hardly ever or never	Some of the time	Often	
3 (n=15,680)	14,978 (96)* (71)**	672 (4) (9)	30 (0.2) (1)	F(12, 1.4e+05) = 1,961, p<0.001
4 (n=5,116)	3,566 (70) (17)	1,502 (29) (20)	48 (1) (2)	
5 (n=3,844)	1,853 (48) (9)	1,825 (48) (24)	166 (4) (7)	
6 (n=3,718)	656 (18) (3)	2,632 (71) (35)	430 (12) (18)	
7 (n=1,454)	127 (9) (1)	648 (45) (9)	679 (47) (28)	
8 (n=735)	20 (3) (0.1)	231 (31) (3)	484 (66) (20)	
9 (n=716)	16 (2) (0.1)	92 (13) (1)	608 (85) (25)	
Total	21,216 (68) (100)	7,602 (24) (100)	2,445 (8) (100)	31,263

* Percentages on the first line correspond to row frequency.

** Percentages on the second line correspond to column frequency.

*

Answers relating to loneliness provide insight into how people's perceptions of their social relationships – or at least the perceptions which they are willing to share publicly – change over time. They tell us little, however, about the quantity of relationships a person has access to and how this fluctuates. In the following section, I look at the more objective concept of social isolation in order to explore trends in the number of relationships a person reports over time.

6.3.2.2. Social isolation

As described in the methods section of this Chapter (see section 6.2.3.2.), I used two measures to assess social isolation in ELSA: an Index of Social Contacts (ISC) and an Index of Close Relationships (ICR).

a) Index of Social Contacts (ISC)

The ISC aimed to capture the quantity of social relationships reported by each individual in ELSA. The six items composing the index are listed in Table 6.28. We see that at each wave, around a quarter (23 to 29%) of respondents lived alone. Around a third of participants spoke or wrote to friends less than once monthly and a quarter of respondents were in contact with their children less than once a month. Contact with family members other than children was slightly lower, with half of individuals not having contact with relatives at least once a month. Around two thirds of the sample were not in employment at each wave (for a more detailed breakdown of employment status, see Table 6.8) and just under a third of people did not belong to any group, club or organisation.

Overall scores on the ISC were derived for between 57% and 69% of the sample at each wave (i.e. data were missing for around a third of the sample each time). The mean score was 2.2 or 2.3 depending on the wave (reminder of the range: 0 to 6), with scores of 2 and 3 being the most common: over 50% of the sample at each wave had access to two or three types of social contact (see Table 6.29). The cross-sectional response patterns show that very few (under 1%) participants scored the highest possible score on the index – that is, did not report having access to any of the relationships covered by the index, be it family, friends or colleagues.

Table 6.28 Cross-sectional summary of the items composing the measure of the quantity of social relationships used to assess social isolation, listed separately

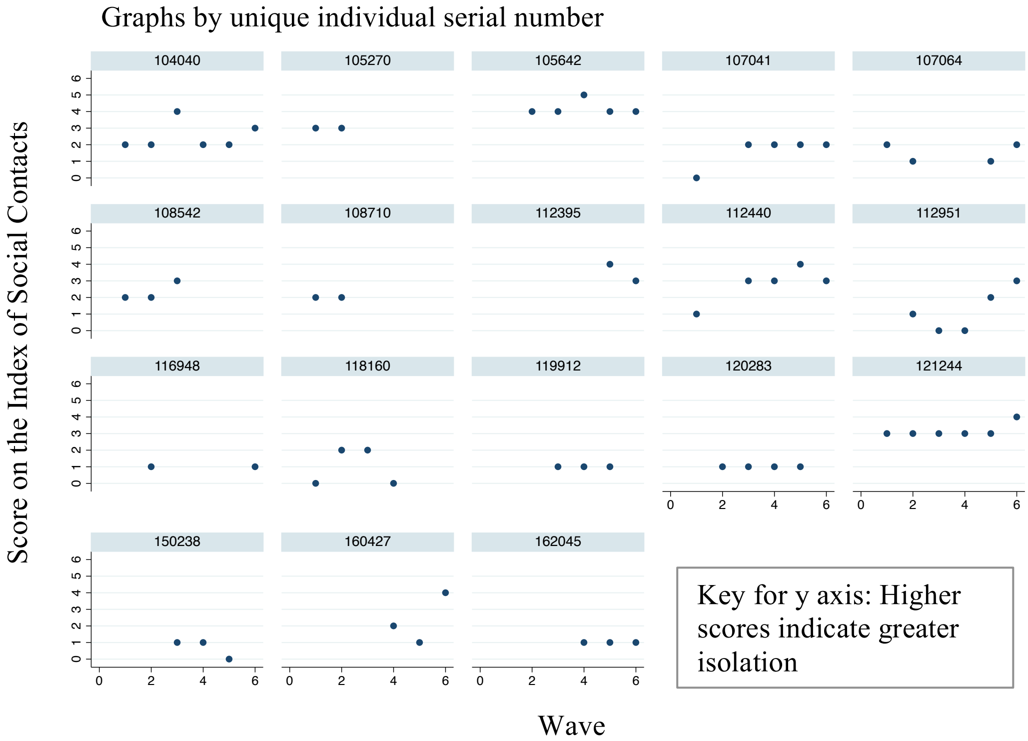
Index item	Wave 1		Wave 2		Wave 3		Wave 4		Wave 5		Wave 6	
	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%
Living arrangement	11,391		8,780		8,810		9,886		9,090		9,132	
Living with others	8,541	75	6,649	76	6,673	76	6,992	71	6,978	77	6,740	74
Living alone	2,850	25	2,131	24	2,137	24	2,894	29	2,112	23	2,392	26
Missing	0	0	0	0	0	0	0	0	0	0	0	0
Frequency of contact												
a) With children	7,890		6,503		6,254		7,375		7,145		6,852	
At least once or twice a month	5,728	73	4,887	75	4,615	74	5,504	75	5,377	75	5,041	74
Less than once or twice a month	2,162	27	1,616	25	1,639	26	1,871	25	1,768	25	1,811	26
Missing	3,501	31	2,277	26	2,556	29	2,511	25	1,945	21	2,280	25
b) With other immediate family	7,905		6,552		6,338		7,468		7,209		6,976	
At least once or twice a month	3,885	49	3,250	50	3,267	52	4,014	54	3,813	53	3,691	53
Less than once or twice a month	4,020	51	3,302	50	3,071	48	3,454	46	3,396	47	3,285	47
Missing	3,486	31	2,228	25	2,472	28	2,418	24	1,881	21	2,156	24
c) With friends	7,628		6,436		6,206		7,458		7,135		6,996	
At least once or twice a month	5,236	69	4,471	69	4,424	71	5,392	72	5,229	73	4,933	71
Less than once or twice a month	2,392	31	1,965	31	1,782	29	2,066	28	1,906	27	2,063	29
Missing	3,763	33	2,344	27	2,604	30	2,428	25	1,955	22	2,136	23
Employment status	11,336		8,754		8,787		9,876		9,056		9,135	
Currently working	3,685	33	2,564	29	3,037	35	3,309	34	2,603	29	2,641	29
Not currently working	7,651	67	6,190	71	5,750	65	6,567	66	6,453	71	6,494	71
Missing	55	0.5	26	0.3	23	0.3	10	0.1	34	0.4	34	0.4
Membership of a club, organisation or society	9,870		7,232		7,060		8,023		7,674		7,553	
Member of at least one group	6,845	69	5,379	74	5,089	72	5,720	71	5,490	72	5,417	72
Not a member	3,025	31	1,853	26	1,971	28	2,303	29	2,184	28	2,136	28
Missing	1,521	13	1,548	18	1,750	20	1,863	19	1,416	16	1,616	18

Table 6.29 Cross-sectional summary of social isolation, focusing on the quantity of social relationships

Index of Social Contacts	Wave 1W		Wave 2		Wave 3		Wave 4		Wave 5		Wave 6	
	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %
Reminder: higher score = greater isolation	6,506	Mean : 2.2 (SD: 1.3)	5,479	Mean: 2.3 (SD: 1.3)	5,315	Mean: 2.2 (SD: 1.3)	6,552	Mean: 2.3 (SD: 1.3)	6,301	Mean: 2.3 (SD: 1.3)	6,154	Mean: 2.3 (SD: 1.3)
0	476	7	355	7	417	8	513	8	473	8	392	6
1	1,395	21	1,266	23	1,196	23	1,442	22	1,401	22	1,338	22
2	1,856	29	1,592	29	1,595	30	1,939	30	1,861	30	1,826	30
3	1,540	24	1,316	24	1,249	24	1,545	24	1,511	24	1,473	24
4	917	14	701	13	632	12	817	13	777	12	811	13
5	288	4	223	4	191	4	245	4	249	4	272	4
6	34	1	26	1	35	1	51	1	29	1	42	1
Missing	4,885	43	3,301	38	3,495	38	3,334	34	2,789	31	2,978	33

To take a look at longitudinal patterns, we can first look at empirical growth plots for 18 randomly selected individuals (see Figure 6.7). These growth plots illustrate the presence of variation within individuals, as well as showing that patterns varied from one participant to another. In only four of the eighteen patterns shown below did participants report the same number of contacts across all the waves in which they took part. Two participants reported fewer contacts over time and five reported more. The remainder of the plots are indicative of fluctuations of varying degrees.

Figure 6.7 Empirical growth plots for 18 randomly selected individuals, showing scores on the measure of social relationship quantity across waves



The extent of pattern variation becomes clear when I extend my description to the 1,273 participants who provided data for all six waves. Altogether, these participants reported 757 different sequences of scores. The patterns with the highest frequencies were scoring 1, 2 or 3 in all six waves - though this was still only the case for 20, 21 and 27 participants respectively. A total of 107 individuals (8%) scored the higher scores of 5 or 6 (scores indicative of isolation) in at least one waves when participants with all six waves of data were considered. A similar proportion of participants with one or two missing waves were isolated in at least one of the waves (10% and 9% respectively).

Subgroup analyses showed that being widowed or in the lowest wealth quintile was associated with greater likelihood of isolation in at least one wave (see Table 6.30). While proportions of respondents being isolated at least once were higher among adults aged 80+ and those with a limiting long-standing illness, these differences did not reach statistical significance.

Table 6.30 Frequency of social isolation measured using the ISC, over the course of six waves – subgroup analyses

Subgroup (characteristic at wave 1)	Frequency of isolation across the six waves – number (%)		
	Never	At least once	Results of statistical test
Aged 80+ (n=16)	14 (88)	2 (13)	p associated with Fisher's exact test=0.638*
Aged <80 (n=3,214)	1,152 (92)	105 (8)	
Widowed (n=108)	84 (78)	24 (22)	$X^2(1) = 29$, $p<0.001$
Not widowed (n=1,165)	1,082 (93)	83 (7)	
Lowest wealth quintile (n=92)	71 (77)	21 (23)	$X^2(1) = 26$, $p<0.001$
Highest four wealth quintiles (n=1,164)	1,078 (93)	86 (7)	
With a limiting long-standing illness (n=301)	263 (87)	38 (13)	$X^2(1) = 9$, $p=0.003$
Without a limiting long-standing illness (n=972)	903 (93)	69(7)	

*For the first subgroup analysis, Fisher's exact test was used instead of the Pearson Chi-square test since the required cell count of 5+ for this latter test was not met.

*

The ISC tells us little, if anything, about the quality of the relationships a person has access to. The Index of Close Relationships (ICR), which I turn to in the next section, aims to explore how many close relationships ELSA participants report and how this changes over time.

b) Index of Close Relationships (ICR)

Four questions were asked in relation to the closeness of respondents' relationships, covering relationships with a) a spouse, b) children, c) other immediate family and d) friends. A third of the sample at each wave did not have a spouse with whom they had a close relationship (see Table 6.31).[15] The number of close relationships with children and other immediate family members ranged from 0 to 17 (mean: 1.3 or 1.2 depending on the wave) and 0 to 70 (mean: 2.7 to 3.2), respectively. Between a sixth and a fifth of respondents did not have children with whom they reported a close relationship and 11% to 23% did not have a family member with whom they enjoyed a close relationship. The number of reported close relationships with friends was especially wide-ranging, from 0 to 98, with means of 3.0 to 4.3 depending on the wave. Between 11 and 23% of people did not have a close relationship with a friend.

To produce a composite measure of close relationships, answers to all four questions were equally weighted in a combined score. Scores were derived for 72% to 86% of participants at each wave (i.e. there was between 14 and 28% of missing data at each wave - see Table 6.32). The distribution of scores was positively skewed (see Figure 6.8), with a mean of 7.9 to 9.2 depending on the wave. The cross-sectional response patterns show that under 1% of participants scored the lowest possible score on the index, i.e. had no close relationships with either family or friends. Taking into account people who only reported one close friend, the proportion of people who were comparatively isolated (i.e. with one or fewer close relationships) at each wave was between 2% and 3% (see Table A6.33, p.335).

Across all six waves, the mean number of social relationships was 8.4 (SD = 5.9). As was the case with social contacts, the number of close relationships reported by participants was not static over time (within SD: 3.6 - see Table A6.34, p.336). Within variation values ranged from 48 to 87, suggesting that some individuals experienced significant increases or decreases in their close relationships networks. Most individuals, however, experienced small drops or increases in their close relationship network. The empirical growth plots for 20 randomly selected individuals show that differences between two waves commonly amounted to one or two relationships gained or lost (see Figure 6.9). When we look at the most isolated of the 1,722 participants with six waves of data, we find that 98 (6%) reported having one or no close relationship at least once over the 10-year study period (proportions were similar among participants with fewer waves: 5% among those with five waves of data, 6% among those with four waves of data – see Table A6.35, p.336). Subgroup analyses did not highlight any differences according to whether people were aged over 80, widowed, less wealthy or had a limiting long-standing illness at baseline (see Table 6.36).

[15] NB: this proportion includes people without a spouse.

Table 6.31 Cross-sectional summary of the items composing the ICR

	Wave 1		Wave 2		Wave 3		Wave 4		Wave 5		Wave 6	
	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %	Number	Mean (SD) or %
Whether the participant has a close relationship with their partner	10,626		8,139		7,950		8,939		8,012		7,945	
Close relationship	6,958	65	5,209	64	4,989	63	5,690	64	5,341	67	5,236	66
Not a close relationship	3,668	35	2,930	36	2,961	37	3,249	36	2,671	33	2,709	34
Missing	765	7	641	7	860	10	947	10	1,078	12	1,224	13
Number of children with whom the respondent has a close relationship*	9,812	1.9 (1.3), 0 to 17	7,388	1.8 (1.3), 0 to 13	7,245	1.8 (1.3), 0 to 12	8,198	1.8 (1.2), 0 to 11	7,595	1.8 (1.3), 0 to 13	7,498	1.8 (1.2), 0 to 17
None	1,626	17	1,397	19	1,333	18	1,513	18	1,356	18	1,292	17
One	2,016	21	1,445	20	1,409	19	1,600	20	1,528	20	1,543	21
Two	3,728	38	2,787	38	2,798	39	3,207	39	2,958	39	2,952	39
Three	1,576	16	1,181	16	1,167	16	1,323	16	1,251	16	1,195	16
Four	549	6	368	6	359	5	374	5	341	4	369	5
Five or more	317	3	210	3	179	2	181	2	161	2	147	2
Missing	1,579	14	1,392	16	1,565	18	1,688	17	1,495	16	1,671	18
Number of family members with whom the respondent has a close relationship	9,221	2.4 (2.9), 0 to 70	6,906	2.5 (3.2), 0 to 67	6,737	2.5 (2.9), 0 to 70	7,714	2.4 (2.8), 0 to 71	7,525	2.4 (2.7), 0 to 50	7,040	2.5 (2.8), 0 to 55
None	2,080	23	1,296	11	1,232	18	1,533	20	1,433	19	1,353	19
One	2,137	23	1,664	24	1,582	23	1,812	23	1,775	24	1,583	22
Two	1,944	21	1,475	21	1,498	23	1,674	22	1,668	22	1,537	22
Three	1,092	12	846	12	858	13	972	13	950	13	872	12
Four	741	8	615	10	636	9	639	8	678	9	613	9
Five to nine	958	10	817	13	747	12	894	12	830	11	880	13
Ten or more	270	3	193	3	184	3	190	2	191	3	202	3
Missing	2,170	19	1,874	21	2,073	24	2,172	22	1,565	17	2,129	23
Number of friends with whom the respondent has a close relationship*	9,460	3.0 (3.7), 0 to 98	7,229	3.6 (4.1), 0 to98	7,003	4.3 (6.9), 0 to 90	8,010	3.4 (3.4), 0 to 90	7,385	3.5 (3.6), 0 to 97	7,438	3.4 (3.2), 0 to 50
None	2,147	23	825	11	742	11	949	12	913	12	1,000	13
One	1,046	11	843	12	750	11	907	11	793	11	808	11
Two	1,997	21	1,669	23	1,588	23	1,817	23	1,609	22	1,631	22
Three	1,246	13	1,105	15	1,078	15	1,258	16	1,197	16	1,195	16
Four	1,152	12	1,094	15	1,013	14	1,163	15	1,102	15	1,050	14
Five to nine	1,331	14	1,264	17	1,318	19	1,487	19	1,260	18	1,343	28
Ten to nineteen	456	5	362	5	343	5	364	5	342	5	360	5
Twenty or more	85	1	66	1	171	2	65	1	67	1	51	1
Missing	1,931	17	1,551	18	1,807	21	1,876	19	1,705	23	1,731	19

* Mean (SD), range

Table 6.32 Cross-sectional description of social isolation as measured using the ICR

	Wave 1		Wave 2		Wave 3		Wave 4		Wave 5		Wave 6	
	Number	**%**	**Number**	**%**	**Number**	**%**	**Number**	**%**	**Number**	**%**	**Number**	**%**
Number of close relationships (encompassing family and friends) – Mean (SD), range	8,410	7.9 (5.4), 0 to 111	6,215	8.6 (6.2), 0 to 133	6,144	9.2 (8.0), 0 to 107	7,110	8.3 (5.1), 0 to 105	6,550	8.4 (5.2), 0 to 108	6,511	8.3 (5.0), 0 to 69
None	54	1	28	0.5	33	0.5	35	0.5	37	1	35	0.5
One to five	2,842	34	1,664	27	1,553	25	1,963	28	1,762	27	1,829	28
Six to ten	3,737	44	2,965	48	2,985	49	3,427	48	3,193	49	3,098	48
Eleven to 20	1,557	19	1,367	22	1,282	21	1,526	21	1,397	21	1,391	21
Twenty-one plus	220	3	191	3	249	4	159	2	161	2	158	2
Missing	2,981	26	2,565	29	2,666	30	2,776	28	2,540	28	2,658	29

Figure 6.8 Scores on the ICR, waves 1 to 6

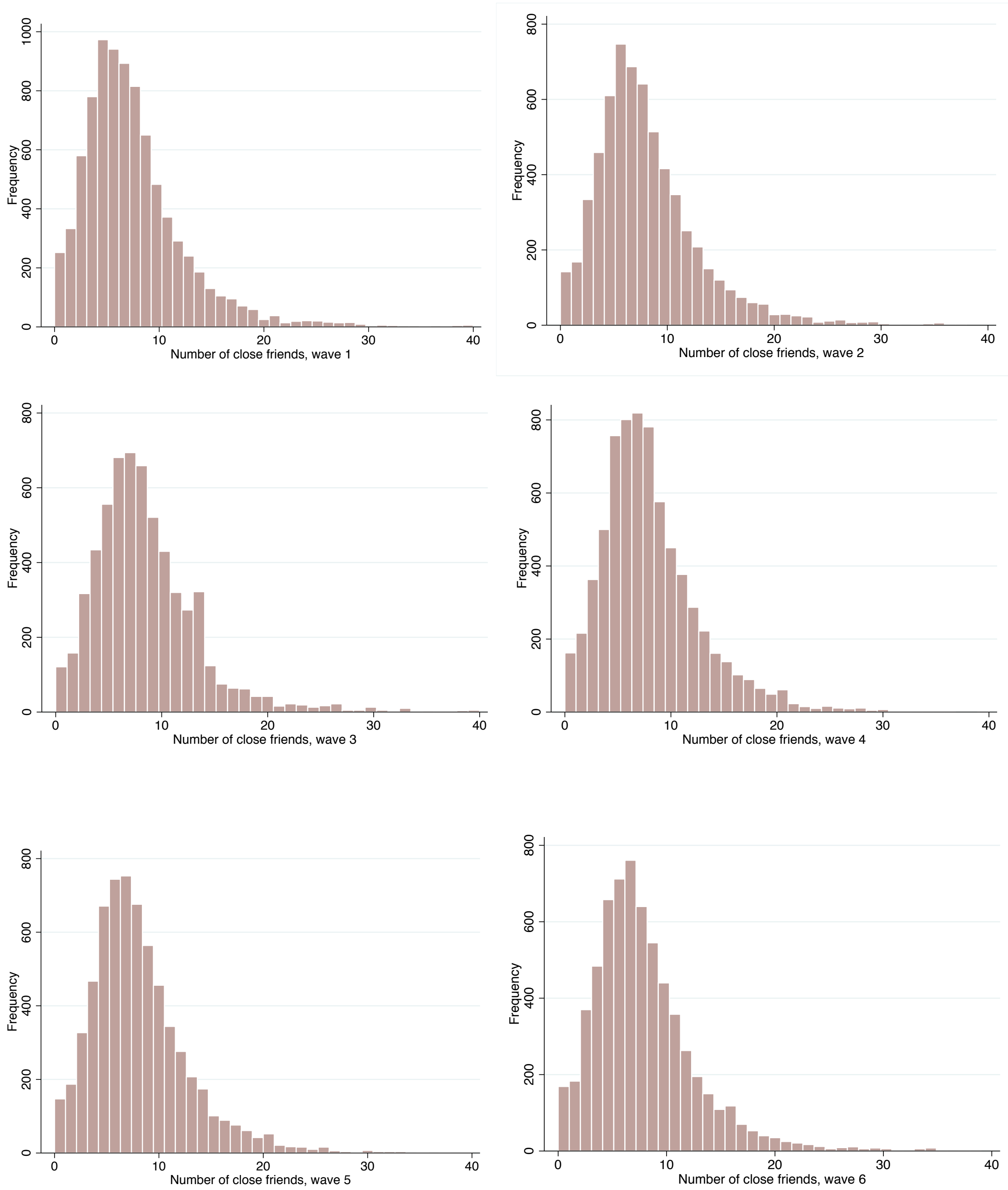


Figure 6.9 Empirical growth plots for 20 randomly selected individuals, showing the number of close relationships reported across waves 1 to 6

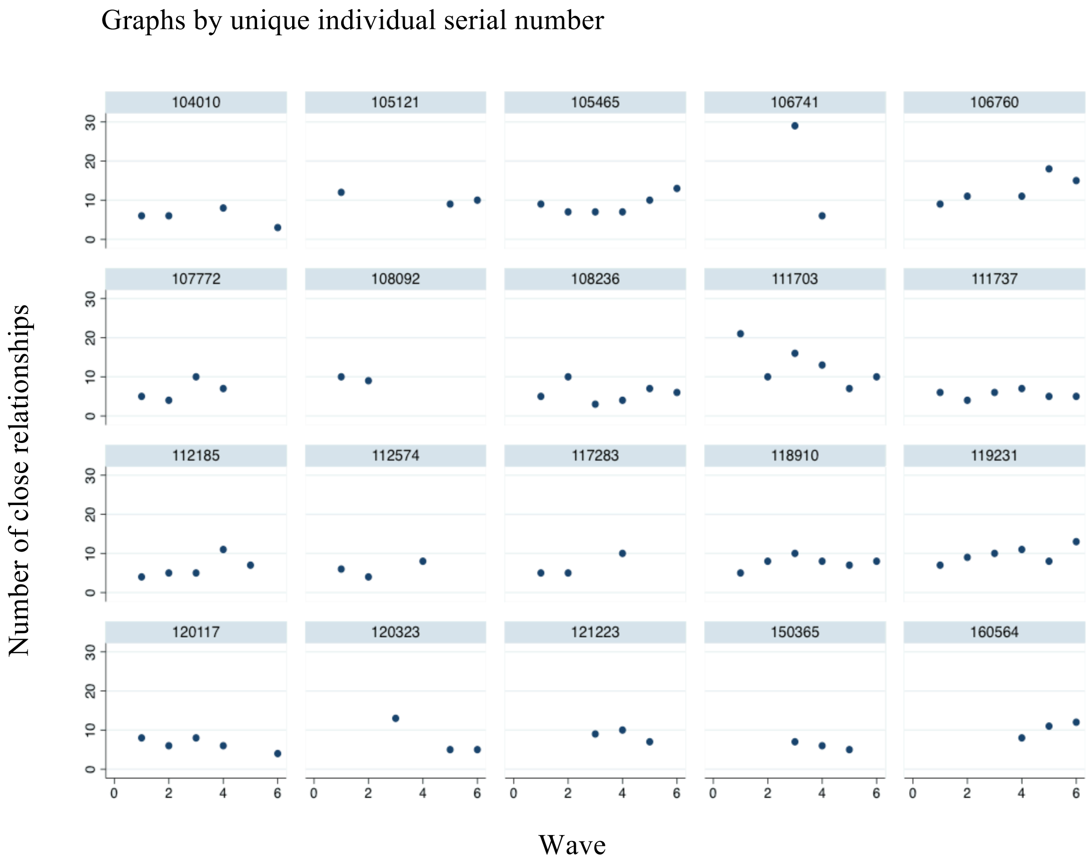


Table 6.36 Frequency of social isolation measured using the ICR, over the course of six waves – subgroup analyses

Subgroup (characteristic at wave 1)	Frequency of isolation across the six waves – number (%)		
	More than one close friend at every wave	**A maximum of one close friend at each wave**	**Results of statistical test**
Aged 80+ (n=21)	19 (91)	2 (10)	p-value associated with Fisher's exact test=0.338*
Aged <80 (n=1,701)	1,605 (94)	96 (6)	
Widowed (n=179)	165 (92)	14 (8)	$X^2(1) = 2$, p=0.194
Not widowed (n=1,543)	1,459 (95)	84 (5)	
Lowest wealth quintile (n=145)	136 (94)	9 (6)	X^2 (1) = 0.1, p=0.822
Highest four wealth quintiles (n=1,548)	1,459 (94)	89 (6)	
With a limiting long-standing illness (n=431)	403 (94)	28 (7)	X^2 (1) = 1, p=0.404
Without a limiting long-standing illness (n=1,291)	1,221 (95)	70 (5)	

*For the first subgroup analysis, Fisher's exact test was used instead of the Pearson chi-square test since the required cell count of 5+ for this latter test was not met.

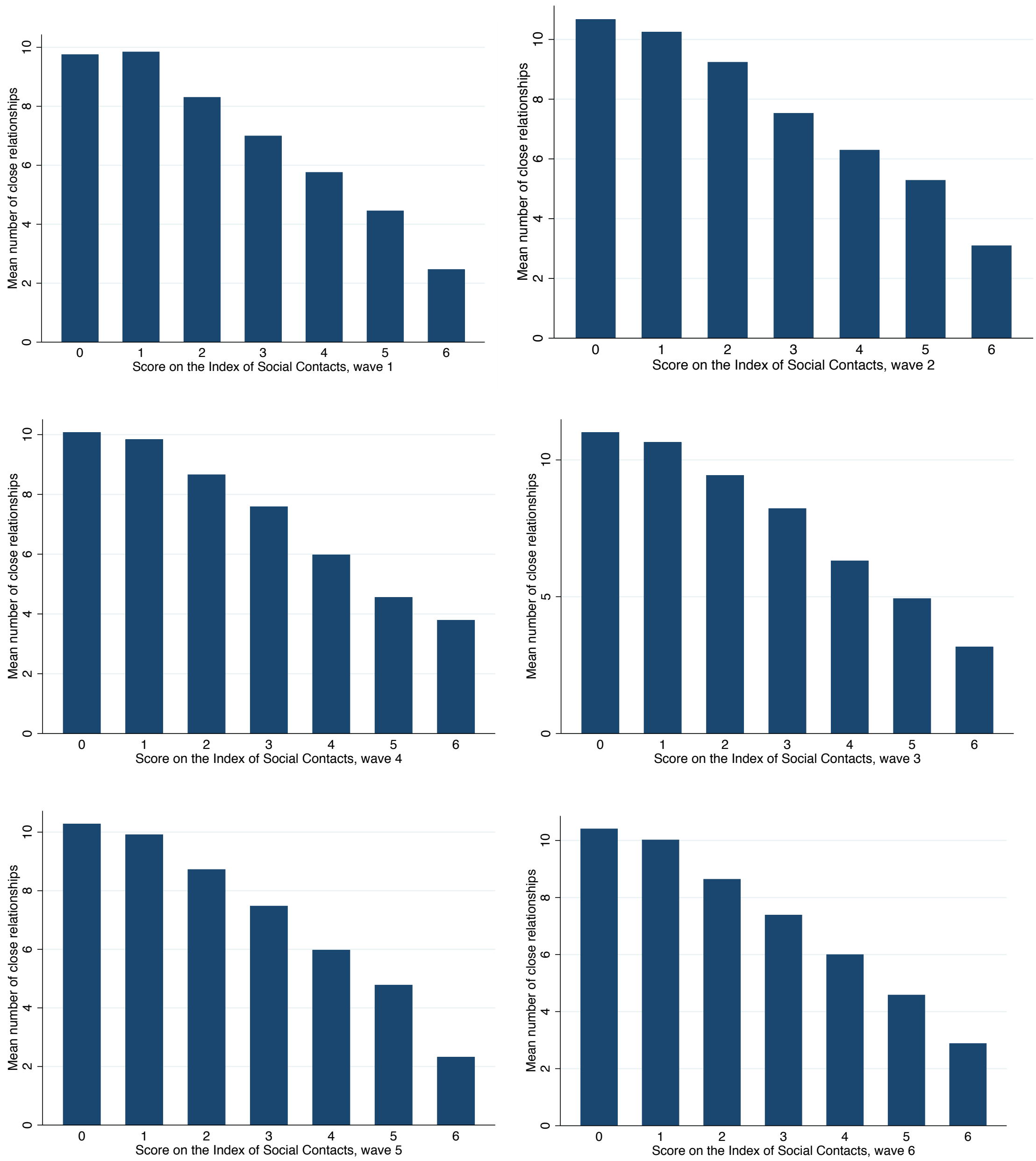
a) Social isolation – quantity versus quality

Clearly, having no partner, family or friends precludes having a close relationship with any of these ties. But do people who potentially have access to such network members necessarily have close relationships with them?

A visual assessment of the association between the two measures of social isolation – the ISC and the ICR – suggests that people with fewer social ties or contacts are more likely to report having fewer close relationships (see Figure 6.10).

Figure 6.10 Mean number of close relationships, by score on the Index of Social Contacts, waves 1 to 6

Reminder: Scores ranged from 0 to 6, with a score of 6 corresponding to being most isolated.



When I dichotomise the two variables to distinguish those who are particularly isolated – i.e. with a maximum of one type of social contact or close relationship – from those with more relationships, I find further evidence of an association between the quantity and quality of relationships: being isolated on the ICS was associated with isolation on the ICR ($F(1, 9{,}523) = 31$, $p<0.001$, see Table 6.37).

Table 6.37 Association between social isolation as measured using the ISC, and social isolation measured with the ICR

NB: The number of observations reported in this table refer to 'person-waves', i.e. each person contributes information more than once. For example, where an individual took part in 3 consecutive waves, they contributed information twice: between the first and second wave, and between the second and third.

Number of social contacts as measured on the ISC	**Number of close relationships – number (%)**		**Result of F test**
	0 or 1	**More than 1**	
None or one, i.e. score of 5 or 6 (n=508)	263 (19)	1,135 (81)	F (1, 11,895) = 990, p<0.001
More than 1 (=23,636)	569 (2)	29,664 (98)	

Whilst there is evidence of an association between the two measures of isolation, this does not mean that having few contacts precludes close relationships. Figure 6.10 shows that people who are classified as socially isolated using the ISC – i.e. scoring 5 or 6 – still report close relationships, suggesting that participants need not interact frequently with people to develop what they perceive to be close relationships; and that frequency of contact tells us little about the quality of a person's relationships. In the remaining section of this chapter, I explore this further by looking at the links between social isolation and loneliness.

6.3.2.3. Association between social isolation and loneliness

Do people with fewer social relationships report feeling lonelier? Analyses using all the waves at which the loneliness questions were asked showed that greater isolation as measured by the ISC was associated with reporting more frequent loneliness across all three measures – the direct question about loneliness in general, the direct question about loneliness in the past week, and the three-item UCLA Loneliness Scale (see Table 6.38 for F-test results relating to each measure and for frequency distributions). Feeling often lonely in general was reported in 22% of instances where people had one or no social contact, compared with 7% of instances where individuals had more than one social contact. When asked whether they had felt lonely much in the past week, in 32% of cases where people were isolated they agreed, compared with 10% among those who were less isolated.

The frequencies reported in Table 6.38 indicate that social isolation as measured by the ISC need not necessarily imply loneliness – at least publicly acknowledged loneliness. Where people reported one or no social contact, in 45% of cases they reported hardly ever or never feeling lonely in general; 68% of the time, they reported not feeling lonely much in the past week.

Turning to the relationship between the number of close relationships reported by participants and their loneliness feelings, analyses across tools confirmed that they were associated (as would be expected given the evidence of association between the ISC and loneliness, and between the ISC and the ICR; see Table 6.39). The proportion of people reporting feeling frequently lonely was higher among those with fewer close relationships (e.g. 25% versus 7% according to the direct question about loneliness in general). Having several close relationships was, however, not a guarantee that someone would be happy about their relationships: in 11% of cases where a participant reported two or more relationships, they also reported feeling frequently lonely in the past week.

Table 6.38 Social isolation as measured using the ISC, and loneliness

NB: The number of observations reported in this table refer to 'person-waves', i.e. each person contributes information as many times as the numbers of waves in which they took part.

Measure of loneliness	Isolation as measured using the ISC		Result of F test based on Chi-squared statistic
	0 or 1 contact	More than one contact	
Direct question about loneliness in general			F(1.98, 19987)= 170, p<0.001
- Hardly ever or never lonely	497 (3%)* (45%)**	16,178 (97%) (70%)	
- Lonely some of the time	359 (6%) (33%)	5,347 (94%) (23%)	
- Often lonely	244 (14%) (22%)	1,541 (86%) (7%)	
Direct question about loneliness in the past week			F(1, 12605) = 493, p<0.001
- Not often lonely in the past week	1,144 (4%) (68%)	30,935 (96%) (90%)	
- Often felt lonely in the past week	533 (13%) (32%)	3,506 (87%) (10%)	
Three-item UCLA Loneliness Scale score			F(6, 64310)= 121, p<0.001
3	385 (3%) (29%)	14,798 (97%) (53%)	
4	181 (4%) (13%)	4,657 (96%) (17%)	
5	175 (5%) (13%)	3,404 (95%) (12%)	
6	238 (7%) (18%)	3,112 (93%) (11%)	
7	131 (10%) (10%)	1,174 (90%) (4%)	
8	94 (16%) (7%)	512 (84%) (2%)	
9	140 (22%) (10%)	504 (78%) (2%)	

* Percentages on the first line correspond to row frequency.

** Percentages on the second line correspond to column frequency for each question.

Table 6.39 Social isolation as measured using the ICR, and loneliness

NB: The number of observations reported in this table refer to 'person-waves', i.e. each person contributes information as many times as the numbers of waves in which they took part.

Measure of loneliness	**Isolation as measured using the ICR**		Result of F test based on Chi-squared statistic
	0 or 1 close relationship	**More than one close relationship**	
Direct loneliness question, in general			
- Hardly ever or never lonely	275 (2%)* (47%)**	17,632 (98%) (69%)	F(2, 21155)= 101, p<0.001
- Lonely some of the time	167 (3%) (28%)	6,077 (97%) (24%)	
- Often lonely	149 (8%) (25%)	1,815 (92%) (7%)	
Direct loneliness question, past week			
- Not often lonely in the past week	696 (2%) (71%)	35,353 (98%) (89%)	F(1, 21155)= 101, p<0.001
- Often felt lonely in the past week	289 (6%) (29%)	4,439 (99%) (11%)	
three-item UCLA Loneliness Scale score			
3	200 (1%) (28%)	16,285 (99%) (52%)	F(6, 67633)=88, p<0.001
4	96 (2%) (13%)	5,147 (98%) (16%)	
5	102 (3%) (14%)	3,794 (97%) (12%)	
6	119 (3%) (16%)	3,584 (97%) (11%)	
7	60 (4%) (8%)	1,341 (96%) (4%)	
8	60 (9%) (8%)	640 (91%) (2%)	
9	90 (13%) (12%)	593 (87%) (2%)	

* Percentages on the first line correspond to row frequency.

** Percentages on the second line correspond to column frequency for each question.

6.4. Discussion

The findings across my analyses are summarised below and discussed in relation to other studies. I consider the strengths and limitations of my investigative approach, and what my findings imply for future research, policy and practice.

6.4.1. Summary of main findings

Four main findings emerged from the descriptive analyses presented in this chapter. First, at the population level, the prevalence of loneliness and social isolation over time was stable. In each wave, 8% of participants reported feeling often lonely in general, and between 12% and 14% of respondents reported feeling lonely much of the time in the past week; between 4% and 5% of the sample had one or fewer social contacts, and between 2% and 3% reported one or no close relationship.

Had loneliness and social isolation been stable experiences, their longitudinal prevalence would not have differed from the cross-sectional figures – since the same people would have been categorised as lonely or isolated at each time point. This was not the case, with longitudinal data showing that loneliness and isolation were more common than cross-sectional figures might have led us to think: 14% of individuals reported feeling often lonely in one or more of the four waves for which data were available (waves 3 to 6); and 30% of participants reported feeling frequently lonely in the past week at one or more of the six waves (waves 1 to 6). Of those who took part in all six waves, 8% presented scores indicative of isolation (scores of 5 or 6) in at least one wave; and 6% of respondents reported one or no close relationship. The stability of prevalence figures at each wave (even when new intakes at waves 3,4 and 6 were ignored – see section 6.3.2.1.a) suggests that individual changes in loneliness were not necessarily attributable to aging.

The third key finding from my analyses was that there was considerable heterogeneity in the longitudinal patterns of loneliness and social isolation reported by ELSA participants. Preliminary analyses using group-based trajectory modelling showed that patterns could not easily be simplified into distinct trajectories such as ‘increasing loneliness’, or ‘decreasing loneliness’. While subgroup analyses showed that the frequency of loneliness and/or social isolation was greater among those aged over 80, widowed, less wealthy or limited by a long-standing illness, they did not highlight any other shared aspects such as similar levels of social relationships or similar trends over time (see for example Table A6.14, p.328). Importantly, my descriptive analyses did not adjust for possible confounders and nor did they take into account changes in circumstances such as bereavement over time; we cannot therefore infer from them that being aged over 80, widowed, less wealthy or reporting a limiting long-standing illness was causally related to increased loneliness or social isolation.

Fourthly, I found evidence that loneliness and social isolation were associated but did not systematically coincide. The proportion of people reporting feeling often lonely was higher among those who reported having few social contacts or close relationships (e.g. feeling often lonely in general was reported in 22% of instances where people had one or no social contact, compared with 7% of instances where individuals had more than one social contact – see section 6.3.2.3). Whilst associated, these were clearly different experiences: having access to social contacts or close relationships did not preclude loneliness, and vice versa.

The purpose of my study was not to assess whether there was agreement between the different measures of loneliness and social isolation; but it is interesting to note that the overall 'picture' provided by the different measures of loneliness and social isolation was similar, in terms of their stability at the population level across waves and their fluctuation within individuals over time.

6.4.2. My findings in context

The analyses presented in this chapter were the first to explore longitudinal patterns of both loneliness and social isolation over more than two waves. Previously, research based on two time-points had highlighted that feelings about social relationships were not static (Tijhuis et al., 1999; Jylha, 2004; Victor and Bowling, 2012). Such analyses were necessarily limited by the number of data points, so that they could only identify an increase, decrease or stability between the two measures available to investigators. Using a maximum of six time-points, my analyses identified that answers to loneliness and social isolation changed significantly over time; and that there was great heterogeneity in longitudinal patterns across participants.

The changeability of loneliness and social isolation within individuals suggests that these experiences may be more related to events (e.g. a change in a person's situation or circumstances) than traits (relatively permanent individual characteristics – see Weiss, 1973). From studies that have looked at risk factors for loneliness and social isolation, we know that a number of situational factors can affect how social relationships and perceptions about these change over time. Circumstances which may lead to an increase in loneliness and social isolation include widowhood, moving away from established social networks and/or a decline in health. The loss of a spouse has consistently been linked to heightened loneliness and social isolation, across different cultures and contexts (Lichtenstein et al., 1996; Samuelsson and Hagberg, 1998; Van Baarsen et al., 1999). Life experiences such as migration, retirement, and entry into care have all been associated with a decrease in the quality and/or quantity of a person's social relationships (Tijhuis et al., 1999; Wu and Penning, 2015; McWhirter, 1990). People who experience a decline in functional capacity or a decline in self-reported health are more likely to experience an increase in loneliness, while new diagnoses of chronic diseases such as cancer can lead to a reduction in social activity (Dykstra et al., 2005; Andreassen et al., 2007). Conversely, certain situational changes can foster social interaction and lead to a decrease in loneliness feelings. The birth of grandchildren, for example, can bring increased contact with children in later life and research indicates that older adults, even in advanced ages, continue to acquire new acquaintances and rekindle weakened ties (Lang, 2000; Bowling et al., 1995; van Tilburg, 1998). While poor health may reduce opportunities for keeping up certain relationships, increased need for help might mobilise helpers and increase one's levels of received support (Miller and McFall, 1991; Stoller and Pugliesi, 1988).

Because I did not seek to explain changes in social relationships in my analyses, but focused on describing patterns instead, I cannot confirm whether the observed heterogeneity across individuals was a consequence of them experiencing changes in their circumstances at different times. What my analyses did indicate was that there was an association between loneliness and social isolation, i.e. that objective characteristics of a person's social network were linked to people's feelings about their relationships. Using a different measure of social relationships, Shankar and Steptoe also noted this association, as well as the fact that many people experienced the one independently from the other (Shankar et al., 2011; Steptoe et al., 2013b). Shankar and Steptoe had only looked at one time point; across multiple waves, my analyses confirmed that loneliness and social isolation were not systematically experienced simultaneously, with participants reporting that they never felt lonely in 45% of cases where they were classed as socially isolated using the ISC (see section 6.3.2.3.).

6.4.3. Strengths and limitations

One of the main strengths of my analyses was the use of data from ELSA, a large representative population cohort. Thanks to the wide range of variables collected in ELSA, I was able to study loneliness and social isolation simultaneously, and to explore potential subgroup differences. Questions about contact with family, friends and the wider community were combined to create a comprehensive measure of social isolation, the ISC. In a field where there is very limited consensus about how best to assess perceptions about relationships and their more objective characteristics, ELSA offered the chance to conduct analyses using several measures, and to compare them.

Until now, studies looking at loneliness or social isolation over time had only relied on two waves of data. The availability of six waves in ELSA meant that I could trace changes over multiple time-points and gain greater insight into the variability of social relationships over time. By comparison with other studies, where the period between two time-points could reach 20 years (Patterson and Veenstra, 2010; Wenger and Burholt, 2004) the fact that ELSA collected data every two years made it a particularly well-suited dataset for studying variation over a comparatively short period of time. Still, it is important to recognize that ELSA could only provide 'snapshots' of loneliness and social isolation, rather than a comprehensive picture of feelings and social interaction over the ten-year study period. Where people gave the same answer in two consecutive waves, it could not be assumed that this was a reflection of stability across the two-year period separating the two time-points.

Different answers to questions about loneliness and isolation may reflect changes in perceptions and/or circumstances; they may also be the result of measurement error (Viswanathan et al., 2013). In common with other measures of social isolation, the validity and reliability of the two indices I used – the ISC and the ICR – is unknown (Shankar et al., 2011; Berkman, 1977; Steptoe et al., 2013b). The extent to which reported contact with others reflects actual contact is unclear and likewise reports about the numbers of close relationships may not accurately reflect people's social networks. Even though the questions used to create the two indices were not labelled as belonging to one self-contained index but rather were taken from different sections of the overall questionnaire, the likelihood of people publicly reporting more social contact and/or closer relationships than they effectively have cannot be ignored (Victor et al., 2005a). As well as validity and reliability issues, the interpretability of a measure such as the three-item UCLA Loneliness Scale is problematic: the wording of each item, coupled with the scoring system, means that higher scores cannot automatically be interpreted as evidence of greater loneliness.

The addition of new members at waves 3, 4 and 6 of ELSA ensured that at each time point, the sample was representative of the target population, i.e. people aged 50 and over living in England. People who only contributed one wave of data were excluded from my longitudinal analyses. Given that individuals who dropped out of the study were more likely to be from lower socio-economic backgrounds, older and in less good health (see Table 6.2), my findings may not be generalizable to more vulnerable groups of the population. The subgroup analyses I performed, to explore whether there were differences according to whether people were aged over 80, widowed, less wealthy or had a limiting long-standing illness, were primarily intended as a means of identifying people with potentially similar social relationship patterns. Relying on baseline information, they were not intended to explain changes over time (which would have required treating them as time-varying variables), and hence can tell us little about how changes in socio-demographic and health-related circumstances affect social relationships.

6.4.4. Implications

The implications of my results for policy, practice and research are considered below.

6.4.4.1. Implications for policy and practice

One of the major challenges for policy-makers, practitioners and service providers is identifying people with chronic loneliness or who are socially isolated, and estimating population prevalence. The figures commonly referred to in policy related documents and in reports from third sector organisations have, up until now, relied on cross-sectional data (Department of Health, 2012; Campaign to End Loneliness, 2011b). Screening and mapping initiatives such as Age UK's loneliness heat maps (Age UK, 2016) use information collected at one point in time only. What the longitudinal analyses presented in this chapter suggest is that this may lead to underestimating the extent of loneliness and social isolation: while only eight per cent of people aged over 50 in England reported feeling often lonely at one time point when asked directly, this rose to between 12% and 14% when people were asked about their feelings over a six year period. For a range of reasons including changes in family circumstances, employment and health, people who may not have been identified as lonely or isolated on one occasion may experience this subsequently. From the perspective of primary prevention – i.e. preventing their occurrence – it is important that efforts to estimate the extent of loneliness and social isolation take into account the changeability of social circumstances over time.

The fluctuations identified in my analyses suggest that, rather than traits, loneliness and social isolation may be more akin to states. From the perspective of intervention design, this implies that targeting the changing context within which these situations are experienced could be more appropriate than focusing on more stable characteristics of the individual. The finding that frequent loneliness or social isolation rarely persisted over a long period of time also bears implications for the content and evaluation of interventions. It may be, for example, that interventions could draw on the solutions which individuals themselves have used to overcome their loneliness. From the ELSA data, it is not possible to say whether people who reported more social contact or less frequent loneliness from one wave to another had engaged in any formal intervention to strengthen their relationships in the interval. When assessing interventions, it will be important to take into account the possibility that factors outside the intervention might have played a significant role in modifying objective, as well as subjective, aspects of social relationships.

6.4.4.2. Implications for research

My analyses point to the fluctuation of loneliness and social isolation over time. While we know that certain factors such as the loss of a spouse, migration or moving into a care home can be risk factors for increasing loneliness and/or social isolation, studies to date have only been able to explore associations based on a maximum of two time points. ELSA, and similar studies in other countries such as the HRS in the US (Sonnega et al., 2014) or TILDA in Ireland (Kearney et al., 2011), offer the opportunity to explore changes over time in more depth, and to consider the implications of events such as widowhood or new health diagnosis for social relationships. The analyses presented here were primarily descriptive. Future studies seeking to predict and explain the variability I found will help to identify factors associated with changes in relationships and potential opportunities for intervention. As the number of waves in ELSA and other studies increases, it will be possible to study patterns of relationships over longer periods of time, so as to build a more comprehensive picture of how social relationships develop in later life.

Complementing analyses of older cohorts with studies of social relationships across the life course would help to identify important factors earlier in life and potentially prevent the occurrence of chronic loneliness or isolation at later ages. Given the limitations of large quantitative studies – e.g. reliance on data collection every two years in the case of ELSA –, qualitative work will be needed to better understand the dynamics and context behind changes in loneliness and social isolation. Diaries, daily updates via mobile applications or interviews are all methods which could help us to gain deeper insight into experiences over time and to contextualise them. They could in particular help to identify triggering events or situations leading to changes in loneliness and social isolation.

Taking into account the ‘instability’ of loneliness and social isolation is important for studying factors that may precipitate these experiences. It is also crucial for understanding the link between social relationships and health. Epidemiological studies have overwhelmingly relied on the measurement of social relationships at one point in time only. Only one of the primary studies reviewed in Chapter 5, for example, measured loneliness or isolation more than once. The findings from this present chapter challenge the pertinence of treating these variables as static: people’s social relationships and perceptions change over time. By categorizing people as lonely or isolated at baseline and not taking into account subsequent developments, we may be ignoring the effects of changes in social relationships. Nor does treating social relationships as time-invariant allow us to study the potentially time-dependent effect of loneliness and social isolation: is it the case, for example, that feeling socially isolated over a longer period of time is associated with a greater likelihood of ill health?

The awareness that no epidemiological studies to date had treated loneliness and social isolation as time-varying variables is what prompted me to address this, using ELSA data. Having established that there was great heterogeneity in participants' answers to questions about social relationships over time, and that, whilst associated, loneliness and social isolation were experienced independently by many, I set out to study both concepts as time-varying variables in survival analyses of non-fatal CVD incidence. The details of how I proceeded and what I found are presented in Chapter 7.

Chapter 7. Loneliness, social isolation and probability of non-fatal cardiovascular disease in the English Longitudinal Study of Ageing

Chapter summary: Epidemiological studies to date have not taken into account the fact that loneliness and social isolation vary over time, and that changes might influence health outcomes (7.1). In this chapter, I adopt a dynamic approach to investigate the cumulative effects over time of loneliness and social isolation on incident non-fatal cardiovascular disease, using data from the English Longitudinal Study of Ageing (7.2). The results of discrete-time survival models adjusting for established risk factors are presented separately for total non-fatal cardiovascular disease incidence, heart disease and stroke (7.3). The chapter concludes with implications for practice, policy and future research (7.4).

7.1. Introduction

The first section of this chapter highlights the gaps in our knowledge of the relationship between loneliness, social isolation and health over time and sets out how I went about addressing these.

7.1.1. Loneliness, social isolation and health over time

One of the key messages from the previous chapter was that answers to questions about loneliness and social isolation change over time. Yet in the systematic review reported in Chapter 5, we saw that only one of the twenty-three studies on incident coronary heart disease (CHD) and stroke measured social relationships at more than one point in time (Thurston and Kubzansky, 2009). Reviews of the links between social relationships and mortality, dementia and self-rated health have similarly highlighted the near absence of studies in which relationships are measured more than once (Holt-Lunstad et al., 2015; Craigs et al., 2014; Kuiper et al., 2015). Because epidemiological studies have predominantly considered loneliness and social isolation as static, we do not know what the implications of changes in answers to questions about social relationships are for health outcomes. Without serial measurements we cannot gauge the proportion of people who may not be classed as lonely or socially isolated at baseline, but who might go onto experiencing these later on – and potentially be at risk of subsequently facing ill health. Conversely, we do not know whether improvements in social relationships have a beneficial influence on health outcomes.

A further limitation of the epidemiological literature is that loneliness and social isolation have often been investigated separately, for example. None of the studies reviewed in Chapter 5 considered both loneliness and social isolation. It is consequently unclear whether the two experiences are independently associated with morbidity, or whether their effects are synergistic (Holt-Lunstad et al., 2015).

A third unanswered question is whether particular groups of people may be at heightened risk of adverse health outcomes following experiences of loneliness or social isolation. A number of factors have been linked to weaker social relationships, such as older age, gender, socio-economic status and prior health status (Pinquart and Sorensen, 2003; Beach and Bamford, 2016; Shankar et al., 2011; Steptoe et al., 2013b). We do not know whether these factors also act as modifiers of the association between social relationships and disease. In the meta-analyses reported in Chapter 5, due to lack of data in the primary studies reviewed, it was not possible to explore potentially modifying effects beyond gender differences. While subgroup analyses produced no evidence that men or women were more likely to be diagnosed with disease following loneliness or social isolation, the strength of this finding is limited by the heterogeneity across studies stemming from the use of different measures to assess loneliness or social isolation and the inclusion or omission of potential confounders in statistical models.

The three gaps in our knowledge summarized above – i.e. whether longitudinal patterns of loneliness and social isolation influence health, whether subjective and objective characteristics of relationships interact in their effects on health and whether certain people may be more likely to develop disease following loneliness or isolation – limit the theoretical basis for designing interventions. Identifying whether certain population subgroups might be at greater risk of adverse health outcomes linked to loneliness and/or social isolation would help to target secondary interventions – i.e. interventions aiming to address deficiencies in social relationships and limit their health implications – to those who might need them most. Analyses that take into account the multi-dimensional and dynamic nature of social relationships are needed to inform the timing of interventions. It may be that one dimension of social relationships is more important than the other in relation to health, which would warrant tailoring interventions to specifically address either perceptions of relationships, or more objective characteristics. If social relationships only have implications for health when they are experienced repeatedly, then interventions will need to consider factors underlying chronic experiences of loneliness and/or social isolation. Conversely, should one instance of severe loneliness or isolation suffice to affect individuals' health and wellbeing, this would be a strong indication of the need for primary prevention strategies.

7.1.2. Study aims and objectives

I set out to investigate whether loneliness and social isolation, treated as time-varying variables, were associated with the probability of incident non-fatal cardiovascular disease (CVD). My objectives were:

- To assess whether loneliness and social isolation were associated with non-fatal CVD, independently of each other and of potential confounders and other CVD risk factors;

- To compare results from survival analyses that treated loneliness and social isolation as static with the results of analyses where they were studied as time-varying variables;

- To identify whether certain factors – specifically, age, gender, wealth and CVD risk profile – moderated the influence of social relationships on CVD incidence.

7.2. Methods

In this section, I detail the methods I used in pursuit of the research objectives listed above, including how I selected the study sample and variables for analyses and which statistical models I applied. As in Chapter 6, tables relating to exploratory or sensitivity analyses are labelled with an 'A' and included in the appendices, to limit interruption in the narrative flow (see Appendix 7.1).

7.2.1. Participants

Participants were selected from the same source as for analyses in Chapter 6, i.e. ELSA (Steptoe et al., 2013a). Details of how ELSA was conducted, including the sampling frame, data collection and response rates to interviews and self-completion questionnaires are provided in Chapter 6 (see section 6.2.1.1). Here I focus on the aspects of particular relevance for my analyses of loneliness, social isolation and incident CVD, including how data on traditional risk factors were collected during a nurse visit carried out at wave 2, and how I selected my analytical sample.

7.2.1.1. ELSA

For the analyses presented in the previous chapter, I relied on data collected during the main interview and in the self-completion questionnaire distributed at each wave. Here, in addition to these two sources, I also used information from the nurse visit conducted in wave 2 of ELSA.

To be eligible for this visit, core members needed to have been interviewed in person (i.e. people interviewed by proxy due to poor health or physical or cognitive disability were not included) (Bridges et al., 2015). During the visit, a trained nurse conducted a series of physical and biomedical performance measures, including blood pressure, grip strength, blood samples, standing, weight, waste and hip measurement, lung function, balance, leg raises, chair rises and hair samples to measure levels of cortisol (Scholes et al., 2008).

The number of nurse visits conducted across the study is presented in Table 7.1, alongside the numbers of interviews and questionnaires completed in that wave. In wave 2, people who took part in a nurse visit represented 88% of core members interviewed in person. Adults who did not participate in this visit were older, less educated and non-white (Bridges et al., 2015).

Table 7.1 Number of main interviews, proxy interviews, self-completion questionnaires and nurse visits at each wave

NB: Numbers include participants who joined the study after wave 1, hence why it is possible for the number of core members in wave 4 to exceed the number of participants in wave 3, and for the number of participants in wave 6 to be higher than in wave5.

Data were obtained from the harmonized dataset available through the UK Data service, and from the technical report for ELSA wave 6 (Bridges et al., 2015).

Wave	**Number of proxy interviews**	**Number of main in-person interviews**	**Number of self-completion questionnaires (% of people who took part in person in the main interviews)**	**Number of nurse visits (% of people who took part in person in the main interviews)**	**Number of people who took part in the main interview, questionnaire and nurse visit (% of people who took part in person in the main interviews)**
Wave 1	158	11,233	10,331 (92)	NA*	NA
Wave 2	92	8,688	7,803 (90)	7,666 (88)	7,029 (81)
Wave 3	167	8,643	7,498 (87)	NA	NA
Wave 4	294	9,592	8,331 (87)	8,213 (86)	7,360 (77)
Wave 5	349	8,741	8,107 (93)	NA	NA
Wave 6	383	8,786	7,903 (90)	7,731 (88)	NC**

*NA: Not applicable. Nurse visits did not take place in waves 1, 3 and 5.
**NC: not calculated. Because the self-completion variable was not available for wave 6 (only the overall number of completed questionnaires was reported in the technical report for wave 6), it was not possible to calculate the number of people who took part in all three data collection procedures – interview, questionnaire and nurse visit – at wave 6.

7.2.1.2. Selection of the analytical sample

I chose wave 2 (data collected in 2004-2005) as the baseline wave since this was the first wave where core participants took part in a nurse visit during which biomarkers pertinent to CVD risk – blood pressure and cholesterol - were measured. All subsequent waves were included in my study, with the latest available wave at the time of analyses being wave 6.

I applied the following eligibility criteria to select the analytical sample: individuals had to have taken part in the main interview, questionnaire and nursing visit at wave 2 of ELSA, and not have reported a diagnosis of heart disease or stroke prior to this wave. The latter criterion was used because I wished to investigate first events, i.e. new incidents of CVD among people who had never been diagnosed with a heart problem or stroke prior to the beginning of the study. In addition to those who were interviewed by proxy at wave 2, I also excluded people who had been interviewed by proxy in waves 3 to 6, since proxy interviews did not include information about individuals' social relationships.

7.2.2. Data retrieval and cleaning

To the dataset created for the analyses reported in Chapter 6 (see section 6.2.2. for a description of how this dataset was generated), I added variables of relevance to the study of CVD incidence identified a priori from the data dictionaries available from the UK Data Service website (web address: https://discover.ukdataservice.ac.uk/series/?sn=200011; see study protocol in Appendix 6.1). These variables were: new diagnosis of heart problem or stroke at each wave, high-density lipoprotein (HDL) and total cholesterol, systolic blood pressure, treatment for hypertension, smoking status, new diabetes diagnosis, use of diabetes medication and haemoglobin A1C level. Each variable is described below in section 7.2.3. All variables were available for download from the Economic and Social Data Service website, specifically from the core data files for ELSA waves 2 to 6, the nurse visit files, and the longitudinal harmonised file (version C – see Phillips at al., 2014) .

Variables were extracted using Stata/SE 14.2 (StataCorp, 2011), and incorporated within the wide format file (i.e. a file where each participant is listed as a separate observation) created for the Chapter 6 analyses. After data had been double-checked and cleaned (see section 6.2.2 for details), a long file version of the dataset was created (i.e. a file where each year of data is listed as a separate observation), to enable longitudinal analyses.

7.2.3. Variables

The variables retrieved for this study were intended to be used either as independent, dependent or covariate variables in my analyses.

7.2.3.1. Independent variables: loneliness and social isolation, waves 2 to 6

a) Loneliness in waves 2 to 6

Two of the three instruments used in ELSA to capture loneliness feelings were used in this study: the direct single-item question about frequency of loneliness in the past week, and the three-item UCLA Loneliness Scale (see section 6.2.3.1. for a detailed description of each measure). Because the third measure about loneliness feelings in general was only included from wave 3 onwards (i.e. not from wave 2, which was the baseline for my study), it was not used here.

I chose the direct, single-item question for my main analyses because I was specifically interested in the frequency, rather than the intensity, of loneliness. To check whether findings were dependent on the tool used to assess loneliness, the three-item UCLA Loneliness Scale was used in sensitivity analyses. I initially contemplated entering the UCLA score as a categorical variable in my sensitivity analyses, since this instrument does not offer a clear cut-off point for distinguishing between frequently lonely and less frequently lonely participants and nor is it a linear scale (see section 6.2.3.1 above for a more detailed discussion of this tool). After recognising that opting for a seven category variable would still mean choosing an arbitrary reference category, I decided to resort to dichotomise the instrument using a score of 6 on the UCLA Scale as the cut-off to distinguish between more and less lonely participants, in line with previous studies (Shankar et al., 2011; Steptoe et al., 2013b). As highlighted in Chapter 6, the interpretability of this cut-off is unclear, since the scale covers both intensity and chronicity of feelings and a score of six does not necessarily indicate greater frequency of negative feelings. Sensitivity analyses were therefore undertaken in the knowledge that any potential discrepancies with the results based on the direct single-item question would need to be interpreted with caution. A reminder of the contents and psychometric properties of each tool is provided in Table 7.2.

Table 7.2 Contents and psychometric properties of the direct single question about loneliness in the past week, and the three-item UCLA Loneliness Scale

Measure of loneliness	Question(s)	Scoring system	Psychometric properties	When and where it was included in ELSA
Direct single-item question about loneliness in the past week (part of the 20-item Centre for Epidemiologic Studies Depression Scale (Radloff, 1977)	Participants were asked whether they would agree or disagree with the following statement: 'Much of the time during the past week, you felt lonely.'	Agreeing was scored as 1, disagreeing was scored as 0.	Some studies have found a correlation between single item approaches and scores on multi-item loneliness scales (de Jong Gierveld and van Tilburg, 1999; Russell et al., 1978; Di Tommaso and Spinner, 1993), which would suggest convergent validity. No data were found re. reliability.	From wave 1 onwards, this question was part of the main interview.
The three-item UCLA Loneliness Scale (Hughes et al., 2004)	The scale includes three questions: 1) How often do you feel you lack companionship? 2) How often do you feel left out? 3) How often do you feel isolated from others?	For each question, respondents are offered the following options: Hardly ever or never (score of 1); some of the time (score of 2); or often (score of 3). Answers are summed to provide a total loneliness score ranging from 3 to 9, with a higher score suggesting greater levels of loneliness.	Using data from the US Health and Retirement Study (HRS),and the Chicago Health, Aging, and Social Relations Study, Hughes reported evidence of: satisfactory reliability (alpha coefficient of reliability = 0.72); discriminant validity (loneliness score was associated with greater likelihood of depressive symptoms and higher scores on scale of perceived stress); and convergent validity (correlation between the self-labelling loneliness statement in the CESD depression index and the Three-Item Loneliness Scale was much higher than the correlation between any	From wave 2 onwards, the scale was included as part of the self-completion questionnaire.

b) Social isolation in waves 2 to 6

To assess individuals' level of social contact, I used the Index of Social Contacts (ISC) developed for the descriptive analyses presented in Chapter 6 (see section 6.2.3.2). The six items composing the index and the scoring system are summarised in Table 7.3. Overall scores range from 0 to 6, with higher scores indicating greater social isolation.

Table 7.3 Scoring criteria for the Index of Social Contacts (ISC)

Item	Criteria for scoring
Household size	Living alone was scored as 1; scored 0 otherwise.
Frequency of contact with children	A score of 1 was allocated where frequency of contact in person, via phone or in writing was lower than once a month; scored 0 otherwise.
Frequency of contact with other immediate family members	A score of 1 was allocated where frequency of contact in person, via phone or in writing was lower than once a month; scored 0 otherwise.
Frequency of contact with friends	A score of 1 was allocated where frequency of contact in person, via phone or in writing was lower than once a month; scored 0 otherwise.
Membership of any organizations, religious groups, or committees	Membership of no organization, group or committee was scored as 1; scored 0 otherwise.
Employment status	Being currently unemployed or having retired was scored as 1; full and part-time employment were scored as 0.

Since I was primarily interested in whether the most isolated individuals were more likely to be newly diagnosed with CVD, I dichotomized the index using 5 as the cut off score: those scoring 5 or 6, i.e. who either had access to none or only one of the relationships covered in the index, were classed as socially isolated.

7.2.3.2. Dependent variables: non-fatal CVD, non-fatal heart problems and non-fatal stroke, waves 2 to 6

At each wave participants were asked whether they had been newly diagnosed by a doctor with a health condition (Taylor et al., 2007). Respondents identified new conditions from a card containing a list of possible diagnoses, including angina, heart attack (myocardial infarction or coronary thrombosis), congestive heart failure, a heart murmur, an abnormal heart rhythm, any other heart trouble and stroke (Phillips et al., 2014). In the harmonized dataset, diagnoses of angina, heart attack, congestive heart failure, a heart murmur, an abnormal heart rhythm and any other heart trouble were collated into one variable, covering all new diagnoses of 'heart problem'. For each wave, the harmonised dataset contained: one variable indicating whether the participant had ever been diagnosed with a heart problem prior to the interview; and whether they reported a new diagnosis of a heart problem since the last interview. Diagnosis of stroke was coded as a separate variable, and again two variables were available: one indicating whether the individuals had ever been diagnosed with a stroke, and a second indicating whether the person reported a new stroke diagnosis since the last wave. To ascertain that new diagnoses corresponded to new events between the two waves (as opposed to diagnoses that had happened earlier but not been reported until much later), I checked codes of new reports against the years and months of diagnosis provided in the core ELSA data files; where the new diagnosis was dated to a prior wave, I amended the data accordingly.

Studies on the validity of self-reported heart conditions have found that respondents may be prone to misclassify specific diagnoses (e.g. angina, acute myocardial infarction, etc.) and that self-reports have more validity when heart disease is defined more broadly (Lampe et al., 1999; O'Donnell et al., 1999). Comparisons of estimates from clinically verified studies with self-reported incident stroke in ELSA's sister study, the Health and Retirement Study, suggest that misreporting is random, and that participant-reported events can be used to study stroke incidence and risk factors (Glymour and Avendano, 2009). Nevertheless, relying on self-report may lead to underestimating incidence, due to people dropping out of longitudinal studies for reasons that may be linked to the outcome of interest (Viswanathan et al., 2013). In ELSA, participants lost to follow-up were more likely to report lower levels of education, be less wealthy, be older and report a limiting long-standing illness (see Table 6.2 in Chapter 6). In the subsample I selected for my study, I found no evidence to suggest that, independently of these socio-demographic and health factors, loneliness and social isolation predicted risk of attrition (see Table A7.4, p.341). Nonetheless, since socio-economic status, age and health are risk factors for loneliness and social isolation as well as CVD (Beach and Bamford, 2016; Pinquart and Sorensen, 2003; Shankar et al., 2011; Steptoe et al., 2013b; Hippisley-Cox et al., 2008), it is possible that people lost to follow-up were both more lonely and isolated, and at greater risk of CVD, compared with individuals who remained in the study.

As well as looking at incidents of heart problems and stroke separately in my analyses, I generated a variable combining both diagnoses, to assess the probability of overall non-fatal CVD. The rationale underlying this approach was that the potential mechanisms linking loneliness and social isolation to adverse health outcomes (see sections 2.3.3. and 2.3.4. in

Chapter 2 for descriptions of the hypothesised pathways) need not be specific to either diagnosis, and that combining the outcomes would allow us to gauge the implications of social relationships for overall CVD incidence with more precision, since a larger number of events could be used in my analyses (Higgins and Green, 2011).

7.2.3.3. Covariates

a) Framingham ten-year CVD risk score at wave 2

With the aim of investigating whether loneliness and social isolation predicted CVD incidence *independently from the factors traditionally taken into account*, I computed the Framingham cardiovascular risk score for each participant. This score, designed for use in primary care to assess general 10-year CVD risk, is calculated based on a gender-specific algorithm incorporating age, high-density lipoprotein (HDL) and total cholesterol, systolic blood pressure, treatment for hypertension, smoking and diabetes (D'Agostino et al., 2008). At wave 2 of ELSA (the baseline wave for my study), blood samples were taken, with written consent, from participants who did not have a clotting or bleeding disorder and were not taking anti-coagulant drugs (i.e. blood was sampled from people who did not already have a heart problem). Samples were testing for total and HDL cholesterol, haemoglobin A1C and for fibrinogen and C-reactive protein at the Royal Victoria Infirmary in Newcastle-upon-Tyne, UK (Gale et al., 2014). Systolic blood pressure was measured three times using an Omron blood pressure monitor with the participant seated; the mean of the last two readings was used for my analysis. Participants were asked about their smoking status and whether they were taking any medication for high blood pressure at the time of interview. I defined prevalent diabetes mellitus based on reported doctor-diagnosed diabetes and/or use of diabetes medication or a haemoglobin A1C level ≥6.5 %, in accordance with the criteria recommended by the International Expert Committee (2009).

b) Total household wealth at wave 2

In addition to the factors included in the Framingham ten-year CVD risk score, I identified socio-economic status as a potential confounder. In this study I used total household wealth, a robust indicator of socio-economic circumstances and standard of living in ELSA which includes financial wealth, the value of any home and other property, the value of business assets, physical wealth such as artwork and jewellery and debt (Phillips et al., 2014; Banks et al., 2003). For my analyses, I divided wealth into quintiles.

c) Age and gender at wave 2

Whilst age and gender are included in the calculation of the Framingham risk score, I also included them separately in my analyses due to their potentially confounding effects.

7.2.4. Statistical analysis

Descriptive statistics were generated for all independent, dependent and covariate variables. Frequency tables were drawn to summarise the distribution of categorical variables, and the mean, standard deviation and range were calculated for continuous data. Event incidence was derived from life tables (Stata, 2015).

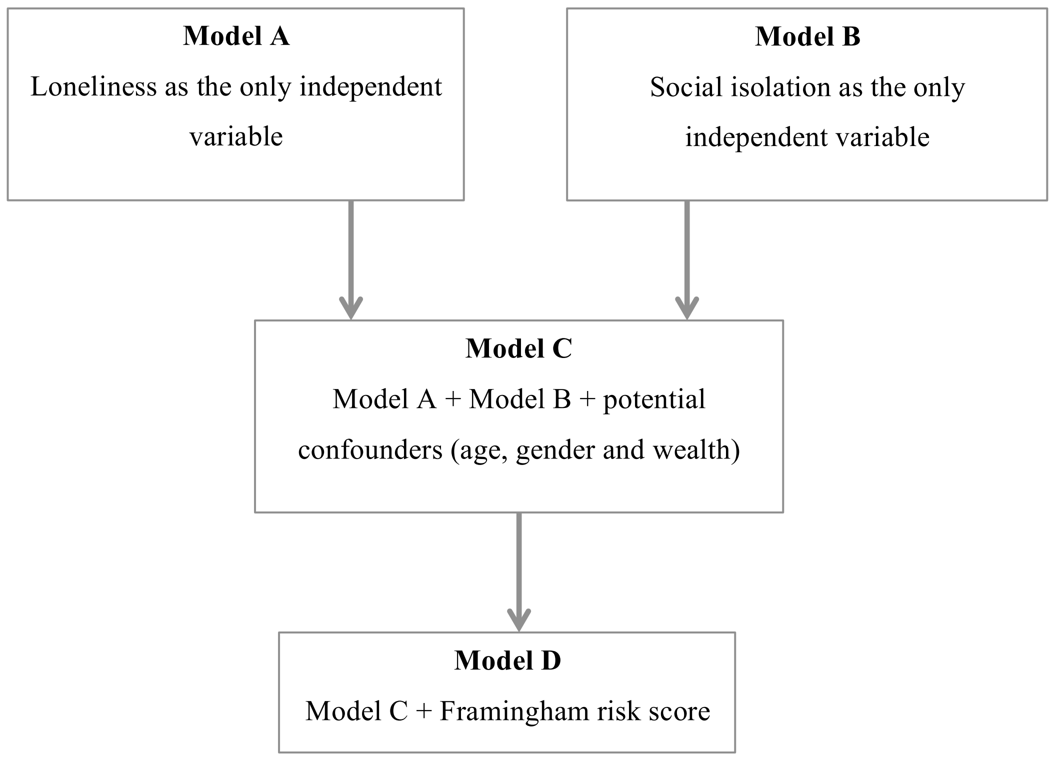
Associations between social relationship measures and CVD incidence were estimated with hazard ratios and 95% confidence intervals computed in discrete-time survival analyses. Discrete-time models were chosen because the exact time at which events (interviews, completion of self-completion questionnaires, nurse visits and CVD events) occurred was unknown, and because such models easily accommodate time-varying variables that have not been measured continuously over time (Allison, 1982). In line with recommendations for events that are not intrinsically discrete (CVD can happen anytime), I used complementary log-log models, rather than logit models which are more appropriate for truly discrete events (Allison, 2010). Complementary log-log regression fits maximum likelihood models with dichotomous dependent variables coded '0' versus 'not 0' (where '0' stands for absent of event) (Stata, 2015).

Three different outcomes were considered: new diagnosis of total non-fatal CVD (i.e. heart disease and stroke combined), new diagnosis of heart disease, and new diagnosis of stroke. For each outcome, I ran four models (see Figure 7.1). First, I ran separate univariate models to look at whether loneliness and social isolation at baseline were associated with the probability of event (models A1 and B1).[16] I then entered both explanatory variables in a model controlling for potential confounders: age, gender and household wealth quintile (model C1). Baseline Framingham score was added to produce a fourth model (D1). The aim of this last model was to investigate whether, independently of the factors used to assess risk of CVD in general practice, loneliness and social isolation were associated with event incidence. The Framingham score was entered as a categorical variable with three levels to replicate the way in which it is used in clinical decision-making: a risk of below 10% is classed as low, between 10% and 20% corresponds to a medium risk, and above 20% is considered high (D'Agostino et al., 2008). The

[16] NB: The number '1' in the label 'Model A1' denotes that a first set of models were run using loneliness and social isolation at baseline only. A second set were then run with loneliness and social isolation as time-varying, with models labeled with a '2' accordingly.

reason I chose this approach over using the Framingham score as a continuous variable was that I wished my analyses to mirror, as closely as possible, the process by which CVD risk is assed in general practice.

Figure 7.1 Diagram illustrating the sequence of models tested for each outcome (total incident CVD, heart problem only and stroke only)



In a second phase, I re-ran the models taking into account answers to questions about loneliness and social isolation across the study period (i.e. not just at baseline). My aim was to look at whether replying reporting feeling lonely once over the course of the study was associated with CVD; and to examine whether there was any evidence of a cumulative effect, whereby the frequency of reports was associated with the probability of being diagnosed with a new event (models A2 to D2). For these analyses, reporting feeling frequently lonely in none, one, two, three or four waves was coded as 0,1,2,3 and 4, and likewise for social isolation. The variable was coded so that exposure reflected the number of times a person reported feeling often lonely in the past week, or was isolated, *prior* to experiencing an event. For ease of interpretation, I used a score of 1 as the reference category for both measures: using this reference score allowed me to compare instances where a person felt lonely or was isolated once versus never, and to compare reporting multiple occasions of loneliness or social isolation with just the once.

For all analyses, T-tests and Wald tests were used to test interactions between loneliness and social isolation, and between potential effect modifiers – age, gender, wealth and CVD risk profile – and social relationships. T statistics were used for single-parameter interaction terms, e.g. where a binary variable interacts with a continuous one or another binary variable; and Wald tests were used for interaction terms with more than two categories. As well as investigating possible differences according to covariates, I ran three sets of sensitivity analyses to check the implications of using different values of independent variables. First, for all the models studied in my primary analyses, I assessed whether entering the Framingham score items separately, rather than using the composite score, affected results. I also examined whether findings based on the three-item UCLA Loneliness Scale differed from those based on the direct single-item loneliness question. Finally, for analyses where loneliness and social isolation were treated as time-varying, I compared the findings based on all waves with those based on ignoring answers to the wave immediately prior to an event. The rationale underlying this last analysis was that loneliness or social isolation immediately prior to an event may be an indication of reverse causality, whereby undiagnosed disease affected objective and/or subjective aspects of social relationships (Ikeda and Kawachi, 2011). For this sensitivity analysis, I generated lagged values of the number of reports of loneliness and social isolation, and re-ran models A to D.

At every stage of my analyses, I checked that the assumptions for discrete time survival analyses using the complementary log-log link function were met. All models satisfied the minimum requirement of 10 events per parameter (Allison, 2010). The proportional hazards assumption was checked by testing whether an interaction term between time and the independent variables was significant. The significance level used was 5%, as for all analyses in this study.

7.2.4.1. Treatment of missing data

I assessed missing data for all the variables in my analyses. The percentage of missing values at baseline ranged from none for age and gender to 28% for CVD risk score and social isolation (see Table 7.5). Taking into account patterns of missingness for the two social relationship variables across the eight-year study period (i.e. not just missingness at baseline but missing answers to questions about social relationships in the follow-up waves), only 63% of the study cohort would have been available for analysis under the traditional listwise deletion method (see Table A7.6, p.347).

Table 7.5 Frequency of missing data at baseline and across waves 2 to 6

Variable	Number of missing observations (%)
At baseline	
Age	0 (0)
Gender	0 (0)
Loneliness	14 (0.3)
Wealth	74 (1)
Social isolation	1,501 (28)
Framingham risk score	1,514 (28)
Components of the Framingham risk score**	
- Diabetes status	0 (0)
- Treatment for hypertension	0 (0)
- Smoking status	4 (0.1)
- Systolic blood pressure	652 (12)
- HDL cholesterol	1,035 (19)
- Total cholesterol	1,031 (19)
*Across waves 2 to 6**	
Loneliness	530 (3)
Social isolation	5,340 (30)

* Frequency for these variables is reported in person-waves, i.e. each individual contributed as many times as the number of waves they took part in.

** In addition to frequency of missingness for the overall Framingham score, each component of the Framingham score is listed separately here to illustrate which items were more likely to be missing.

I addressed the problem of missing data using multiple imputation by chained equations, under the assumption that values were missing at random (MAR – see Little and Rubin, 1987). When missingness is beyond the researcher's control – as in the case of secondary data analysis where data have already been collected –, its distribution is not known and MAR is only an assumption (Schafer and Graham, 2002). It is not possible to test whether MAR holds in a dataset, unless follow-up data are obtained from non-respondents (Glynn et al., 1993; Graham and Donaldson, 1993), or an unverifiable model is hypothesised (Little and Rubin, 1987, Chapter 11). Since data were not collected from ELSA non-respondents and I did not have data model, I explored whether loneliness or social isolation at one wave predicted missingness in these same variables at the next using fixed effect logit models. I chose fiixed rather than random effects models for the following reasons: the focus of my analyses was change *within* *individuals*, both variables varied significantly within people over time (see the variability identified in my Chapter 6 analyses); and fixed effects models are less vulnerable to omitted variable bias – which I knew to be highly likely, given that I was only conducting exploratory univariate analyses (Allison, 2009). The results from these univariate analyses did not suggest that loneliness and social isolation in one wave were associated with missingness at the next (see Tables A7.6 and A7.7, p.347), a finding which gives some basis for the MAR assumption: since we know from the analyses in Chapter 6 that answers in one wave were correlated with answers at the next, if missingness had been linked to values in the previous wave this could have been an indication that the MAR assumption was implausible. Still, departure from MAR cannot be ruled out.

To generate the imputed datasets, the event indicator, duration of follow-up, baseline age, gender, baseline total household wealth, baseline HDL cholesterol, baseline total cholesterol, baseline systolic blood pressure, baseline treatment for hypertension, baseline smoking status, baseline diabetes status and loneliness and social isolation at each wave were included in the imputation model (White et al., 2011). In accordance with the guidelines suggested by Spratt for multiple imputation in longitudinal studies, twenty-five imputed datasets were generated (Spratt et al., 2010). Analyses on each dataset were pooled according to Rubin's rules (Little and Rubin, 1987). For each dataset, the Framingham score was generated based on the imputed values of its individual components. As shown in Table 7.8, across datasets, the distribution of imputed values for all the variables in my analyses was very similar to that of observed values: continuous variables shared the same mean and differences in the distributions of categorical variables rarely exceeded one percentage point.

After conducting my analyses with the imputed data, I re-ran them using listwise deletion (i.e. omitting missing data). Since results were similar across both methods, I reported imputed results in the main body of this chapter, and provided results from listwise deletion in the appendix for comparison (see Appendix 7.2).

All statistical analyses were conducted using Stata SE 14.2 (StataCorp, 2011). An annotated Stata 'do file' listing all stages of the analysis is provided in Appendix 7.1.

7.3. Results

In the following section, before presenting the findings from my survival analyses, I describe the study sample at baseline and rates of CVD incidence over the eight-year study period. Note that whenever I refer to 'wave 2', this designates wave 2 of ELSA (i.e. the baseline wave for my analyses), rather than the second wave of my study. I have retained ELSA's numbering so that my analyses can be situated within the wider context of the on-going panel study – and potentially be built upon as the number of waves available to researchers increases with time.

7.3.1. Study population

Of the 8,780 core members who participated in wave 2 of ELSA (i.e. the baseline for my study), 92 (1%) were interviewed by proxy in that wave and were therefore not eligible for a nursing visit (see Table 7.1 above). Eighty-one per cent (7,029) of those who were interviewed in person completed a questionnaire and took part in the nurse visit. Of these, 1,290 people reported having been diagnosed with a heart problem prior to wave 2 and 308 reported having had a stroke (116 people reported both diagnoses). After excluding these participants, 5,547 people remained. Of these, 216 individuals went on to be interviewed by proxy in one or more subsequent waves and were excluded from my study sample. Altogether, 5,331 people were eligible for my analyses.

Table 7.8 Sample characteristics at baseline (ELSA wave 2)

NB: Joint cells across the observed and imputed data correspond to variables for which there were no missing data (e.g. age), or where the same thresholds were used to impute categorical data (e.g. wealth).

Variables with no missing values*		
Variable	Analytic sample	
Age – mean (SD)	64.9 (8.8), 52 to 90+**	
Gender – proportion (%)		
Female	3,002 (56)	
Male	2,329 (44)	
Total household wealth – range, in £		
1 (lowest quintile)	Up to £82,700	
2	82,800-170,520	
3	170,612- 246,500	
4	246,900-393,200	
5 (highest quintile)	393,260-9,297,227	
Variables with missing values		
Variable	Observed data	Imputed data (%)
Framingham CVD 10-year risk score, categorised (%)		
Low	954 (25)	24
Medium	1,468 (38)	38
High	1,395 (37)	38
Framingham CVD risk score components		
Diabetes status – proportion (%)		
Diabetic	396 (7)	7
Not diabetic	4,935 (93)	93
Treatment for hypertension – proportion (%)		
Yes	697 (13)	13
No	4,634 (87)	87
Smoking status – proportion (%)		
Current smoker	768 (14)	14
Not currently smoking	4,559 (86)	86
Systolic blood pressure (mmHg) – mean (SD)	135.0 (18.5), 80 to 259	135.0 (18.3), 80 to 259
HDL cholesterol (mg/dL) – mean (SD)	59.7 (14.8), 19.3 to 139.2	59.7 (14.8), 19.0 to 139.2
Total cholesterol (mg/dL) – mean (SD)	234.0 (44.9), 81.2 to 475.6	233.9 (44.7), 81.2 to 475.6

* Or, in the case of household wealth, where the same thresholds used to split the variable into quintiles were used to impute the missing responses – i.e. the same thresholds apply for both the observed and imputed dataset.

**Note that all ages over 90 are coded as 90 in ELSA. In wave 2, there were twenty-four individuals coded as aged 90.

Descriptive characteristics of participants for both the observed and imputed datasets are summarised in Table 7.8. More than a third of the sample had a Framingham score of over 20%, indicating a high risk of CVD. To check whether this was a plausible proportion, I compared the distribution of CVD risk factors in my sample with the wave 2 ELSA sample used by Gale and colleagues in their study on CVD risk and frailty status (Gale et al., 2014). The distributions of Framingham risk score components (smoking status, diabetes, systolic blood pressure etc.) were very similar in both samples, suggesting that the high proportion of people classified as being at risk of CVD in my sample was not due to error when implementing the algorithm. Rather, the high proportion of people at risk is likely to stem from the fact that the Framingham risk score tends to over-predict risk in UK-based cohorts (Collins and Altman, 2012). For this reason, the National Institute for Health and Clinical Excellence (NICE) recommends that UK practitioners use the QRISK2 algorithm instead (National Institute for Health and Clinical Excellence, 2014). Compared with the Framingham score, QRISK2 shows better agreement between observed and predicted risk of CVD in the UK (Collins and Altman, 2012). Unfortunately, because ELSA did not collect information on all of the elements used to calculate the QRISK2 score (e.g. occurrence of angina or heart attack in a first degree relative aged under 60), it was not possible to use this tool. The Framingham score was chosen as the best available alternative.

In line with the findings from Chapter 6 based on a larger sample, the frequencies of loneliness and social isolation reports summarised in Table 7.9 show that loneliness was more common than social isolation. Table 7.10 confirms the limited overlap between the two experiences: in under a third of instances where people were socially isolated, this was accompanied by loneliness; and in only 12% of cases where people repeated feeling lonely did this correspond with being socially isolated.

Table 7.9 Frequency of loneliness and social isolation in ELSA, waves 2 to 6

Measure of social relationships	Observed data – number (%)	Imputed data – %
Loneliness – single direct question about the past week		
Not lonely at any wave	2,819 (77)	73
Once lonely during follow-up	436 (12)	14
Twice lonely	199 (5)	6
Thrice lonely	121 (3)	4
Four times lonely	101 (3)	3
Loneliness – Three-item UCLA Loneliness Scale		
Not lonely at any wave	2,051 (67)	75
Once lonely during follow-up	414 (14)	13
Twice lonely	223 (7)	6
Thrice lonely	187 (6)	4
Four times lonely	190 (6)	4
Social isolation, measured using the ISC		
Not isolated at any wave	1,451 (92)	87
Once isolated	62 (4)	6
Twice isolated	33 (2)	3
Thrice isolated	19 (1)	2
Four times isolated	18 (1)	2

Table 7.10 Cross-sectional patterns of loneliness and social isolation responses across waves 2 to 6

NB: Frequency is reported in person-waves, i.e. each individual contributed as many times as the number of waves they took part in.

Patterns of loneliness and isolation	Observed data	Imputed data
	Number of person-waves (%)	%
Not isolated or lonely	10,862 (87)	86
Lonely but not Isolated	1,071 (9)	9
Isolated but not Lonely	368 (3)	3
Isolated and lonely	149 (1)	1

7.3.2. CVD events

Over a mean follow-up period of 6.7 years (minimum: 2.0, maximum: 8.0, standard deviation: 1.1), a total of 687 first CVD events were recorded: 556 new heart conditions and 131 stroke events. The breakdown of events per study interval (i.e. between waves 2 and 3, 3 and 4, 4 and 5 and 5 and 6) is provided in Table 7.11.

Table 7.11 Breakdown of new CVD events, per study interval

Interval	Number of participants at the start of the interval	New CVD events	Number of people censored*
First interval, between ELSA waves 2 and 3	5,331	124 (101 heart problems, 23 strokes)	485
Second interval, between ELSA waves 3 and 4	4,724	196 (153 heart problems, 43 strokes)	403
Third interval, between ELSA waves 4 and 5	4,129	186 (151 heart problems, 35 strokes)	311
Fourth interval, between ELSA waves 5 and 6	3,636	181 (151 heart problems, 30 strokes)	3,461

* I.e. people lost to follow-up or who had not experienced the event by the end of the study.

Sixteen people reported new diagnoses of stroke and heart problems in the same wave (2 in wave 3, 4 in wave 4, 3 in wave 5 and 7 in wave 6). In analyses where the outcome of interest was total CVD incidence, simultaneous events were only counted as one occurrence. Because it was not possible to determine, from the ELSA data, which of the two events occurred first, simultaneous events were dropped from the analyses where stroke and heart outcomes were investigated separately. This decision ensured consistency with the overall study objective, which was to look at first diagnoses only.

7.3.3. Loneliness and social isolation at baseline, and incident CVD

The first stage of my survival analyses was to investigate whether loneliness and social isolation at baseline were associated with the probability of developing CVD. My aim was to compare the results based on models in which loneliness and social isolation were treated as static, with the results from dynamic models where the variation of social relationship measures over time was taken into account (see section 7.3.4).

To get a sense of the patterning of event occurrence, I tabulated events according to loneliness or social isolation at baseline, based on the observed (non-imputed) data (see Table 7.12). This showed that a limited number of events had occurred among the isolated group, reflecting the low prevalence of social isolation at baseline. The only new diagnosis of stroke among individuals isolated at baseline was reported in conjunction with a new diagnosis of heart problems – i.e. there were no instances among isolated participants where stroke was the first CVD event as far as we could tell from ELSA. Social isolation at baseline was therefore dropped from the analyses focusing on stroke incidence.

Table 7.12 Loneliness and social isolation at baseline, and new diagnoses of CVD

Social relationship variables	New CVD diagnosis				
	No event	Event			
		Total CVD	Heart problem	Stroke	Number of people reporting simultaneous events
Lonely at baseline	498	95	78	17	0
Not lonely at baseline	4,150	590	476	114	16
Isolated at baseline	135	17	16	1	1
Not isolated at baseline	3,206	486	395	91	13

Using the imputed datasets, associations were formally tested for in univariate and multivariate regression models (see Table 7.13). In the following three sections., results are presented separately for each outcome.

7.3.3.1. Loneliness, social isolation and all non-fatal CVD events

In univariate analyses, baseline loneliness (Hazard Ratio (HR): 1.39, 95% confidence interval (CI): 1.12 to 1.72), but not social isolation (HR: 0.98, 95% CI: 0.62 to 1.55), was associated with an increased probability of being newly diagnosed with CVD. When potential confounders – age, gender and wealth – and both loneliness and social isolation were included in the model, the influence of loneliness was reduced (hazard ratio: 1.23, 95% confidence interval: 0.98 to 1.54). Social isolation, meanwhile, appeared to have a potentially protective effect (HR: 0.66, 95% CI: 0.42 to 1.06). Since, for both loneliness and social isolation, the confidence intervals included the value of 1, we cannot exclude the possibility that neither variable had any effect. The addition of CVD risk status as measured by the Framingham score did not change the magnitude and direction of the associations for either loneliness or social isolation.

Table 7.13 Association between loneliness and social isolation at baseline (ELSA wave 2), and CVD incidence between waves 2 and 6

	Total cardiovascular disease			Heart disease			Stroke		
Explanatory variable	**Hazard Ratio**	**95% Confidence**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Model A1 : Loneliness only									
Loneliness	1.39	1.12-1.72	0.003	1.42	1.12-1.81	0.004	1.45	0.86-2.42	0.160
Model B1 : Social isolation only									
Social isolation	0.98	0.62-1.55	0.927	1.14	0.71-1.81	0.586	NC*	NC	NC
Model C1 : Loneliness, social isolation, age, gender and wealth									
Loneliness	1.23	0.98-1.54	0.070	1.26	0.99-1.62	0.064	1.12	0.66-1.90	0.667
Social isolation	0.66	0.42-1.06	0.083	0.80	0.50-1.28	0.348	NC	NC	NC
Age (one year increase)	1.05	1.04-1.06	<0.001	1.05	1.04-1.06	<0.001	1.07	1.05-1.09	<0.001
Gender (male)	1.08	0.92-1.25	0.356	1.04	0.88-1.23	0.661	1.12	0.78-1.63	0.538
Wealth									
First (lowest)	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Second quintile	0.89	0.70-1.13	0.341	0.87	0.67-1.13	0.301	0.99	0.57-1.70	0.957
Third quintile	0.89	0.70-1.13	0.336	0.87	0.67-1.14	0.319	1.01	0.58-1.74	0.979
Fourth quintile	0.90	0.71-1.14	0.396	0.90	0.69-1.17	0.436	0.95	0.55-1.66	0.861
Fifth quintile	0.88	0.69-1.13	0.323	0.94	0.72-1.23	0.650	0.59	0.30-1.13	0.113
Model D1: Loneliness, social isolation, age, gender, wealth and CVD risk score									
Loneliness	1.22	0.98-1.53	0.079	1.25	0.98-1.60	0.076	1.14	0.67-1.93	0.628
Social isolation	0.67	0.42-1.06	0.089	0.81	0.50-1.29	0.372	NC	NC	NC
One year increase in age	1.04	1.03-1.06	<0.001	1.04	1.03-1.05	<0.001	1.07	1.04-1.09	<0.001
Gender (male)	0.96	0.79-1.15	0.639	0.92	0.75-1.14	0.448	1.05	0.67-1.64	0.841
Wealth									
First (lowest)	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Second quintile	0.90	0.71-1.15	0.406	0.88	0.67-1.15	0.352	0.99	0.57-1.72	0.981
Third quintile	0.90	0.71-1.15	0.396	0.88	0.68-1.16	0.372	1.02	0.59-1.76	0.955
Fourth quintile	0.93	0.73-1.18	0.536	0.93	0.71-1.21	0.578	0.96	0.55-1.68	0.887
Fifth quintile	0.92	0.72-1.17	0.483	0.97	0.74-1.28	0.846	0.60	0.31-1.16	0.130
Framingham score									
Low	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Medium	1.35	1.03 - 1.76	0.030	1.52	1.12-2.07	0.007	0.75	0.39-1.44	0.384
High	1.48	1.07-2.03	0.016	1.55	1.08-2.23	0.017	1.04	0.50-2.15	0.926

* NC: Not Calculated, due to insufficient numbers of strokes among isolated individuals.

7.3.3.2. Loneliness, social isolation and heart problems

When only new diagnoses of heart conditions were considered, results were similar to those based on overall CVD. In the univariate model, loneliness was associated with an increased likelihood of new diagnosis (HR: 1.42, 95% CI: 1.12, to 1.81). Once social isolation, age, gender, wealth and the Framingham score were added, this effect diminished (HR: 1.25, 95% confidence interval: 0.98 to 1.60). The unadjusted hazard ratio for social isolation was not indicative of a statistically significant effect (HR: 1.14, 95% CI: 0.71 to 1.81); the point estimate in multivariate analyses suggested a possible protective effect (HR: 0.81), though the wide confidence interval precluded any robust conclusions (95% CI: 0.50 to 1.29).

7.3.3.3. Loneliness and stroke

Because too few stroke events prior to heart diagnosis were reported among people who were socially isolated at baseline, it was not possible to explore the association of social isolation with stroke. Scarcity of events meant that models for which stroke was the specified outcome and where social isolation was entered as an explanatory variable could not be run, due to the set of omitted variables not being consistent across imputed datasets. It was therefore only possible to explore the association between loneliness and stroke.

In univariate analysis, there was some evidence to suggest that loneliness may be associated with an increased risk of event (HR: 1.45, 95% CI: 0.86 to 2.42). Once covariates were added, this effect decreased considerably (model D1, HR: 1.14, 95% CI: 0.67 to 1.93). Note that failure to detect a statistically significant effect here may be due to the comparatively low incidence of stroke events, limiting the analysis' statistical power and its chance of detecting a true effect (Button et al., 2013).

7.3.3.4. Testing the proportional hazards assumption

Interactions between covariates and time were investigated to check that the proportional hazards assumption was met for all the models presented above. Across all three outcomes studied, there was no evidence of interaction between any of the independent variables and time (see Table A7.14, p.348). This finding implies that neither loneliness nor social isolation had a time-dependent effect on the outcomes – i.e. that their effects did not vary over time.[17]

[17] NB: A time-dependent effect is not to be confused with the effect of a time-varying variable. Investigating a time-dependent effect signifies checking whether the effect of a variable is constant, or fluctuates, with time; studying the effect of a time-varying variable, meanwhile, aims to determine whether a variable that is not constant over time is associated with the outcome (see Chapter 31 by Allison in Hancock and Mueller, 2010).

7.3.3.5. Investigating potential interactions between covariates

Interactions between all independent variables in model D1 were tested for to explore potential effect modification. Detailed results are reported in the appendices (see Table A7.15, p.351). No statistically significant interaction between loneliness and social isolation was found. Nor was there any evidence that gender or wealth modified the effects of loneliness or social isolation. Interactions between loneliness and age were significant in the overall CVD and stroke analyses (p-values associated with the T-statistic for interaction with age: 0.040 in the model with all CVD events as the outcome, 0.025 in the model for stroke), as were interactions between loneliness and CVD risk category (p-values associated with Wald test =0.017 in the model with all CVD events as the outcome, p=0.003 in the stroke only model). When both interaction terms (loneliness and age, and loneliness and CVD risk category) were added to model D1, interactions were no longer significant in analyses of overall CVD events (interaction with age: p=0.415; interaction with CVD risk category: p=0.102, see Table A7.16, p.352); nor was the interaction term between loneliness and age significant any longer in analyses where stroke was the outcome of interest (p=0.565). The interaction term between CVD risk category and loneliness, however, remained significant (p=0.033) in the stroke analyses (see Table A7.17, p.353). The direction of the interaction suggested that loneliness had negative implications for people at low risk of CVD, but protective among people at medium and high risk. Among those who were at low risk of CVD according to the Framingham score, all else being equal, lonely individuals were 5.9 times more likely to develop stroke compared to people who were not lonely. For people at medium and high risk of CVD, the hazards of developing stroke were respectively 0.8 and 0.6, when comparing lonely with non-lonely individuals and maintaining all other variables equal. This finding – of loneliness being more problematic among participants with lower CVD risk – is plausible if we consider the different risk factors for stroke, and the different ways in which loneliness might lead to worse health: it may be that loneliness is linked to characteristics that are not captured in the Framingham risk score, but that are nevertheless associated with the risk of having an event, such as diet, exercise or mental health conditions. These factors may be the pathways through which loneliness affects health outcomes among people who would otherwise, using a tool such as the Framingham score, be considered at low risk. Alternatively, it may be that loneliness feelings are a reflection of, rather than a trigger for, these mechanisms (e.g. physical inactivity leading to low self-esteem and loneliness). Among people who are at heightened risk of CVD because of smoking, high blood pressure, or other factors captured in the Framingham score, it may be that these are also linked to loneliness feelings – but that by controlling for this risk score, the effect of loneliness is removed.

7.3.3.6. Sensitivity analyses

Two sensitivity analyses were conducted: first, all models were re-run using a dichotomous measure based on the three-item UCLA Loneliness Scale, to check whether my findings varied according to the measure of loneliness used. In a second series of analyses, all the items contributing to the Framingham score were entered as separate variables in the models, to investigate whether this affected results. When using the dichotomized measure of loneliness based on a cut-off of 6 on the three-item UCLA Loneliness Scale, the magnitude of effect was somewhat lower than the estimates found for the direct loneliness question. In univariate analyses, the hazard of being newly diagnosed with either stroke or a heart problem was 21% greater among people who were classed as lonely (95% confidence interval: 1.00 to 1.46, see Table A7.18, p.353), compared with 39% in the main analyses (see Table 7.13). When all covariates were added, scoring more than 6 on the three-item UCLA Loneliness Scale was associated with an increased risk of 18% (95% CI: 0.97 to 1.43 – see Table A7.19, p.354). This result was close to the point estimate of 1.22 obtained in the main analyses using the dichotomized direct loneliness question. Similarly to when the direct question was used, the inclusion of 1 in the confidence interval meant that absence of effect could not be ruled out.

When all of the items used to calculate the Framingham score were entered separately in model D1, the estimates for loneliness and social isolation were very similar to those obtained in the primary analyses (see Table A7.20, p.358). In the model with all CVD events as the outcome, the point estimate for loneliness was 1.21 (95% CI: 0.97 to 1.51) and 0.68 for social isolation (95% CI: 0.43 to 1.09). When heart and stroke were considered separately, point estimates were respectively 1.25 (95% CI: 0.97 to 1.60) and 1.11 (95% CI: 0.65 to 1.88) for loneliness, and 0.83 (95% CI: 0.52 to 1.33) for social isolation (for heart problems only – no estimate was generated for stroke, due to the near absence of events among people categorized as isolated at baseline).

7.3.4. Loneliness and social isolation over the course of the 8-year study period, and incident CVD

The second stage of my survival analyses was to re-run the statistical models taking into account the longitudinal frequencies of loneliness and social isolation. The results from these models are presented in Table 7.21 and presented separately for each outcome below.

7.3.4.1. Frequency of loneliness and social isolation, and non-fatal CVD events

In univariate analyses, never reporting feeling lonely was associated with a decreased likelihood of event (HR: 0.69, 95% CI: 0.55 to 0.86). Comparing multiple reports of loneliness with single instances, there was no evidence that feeling lonely more than once was associated with greater event risk (e.g. comparing three loneliness reports versus one, HR: 1.06, 95% CI: 0.61 to 1.85). Once potential confounders and CVD risk category were added to the model, this finding persisted: participants who never reported loneliness were less likely to develop CVD than those who reported feeling lonely once (HR: 0.74, 95% CI: 0.59 to 0.92). When people who reported feeling lonely *at least once* across the study period were combined into one category (i.e. when the measure of loneliness was dichotomised to compare never lonely versus one or more times lonely), CVD hazard comparing never versus lonely at least once was 0.75 (95% CI: 0.62 to 0.91). There was no difference in effect between reporting loneliness once, twice, three or four times. Given the small proportion of people who repeatedly reported feeling lonely, the absence of any observed difference may be due to low statistical power.

The unadjusted hazard ratios and confidence intervals for social isolation were not indicative of any effect (see the results reported for model B2 in Table 7.21). The results from models C2 and D2 hinted at the possibility that never being isolated might, once confounders, CVD risk and loneliness had been controlled for, predict greater likelihood of CVD (e.g. model D2, HR: 1.67, 95% CI: 0.98 to 2.85). There was no evidence that multiple instances of social isolation, when compared with a single occurrence, were associated with CVD events.

Table 7.21 Association between loneliness and social isolation in waves 2 to 5, and CVD incidence between waves 2 and 6

Explanatory variable	Total cardiovascular disease			Heart disease			Stroke		
	Hazard Ratio (HR)	95% Confidence Interval (CI)	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Model A2 : Loneliness only									
Loneliness									
Never	0.69	0.55-0.86	0.001	0.73	0.57-0.93	0.013	0.53	0.33-0.85	0.009
Once	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Twice	0.96	0.64-1.42	0.827	1.03	0.66-1.61	0.890	0.64	0.24-1.71	0.371
Three times	1.06	0.61-1.85	0.832	1.26	0.71-2.26	0.430	0.39	0.05-1.71	0.357
Four times	1.41	0.68-2.96	0.353	1.58	0.72-3.48	0.259	1.02	0.13-7.84	0.986
Model B2 : Social isolation only									
Social isolation									
Never	1.15	0.68-1.97	0.599	1.05	0.63-1.77	0.840		NC*	
Once	1.00 (reference)			1.00 (reference)					
Twice	1.38	0.60-3.16	0.450	1.26	0.54-2.94	0.594			
Three times	0.89	0.22-3.53	0.866	1.00	0.26-3.82	0.998			
Four times	1.01	0.19-5.48	0.993	1.11	0.21-5.89	0.903			
Model C2 : Loneliness, social isolation, age, gender and wealth									
Loneliness									
Never	0.74	0.59-0.92	0.009	0.77	0.60-1.00	0.041	0.63	0.39-1.04	0.069
Once	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Twice	0.92	0.62-1.36	0.667	0.99	0.63-1.55	0.877	0.57	0.21-1.53	0.266
Three times	0.93	0.53-1.62	0.790	1.12	0.63-2.00	0.710	0.31	0.04-2.29	0.250
Four times	1.32	0.63-2.76	0.463	1.46	0.66-3.25	0.348	0.82	0.11-6.30	0.847
Social isolation									
Never	1.68	0.98-2.86	0.057	1.48	0.88-2.49	0.140		NC	
Once	1.00 (reference)			1.00 (reference)					
Twice	1.27	0.55-2.89	0.573	1.16	0.50-2.70	0.735			
Three times	0.78	0.19-3.12	0.721	0.87	0.22-3.36	0.837			
Four times	0.83	0.15-4.52	0.829	0.90	0.17-4.79	0.903			
Model D2: Loneliness, social isolation, age, gender, wealth and CVD risk score									
Loneliness									
Never	0.74	0.59-0.93	0.009	0.77	0.60-1.00	0.049	0.64	0.39-1.04	0.073
Once	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Twice	0.91	0.61-1.36	0.648	0.98	0.63-1.53	0.930	0.58	0.22-1.56	0.283
Three times	0.92	0.53-1.60	0.762	1.10	0.61-1.97	0.750	0.32	0.04-2.35	0.262
Four times	1.30	0.62-2.73	0.485	1.44	0.65-3.19	0.372	0.83	0.11-6.37	0.854
Social isolation									
Never	1.67	0.98-2.85	0.058	1.47	0.88-2.48	0.144		NC	
Once	1.00 (reference)			1.00 (reference)					
Twice	1.27	0.55-2.89	0.575	1.16	0.50-2.70	0.732			

* NC: Not Calculated. Because social isolation was rare, and there were few strokes, not all frequencies of social isolation were associated with at least one event (i.e. there were empty

cells in tabulations). Frequency of social isolation was therefore not included in the models where stroke was the sole outcome.

7.3.4.2. Frequency of loneliness and social isolation, and heart problems

The findings based on all CVD events were echoed in the analyses focusing on heart problems. Reporting loneliness once was associated with a greater risk of event (model D2, comparing never versus once lonely, HR: 0.77, 95% CI: 0.60 to 1.00); there was no evidence to suggest that greater frequency of reports predicted risk. Estimates and confidence intervals relative to frequency of social isolation did not provide any conclusive evidence of effect.

7.3.4.3. Frequency of loneliness and stroke

As was the case in the first set of analyses using baseline information about social relationships (see section 7.3.3.3), because there were comparatively few stroke events without any prior history of CVD and social isolation was not a common experience, there were not enough events per number of social isolation reports to investigate the association between social isolation and stroke. Analyses therefore focused on the association between loneliness and stroke.

Similarly to the evidence relating to heart problems, a single report of loneliness was associated with an increased probability of stroke in the univariate model (comparing never versus one report of loneliness, HR: 0.53, 95% CI: 0.33 to 0.85). In multivariate models, while point estimates still pointed to an increased risk, the effect was no longer statistically significant. This could be a consequence of comparatively low stroke incidence and statistical power, as suggested by the wider confidence intervals observed in the stroke analyses, compared with the results for heart conditions.

7.3.4.4. Investigating potential interactions between loneliness or social isolation, and covariates

Due to the low proportions of people repeatedly reporting feeling lonely or being isolated, it was only possible to investigate interactions between social relationships and age, and loneliness and gender. Interaction terms were added to model D2 for overall CVD outcomes, and for heart problems (there were too few events for stroke). There was no evidence that the effect of social isolation was modified by age, or that estimates for loneliness varied according to gender (see Table A7.22, p.362). The interaction term between loneliness and baseline age, however, was significant (in the model with overall CVD as the outcome, $p = 0.005$; in the model with heart problems only as the outcome, p = 0.020). More specifically, what estimates indicated was that the effect of reporting feeling loneliness once versus never decreased with age: for example, all else being equal, CVD hazard among individuals aged 60 at baseline who did not report loneliness was 0.59 times that among those who reported loneliness once; for people aged 70, the ratio was 0.77; and for those aged 80, this was 0.95. When only heart problems were considered, all else being equal, the hazard of reporting a new event among non-lonely participants aged 60 was 0.64 times that among their once lonely counterparts; the ratio was 0. 68 for people aged 70; and 0.95 among those aged 80.

7.3.4.5. Sensitivity analyses

Repeating the sensitivity analyses conducted for the baseline analyses, models were re-run with the Framingham score items entered separately, to compare results with those based on the overall Framingham risk score. The dichotomous measure of loneliness based on the three-item UCLA Loneliness score was also used, to compare findings with those based on the direct loneliness measure.

Entering the Framingham separately produced very similar results to those where the overall score was used (see Tables A7.23 and A7.24, pp.362-63). In multivariate analyses, never reporting loneliness was associated with a hazard of CVD of 0.74 (95% confidence interval: 0.59 to 0.93), compared with the reference category of reporting loneliness once.

When the three-item UCLA score was used to distinguish between lonely versus non-lonely individuals, the point estimate associated with feeling lonely once suggested that this was linked to an increased risk of CVD (hazard ratio, comparing never versus once lonely: 0.87, 95% confidence interval: 0.70 to 1.09), though this effect did not reach statistical significance. There was no evidence to suggest that multiple reports of loneliness were linked to greater risk of CVD (see Table A7.25, p.364).

A further sensitivity analysis was performed, using the lagged values of loneliness and social isolation reports, to see whether findings were modified when answers to the wave immediately prior to an event were ignored. Whilst effect estimates pointed to never-lonely individuals potentially being at lesser risk of event (e.g. in analyses where all CVD outcomes were considered, hazard ratio comparing never versus once lonely in multivariate analyses: 0.86, 95% confidence interval: 0.66, 1.13), confidence intervals did not exclude 1 and so absence of effect could not be ruled out (see Table A7.26, p.365). The fact that a significant effect was observed when all waves were considered, but not when the wave immediately prior to event was dropped, suggests that the effect identified in main analyses could be an indication of reverse causality.

7.4. Discussion

The main findings from my analyses are summarised below and discussed in relation to the literature. I consider the strengths and weakness of my investigative approach and the implications of my findings from policy, practice and research.

7.4.1. Summary of main findings

The findings from the survival analyses reported in this chapter can be summarized in four main messages. First, reporting feeling lonely much of the time in the past week, independently of social isolation, was associated with an increased risk of new non-fatal cardiovascular events. Results based on treating loneliness as a time-varying variable were indicative of a stronger effect than those using baseline loneliness only. In analyses where loneliness was treated as time-invariant, the hazard of reporting a new CVD event was 22% greater among lonely individuals, compared with non-lonely participants (HR: 1.22, 95% CI: 0.98 to 1.60). When loneliness was studied as time-varying, CVD hazard was 33% higher among individuals who reported feeling lonely at least once, compared with never feeling lonely (HR: 1.33, 95% CI: 1.10 to 1.60).[18]

Secondly, there was no evidence to suggest that social isolation was associated with a greater risk of non-fatal CVD. In fact, the point estimates for social isolation obtained from multivariate models suggested that individuals who were socially isolated might be less likely to report a non-fatal event (e.g. compared with those who were isolated once, participants who were not isolated in any wave had a 67% greater risk of reporting a new diagnosis compared with people who were isolated once: HR: 1.67, 95% CI: 0.98 to 2.85).

Thirdly, among participants who reported feeling lonely or socially isolated at least once, there was no evidence to suggest that the number of reports (once, two, three or four times) affected CVD risk. In other words, reporting feeling lonely or socially isolated once or four times was not differentially associated with new diagnosis of event.

Finally, there was some evidence to suggest that younger adults were more likely to report a new diagnosis following experiences of loneliness. In analyses where social relationships were treated as time-varying, loneliness among younger individuals was associated with a greater risk

[18] NB: In Table 7.20, I used once lonely or isolated as the reference category. To produce the estimate reported here and allow comparison with the baseline analyses, I have used ‘never lonely’ as the reference category and grouped participants reporting loneliness once, twice, three or four times into a ‘more than once category’.

of event than among older participants.

7.4.2. *My findings in context*

The findings reported in this chapter allow us to go beyond what we know from the literature summarised in Chapter 5. No previous study had compared the implications of loneliness and social isolation for incident CVD. My analyses of ELSA indicate that loneliness, rather than social isolation, may be more problematic for CVD risk – at least for non-fatal events. The hazard of reporting a new CVD diagnosis was 33% greater for participants who replied feeling lonely at least once over an eight-year period, compared with participants who never reported feeling lonely. This association persisted when the main biological and behavioural CVD risk factors were controlled for, suggesting that the mechanisms at play may be more to do with psychological pathways (e.g. depression, anxiety, self-esteem) and/or other behaviours, including alcohol consumption and physical activity. Prospective longitudinal studies have linked loneliness to higher levels of depressive symptoms (Cacioppo et al., 2010; Luo et al., 2012) and reviews of the literature have highlighted loneliness as a risk factor for both higher alcohol consumption and lower physical activity (Pels and Kleinert, 2016; Åkerlind and Hörnquist, 1992). Since health-related behaviours and psychological states can in turn influence loneliness, it is important to bear in mind that the latter may be a marker or 'symptom', rather than a cause, of the former; based on my data and analyses, we cannot assume that loneliness was a causal factor and further analyses will be needed to disentangle potential reverse causality and synergistic effects.

I used a more conservative approach to the study of social isolation than found in most studies of social relationships (see Appendix 5.4 for details of the measures used in studies of cardiovascular disease). The measure I designed was intended to capture absolute, rather than relative, absence of contacts with others. While the studies reviewed in Chapter 5 indicated that having fewer contacts was associated with greater disease risk, my results suggest that having very little, if any, interaction with others may not lead to incident non-fatal CVD. Many of the studies that contributed to my meta-analyses relied on measurement tools that explicitly targeted more objective characteristics of relationships (e.g. network size or frequency of interaction) but in practice often tapped into perceptions of relationships (e.g. in the Lubben Social Network Scale: 'How many relatives do you feel close to? That is how many of them do you feel at ease with can talk about private matters or can call for help?'; and 'Do you have any close friends?' – see Lubben, 1988). The findings from the meta-analyses may therefore be echoing the findings from my secondary analyses of ELSA data, namely the importance of perceptions of social relationships. Alternatively, it may be that my measure of social isolation was ill-suited to capturing the benefits of having access to other people – i.e. the number of contacts may not be as important as the number of contacts *who could provide support*, for instance.

Importantly, my analyses did not include fatal events. Since other researchers have found that social isolation, but not loneliness, predicted increased risk of mortality among ELSA participants, we should be wary of generalizing these findings to non-fatal events (Steptoe et al., 2013b). There are two main explanations for why my findings contrast with those of Steptoe. First, it could be that socially isolated individuals are more likely to die prematurely, in which case this would constitute a competing risk, with fatal events precluding the occurrence of non-fatal ones. In my study, I found no evidence to suggest that social isolation was associated with increased risk of drop-out; but due to not having requested access to mortality records from the National Health Service central data registry (a process which would have required more time than was available during my PhD), I was not able to check whether it was linked to greater likelihood of death. Future analyses in which both fatal and non-fatal events are taken into account will help to test whether my findings apply to all CVD events, or to non-fatal ones only. A second reason for the contrasting findings between my study and that of Steptoe and colleagues is that we used different measures of loneliness and social isolation: while they used the Shankar index and the UCLA Loneliness scale, I used a modified version of the Shankar index and a direct loneliness question. Further empirical work replicating the analyses conducted by Steptoe using the measures I selected, and replicating my analyses using the Steptoe measures, would shed light on whether the use of different instruments modifies results.

Many of the studies reviewed in Chapter 5 controlled for variables that may be on the causal pathway, such as smoking status or high blood pressure. This was also the case of my study, though by separating the step between adjusting for confounders and adjusting for confounders and CVD risk, I was able to monitor the effect of adding in variables that may explain the effect of social relationships on health. What comparisons between models C and D showed was that incorporating CVD risk into the model made very little difference to the estimates for loneliness and social isolation – i.e. their effects did not appear to be mediated by the factors that make up the Framingham score. The fact that evidence of an association between loneliness and incident CVD persisted when the more commonly recognized risk factors were adjusted for suggests that loneliness may be influencing physical health via mechanisms not incorporated in the risk score, such as mental ill health or physical activity. An alternative explanation, supported by my sensitivity analyses excluding the loneliness reports immediately prior to an event, is that loneliness may be a marker, or a consequence, of these mechanisms, rather than preceding them. Such a hypothesis does not contradict the finding that, independently of the Framingham score, loneliness predicted an increased risk of outcome; though it raises the question of whether loneliness may or may not be aetiologically related to disease.

7.4.3. *Strengths and limitations*

As with the analyses presented in Chapter 6, this study drew on the strengths of ELSA: its large sample of nationally representative adults aged over 50, the availability of robust socio-demographic and biomarker variables and regular follow-up every two years. The data collected during nurse visits allowed me to incorporate the main risk factors routinely considered when assessing patients for CVD risk in the UK into my analyses (Collins and Altman, 2012). The longitudinal design of the study meant that I could focus on the prospective association between social relationships and event occurrence, though I acknowledge that reverse causation where deficiencies in social relationships are the result of subclinical disease remains a possibility. In common with other observational studies, causality cannot be assumed here, nor can confounding by unmeasured causes be excluded. In particular, the inclusion of only one measure of socio-economic status, household wealth, means that confounding by socio-economic position as measured by education level or social class cannot be excluded. Future analyses using multiple indicators of deprivation will help to strengthen the evidence on the role of socio-economic factors in shaping the association between relationships and health.

New CVD events were self-reported by participants at every wave. While this is generally recognized as a relatively robust measure of outcomes such as myocardial infarction or stroke, it may be that participants omitted to report certain events, or that the month and year of diagnosis they provided was not accurate – which would mean that events were wrongly coded as occurring between waves 2 and 3 instead of 3 and 4, for example. Whenever month and year were provided, I double-checked the data for consistency across waves; for events where no date was provided, I had no choice but to rely on the code at interview. Had accuracy of outcome recording been the main concern for my study, I would have used a different dataset; the important advantage of ELSA was that it repeatedly measured social isolation and loneliness. The methods I used can easily be replicated for other outcomes, and it will be useful to compare findings based on other conditions in future.

Using the baseline data on age, gender, wealth and CVD risk factors collected in ELSA, I was able to explore their potential effect on the relationship between loneliness or social isolation and disease outcome. Because not all variables were collected at each wave (e.g. the nurse visit was carried out every four years, i.e. in alternate waves), I did not venture into investigating whether, when treated as time-varying, the relationship between factors such as wealth or CVD risk factors and social relationships changed. Nor did I study the implications of specific changes in circumstances, such as bereavement, retirement or migration. Given the changeability in loneliness and social isolation reports evidenced in Chapter 6, and the finding that chronicity was not associated with an difference in effect, changes in a person's circumstances may be key to increasing our understanding of how social relationships influence health. The challenge for future research will be to capture the dynamic relationship between these changes and fluctuations in loneliness or social isolation. Collecting data every two years, as is done in ELSA, may not be sufficiently frequent for this. Indeed, for my analyses, we should be careful not to assume continuity between reports at each wave. Because loneliness and social isolation fluctuate over time, the data I relied on should at best be seen as a discrete indicator of what are likely to be far more frequent changes between time points.

In my models, I included the main risk factors routinely considered when assessing heart disease and stroke risk in general practice in the UK (Hippisley-Cox et al., 2008), except for family history of CVD for which there were no data in ELSA. Entering each of the Framingham score items separately in my models did not produce different results from those obtained when the risk score was used as a summary variable. Among these factors are smoking status, cholesterol and blood pressure, all of which have been identified as possible outcomes following exposure to chronic loneliness or social isolation (Dyal and Valente, 2015; Grant et al., 2009; Hawkley et al., 2010). Adding these variables into my survival models did not affect the effect estimates, suggesting that these were neither mediating nor moderating factors of the association between social relationships and CVD incidence (see Tables 7.13 and 7.21).

Potential effect modifiers and/or variables on the pathway to ill health which I did not explore include ethnicity, marital status, mental illness and psychological distress, diet and exercise (see Chapter 2 for an overview of the different hypothesised pathways through which social relationship are linked to health outcomes). While there is limited evidence on the distribution of loneliness and social isolation among older adults from different ethnic minorities (Victor et al., 2012), research on social participation and isolation among working adults has identified differences in patterns of activity across ethnic groups: analyses adjusting for age, partnership status, children, long-term illness, carer status, education, work history and income have shown that Indian, Bangladeshi and Pakistani women were less likely to participate in organised activities when compared with White British women, for example (Platt, 2009). There are very few ethnic minority participants in ELSA (they constitute 3% of the initial ELSA sample) and information on ethnic group membership is restricted to white versus non-white, making it an ill-suited dataset for exploring differences between people with different ethnic origins (Steptoe et al., 2013a). Still, a posthoc examination of the prevalence of loneliness and social isolation according to ethnicity indicated that there were no differences in social isolation levels but that non-white participants were more likely to report feeling frequently lonely (27% of non-whites reported feeling frequently lonely in the past week compared with 11% of non-whites, Pearson X^2 <0.001; see Tables A7.27 and A7.28, pp. 366-67). This suggests that ethnicity is a plausible effect modifier of the relationship between loneliness and CVD risk, and that future analyses would benefit from taking ethnicity into account. Marital status, mental health, diet and exercise are other potential effect modifiers which will need exploring in future analyses. I did not include marital status in my analyses because this could be considered a component of social isolation; but it may help to explain the relationship I found between loneliness and health, since partnership status has been linked to both perceptions of relationships and CVD risk (Molloy et al., 2009; Pinquart and Sorensen, 2003). My primary reason for not including mental health, diet and exercise was that these may be both effect modifiers and on the causal pathway between loneliness and disease onset (see Chapter 2); including them in survival models would not have provided any helpful indication of whether loneliness preceded, or followed, them. Future analyses better suited to disentangling moderating and mediating effects (e.g. structural equation modelling) will help to shed further light on the mechanisms underlying the association between social relationships and health.

My analyses relied on a sample of participants who were in good enough health to take part in face-to-face interviews. According to the stress-buffering hypothesis, people who are in vulnerable situations may be particularly at risk of ill health following loneliness or social isolation (Cohen et al., 2000a). Since people interviewed by proxy were excluded from the study sample, we should exercise caution when considering the implications of my findings for people with a physical or cognitive disability. Further research is needed to establish whether their social relationships are more strongly associated with worsening health outcomes.

The primary measure of loneliness I used in my analyses was the direct question included in the Centre for Epidemiologic Studies Depression Scale (CESD – see Radloff, 1977). The advantage of using this tool was that it was administered as part of the main interview and hence had very little missing data (3% across all the waves for my analyses). I was aware that a direct measure of loneliness may not capture the feelings of participants who were reluctant to publicly report them, and conducted sensitivity analyses using the three-item UCLA Loneliness Scale. Findings were very similar across the two measures. Unfortunately, it was not possible to conduct similar sensitivity analyses for the measure of social isolation I used. As with all other self-reported measures of social networks or interactions, the validity of such instruments is unknown, and caution should be exercised when interpreting their significance.

To limit the potential bias arising from missing data, I used multiple imputation by chained equations. The assumption underlying this method is that the data are MAR, i.e that the pattern of missingness is not dependent on the values of the missing variables. Whilst I found no evidence to suggest that previous responses to the social relationship measures was associated with missingness in the next wave, the possibility that data were not MAR cannot be excluded. In many realistic cases, researchers have shown that an erroneous assumption of MAR (such as failing to take into account a correlate or cause of missingness) only has a minor impact on estimates and standard errors (Collins et al., 2001). While no sensitivity analyses were run to check whether departure from the MAR assumption affected my results, there was no strong reason to believe that my study was different from other longitudinal studies where failure to account for the cause of missingness only introduced minor bias (Graham et al., 1997).

Aside from the treatment of missing data, a last factor may have introduced bias and limited the generalizability of my findings: not modelling fatal CVD events or any other causes of death as a competing risk. The absence of robust mortality data in the ELSA datasets made available by the UK Data Service website meant that I was not able to incorporate fatal events into my analyses. Whilst I found no evidence that loneliness or social isolation were associated with greater risk of drop-out, future analyses taking fatal events into account will help to test whether findings are similar when all CVD events are taken into account. These would also enable us to study whether prognosis differs according to social relationship characteristics.

7.4.4. Implications

The implications of my findings for practice, policy and research are discussed below.

7.4.4.1. Implications for practice and policy

The finding that lonely individuals are at increased risk of new heart conditions and stroke supports taking perceptions of social relationships into account when assessing patients' risk of CVD. The direct question included in the ELSA interview may be a useful tool for practitioners to identify people who would not be flagged up as being at risk of CVD with tools such as QRISK2 or the Framingham score, but who are nonetheless more likely to experience the event – whether due to loneliness, or other unmeasured factors. My analyses suggested that loneliness may be a particularly useful marker of risk among younger older adults. Because individuals may not wish to publicly discuss negative feelings about their entourage, asides from directly asking patients about loneliness, it will be important to consider other, indirect, means of assessing loneliness, such as multi-item questionnaires.

In my analyses, repeated instances of loneliness, compared with only reporting loneliness once, were not associated with a higher risk of non-fatal CVD. One of the implications of this finding is that it may be particularly difficult for secondary and tertiary prevention strategies to positively affect health outcomes. Once people have experienced loneliness, be it only for a comparatively short period of time, the implications for health may not be modifiable. If loneliness reflects undiagnosed symptoms, then targeting people who already feel lonely may not reduce CVD risk. Another implication of the similarity of effect across one or more reports of loneliness is the apparent absence of a 'resilience' mechanism, whereby individuals might have found ways of successfully preventing the adverse outcomes associated with chronic loneliness. In the absence of any evidence pointing to the health benefits of improvements in loneliness, primary prevention strategies could be a more promising way of tackling loneliness and its adverse health implications.

7.4.4.2. Implications for research

The analyses presented in this chapter are the first example of how we might study the association between repeated measures of loneliness, social isolation and incident health outcomes. ELSA and other datasets include a range of physical and mental health outcomes, and the analytical approach I used could be employed to investigate whether loneliness and social isolation are associated with them. The methodological angle I took – i.e. treating social relationships as time-varying in survival analyses – is one way in which the data could be analysed; future studies should take advantage of the increasing availability of repeated measures in cohorts to explore other approaches. For example, serial measurements could be used to research how changes in social relationships prospectively affect health outcomes; and the potentially time-varying effects of loneliness or isolation could be investigated using datasets with more precise measures of time than those available in ELSA.

Without repeated measures of relationships over time, it would not have been possible to explore whether multiple reports of frequent loneliness or social isolation were differentially associated with CVD risk. The fact that I found no evidence of multiple loneliness reports being associated with a greater hazard of incident CVD when compared with one instance only should not be interpreted as meaning that there is no need to collect information about social relationships on multiple occasions. On the contrary, we need repeated measures so that we can gain insight into the different profiles of loneliness and adapt interventions accordingly. People who are chronically lonely over a prolonged period of time are likely to require different approaches from those who have moved into loneliness following a life-changing events, for example. Repeated measures over time will also be useful to explore whether the implications of loneliness and social isolation vary over time, e.g. whether loneliness or isolation in younger life is associated with worse or better outcomes than in later life, for example.

My analyses focused on one dataset, and on individual-level factors; replicating them on comparable data, such as the Health and Retirement Study (Sonnega et al., 2014) or the Irish Longitudinal Study of Ageing (Kearney et al., 2011) would help to gain insight into the context within which loneliness and social isolation, and their health implications, are shaped. Datasets such as the French Gazel cohort (Goldberg et al., 2007), which initially targeted a working age population and has followed them into retirement, offer the opportunity to replicate analyses based on younger cohorts and to take a more comprehensive approach to the study of social relationships over the lifecourse. Taking context and timeframe into account will be particularly important if research is to inform the design of interventions that can successfully address loneliness and its health implications.

Chapter 8. Discussion

Chapter summary: The overall aim of my doctoral work was to further our understanding of the link between social relationships and health. To achieve this I designed a novel classification of measures of social relationships (Chapter 4) and used it to systematically review the evidence relating to incident cardiovascular disease (Chapter 5). To address the gaps identified from this review, I explored patterns of loneliness and social isolation over time in the English Longitudinal Study of Ageing (Chapter 6). For the first time, I analysed whether repeated exposure to loneliness or social isolation was associated with incident cardiovascular disease (Chapter 7). In this final chapter I summarise the contribution that I have made to the research evidence (8.1). Highlighting what we now know, and pointing to the new questions arising from my analyses, I reflect on the study's strengths and identify opportunities for building on the gaps with future research (8.2). Beyond the academic literature, my findings have implications for policy and practice; I discuss these with reference to the assumptions underlying the intervention strategies currently promoted in the UK, considering how these strategies can be strengthened in future (8.3).

8.1. Summary of the main messages from my study

The aim of my doctoral work was to further our understanding of the health implications of social relationships. Specifically, I set out to:

a) Bring clarity to the epidemiological literature on social relationships;

b) Investigate the link between loneliness and/or social isolation, and incident cardiovascular disease (CVD);

c) Identify whether certain subgroups may be at greater risk of incident CVD following loneliness or social isolation.

Taking each of these aims in turn, I summarise the key messages from my work in the three sections below.

8.1.1. Bringing conceptual clarity to the epidemiological literature

To bring clarity to the epidemiological literature on social relationships, I designed a novel way of classifying the measures used by researchers to capture objective and subjective aspects of relationships. This is the first time that such a classification has been proposed. Without a common framework, it was up until now difficult to know how measurement tools with distinct labels and developed from different theoretical perspectives compared to one another. Through identifying two dimensions by which each measure can be assessed – i.e. whether the measure targets structural or functional characteristics and the degree of subjectivity expected of respondents – the classification presented in Chapter 4 was a first step in a) helping researchers to adopt a conceptually clear approach and b) enabling research into how different dimensions of social relationships are linked to health and wellbeing.

The new classification makes it clear to researchers and readers of research that the large number of existing social relationship measures include a range of different questions. These questions differ with regard to what they explicitly target (e.g. the availability of social resources, or the presence of negative feelings) and how they are phrased – e.g. whether they ask people to count the number of people they speak to, or whether they ask people about their satisfaction with their frequency of contact with others. Within one tool, it is common to find items phrased in different ways and/or targeting different aspects of relationships. This raises the question of what the overall tool seeks to capture – and whether it succeeds.

As well as highlighting heterogeneity across and within instruments, the new classification illustrates the overlap between them. Despite being labelled as measuring distinct domains, such as social support or social network, tools often share questions or target the same domains (e.g. perceptions of relationship adequacy). When studying the health implications of different social relationship characteristics, being aware of this overlap is crucial. Our ability to disentangle different pathways linking relationships to health depends on clarity over what is being measured. If a multi-item questionnaire includes questions about both loneliness and social isolation (e.g. the OARS Social Resource Scale), how can we attribute effects to either one or the other? When reviewing the literature, having a clear sense of the similarities and differences across studies is essential, since it forms the basis of decisions about how we group, analyse and interpret the evidence. Where there is overlap between measures this can justify pooling studies together. Conversely, where tools are clearly examining distinct concepts, looking at the evidence separately will yield more meaningful results. Previous research has already found perceptions of social support to be a better predictor of adjustment to stressful life events than received support, for example (Wethington and Kessler, 1986; Kessler and McLeod, 1985). In my ELSA analyses loneliness, but not social isolation, predicted increased risk of CVD. No one concept and/or measure is likely to fit all purposes and capture the different aspects of social relationships. It will be important for future investigators to have a clear hypothesis as to which dimension of relationships they wish to focus on, so that they can identify appropriate measurement tools.

In summary, the key message from Chapter 4 is that being clear about what is being measured is important if we are to better understand the links between social relationships and health. I have disseminated this message and presented the new classification at conferences and seminars (including the British Society for Gerontology Annual Conference in 2015, Campaign to End Loneliness Research seminar in 2016) and in an article published in *BMJ Open* (Valtorta et al., 2016b). I purposefully chose to publish in a medical journal to attract the attention of researchers who would not necessarily be familiar with the heterogeneity of social relationship measures. Encouragingly, the *BMJ Open* article has motivated epidemiologists at University College London to organise a one-day research workshop in 2017 to discuss measures of social relationships and explore ways of testing the validity and reliability of my classification – a valuable opportunity to build on my doctoral work and promote clarity in the field.

8.1.2. Investigating the link between loneliness, social isolation and incident CVD

I used the classification presented in Chapter 4 to identify studies that measured loneliness and social isolation and investigated their association with incident CVD. The results of the review reported in Chapter 5 showed that having fewer relationships and/or feeling unhappy about one's relationships was associated with a 29% increased risk of developing coronary heart disease, and a 32% increased risk of stroke. This was the first review to investigate whether loneliness or social isolation were risk factors for new diagnoses of CVD. Previous studies focusing on mortality had identified both experiences as determinants of premature death; but it was not clear whether this was because lonely or isolated individuals had a worse prognosis, or whether they were more likely to become ill. By synthesising the evidence from longitudinal rather than cross-sectional studies and including only participants without prior CVD, I was able to identify social relationships as risk factors for morbidity and not just mortality, providing new evidence of the negative association between deficiencies in social relationships and health.

The results from my systematic review were published in *Heart* (Valtorta et al., 2016c) and have received extensive media coverage. As of 19th December 2016, the article was listed in the top 5% of research outputs scored by Altmetric, an indicator of the amount of attention received from the press and the wider public (https://www.altmetric.com). The message that social relationships are important for remaining in good health is a popular one, and has generated much discussion about what we can do to strengthen relationships in future (see for example Holt-Lunstad, 2016) .

Perhaps unsurprisingly, the gaps in our knowledge identified by my review have been less widely debated by readers and campaigners. They are no less important. In particular, the absence of studies measuring both loneliness and social isolation, and reliance on single rather than repeated measures of social relationships, meant that health implications over time were unknown. It is to address this gap that I set out to explore patterns of loneliness and social isolation in the English Longitudinal Study of Ageing (ELSA). What I found and reported in Chapter 6 was that loneliness and social isolation fluctuated substantially over time, both within and across individuals; and that the two experiences, while correlated, were distinct and warranted being studied as separate entities in epidemiological studies.

My analyses of loneliness and social isolation were the first to span across more than two waves of data. Applying the knowledge that I acquired from looking at how responses change over time, I was able to study the links between loneliness and social isolation as time-varying factors and incident CVD in ELSA. Using discrete-time survival modelling, I identified loneliness as a risk factor for developing a heart condition or stroke (comparing one v. no report of loneliness across an eight-year study period, hazard ratio: 1.36, 95% confidence interval: 1.09 to 1.71). This association was independent of social isolation, gender, wealth and commonly recognised risk factors for CVD. Repeated exposure to loneliness did not predict greater CVD risk, when compared with one-off reports of loneliness. There was no indication that social isolation moderated the effect of loneliness.

In ELSA, social isolation did not emerge as a risk factor for CVD. Adults who were not isolated in any of the study waves appeared to be at greater risk of reporting a non-fatal event (e.g. participants who were not isolated in any wave had a 71% greater risk of reporting a new diagnosis compared with people who were isolated once, 95% confidence interval: 1.00 to 2.89), suggesting that the benefits of social contact may have been outweighed by their potentially detrimental effects on health. The measure I used to capture social isolation focused on relationship quantity, whereas the studies reviewed in Chapter 5 often touched on their quality too (e.g. in the Berkman-Syme Social Network Index, used in six of the reviewed studies, participants are asked 'How many close friends do you have? How many relatives do you have that you feel close to?'). What my findings suggest is that perceptions of relationships, rather than their quantity, may be more important for predicting risk of CVD.

8.1.3. Identifying groups that may be at greater risk of incident CVD following loneliness or social isolation

My ELSA analyses uncovered no evidence that gender or wealth moderated the effect of social relationships. The increased CVD risk associated with loneliness was greater among younger cohort members (there was a 76% increased risk among those aged 60 when comparing lonely to non-lonely individuals; the increase was only 35% among those aged 70 and 3% among people aged 80). There was some indication that loneliness may predict stroke more strongly among people who would otherwise, based on the risk factors usually taken into account when assessing CVD Risk, not be considered at risk of stroke. These differences – according to age and CVD risk – were observed independently of traditional risk factors for CVD, suggesting that these were not the sole mechanisms through which loneliness might affect disease risk.

8.2. Critique of the overall study design

A key strength of my doctoral work is its grounding in systematic methods and the efforts made to achieve conceptual clarity. Without an informed overview of the tools used to assess relationships in epidemiological studies, it would not have been possible to set clear empirically-derived criteria for inclusion in my systematic review; this is why I produced the classification of tools. In the absence of longitudinal studies of loneliness and social isolation, I also needed to conduct thorough exploratory analyses of patterns of answers in ELSA. Only once I had investigated how the variables behaved over time could I appropriately code them in survival analyses.

In my secondary analyses of non-fatal outcomes in ELSA, I was particularly careful to use measurement tools that did not overlap, so as to clearly distinguish between the more objective situation of social isolation, and the subjective experience of loneliness. I developed a comprehensive index of social isolation that covered contact with family and friends, community engagement and colleagues. Unlike previous studies that used ELSA data (Shankar et al., 2011; Steptoe et al., 2013b), this index took into account contact with household members other than spouses, and access to work colleagues – two potentially important sources of social interaction (Collins et al., 2016; Rothon et al., 2012). As with other extant self-report measures of social isolation, whether the index I designed accurately reflects access to relationships with others is unknown and future work is needed to evaluate its validity and reliability. Diaries and other means of monitoring contact such as self-report via digital devices, or third-party observations, are examples of sources from which data could be gathered to assess whether the index succeeds in capturing the frequency with which people interact with others. Smaller scale studies and interviews could help to identify items that might be missing from extant indices, and to gauge the interpretability of items and scoring. Repeated administration over short periods of time and comparisons between answers to different tools would provide further insights into the instrument's reliability.

Studying loneliness and social isolation simultaneously allowed me to clarify their distinct associations with incident non-fatal CVD and to highlight that perceptions of relationships may be particularly important. In ELSA, reports of feeling lonely much of the time in the past week were associated with an increased risk of developing CVD, independently of social isolation. Experiencing isolation, on the other hand, appeared to have a protective effect. Isolated individuals may be protected from the potentially negative influences of social relationships, including stress-inducing interactions and behaviours such as excessive alcohol consumption (Rosenquist et al., 2010). The implications of loneliness, meanwhile, could stem from psychological mechanisms such as depression (Cacioppo et al., 2006b; Kawachi and Berkman, 2001), a known risk factor for CVD (Lichtman et al., 2008). Future ELSA analyses could be conducted to study the potentially mediating effect of mental health and/or the effect of changes in circumstances such as widowhood or migration. To gain insight into how loneliness and social isolation shape a person's daily routine, or why it is that someone might feel repeatedly or temporarily lonely, it will be necessary to design qualitative studies that can offer insights into the nuances and diversity of experiences. These insights would be particularly valuable for understanding the heterogeneity of loneliness and social isolation patterns observed in ELSA, and for shedding light on the within-individual variations in loneliness and social isolation over time.

My ELSA analyses uncovered differences in the association between loneliness and incident CVD according to age and Framingham risk category. The increased CVD risk associated with feeling lonely was greater among younger participants, suggesting that social relationships may play a greater role in predicting health outcomes among younger older adults. Meanwhile, the finding that lonely people with lower CVD risk score were more likely to develop a stroke than lonely people with higher CVD risk score could be an indicator of the limitations of the CVD Framingham risk score when applied to a UK population (Collins and Altman, 2012).

An important question is whether my study of loneliness, social isolation and health can further our understanding of whether social relationships are causally linked to subsequent health outcomes. With reference to Gordis' guidelines on temporality, plausibility, strength and consistency, my findings, when added to the existing literature, do support a possible causal relationship (Gordis and Forgione, 2014). I found that loneliness and social isolation *prior* to events predicted the risk of disease, both in the meta-analyses and in the secondary analyses of ELSA. All of the results from my analyses were plausible in so far as they could be explained by mechanisms such as mental health and/or health-related behaviours for which there is growing research evidence (see Chapter 2 for a summary of the literature on mechanisms and pathways). Concepts close to loneliness, such as the presence of depressive symptoms, have been identified as risk factors for stroke as well as heart disease, suggesting that loneliness is a plausible determinant (Lichtman et al., 2008). The magnitude of the association between loneliness and incident non-fatal CVD in ELSA, around 30%, was similar to the pooled estimates in my meta-analyses, as well as being comparable to the increased CVD risk associated with other psychosocial factors such as job strain and anxiety (Roest et al., 2010; Fransson et al., 2015).

My findings did not uniformly support causality. The absence of a dose-relationship effect in ELSA – increased numbers of loneliness reports did not predict increased risk of non-fatal CVD in my survival analyses – is perhaps the strongest indicator of loneliness possibly not being a causal factor, but rather a marker of risk. Future analyses based on datasets other than ELSA are needed to provide comparisons with the effects I found, to check consistency across different settings. If similar results are obtained using different data, this will strengthen the case for causality – as would obtaining comparable estimates for other health outcomes, such as fatal CVD.

It is important to recognise that the two concepts I used to study social relationships, loneliness and social isolation, are measured at the individual level; they are intended to capture the experiences of each participant, as opposed to a concept like social capital, which targets social relationships at the group level (Putnam, 2000). Reliance on individual level measures and use of a single national dataset means that my study can tell us little, if anything, about the role of context – e.g. the influence of cultural, political and social values at the level of society. In Chapter 2, we saw that these factors have the potential to shape individual level relationships and their links with health in a variety of ways, e.g. through defining labour market structures or excluding certain populations from access to health, social care and other resources. When interpreting my findings, we should avoid seeking explanations at the individual level only. Societal inequality and atomization at the community level have consistently been linked to reduced trust and heightened perceptions of relative deprivation, leading to negative outcomes in wellbeing and health (O'Rand, 2001; Wilkinson and Pickett, 2010). Future comparative studies across different settings, and analyses incorporating group and society-level information, will be needed to complement the analyses presented here and to contextualise them. Without a better understanding of the role of context, interventions may fail to tackle the structural dynamics underlying deficiencies in social relationships and health inequity.

As well as contextualising the relationship between loneliness, social isolation and health at the macro level, taking a life course approach is another way in which we can hope to increase our knowledge of the factors shaping social relationships in future. For my analyses, ELSA offered the opportunity to include younger participants than commonly found in 'ageing' cohorts (aged 50+); but it provided no insight into social relationship patterns earlier in life. What we know from the limited evidence on childhood experiences is that isolation in early life predicts isolation in adolescence and adulthood (Caspi et al., 2006), and that it is associated with smoking, obesity and psychological distress in adulthood (Lacey et al., 2014). Future longitudinal studies will be needed to clarify how dynamics of social relationships in adults of working age are linked to relationship patterns and health outcomes in later life.

My analyses of the relationship between loneliness, social isolation and health in ELSA relied on quantitative data. Whilst answers to questionnaires allowed me to study changes in social relationships within individuals over time and to highlight an association between loneliness and CVD, they provided limited insight into the reasons behind fluctuations and the possible mechanisms linking loneliness to health. In future, qualitative interview data could provide in depth data on the dynamics of social relationships and help us to understand the reasons behind reported changes in perceptions and objective characteristics of relationships. Interviews could also help to uncover the role of past experiences in shaping relationships in later life, and shed light on the coping mechanisms developed by older adults faced with chronic loneliness in later life.

8.3. Implications for policy and practice

In England, the societal implications of social relationships have recently attracted growing attention from policy-makers. In 2011, a national Campaign to End Loneliness was set up by four charities and Manchester city council, in a drive to raise awareness of the issue of loneliness and isolation among older adults (Campaign to End Loneliness, 2011a). This campaign is recognised as having led to the inclusion of these challenges in the 2012 White Care and Support White Paper, and in the strategic plans of health and wellbeing boards (Charities Evaluation Services, 2013). So far, efforts have principally concentrated on finding ways of identifying lonely and/or socially isolated individuals, and on rekindling social ties among older adults through interventions such as befriending or group activities delivered by third sector organisations (Windle et al., 2011). The expectation is that by tackling loneliness and social isolation in later life, this will reduce the burden of morbidity and mortality (Valtorta, 2016).

In general, we should be cautious about assuming that interventions to strengthen social relationships and improve perceptions can positively affect health outcomes. The estimates generated from my analyses are based on comparisons *between* individuals, rather than *within*; and there is no evidence, in the rest of the literature, that the effects of loneliness and social isolation are modifiable. In relation to pregnancy outcomes for example, research has consistently linked lack of social support to poor outcomes such as low birth weight; but antenatal interventions to improve social support have consistently failed to improve outcomes (Hodnett et al., 2010). One of the reasons for this may be that these interventions are not powerful enough to counter the stressors in participants' lives; and/or that these targeted interventions do not replicate the benefits of social relationships which individuals have nurtured over the life course.

Combined with the absence of evidence of effective interventions, the fact that repeated reports of loneliness did not predict greater risk of incident non-fatal CVD in ELSA suggests that primary prevention strategies – i.e. seeking to prevent the occurrence of chronic loneliness – may be particularly pertinent. At present, primary prevention is quasi absent from the intervention discourse on tackling loneliness, social isolation and associated health problems (Valtorta, 2016). In the remainder of this chapter, I outline how my findings could inform such primary prevention strategies, as well as how they might be used to strengthen secondary and tertiary prevention initiatives (respectively aimed at preventing adverse health outcomes among lonely or isolated individuals, and seeking to minimize the health implications of social relationship deficiencies).

8.3.1. Implications for primary prevention strategies: preventing modifiable loneliness and social isolation risk factors, and anticipating the others

Echoing other studies of loneliness in later life, my ELSA analyses showed that chronic loneliness was reported by a minority of older adults: at any one point in time, 8% of ELSA participants stated that they often felt lonely when asked directly, and the same proportion reported high scores of 7 to 9 on the UCLA Loneliness Scale (Victor et al., 2005a; Victor and Yang, 2012). Social isolation was experienced by even fewer participants, around 5% of participants at each wave. Clearly, based on these prevalence figures, neither loneliness nor social isolation are inevitable concomitants of ageing. It is true that, in my exploratory analyses, participants aged over 80 were more likely to report chronic loneliness; but even then, three quarters of individuals aged 80+ did not report being unhappy about their relationships. Rather than approach deficiencies in social relationships as a problem associated with later life, my findings support considering what other factors are associated with loneliness and isolation, and tackling these.

In ELSA, participants who were widowed, in the lowest wealth quintile or who reported a limiting long-standing illness were more likely to report feeling intensely lonely at least once over the course of a ten-year period. Experiencing social isolation was close to three times more common among bereaved individuals and those in the lowest wealth quintile. Tackling modifiable factors, such as improving people's socio-economic circumstances, could decrease people's likelihood of experiencing chronic loneliness or social isolation – in turn potentially reducing the burden of negative health outcomes associated with social relationship deficiencies. In other words, tackling loneliness and social isolation need not focus exclusively on strengthening people's social relationships. At the macro level described in Chapter 2, policies and interventions explicitly concerned with domains as diverse as housing, education, employment or access to healthcare, in so far as they affect risk factors for loneliness and social isolation and directly shape social relationships and expectations, could be important leavers of action.

Where situations cannot be avoided, as with the advent of older age and widowhood, accompanying people who are about to enter these vulnerable stages of life, or who have recently experienced them, could help to prevent chronic loneliness or isolation. Third sector organisations who support widowed individuals and/or older adults, but also community service providers and informal networks, are well placed to identify subjects at risk, and to either directly help or signpost people to relevant local activities and initiatives.

8.3.2. Implications for secondary prevention strategies: acknowledging the variability of loneliness and social isolation

In the UK, the focus of intervention strategies to date has been on improving the social relationships of people who feel lonely, or who are socially isolated (Valtorta, 2016). Evaluative studies have already pointed to the difficulty of improving people's feelings about their relationships, emphasising that examples of successful initiatives are rare and that they require a robust theoretical framework and tailored, long-term resources (Dickens et al., 2011). The heterogeneity in ELSA responses over time are a further indication of the complexity underlying both perceptions of social relationships and more objective network characteristics. Very few adults reported constant levels of loneliness or social interaction, and the challenge for interventions is to take into account the many factors that influence social relationships.

Loneliness and social isolation are, by definition, distinct concepts; what my analyses indicate is that they are, in practice, often experienced separately. Given that loneliness is not necessarily accompanied by social isolation, it is perhaps not surprising that many of the solutions promoted to date, which primarily rely on increasing social interaction, have not been shown to effectively improve participant's feelings. While openly labelling interventions as targeting loneliness may be problematic due to stigmatisation, it will be important for future interventions to be clear on which aspect of social relationships it is that they seek to improve. If it is perceptions, then acknowledging that these do not necessarily simply reflect a more objective reality will be key.

8.3.3. *Implications for tertiary prevention strategies: improving the evidence base, targeting potential mechanisms, and incorporating assessments into patient care*

Many tertiary interventions have been developed to strengthen the social relationships of people who feel lonely or are isolated and/or experience ill health. These range from community education groups to sports activities, choirs and befriending schemes. NHS England has been promoting access to such non-clinical interventions which are delivered by voluntary services and community groups and seen as a potential solution to alleviating pressure on health and social care services (Dyson, 2014). Through social prescribing, general practitioners have a non-medical referral option which they can use alongside existing treatments to improve patients' health and wellbeing. In the absence of robust evidence, the effectiveness of social prescribing is currently unclear. Studies to date have mainly described evaluations of pilot projects and do not provide sufficient detail to gauge impact on health and wellbeing, service use and costs (Centre for Reviews and Dissemination, 2015).

The findings from my systematic review and survival analyses do suggest that tertiary strategies such as social prescribing could help to minimize the health implications of deficiencies in social relationships, and that social relationships should be taken into account when caring for patients and service users. Social relationships can be used as a lever to promote and support improvements in behaviours relating to health such as physical exercise, diet and smoking cessation, and interventions relying on the involvement of close relationships in medical care have the potential to positively effect adherence to advice and medication (Holt-Lunstad & Smith, 2016). In ELSA, loneliness predicted increased disease risk independently of the risk factors commonly recognized for CVD, implying that solutions may require focusing on other mechanisms such as physical activity and/or mental health and wellbeing to prevent the development of CVD. In turn, intervening via these mechanisms could improve people's loneliness feelings.

In elderly care and family practice, if lonely and isolated patients are being treated more often than others, then health practitioners are well placed to play a key role in identifying those at highest risk. One of the challenges this raises is developing a means of assessment that captures the multifaceted nature of loneliness while being easily incorporated into day-to-day practice. Because individuals might not wish to publicly admit to frequent loneliness feelings, using a direct single question may not be sufficient. Familiarity with the range of tools available is likely to require that social relationships and associated social circumstances be covered in medical, nursing and social care education in future (Holt-Lunstad & Smith, 2016).

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As responses to the challenge of persistent loneliness and social isolation develop, it will be important to monitor and evaluate their effects via robust studies, taking into account the complexity of the association between social relationships and health. The success of future strategies will depend on careful consideration of the macro-level context within which objective and subjective aspects of social relationships, and health, are shaped. Importantly, replacing deficits in 'natural' social relationships with services such as befrienders may have a different outcome to preserving a person's social convoy; future evaluative research will be needed to determine the comparative effects of both strategies. Effective cooperation between policy-makers, the third sector, practitioners, service users and researchers will be key to furthering our understanding of how best to tackle this public health and societal issue.

Appendix 4.1 List of tools identified, with references

Tool	Studies in which the tool was used
Berkman-Syme Social Network Index (Berkman and Breslow, 1983)	Avendano, M, Kawachi, I, Van Lenthe, F, et al. 2006, 'Socio-economic status and stroke incidence in the US elderly: the role of risk factors in the EPESE study', *Stroke*, vol. 37, 6, 1368-73. Eng, PM, Rimm, EB, Fitzmaurice, G, Kawachi, I 2002, 'Social ties and change in social ties in relation to subsequent total and cause-specific mortality and coronary heart disease incidence in men', *American Journal of Epidemiology*, vol. 55, 8, 700-09. Gafarov, VV, Panov, DO, Gromova, EA, et al. 2013, 'The influence of social support on risk of acute cardiovascular diseases in female population aged 25-64 in Russia', *International Journal of Circumpolar Health*, vol. 72, 21210. Kang, SH, Bloom, JR 1996, 'Social support and cancer screening among older black Americans', *Journal of the National Cancer Institute*, vol. 85, 737-42. Kawachi, I, Colditz, GA, Ascherio, A, et al. 1996, 'A prospective study of social networks in relation to total mortality and cardiovascular disease in men in the USA', *Journal of Epidemiology and Community Health*, vol. 50, 3, 245-51. Parboosingh, EJ, Larsen, DE 1987, 'Factors influencing frequency and appropriateness of utilization of the emergency room by the elderly', *Medical Care*, vol. 25, 12, 1139-47. Sykes, D, Arveiler, D, Salters, CP, et al. 2002, 'Psychosocial risk factors for heart disease in France and Northern Ireland: the Prospective Epidemiological Study of Myocardial Infarction (PRIME)', *International Journal of Epidemiology*, vol. 31, 6, 1227-34.
11-item de Jong Gierveld Loneliness Scale (de Jong Gierveld and van Tilburg, 2006)	Iecovich, E, Biderman, A 2012, 'Attendance in adult day care centers and its relation to loneliness among frail older adults', *International Psychogeriatrics*, vol. 24, 3, 439-48. Kempen, GI, Suurmeijer, TP, 1991, 'Factors influencing professional home care utilization among the elderly', *Social Science & Medicine*, vol. 32, 1, 77-81.
35-item Duke Social Support Index (Landerman et al., 1989)	Hastings, SN, George, LK, Fillenbaum, GG, Park, RS, Burchett, BM, Schmader, KE 2008, 'Does lack of social support lead to more ED visits for older adults?', *The American Journal of Emergency Medicine,* vol. 26, 4, 454-61.
11-item Duke Social Support Index (Powers et al., 2004)	Strodl, E, Kenardy, J, Aroney, C 2003, 'Perceived stress as a predictor of the self-reported new diagnosis of symptomatic CHD in older women', *International Journal of Behavioral Medicine*, vol. 10, 3, 205-20. Strodl, E, Kenardy, J 2008, 'The 5-item mental health index predicts the initial diagnosis of nonfatal stroke in older women', *Journal of Women's Health*, vol. 17, 6, 979-86.
4-item Duke Social Support Index	Longman, JM, Rolfe, MI, Passey, MD, et al. 2012, 'Frequent hospital admission of older people with chronic disease: a cross-sectional

(Longman et al., 2012)	survey with telephone follow-up and data linkage', *BMC Health Services Research,* vol. 12, 373.
Duke-UNC Functional Social Support Questionnaire (Broadhead et al., 1988)	Ottenbacher, KJ, Graham, JE, Ottenbacher, AJ, et al. 2012, 'Hospital readmission in persons with stroke following postacute inpatient rehabilitation', *The Journals of Gerontology: Series A, Biological Sciences and Medical Sciences*, vol. 67, 8, 875–81. Stoddart, H, Whitley, E, Harvey, I, Sharp, D 2002, 'What determines the use of home care services by elderly people?', *Health & Social Care in the Community*, vol. 10, 5, 348-60.
ENRICHD Social Support Inventory (ESSI) (Mitchell et al., 2003)	Coventry, PA, Gemmell, I, Todd, CJ 2011, 'Psychosocial risk factors for hospital readmission in COPD patients on early discharge services: a cohort study', *BMC Pulmonary Medicine*, vol.11.
Gijón Scale for the elderly's social-family assessment, family and social relationships subscales (García-González et al., 1999)	Lorén Guerrero, L, Gascón Catalán, M 2011, 'Biopsychosocial factors related to the length of hospital stay in older people', *Revista Latino-Americana de Enfermagem*, vol. 19, 6, 1377-84.
12-item Interpersonal Support Evaluation List (ISEL) (Cohen et al., 1985)	Eakin, EG, Strycker, LA 2001, 'Awareness and barriers to use of cancer support and information resources by HMO patients with breast, prostate, or colon cancer: patient and provider perspectives', *Psycho-oncology*, vol. 10, 2, 103-13.
Interview Measure of Social Relationships (Brugha et al., 1987)	Lesage, AD, Charron, M, Punti, R, et al. 1994, 'Factors related to admission of new patients consulting geriatric psychiatric services in Montreal', *International Journal of Geriatric Psychiatry,* vol.9, 8, 663-72.
Litwin Support Network Types (Litwin, 1997)	Litwin, H, 1997, 'Support network type and health service utilization', *Research on Aging*, vol. 19, 274–99.
10-item Lubben Social Network Scale (Lubben, 1988)	Nagayoshi, M, Everson-Rose, SA, Iso, H, Mosley, TH, Rose, KM, Lutsey PL, 'Social network, social support, and the risk of incident stroke: the atherosclerosis risk in communities study', *Circulation* 2014, vol. 129, 2868-73. Player, MS, King, DE, Mainous, AG 3rd, Geesey, ME 2007, 'Psychosocial factors and progression from prehypertension to hypertension or coronary heart disease', *Annals of Family Medicine*, vol. 5, 5, 403-11. Mistry, R, Rosansky, J, McGuire, J, McDermott, C, Jarvik, L, UPBEAT Collaborative Group 2001, 'Social isolation predicts re-hospitalization in a group of older American veterans enrolled in the UPBEAT Program', *International Journal of Geriatric Psychiatry*, vol.16, 950-59. Stoddart, H, Whitley, E, Harvey, I, Sharp, D 2002, 'What determines the use of home care services by elderly people?', *Health & Social Care in the Community*, vol. 10, 5, 348-60.
6-item Lubben Social Network Scale (Lubben et al., 2006)	Iliffe, S, Kharicha, K, Harari, D, Swift, C, Gillmann, G, Stuck, AE 2007, 'Health risk appraisal in older people 2: the implications for clinicians and commissioners of social isolation risk in older people', *British Journal of General Practice*, vol. 57, 537, 277-82.

	Kobayashi, KM, Cloutier-Fisher, D, Roth, M 2009, 'Making meaningful connections: a profile of social isolation and health among older adults in small town and small city, British Columbia', *Journal of Aging and Health*, vol. 21, 2, 374-97. Nelms, L, Johnson, V, Teshuva, K, Foreman, P, Stanley, J 2009, 'Social and health factors affecting community service use by vulnerable older people', *Australian Social Work*, vol. 62, 4, 507-24. Simning, A, Van Wijngaarden, E, Fisher, SG, Richardson, TM, Conwell, Y 2012, 'Mental healthcare need and service utilization in older adults living in public housing', *American Journal of Geriatric Psychiatry*, vol. 20, 5, 441-51.
Medical Outcomes Study (MOS) Social Support Survey (Sherbourne and Stewart, 1991)	de Boer, AG, Sprangers, MA, Speelman, HD, de Haes, HC 1999, 'Predictors of health care use in patients with Parkinson's disease: a longitudinal study', *Movement Disorders*, vol. 14, 5, 772-79.
Multidimensional Scale of Perceived Social Support (MSPSS) (Zimet et al., 1988)	Contrada, RJ, Boulifard, DA, Hekler, EB, et al. 2008, 'Psychosocial factors in heart surgery: presurgical vulnerability and postsurgical recovery', *Health Psychology*, vol. 27, 3, 309-19. Simning A, Van Wijngaarden, E, Fisher, SG, Richardson, TM, Conwell, Y 2012, 'Mental healthcare need and service utilization in older adults living in public housing', *American Journal of Geriatric Psychiatry,* vol. 20, 5, 441-51.
Negative Affect Scale (Bradburn, 1969)	Burnette, D, Mui, AC 1995, 'In-home and community-based service utilization by three groups of elderly Hispanics: a national perspective', *Social Work Research*, vol. 19, 4, 197-206. Tran, TV, Dhooper, SS, McInnis-Dittrich, K 1997, 'Utilization of community-based social and health services among foreign born Hispanic American elderly', *Journal of Gerontological Social Work*, vol. 28, 4, 23-43.
Nottingham Health Profile Social Isolation subscale (Hunt et al., 1981)	Naughton, C, Drennan, J, Treacy, P, et al. 2011, 'How different are older people discharged from emergency departments compared with those admitted to hospital?', *European Journal of Emergency Medicine*, vol. 18, 1, 19-24.
Older Americans Research and Service Center (OARS) Social Resource Scale (Fillenbaum, 1988)	Almagro, P, Barreiro, B, De Echaguen, AO, et al. 2006, 'Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease', *Respiration*, vol. 73, 3, 311-17. Mcauley, WJ, Arling, G 1984, 'Use of in-home care by very old-people', *Journal of Health and Social Behavior*, vol. 25, 1, 54-64. McCusker, J, Healy, E, Bellavance, F, Connolly, B 1997, 'Predictors of repeat emergency department visits by elders', *Academic Emergency Medicine*, vol. 4, 6, 581-88.
Oslo-3 Social Support Scale (Boen et al., 2010)	Boen, H, Dalgard, OS, Johansen, R, Nord, E 2010, 'Socio-demographic, psychosocial and health characteristics of Norwegian senior centre users: a cross-sectional study', *Scandinavian Journal of Public Health*, vol. 38, 5, 508-17.
Personal Resource Questionnaire (PRQ2000) (Weinert, 1984)	Chen, Y-J, Narsavage, GL 2006, 'Factors related to chronic obstructive pulmonary disease readmission in Taiwan', *Western Journal of Nursing Research*, vol. 28, 1, 105-24.

University of California, Los Angeles (UCLA) Loneliness Scale (Russell et al., 1978)	[5-item version] Auslander, GK, Soffer, M, Auslander, BA 2003, 'The supportive community: help seeking and service use among elderly people in Jerusalem', *Social Work Research*, vol. 27, 4, 209-21. [10-item version] Cheng, ST 1992, 'Loneliness-distress and physician utilization in well-elderly females', *Journal of Community Psychology*', vol. 20, 1, 43-56. [9-item version] Penning, MJ 1995, 'Health, social support, and the utilization of health services among older adults', *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*', vol. 50, 5, S330-39.
Wenger Support Network Typology (Wenger, 1991)	Eustace, A, Denihan, A, Bruce I, Cunningham, C, Coakley, D, Lawlor, BA 2001, 'Depression in the community dwelling elderly: do clinical and sociodemographic factors influence referral to psychiatry?', *International Journal of Geriatric Psychiatry,* vol. 16, 10, 975-79. Naughton, C, Drennan, J, Treacy, P, et al. 2010, 'The role of health and non-health-related factors in repeat emergency department visits in an elderly urban population', *Emergency Medicine Journal*, vol. 27, 9, 683-87. Naughton, C, Drennan, J, Treacy, P, et al. 2011, 'How different are older people discharged from emergency departments compared with those admitted to hospital?', *European Journal of Emergency Medicine*, vol. 18, 1, 19-24.
A measure of social isolation (LaVeist et al., 1997)	LaVeist, TA, Sellers, RM, Brown, KA, Nickerson, KJ 1997, 'Extreme social isolation, use of community-based senior support services, and mortality among African American elderly women', *American Journal of Community Psychology*, vol. 25, 5, 721-32
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A measure of social anchorage (Rennemark et al., 2009)	Rennemark, M, Holst, G, Fagerstrom, C, Halling, A 2009, 'Factors related to frequent usage of the primary healthcare services in old age: findings from The Swedish National Study on Aging and Care', *Health & Social Care in the Community*, vol. 17, 3, 304-11.
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An index of social support (Lai, 2006)	Lai, DW 2004, 'Use of home care services by elderly Chinese immigrants', *Home Health Care Services Quarterly*, vol. 23, 3, 41-56. Lai, DWL, Kalyniak, S 2005, 'Use of annual physical examinations by Aging Chinese Canadians', *Journal of Aging and Health*, vol. 17, 5, 573-91. Lai, DWL 2006, 'Predictors of use of senior centers by elderly Chinese immigrants in Canada', *Journal of Ethnic & Cultural Diversity in Social Work: Innovation in Theory, Research & Practice*, vol. 15, 12, 97-121.

A measure of living arrangements and informal care (Crets, 1996)	Crets, S 1996, 'Determinants of the use of ambulant social care by the elderly', *Social Science & Medicine*, vol. 43, 12, 1709-20.
A measure of satisfaction with social support (Feld and George, 1994)	Feld, S, George, LK 1994, 'Moderating effects of prior social resources on the hospitalizations of elders who become widowed', *Journal of Aging and Health*, vol. 6, 275-95.
A measure of social integration (Orth-Gomer et al., 1993)	Orth-Gomer, K, Rosengren, A, Wilhelmsen, L 1993, 'Lack of social support and incidence of coronary heart disease in middle-aged Swedish men', *Psychosomatic Medicine*, vol. 55, 1, 37-43. Rosengren, A, Wilhelmsen, L, Orth-Gomer, K 2004, 'Coronary disease in relation to social support and social class in Swedish men. A 15 year follow-up in the study of men born in 1933', *European Heart Journal*, vol. 25, 1, 56-63.
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A measure of social network (Reed et al., 1983)	Reed, D, McGee, D, Yano, K, Feinleib, M 1983, 'Social networks and coronary heart disease among Japanese men in Hawaii', *American Journal of Epidemiology*, vol. 117, 4, 384-96.
A measure of social network (Reed et al., 1984)	Reed, D, McGee, D, Yano, K 1984, 'Psychosocial processes and general susceptibility to chronic disease', *American Journal of Epidemiology,* vol. 119, 3, 356-70.
A measure of social support (Tran et al., 1997)	Tran, TV, Dhooper, SS, McInnis-Dittrich, K 1997, 'Utilization of community-based social and health services among foreign born Hispanic American elderly', *Journal of Gerontological Social Work*, vol. 28, 4, 23-43.
A measure of social support (Andre-Petersson et al., 2006)	Andre-Petersson, L, Hedblad, B, Janzon, L, Ostergren, PO 2006, 'Social support and behavior in a stressful situation in relation to myocardial infarction and mortality: who is at risk? Results from prospective cohort study 'Men born in 1914', Malmo, Sweden', *International Journal of Behavioral Medicine*, vol. 13, 4, 340-47.
A measure of social support (Ikeda et al., 2008)	Ikeda, A, Iso, H, Kawachi, I, et al. 2008, 'Social support and stroke and coronary heart disease: the JPHC study cohorts II', *Stroke*, vol. 39, 3, 768-75.
A measure of social support (Kuper et al., 2006)	Kuper, H, Adami, HO, Theorell, T, Weiderpass, E. 2006, 'Psychosocial determinants of coronary heart disease in middle-aged women: a prospective study in Sweden', *American Journal of Epidemiology*, vol. 164, 4, 349-57.
An social network index (Rutledge et al., 2008)	Rutledge, T, Linke, SE, Olson, MB, et al. 2008, 'Social networks and incident stroke among women with suspected myocardial ischemia', *Psychosomatic Medicine*, vol. 70, 3, 282-87.
Social network type (Coe et al., 1984)	Coe, RM, Wolinsky, FD, Miller, DK, Prendergast, JM 1984, 'Social network relationships and use of physician services. A reexamination.' *Research on Aging*, vol. 6, 2, 243-56. Coe, RM, Wolinsky, FD, Miller, DK, Prendergast, JM 1984, 'Complementary and compensatory functions in social network relationships among the elderly', *Gerontologist*, vol. 24, 4, 396-400.
Social network type – family (Coe et al., 1985)	Coe, RM, Wolinsky, FD, Miller, DK, Prendergast, JM 1985, 'Elderly persons without family support networks and use of health services. A follow-up report on social network relationships', *Research on Aging,* vol. 7, 4, 617-22.

Multi-item measures combining questions about frequency of contact with others and participation in activities, e.g. 'Over the last month were you able to: 1) attend events out- side of your home (e.g., community or social event); 2) visit friends or family in their own home?' (Molloy et al., 2010)	John, R, Roy, LC, Dietz, TL 1997, 'Setting priorities in aging populations: formal service use among Mexican American female elders', *Journal of Aging & Social Policy*, vol. 9, 1, 69-85. Krout, JA, Cutler, SJ, Coward, RT 1990, 'Correlates of Senior Center Participation - a National Analysis', *Gerontologist*, 30, 1, 72-79. Molloy, GJ, McGee, HM, O'Neill, D, Conroy, RM 2010, 'Loneliness and emergency and planned hospitalizations in a community sample of older adults', *Journal of the American Geriatrics Society*, vol. 58, 8, 1538-41. Stump, TE, Johnson, RJ, Wolinsky, FD 1995, 'Changes in physician utilization over time among older adults', *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* vol. 50, 1, S45-S58. Wolinsky, FD, Johnson, RJ 1991, 'The use of health services by older adults', *Journal of Gerontology*, vol. 46, 6, S345-57.
Question(s) about frequency of face to face and/or phone contact with family and/or friends and/or neighbours, e.g.: 'How many times during the past week did you spend some time with someone who does not live with you?' (Hyduk, 1996)	Aliyu, MH, Adediran, AS, Obisesan, TO 2003, 'Predictors of hospital admissions in the elderly: analysis of data from the longitudinal study on aging' *Journal of the National Medical Association*, vol. 95, 12, 1158-67. Almind, G, Holstein, BE, Holst, E, Due, P 1991, 'Old persons' contact with general practitioners in relation to health: a Danish population study', *Scandinavian Journal of Primary Health Care*, vol. 9, 4, 252-58. Auslander, GK, Soffer, M, Auslander, BA 2003, 'The supportive community: help seeking and service use among elderly people in Jerusalem', *Social Work Research*, vol. 27, 4, 209-21. Barefoot, JC, Gronbaek, M, Jensen, G, Schnohr, P, Prescott E 2005, 'Social network diversity and risks of ischemic heart disease and total mortality: findings from the Copenhagen City Heart Study', *American Journal of Epidemiology*, vol. 161, 10, 960-67. Burnette, D, Mui, AC 1995, 'In-home and community-based service utilization by three groups of elderly Hispanics: a national perspective', *Social Work Research*, vol. 19, 4, 197-206. Burnette, D, Mui, AC 1999, 'Physician utilization by Hispanic elderly persons - National perspective', *Medical Care*, vol. 37, 4, 362-74. Callahan, CM, Wolinsky, FD 1995, 'Hospitalization for major depression among older Americans', *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*', vol. 50, 4, M196-202. Calsyn, RJ, Winter, JP 1999, 'Who attends senior centers?', *Journal of Social Service Research*, vol. 26, 2, 53-69. Chappell, NL 1985, 'Social support and the receipt of home care services', *Gerontologist*, 25, vol. 1, 47-54. Chappell, NL, Blandford, AA 1987, 'Health-service utilization by elderly persons', *Canadian Journal of Sociology*, vol. 12, 3, 195-215.

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	Walter-Ginzburg, A, Chetrit, A, Medina, C, Blumstein T, Gindin J, Modan, B 2001, ‘Physician visits, emergency room utilization, and overnight hospitalization in the old-old in Israel: the Cross-Sectional and Longitudinal Aging Study (CALAS)’, *Journal of the American Geriatrics Society* 2001, vol. 49, 5, 549-56. West, GE, Delisle, MA, Simard, C, Drouin, D 1996, ‘Leisure activities and service knowledge and use among the rural elderly’, *Journal of Aging and Health*, vol. 8, 2, 254-79. Wilkins, K, Beaudet, MP 2000, ‘Changes in social support in relation to seniors' use of home care’, *Health Reports*, vol. 11, 4, 39-47. Wolinsky, FD & Johnson, RJ 1991 ‘The use of health services by older adults. *Journal of Gerontology*’, vol. 46, 6, S345-57.
Question(s) about the geographical proximity of family and friends (Nagga et al., 2012)	Nagga, K, Dong, HJ, Marcusson, J, Skoglund, SO, Wressle, E 2012, ‘Health-related factors associated with hospitalization for old people: comparisons of elderly aged 85 in a population cohort study’, *Archives of Gerontology and Geriatrics,* vol. 54, 2, 391-97.
Question(s) about the number of close friends or relatives, e.g. asking respondents for the 'number of friends [they] feel close to' (Lee et al., 2008)	Chappell, NL 1985, ‘Social support and the receipt of home care services’, *Gerontologist*, vol. 25, 1, 47-54. Feld, S, George, LK 1994 ‘Moderating effects of prior social resources on the hospitalizations of elders who become widowed’, *Journal of Aging and Health*, vol. 6, 275-95. Lee, BW, Conwell, Y, Shah, MN, Barker, WH, Delavan, RL, Friedman, B 2008, ‘Major depression and emergency medical services utilization in community-dwelling elderly persons with disabilities’, *International Journal of Geriatric Psychiatry*’, vol. 23, 12, 1276-82.
Question(s) about participation in social activities such as going to the cinema, sport events, church attendance or volunteering, e.g. 'In the past two weeks, did you go to a show or movie, sports event, club meeting, classes or other group event?' (Kovar et al., 1992)	Aliyu, MH, Adediran, AS, Obisesan, TO 2003, ‘Predictors of hospital admissions in the elderly: analysis of data from the longitudinal study on aging’, *Journal of the National Medical Association*, vol. 95, 12, 1158-67. Auslander, GK, Soffer, M, Auslander, BA 2003, ‘The supportive community: help seeking and service use among elderly people in Jerusalem’, *Social Work Research*, vol. 27, 4, 209-21. Mechakra-Tahiri, SD, Zunzunegui, MV, Dubé, M, Préville, M 2011, ‘Associations of social relationships with consultation for symptoms of depression: a community study of depression in older men and women in Québec’, *Psychological Reports*, vol. 108, 2, 537-52. Starrett, RA, Todd, AM, Deleon, L 1989, ‘A Comparison of the social-service utilization behavior of the Cuban and Puerto-Rican elderly’, *Hispanic Journal of Behavioral Sciences*, vol. 11, 4, 341-53. Starrett, RA, Decker, JT, Araujo, A, Walters, G 1989, ‘The Cuban elderly and their service use’, *Journal of Applied Gerontology*, vol. 8, 1, 69-85. Starrett, RA, Bresler, C, Decker, JT, Walters, GT, Rogers, D 1990, ‘The role of environmental awareness and support networks in Hispanic elderly persons' use of formal social services’, *Journal of*

	Community Psychology, vol. 18, 3, 218-27.
Question(s) about the perceived availability of emotional, tangible, informational and/or other support, e.g. 'Is there someone who would give you any help at all if you were sick or disabled, for example your husband/wife, a member of your family, or a friend?' (Barresi and McConnell, 1987)	Alkema, GE, Reyes, JY, Wilber, KH 2006, 'Characteristics associated with home- and community-based service utilization for Medicare managed care consumers', *Gerontologist*, vol. 46, 2, 173-82. Barresi, CM & McConnell, DJ 1987, 'Adult day care participation among impaired elderly', *Lifestyles*, vol. 8, 3-4, 82-94. Black, BS, Rabins, PV, German, P, McGuire, M, Roca, R 1993, 'Need and unmet need for mental health care among elderly public housing residents', *Gerontologist*, vol. 37, 6, 717-28. Clay, OJ, Roth, DL, Safford, MM, Sawyer, PL, Allman, RM 2011, 'Predictors of overnight hospital admission in older African American and Caucasian Medicare beneficiaries', *Journals of Gerontology Series A - Biological Sciences and Medical Sciences*, vol. 66, 8, 910-16. Ginsberg, G, Israeli, A, Cohen, A, Stessman, J 1996, 'Factors predicting emergency room utilization in a 70-year-old population', *Israel Journal of Medical Sciences*, vol. 32, 8, 649-64. Hyduk, CA 1996, 'The dynamic relationship between social support and health in older adults: assessment implications', *Journal of Gerontological Social Work*, vol. 27,1-2, 149-65. Jackson, SA, Shiferaw, B, Anderson, RT, Heuser, MD, Hutchinson, KM, Mittelmark, MB 2002, 'Racial differences in service utilization: the Forsyth County Aging Study', *Journal of Health Care for the Poor & Underserved*, vol. 13, 3, 320-33. Korten, AE, Jacomb, PA, Jiao, Z, et al. 1998, 'Predictors of GP service use: a community survey of an elderly Australian sample', *Australian and New Zealand Journal of Public Health*, vol. 22, 5, 609-15. Krause, N 2010, 'Close companions at church, health, and health care use in late life', *Journal of Aging and Health*, vol. 22, 4, 434-53. Mechakra-Tahiri, SD, Zunzunegui, MV, Dubé, M, Préville, M 2011, 'Associations of social relationships with consultation for symptoms of depression: a community study of depression in older men and women in Québec', *Psychological Reports*, vol. 108, 2, 537-52. Molloy, GJ, McGee, HM, O'Neill, D, Conroy, RM 2010, 'Loneliness and emergency and planned hospitalizations in a community sample of older adults', *Journal of the American Geriatrics Society*, vol. 58, 8, 1538-41. Preville, M, Vasiliadis, HM, Boyer, R, et al. 2009, 'Use of health services for psychological distress symptoms among community-dwelling older adults', *Canadian Journal on Aging*, vol. 28, 1, 51-61. Rittner, B & Kirk, AB 1995, 'Health care and public transportation use by poor and frail elderly people', *Social Work*, vol. 40, 3, 365-73. Wan, TT 1987, 'Functionally disabled elderly. Health status, social support, and use of health services', *Research on Aging*, vol. 9, 1, 61-

	78. Wilkins, K & Beaudet, MP 2000, 'Changes in social support in relation to seniors' use of home care', *Health Reports*, vol. 11, 4, 39-47.
Question(s) about received support, e.g. asking participants whether they received assistance during the past month with 7 tasks, including shopping, housework or going to the doctor (Auslander et al., 2003)	Auslander, GK, Soffer, M, Auslander, BA 2003, 'The supportive community: help seeking and service use among elderly people in Jerusalem', *Social Work Research*, vol. 27, 4, 209-21. Bazargan, M, Bazargan, S, Baker, RS 1998, 'Emergency department utilization, hospital admissions, and physician visits among elderly African American persons', *Gerontologist*, vol. 38, 1, 25-36. Chappell, NL & Blandford, AA 1987, 'Health-service utilization by elderly persons', *Canadian Journal of Sociology*, vol. 12, 3, 195-215. Cho, E 2007, 'The effects of nonprofessional caregivers on the rehospitalization of elderly recipients in home healthcare', *Advances in Nursing Science*, vol. 30, 3, E1-12. Choi, NG & Wodarski, JS 1996, 'The relationship between social support and health status of elderly people: does social support slow down physical and functional deterioration?', *Social Work Research*, vol. 20, 1, 52-63. Crets, S 1996, 'Determinants of the use of ambulant social care by the elderly', *Social Science & Medicine*, vol. 43, 12, 1709-20. Frederiks, CMA, Wierik, MJM, Van Rossum, HJL 1991, 'Factors associated with differential utilization of professional care among elderly people: Residents of old people's homes compared to elderly people living at home', *Acta Hospitalia*, vol. 31, 3, 33-45. Hakim, EA & Bakheit, AM 1998, 'A study of the factors which influence the length of hospital stay of stroke patients', *Clinical Rehabilitation*, vol. 12, 2, 151-56. Houde, SC 1998, 'Predictors of elders' and family caregivers' use of formal home services', *Research in Nursing & Health*, vol. 21, 6, 533-43. Jackson, SA, Shiferaw, B, Anderson, RT, Heuser, MD, Hutchinson, KM, Mittelmark, MB 2002, 'Racial differences in service utilization: the Forsyth County Aging Study', *Journal of Health Care for the Poor & Underserved*, vol. 13, 3, 320-33. John, R, Roy, LC, Dietz, TL 1997, 'Setting priorities in aging populations: formal service use among Mexican American female elders', *Journal of Aging & Social Policy,* vol. 9, 1, 69-85. Kim, H-S, Miyashita, M, Harada, K, Park, J-H, So, J-M, Nakamura, Y 2012, 'Psychological, social, and environmental factors associated with utilization of senior centers among older adults in Korea', *Journal of Preventive Medicine and Public Health*, vol. 45, 4, 244-50. Larsson, K, Thorslund, M, Forsell, Y 2004, 'Dementia and depressive symptoms as predictors of home help utilization among the oldest old: population-based study in an urban area of Sweden', *Journal of Aging*

	and Health, vol. 16, 5, 641-68. Li, LW 2004, 'Caregiving network compositions and use of supportive services by community-dwelling dependent elders', *Journal of Gerontological Social Work*, vol. 43, 2-3, 147-64. Miner, S 1995, 'Racial differences in family support and formal service utilization among older persons: a nonrecursive model', *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, vol. 50, 3, S143-53. Nelms, L, Johnson, V, Teshuva, K, Foreman, P, Stanley, J 2009, 'Social and health factors affecting community service use by vulnerable older people', *Australian Social Work*, vol. 62, 4, 507-24. Penning, MJ 1995, 'Health, social support, and the utilization of health services among older adults', *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, vol. 50, 5, S330-39. Safran, DG, Graham, JD, Osberg, JS 1994, 'Social supports as a determinant of community-based care utilization among rehabilitation patients', *Health Services Research,* vol. 28, 6, 729-50. Smith, GC 2003, 'Patterns and predictors of service use and unmet needs among aging families of adults with severe mental illness', *Psychiatric Services*, vol. 54, 6, 871-77. Tomassini, C, Glaser, K, Stuchbury, R 2007, 'Family disruption and support in later life: a comparative study between the United Kingdom and Italy', *Journal of Social Issues*, vol. 63, 4, 845-63.
Question(s) about satisfaction with social relationships and/or participation, e.g. asking participants whether they believe their present level of social activities to be adequate (Callahan and Wolinsky, 1995)	Auslander, GK, Soffer, M, Auslander, BA 2003, 'The supportive community: help seeking and service use among elderly people in Jerusalem', *Social Work Research*, vol. 27, 4, 209-21. Blalock, SJ, Byrd, JE, Hansen, RA, et al. 2005, 'Factors associated with potentially inappropriate drug utilization in a sample of rural community-dwelling older adults', *American Journal Geriatric Pharmacotherapy*, vol. 3, 3, 168-79. Boen, H, Dalgard, OS, Johansen, R, Nord, E 2010, 'Socio-demographic, psychosocial and health characteristics of Norwegian senior centre users: a cross-sectional study', *Scandinavian Journal of Public Health*, vol. 38, 5, 508-17. Callahan, CM, Wolinsky, FD 1995, 'Hospitalization for major depression among older Americans', *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, vol. 50, 4, M196-202. Chappell, NL 1985, 'Social support and the receipt of home care services', *Gerontologist*, vol. 25, 1, 47-54. Conforti, DA, Basic, D, Rowland, JT 2004, 'Emergency department admissions, older people, functional decline, and length of stay in hospital', *Australasian Journal on Ageing*, vol. 23, 4, 189-94.
Question(s) about the size of a person's network , e.g.	Chappell, NL 1985, 'Social support and the receipt of home care services', *Gerontologist*, vol. 25, 1, 47-54.

number of friends and relatives outside the household (Chappell and Blandford, 1987)	Chappell, NL, Blandford, AA 1987, 'Health-service utilization by elderly persons', *Canadian Journal of Sociology*, vol. 12, 3, 195-215. Feld, S & George, LK 1994, 'Moderating effects of prior social resources on the hospitalizations of elders who become widowed', *Journal of Aging and Health*, vol. 6, 275-95. Vogt, TM, Mullooly, JP, Ernst, D, Pope, CR, Hollis, JF 1992, 'Social networks as predictors of ischemic heart disease, cancer, stroke and hypertension: incidence, survival and mortality', *Journal of Clinical Epidemiology*, vol. 45, 6, 659-66. Wan, TT 1987, 'Functionally disabled elderly. Health status, social support, and use of health services', *Research on Aging*, vol. 9, 1, 61-78.
Question about time spent alone (Ginsberg et al., 1996)	Ginsberg, G, Israeli, A, Cohen, A, Stessman, J 1996, 'Factors predicting emergency room utilization in a 70-year-old population', *Israel Journal of Medical Sciences*, vol.32, 8, 649-64.
Single-item question about feeling lonely, e.g.: 'How often in the last 12 months have you been bothered by loneliness?' (Molloy et al., 2010)	Almind, G, Holstein, BE, Holst, E, Due, P 1991, 'Old persons' contact with general practitioners in relation to health: a Danish population study', *Scandinavian Journal of Primary Health Care*, vol. 9, 4, 252-58. Calsyn, RJ & Winter JP 1999, 'Who attends senior centers?', *Journal of Social Service Research*, vol. 26, 2, 53-69. Eaker, ED, Pinsky, J, Castelli, WP 1992, 'Myocardial infarction and coronary death among women: psychosocial predictors from a 20-year follow-up of women in the Framingham Study', *American Journal of Epidemiology*, vol. 135, 8, 854-64. Frederiks, CMA, Wierik, MJM, Van Rossum, HJL 1991, 'Factors associated with differential utilization of professional care among elderly people: residents of old people's homes compared to elderly people living at home', *Acta Hospitalia,* vol. 31, 3, 33-45. Ginsberg, G, Israeli, A, Cohen, A, Stessman, J 1996, 'Factors predicting emergency room utilization in a 70-year-old population', *Israel Journal of Medical Sciences*, vol. 32, 8, 649-64. Lofvenmark, C, Mattiasson, A-C, Billing, E, Edner, M 2009, 'Perceived loneliness and social support in patients with chronic heart failure', *European Journal of Cardiovascular Nursing*, vol. 8, 4, 251-58. Molloy, GJ, McGee, HM, O'Neill, D, Conroy, RM 2010, 'Loneliness and emergency and planned hospitalizations in a community sample of older adults', *Journal of the American Geriatrics Society*, vol. 58, 8, 1538-41. Nagga, K, Dong, HJ, Marcusson, J, Skoglund, SO, Wressle, E 2012, 'Health-related factors associated with hospitalization for old people: comparisons of elderly aged 85 in a population cohort study', *Archives of Gerontology and Geriatrics,* vol. 54, 2, 391-97. Thurston, RC & Kubzansky, LD 2009, 'Women, loneliness, and

	incident coronary heart disease', *Psychosomatic Medicine*, vol. 71, 8, 836-42.

Appendix 5.1 Forms used in the systematic review

A) Study screening checklist

Study details (citation):

Date screened:

Reviewer:

Question	Yes	No	Unclear	Other/comments
Was the study set in a high-income country?				
Was it a longitudinal observational study?				
Was loneliness and/or social isolation included as a predictor variable?				
Was loneliness and/or social isolation measured using a tool eligible for inclusion in this review?	Loneliness ('explicit') ☐ Social isolation ('explicit') ☐ Loneliness ('implicit') ☐ Social isolation ('implicit') ☐ Combined ☐ Other ☐			
Did the study include a measure of individual ill health as an outcome variable?				
Did the study report data linking loneliness and/or social isolation and ill health?				
	Yes	No	Unclear (need more information)	Other/comments
Final decision				

B) Data extraction form

Date of data extraction:

GENERAL INFORMATION			
	Data as reported	Location in source	Reviewer's comments
First author			
Year of publication			
Title			
Type of publication			
GENERAL STUDY CHARACTERISTICS			
	Data as reported	Location in source	Reviewer's comments
Aim of the study			
Study design			
Source of the data (e.g. name of cohort)			
Date of data collection			
Length of follow-up			
Country			
Population			
Exclusion criteria			
Method of recruitment			
Type of sample			
Participation rate			
Initial sample size			
Final sample size			
PARTICIPANTS			
Age	Mean: SD: Range:		
Gender	Men: Women:		
Ethnicity			
Socio-economic status			
Relationship status			
Disability status			
Severity of illness			
Comorbidities			
MEASURE(S) OF LONELINESS AND/OR SOCIAL ISOLATION			

What the study authors say they are measuring			
Tool used			
Is this a measure of loneliness, social isolation or both according to the definitions used in this review?			
How many/what proportion of the people in the study were classed as lonely and/or isolated?			
MEASURE(S) OF HEALTH			
Disease or condition of interest			
Tool used			
Description of tool			
How many/what proportion of the people in the study had the disease?			
ANALYSIS			
Type of independent variable			
Type of dependent variable			
Treatment effect measure			
Statistical methods used to analyse the data			
Confounders controlled for			
RESULTS & CONCLUSIONS			
Findings of relevance			
Authors' conclusion(s)			
OTHER INFORMATION			

References to other relevant studies			
Correspondence required for further study information			
ANY OTHER NOTES/COMMENTS			

Key:

NA – Not applicable ; NR – Not reported

C) Risk of bias and precision assessment tool for observational studies

STUDY DETAILS (citation):

Date assessed:

Reviewer:

Domain	Description: summarise evidence from text and any further comments	Judgement
External validity		
Sampling bias Was the sample collected in such a way that some members of the intended population were less likely to be included than others?		Yes Unclear No
Non-response bias Did respondents differ from non-respondents in ways likely to have increased risk of bias?		Yes Unclear No
Missing data Did subjects with data at baseline differ from subjects with missing data in ways likely to have increased risk of bias?		Yes Unclear No
Internal validity		
Differential loss to follow-up Did subjects lost to follow-up differ from subjects who remained in the study in ways likely to have increased risk of bias?		Yes Unclear No
Measurement error - exposure Were the tools used to measure loneliness and/or social isolation valid and reliable?		Yes Unclear No
Measurement error – outcome		Yes Unclear No
Detection bias (blinding of outcome assessor) NB: only applies to outcome where this was assessed by means other than self-report.		Yes Unclear No
Risk of confounding		Yes Unclear No
Threats to precision		
Study size Was the study size adequate?		Yes Unclear No

Appendix 5.2 Electronic search strategy, June 2014

PHD researcher: Nicole Valtorta

Project Loneliness

Information Specialist: Rocio Rodriguez Lopez

rocio.lopez@york.ac.uk

Databases:

MEDLINE (Ovid SP), 1946 – current;
Embase (Ovid SP), 1974 – current;

Cumulative Index to Nursing and Allied Health Literature Plus (CINAHL Plus) (EBSCO), 1937 – current;

PsycINFO (Ovid SP), 1887 – current;
Applied Social Sciences Index and Abstracts (ASSIA) (ProQuest), 1987 – current;
Science Citation Index (SCI) Web of Science Core Collection, 1898 – current,
Cochrane Library (Wiley), 1898 - current;
Social Policy & Practice (Ovid SP), 1981 – current;

National Database of Ageing Research (NDAR), 1955 – current (http://www.cpa.org.uk/research/ndar_about.html);

Grey literature will be identified via the following databases:

Open Grey, http://www.opengrey.eu;
The Health Management Information Consortium (HMIC);

The British Library electronic theses database (ETHOS), http://ethos.bl.uk/Home.do;

The Networked Digital Library of Theses and Dissertations (NDLTD), http://www.ndltd.org
NHS Evidence
Social Care Institute for Excellence (SCIE)
National Institute for Health and Social Care (NICE)

We applied search filters for cohort studies and case control studies to the bibliographic databases.

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Searched online 10/06/14
Strategy saved as: Loneliness_Medline
Search Strategy:
----
loneliness/ (2206)
social isolation/ (10940)
social alienation/ (1309)
social support/ (51329)
community networks/ (5430)
social distance/ (1444)
interpersonal relations/ (55367)
Friends/ (2680)
psychosocial deprivation/ (1817)
Social Participation/ (545)
(lonely or loneliness or solitude).ti,ab. (3910)
((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (19533)
(social wellbeing or social health or social capital).ti. (1205)
or/1-13 (134819)
exp cohort studies/ (1353453)
cohort$.tw. (280225)
controlled clinical trial.pt. (88473)
epidemiologic methods/ (29786)
exp case-control studies/ (662637)
(case$ and control$).tw. (331312)
or/15-20 (1913522)
and/14,21 (15308)

15308 total results saved to Endnote library marked ‘Loneliness_MEDLINE_12/06/2014’ in Custom 4 field.

Database: Embase <1974 to 2014 May 21>
Searched online 10/06/14
Strategy saved as: Loneliness_Embase
Search Strategy:
----

loneliness/ (4228)
social isolation/ (16196)
social support/ (57277)
social network/ (5514)
social distance/ (1254)
human relation/ (74781)
friend/ (7427)
social participation/ (1656)
(lonely or loneliness or solitude).ti,ab. (5011)
((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (22322)
(social wellbeing or social health or social capital).ti. (1324)
or/1-11 (169946)
exp cohort analysis/ (169035)
exp longitudinal study/ (66901)
exp prospective study/ (252031)
exp follow up/ (802138)
cohort$.tw. (398447)
exp case control study/ (85440)
(case$ and control$).tw. (430935)
or/13-19 (1739589)
and/12,20 (14999)

14999 total results saved to Endnote library marked 'Loneliness_EMBASE_16/06/2014' in Custom 4 field.

CINAHL Plus
Searched online 10/06/14
Strategy saved as: Loneliness_Cinahl
Search Strategy:

S1 MH "Loneliness" 1,850
S2 MH "Social Isolation" 4,620
S3 MH "Social Alienation"   345
S4 (MH "Community Networks") 1,838
S5 (MH "Social Support (Iowa NOC)") 1
S6 (MH "Interpersonal Relations") 28,197
S7 (MH "Friendship") 3,021
S8 (MH "Psychosocial Deprivation") 309
S9 (MH "Social Participation") 805
S10 TX (lonely or loneliness or solitude) 3,235
S11 TI ((social* or societ* or perce* or person*) N3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)) 12,223

S12 TI (social wellbeing or social health or social capital) 5,601
S13 (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12) 54,445
S14 (MH "Prospective Studies+") 235,966
S15 (MH "Case Control Studies+") 46,468
S16 TX cohort or longitudinal or prospective or retrospective 382,781
S17 (MH "Epidemiology") 3,662
S18 ((case* and control*) or (case adj3 comparison*) or case-comparison or control group*) 123,750
S19   S14 OR S15 OR S16 OR S17 OR S18 479,472
S20   S13 AND S19 5,959

5959 total results saved to Endnote library marked ‘Loneliness_CINAHL_16/06/2014’ in Custom 4 field.

Database: PsycINFO <1806 to June Week 1 2014>
Searched online 16/06/14
Strategy saved as: Loneliness_PsycInfo
Search Strategy:
Filter: http://libguides.sph.uth.tmc.edu/ovid_psycinfo_filter_examples
----
social networks/ (6999)
interpersonal interaction/ (29250)
social interaction/ (18274)
social support/ (26953)
exp social isolation/ (5912)
loneliness/ (2958)
Alienation/ (2127)
social interaction/ (18274)
Interpersonal Communication/ (13042)
Interpersonal Relationships/ (12183)
Friendship/ (7324)
Interpersonal Interaction/ (29250)
exp social deprivation/ (6583)
(lonely or loneliness or solitude).ti,ab. (7576)
((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (36277)
(social wellbeing or social health or social capital).ti. (2026)
or/1-16 (136994)
((cohort or longitudinal or prospective or retrospective).ti,ab,id. or longitudinal study.md. or prospective study.md. or retrospective study.md.) not "Literature Review".md. (183596)
epidemiology/ (37902)
((case* adj5 control*) or (case adj3 comparison*) or case-comparison or control group*).ti,ab,id. not "Literature Review".md. (66734)
or/18-20 (275226)
and/17,21 (10677)

10677 total results saved to Endnote library marked ‘Loneliness_PsycInfo_16/06/2014’ in Custom 4 field.

ASSIA: Applied Social Sciences Index and Abstracts
Searched online 10/06/14
Strategy saved as: Loneliness_ASSIA
Search Strategy:

Set#: S25 Searched for: (SU.EXACT("Loneliness") OR SU.EXACT.EXPLODE("Isolation" OR "Purdah" OR "Seclusion") OR SU.EXACT("Alienation") OR SU.EXACT.EXPLODE("Computer based social support" OR "Perceived social support" OR "Social support") OR SU.EXACT("Interpersonal networks") OR SU.EXACT("Social distance") OR SU.EXACT("Interpersonal relationships") OR SU.EXACT.EXPLODE("Close friends" OR "Companions" OR "Confidants" OR "Friends") OR (SU.EXACT("Close friendships") OR SU.EXACT("Friendships")) OR SU.EXACT("Social deprivation") OR SU.EXACT("Social participation") OR (ti((lonely OR loneliness OR solitude)) OR ab((lonely OR loneliness OR solitude))) OR ti(((social* OR societ* OR perce* OR person*) NEAR/3 (isolation OR isolated OR alienation OR alienated OR relation* OR detachment OR detached OR contact OR link OR tie OR ties OR support* OR network* OR participation OR activ* OR engage* OR connect* OR disconnect* OR cohesion OR cohesive OR embedded* OR vulnerab* OR interact*))) OR ti((social wellbeing OR social health OR social capital))) AND (SU.EXACT.EXPLODE("Cohort analysis" OR "Longitudinal studies") OR (ti(cohort) OR ab(cohort)) OR SU.EXACT("Epidemiology") OR SU.EXACT("Case controlled studies") OR (case$ and control$)) 519°

Set#: S24 Searched for: SU.EXACT.EXPLODE("Cohort analysis" OR "Longitudinal studies") OR (ti(cohort) OR ab(cohort)) OR SU.EXACT("Epidemiology") OR SU.EXACT("Case controlled studies") OR (case$ and control$) 20191*

Set#: S23 Searched for: (case$ and control$) 5269*

Set#: S22 Searched for: SU.EXACT("Case controlled studies") 246°

Set#: S21 Searched for: SU.EXACT("Epidemiology") 1842°

Set#: S20 Searched for: ti(cohort$) OR ab(cohort$) 10748*

Set#: S18 Searched for: SU.EXACT.EXPLODE("Cohort analysis" OR "Longitudinal studies") 4417*

Set#: S17 Searched for: SU.EXACT("Loneliness") OR SU.EXACT.EXPLODE("Isolation" OR "Purdah" OR "Seclusion") OR SU.EXACT("Alienation") OR SU.EXACT.EXPLODE("Computer based social support" OR "Perceived social support" OR "Social support") OR SU.EXACT("Interpersonal networks") OR SU.EXACT("Social distance") OR SU.EXACT("Interpersonal relationships") OR SU.EXACT.EXPLODE("Close friends" OR "Companions" OR "Confidants" OR "Friends") OR (SU.EXACT("Close friendships") OR SU.EXACT("Friendships")) OR SU.EXACT("Social deprivation") OR SU.EXACT("Social participation") OR (ti((lonely OR loneliness OR solitude)) OR ab((lonely OR loneliness OR solitude))) OR ti(((social* OR societ* OR perce* OR person*) NEAR/3 (isolation OR isolated OR alienation OR alienated OR relation* OR detachment OR detached OR contact OR link OR tie OR ties OR support* OR network* OR participation OR activ* OR engage* OR connect* OR disconnect* OR cohesion OR cohesive OR embedded* OR vulnerab* OR interact*))) OR ti((social wellbeing OR social health OR social capital))

17362*

Set#: S16 Searched for: ti((social wellbeing or social health or social capital)) 3141°

Set#: S15 Searched for: ti(((social* OR societ* OR perce* OR person*) N/3 (isolation OR isolated OR alienation OR alienated OR relation* OR detachment OR detached OR contact OR link OR tie OR ties OR support* OR network* OR participation OR activ* OR engage* OR connect* OR disconnect* OR cohesion OR cohesive OR embedded* OR vulnerab* OR interact*))) 7660*

Set#: S12 Searched for: ti((lonely or loneliness or solitude)) OR ab((lonely or loneliness or solitude)) 1349°

Set#: S11 Searched for: SU.EXACT("Social participation") 237°

Set#: S10 Searched for: SU.EXACT("Social deprivation") 108°

Set#: S9 Searched for: SU.EXACT("Close friendships") OR SU.EXACT("Friendships") 892°

Set#: S8 Searched for: SU.EXACT.EXPLODE("Close friends" OR "Companions" OR "Confidants" OR "Friends") 1137°

Set#: S7 Searched for: SU.EXACT("Interpersonal relationships") 1531°

Set#: S6 Searched for: SU.EXACT("Social distance") 131°

Set#: S5 Searched for: SU.EXACT("Interpersonal networks") 16°

Set#: S4 Searched for: SU.EXACT.EXPLODE("Computer based social support" OR "Perceived social support" OR "Social support") 3937°

Set#: S3 Searched for: SU.EXACT("Alienation") 209°

Set#: S2 Searched for: SU.EXACT.EXPLODE("Isolation" OR "Purdah" OR "Seclusion") 832°

Set#: S1 Searched for: SU.EXACT("Loneliness")591°

519 total results saved to Endnote library marked ‘Loneliness_ASSIA_16/06/2014’ in Custom 4 field

Cochrane Library (includes CDSR, DARE, CENTRAL, HTA and NHSEED)
Searched online 11/06/14
Strategy saved as: Loneliness_Cochrane
Search Strategy:

#1 MeSH descriptor: [Loneliness] this term only 53
#2 MeSH descriptor: [Social Isolation] this term only 134
#3 MeSH descriptor: [Social Alienation] this term only 17
#4 MeSH descriptor: [Social Support] this term only 2368
#5 MeSH descriptor: [Community Networks] this term only 126
#6 MeSH descriptor: [Social Distance] this term only 68
#7 MeSH descriptor: [Interpersonal Relations] this term only 1536
#8 MeSH descriptor: [Friends] this term only 85
#9 MeSH descriptor: [Psychosocial Deprivation] this term only 47
#10 MeSH descriptor: [Social Participation] this term only 16
#11 (lonely or loneliness or solitude):ti,ab 138
#12 ((social* or societ* or perce* or person*) near/3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)):ti 1031
#13 (social wellbeing or social health or social capital):ti 201
#14 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 4987

4987 Of total results in Cochrane Library 40 were from CDSR, 277 from DARE, 4507 from CENTRAL, 41 from HTA, and 96 from NHSEED. Results saved to Endnote library marked Loneliness_COCHRANE_CDSR_16/06/2014, Loneliness_DARE_16/06/2014, Loneliness_HTA_16/06/2014 in Custom 4 field.

Science Citation Index (SCI)
Searched online 10/06/14
Strategy saved as: Loneliness_SCI
Search Strategy:

1639 total results saved to Endnote library marked 'Loneliness_SCI_16/06/2014' in Custom 4 field.

Social Policy and Practice
Searched online 10/06/14
Strategy saved as: Loneliness_Social_Policy_Practice
Search Strategy:
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1. (lonely or loneliness or solitude).ti,ab. (933)
2. ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (2969)
3. (social wellbeing or social health or social capital).ti. (465)
4. 1 or 2 or 3 (4224)
5. cohort$.tw. (3214)
6. (case$ and control$).tw. (1887)
7. longitudinal.tw. (4895)
8. 5 or 6 or 7 (9331)
9. 4 and 8 (246)

246 total results saved to Endnote library marked 'Loneliness_SPP_16/06/2014' in Custom 4 field.

Database: HMIC Health Management Information Consortium <1979 to March 2014>
Searched online 10/06/14
Strategy saved as: Loneliness_HMIC
Search Strategy:
----

1. Loneliness/ (77)
2. social isolation/ (163)
3. social alienation/ (48)
4. social support/ (462)
5. exp Social networks/ (720)
6. interpersonal relations/ (550)
7. Friends/ (42)
8. participation/ (672)
9. (lonely or loneliness or solitude).ti,ab. (265)
10. ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (925)
11. (social wellbeing or social health or social capital).ti. (214)
12. or/1-11 (3175)
13. exp cohort studies/ (1027)
14. cohort$.tw. (6474)
15. case control studies/ (136)
16. (case$ and control$).tw. (4081)
17. or/13-16 (10223)
18. and/12,17 (91)

91 total results saved to Endnote library marked ‘OKIS_HMIC_16/06/2014’ in Custom 4 field.

Open Grey, 22 records
The British Library electronic theses database (ETHOS) 22 records
The Networked Digital Library of Theses and Dissertations (NDLTD), 197 records
NHS Evidence 16 records
Social Care Institute for Excellence (SCIE) 2
National Institute for Health and Social Care (NICE) 0
Search: loneliness or “social isolation”

Total Results

Database	Results	After deduplication	Custom 4 field
MEDLINE and MEDLINE In-Process	15308	14743	Loneliness_MEDLINE_12/06/2014
EMBASE	14999	7726	Loneliness_EMBASE_16/06/2014
CINAHL	5959	2949	Loneliness_CINAHL_16/06/2014
PsycInfo	10677	8555	Loneliness_PsycInfo_16/06/2014
Cochrane Database of Systematic Reviews (CDSR)	40	35	Loneliness_COCHRANE_ CDSR_16/06/2014
Database of Abstracts of Reviews of Effects (DARE)	277	263	Loneliness_DARE_16/06/2014
Health Technology Assessment Database	41	40	Loneliness_HTA_16/06/2014
NHS EED	96	67	Loneliness_NHSEED_16/06/2014
ASSIA	519	152	Loneliness_DARE_16/06/2014
Sciences Citation Index (SCI)	1639	602	Loneliness_SCI_16/06/2014
Social Policy and Practice	246	80	Loneliness_SPP_16/06/2014
HMIC	93	43	Loneliness_HMIC_16/06/2014
Opengrey	22	15	Loneliness_OPENGREY_23_06_2014
NDLTD	198	144	Loneliness_NDLTD_23_06_2014
NDAR	7	6	Loneliness_NDAR_23_06_2014
ETHOS	22	2	Loneliness_ETHOS_23_06_2014
NHS Evidence	16	16	Loneliness_NHS_Evidence_16_06_2014
Social Care Institute for Excellence (SCIE)	2	1	Loneliness_SCIE_16_06_2014
Total	50161	35438	

All results saved to Endnote X7 library 'Lonelinessenl'

Appendix 5.3 Updated electronic search strategy, May 2015

Researcher: Nicole Valtorta

Searcher: Melissa Harden, Information Specialist, CRD

Previous database and grey literature searches undertaken in June 2014 were updated in May 2015 to identify any material published during the period June 2014 – May 2015.

The update search was narrowed to include material on loneliness and coronary heart disease or loneliness and stroke, where this was practical. As with the previous search in June 2014, retrieval was restricted to cohort or case control studies in the bibliographic databases.

The following databases were searched:

MEDLINE (Ovid), 1946 – to April Week 4 2015
MEDLINE In-Process and Other Non-indexed Citations (Ovid), May 04, 2015
Embase (Ovid), 1974 – 2015 May 05

Cumulative Index to Nursing and Allied Health Literature Plus (CINAHL Plus) (EBSCO), 1937 – 20150501

PsycINFO (Ovid), 1887 – April Week 4 2015
Applied Social Sciences Index and Abstracts (ASSIA) (ProQuest), 1987 – current
Science Citation Index (SCI) Web of Science Core Collection, 1900 – 2015-05-06
Cochrane Library (Wiley), 1898 - current
Social Policy & Practice (Ovid SP), 1981 – 201503

The following sources of grey literature were searched:

National Database of Ageing Research (NDAR) (http://www.cpa.org.uk/research/ndar_about.html)
Open Grey, http://www.opengrey.eu
The Health Management Information Consortium (HMIC) (Ovid), 1979 to March 2015

The British Library electronic theses database (ETHOS), http://ethos.bl.uk/Home.do

The Networked Digital Library of Theses and Dissertations (NDLTD), http://www.ndltd.org
NHS Evidence
Social Care Institute for Excellence (SCIE)
National Institute for Health and Social Care (NICE)

Results were downloaded into EndNotex7 and de-duplicated. After de-duplication a total of 477 records were identified.

Literature search strategies

Bibliographic database search strategies:

Ovid MEDLINE(R) <1946 to April Week 4 2015>
Searched on: 5th May 2015
Records retrieved: 82

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1 Loneliness/ (2334)
2 social isolation/ (11216)
3 Social Alienation/ (1315)
4 social support/ (53479)
5 Community Networks/ (5698)
6 Social Distance/ (1604)
7 Interpersonal Relations/ (57128)
8 Friends/ (2907)
9 Psychosocial Deprivation/ (1841)
10 Social Participation/ (720)
11 (lonely or loneliness or solitude).ti,ab. (3784)
12 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (18983)
13 (social wellbeing or social well-being or social health or social capital).ti. (1254)
14 or/1-13 (138058)
15 exp Cohort Studies/ (1424917)
16 cohort$.tw. (278597)
17 controlled clinical trial.pt. (89252)
18 Epidemiologic Methods/ (29851)
19 exp case-control studies/ (710359)
20 (case$ and control$).tw. (320103)
21 or/15-20 (1961576)
22 and/14,21 (15992)
23 exp Cerebrovascular Disorders/ (288957)
24 stroke$.ti,ab. (147442)
25 (cerebrovasc$ or cerebral vascular or CVA$ or poststroke).ti,ab. (45846)
26 (cerebral or cerebellar or brain$ or vertebrobasilar).ti,ab. (909572)
27 (infarct$ or isch?emi$ or thrombo$ or emboli$).ti,ab. (698350)
28 26 and 27 (96827)
29 (cerebral or intracerebral or intracranial or parenchymal).ti,ab. (359563)
30 (brain or intraventricular or brainstem or cerebellar).ti,ab. (738831)
31 (infratentorial or supratentorial or subarachnoid).ti,ab. (31247)
32 29 or 30 or 31 (987338)
33 (haemorrhage or hemorrhage or haematoma or hematoma).ti,ab. (148043)
34 (bleed$ or aneurysm).ti,ab. (196786)
35 33 or 34 (316105)
36 32 and 35 (65766)
37 23 or 24 or 25 or 28 or 36 (401358)
38 22 and 37 (329)

39 exp Cardiovascular Diseases/ (1929245)

40 (cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar$ or angina or isch?emi$).ti,ab. (1410680)

41 39 or 40 (2479083)

42 22 and 41 (1255)

43 38 or 42 (1278)

44 limit 43 to ed=20140601-20150501 (82)

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <May 04, 2015>
Searched on: 5th May 2015
Records retrieved: 6

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1 Loneliness/ (0)
2 social isolation/ (0)
3 Social Alienation/ (0)
4 social support/ (0)
5 Community Networks/ (0)
6 Social Distance/ (0)
7 Interpersonal Relations/ (0)
8 Friends/ (0)
9 Psychosocial Deprivation/ (0)
10 Social Participation/ (0)
11 (lonely or loneliness or solitude).ti,ab. (436)
12 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (2050)
13 (social wellbeing or social well-being or social health or social capital).ti. (160)
14 or/1-13 (2588)
15 exp Cohort Studies/ (0)
16 cohort$.tw. (33629)
17 controlled clinical trial.pt. (36)
18 Epidemiologic Methods/ (0)
19 exp case-control studies/ (0)
20 (case$ and control$).tw. (32135)
21 or/15-20 (63449)
22 and/14,21 (111)
23 exp Cerebrovascular Disorders/ (0)
24 stroke$.ti,ab. (15157)
25 (cerebrovasc$ or cerebral vascular or CVA$ or poststroke).ti,ab. (3447)
26 (cerebral or cerebellar or brain$ or vertebrobasilar).ti,ab. (65730)
27 (infarct$ or isch?emi$ or thrombo$ or emboli$).ti,ab. (45369)
28 26 and 27 (7941)
29 (cerebral or intracerebral or intracranial or parenchymal).ti,ab. (23219)
30 (brain or intraventricular or brainstem or cerebellar).ti,ab. (55281)
31 (infratentorial or supratentorial or subarachnoid).ti,ab. (2492)
32 29 or 30 or 31 (70847)
33 (haemorrhage or hemorrhage or haematoma or hematoma).ti,ab. (11818)
34 (bleed$ or aneurysm).ti,ab. (16990)
35 33 or 34 (26120)

36 32 and 35 (5967)
37 23 or 24 or 25 or 28 or 36 (25639)
38 22 and 37 (2)
39 exp Cardiovascular Diseases/ (0)
40 (cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar$ or angina or isch?emi$).ti,ab. (94367)
41 39 or 40 (94367)
42 22 and 41 (4)
43 38 or 42 (6)

Ovid Embase <1974 to 2015 May 05>
Searched on: 7th May 2015
Records retrieved: 266

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1 loneliness/ (4586)
2 social isolation/ (17232)
3 social support/ (62059)
4 social network/ (6896)
5 social distance/ (1473)
6 human relation/ (78602)
7 friend/ (8832)
8 social participation/ (2301)
9 (lonely or loneliness or solitude).ti,ab. (5448)
10 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or 291aemor* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (24398)
11 (social wellbeing or social well-being or social health or social capital).ti. (1562)
12 or/1-11 (183400)
13 exp cohort analysis/ (199655)
14 exp longitudinal study/ (76722)
15 exp prospective study/ (288111)
16 exp follow up/ (908784)
17 cohort$.tw. (469736)
18 exp case control study/ (99433)
19 (case$ and control$).tw. (473567)
20 or/13-19 (1968157)
21 and/12,20 (16965)
22 exp cerebrovascular disease/ (416807)
23 stroke$.ti,ab. (239092)
24 (cerebrovasc$ or cerebral vascular or CVA$ or poststroke).ti,ab. (68077)
25 (cerebral or cerebellar or brain$ or vertebrobasilar).ti,ab. (1213236)
26 (infarct$ or isch?emi$ or thrombo$ or emboli$).ti,ab. (1004527)
27 25 and 26 (142936)
28 (cerebral or intracerebral or intracranial or parenchymal).ti,ab. (485210)
29 (brain or intraventricular or brainstem or cerebellar).ti,ab. (986854)
30 (infratentorial or supratentorial or subarachnoid).ti,ab. (43486)
31 28 or 29 or 30 (1318373)
32 (haemorrhage or 291aemorrhage or haematoma or hematoma).ti,ab. (208631)
33 (bleed$ or aneurysm).ti,ab. (295298)
34 32 or 33 (460192)
35 31 and 34 (97523)
36 22 or 23 or 24 or 27 or 35 (594693)
37 21 and 36 (481)
38 exp cardiovascular disease/ (3166743)
39 (cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar$ or angina or isch?emi$).ti,ab. (1993206)
40 38 or 39 (3772298)
41 21 and 40 (1737)
42 limit 41 to em=201418-201519 (247)

43 (“201591” or “201592” or “201593”).em. (347941)
44 41 and 43 (19)
45 42 or 44 (266)

CINAHLPlus via EBSCO (1937 – 20150501)
Searched on: 7th May 2015
Records retrieved: 33

#	Query	Results
S44	S42 AND S43	33
S43	EM 20140501-	335,745
S42	S37 OR S41	435
S41	S20 AND S40	421
S40	S38 OR S39	439,482
S39	TI ((cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar* or angina or isch#emi*)) OR AB ((cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar* or angina or isch#emi*))	221,002
S38	(MH "Cardiovascular Diseases+")	363,695
S37	S20 AND S36	134
S36	S21 OR S22 OR S23 OR S24 OR S27 OR S35	85,518
S35	S31 AND S34	8,780
S34	S32 OR S33	35,530
S33	TI ((bleed* or aneurysm)) OR AB ((bleed* or aneurysm))	21,323
S32	TI ((haemorrhage or hemorrhage or haematoma or hematoma)) OR AB ((haemorrhage or hemorrhage or haematoma or hematoma))	16,686
S31	S28 OR S29 OR S30	84,952
S30	TI ((infratentorial or supratentorial or subarachnoid)) OR AB ((infratentorial or supratentorial or subarachnoid))	3,574
S29	TI ((brain or intraventricular or brainstem or cerebellar)) OR AB ((brain or intraventricular or brainstem or cerebellar))	56,812
S28	TI ((cerebral or intracerebral or intracranial or parenchymal)) OR AB ((cerebral or intracerebral or intracranial or parenchymal))	34,451
S27	S25 AND S26	10,805
S26	TI (((infarct* or isch#emi* or thrombo* or emboli*)) OR AB ((infarct* or isch#emi* or thrombo* or emboli*))	79,821
S25	TI ((cerebral or cerebellar or brain* or vertebrobasilar)) OR AB ((cerebral or cerebellar or brain* or vertebrobasilar))	76,262

S24	TI ((cerebrovasc* or cerebral vascular or CVA* or poststroke)) OR AB ((cerebrovasc* or cerebral vascular or CVA* or poststroke))	7,924
S23	TI stroke* OR AB stroke*	45,397
S22	(MH "Stroke Patients")	2,690
S21	(MH "Cerebrovascular Disorders+")	66,600
S20	S13 AND S19	6,596
S19	S14 OR S15 OR S16 OR S17 OR S18	532,266
S18	((case* and control*) or (case N3 comparison*) or case-comparison or control group*)	135,008
S17	MH "Epidemiology"	4,115
S16	TX (cohort or longitudinal or prospective or retrospective)	426,986
S15	MH "Case Control Studies+"	51,303
S14	MH "Prospective Studies+"	261,881
S13	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12	59,012
S12	TI (social wellbeing or social well-being or social health or social capital)	6,349
S11	TI ((social* or societ* or perce* or person*) N3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*))	13,448
S10	TX (lonely or loneliness or solitude)	3,512
S9	MH "Social Participation"	1,121
S8	MH "Psychosocial Deprivation"	320
S7	MH "Friendship"	3,290
S6	MH "Interpersonal Relations"	30,197
S5	MH "Social Support (Iowa NOC)"	1
S4	MH "Community Networks"	1,956
S3	MH "Social Alienation"	380
S2	MH "Social Isolation"	4,927
S1	MH "Loneliness"	2,041

Ovid PsycINFO <1806 to April Week 4 2015>
Searched on: 7th May 2015
Records retrieved: 22

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1 social networks/ (7924)
2 interpersonal interaction/ (29814)
3 social interaction/ (19400)
4 social support/ (28446)
5 exp social isolation/ (6216)
6 loneliness/ (3177)
7 Alienation/ (2182)
8 social interaction/ (19400)
9 Interpersonal Communication/ (13369)
10 Interpersonal Relationships/ (13364)
11 Friendship/ (7726)
12 Interpersonal Interaction/ (29814)
13 exp social deprivation/ (6915)
14 (lonely or loneliness or solitude).ti,ab. (8109)
15 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (38740)
16 (social wellbeing or social well-being or social health or social capital).ti. (2373)
17 or/1-16 (144694)
18 ((cohort or longitudinal or prospective or retrospective).ti,ab,id. or longitudinal study.md. or prospective study.md. or retrospective study.md.) not "Literature Review".md. (200900)
19 epidemiology/ (40183)
20 ((case* adj5 control*) or (case adj3 comparison*) or case-comparison or control group*).ti,ab,id. not "Literature Review".md. (71503)
21 or/18-20 (298325)
22 and/17,21 (11506)
23 exp cerebrovascular disorders/ (20008)
24 stroke$.ti,ab. (23388)
25 (cerebrovasc$ or cerebral vascular or CVA$ or poststroke).ti,ab. (6260)
26 (cerebral or cerebellar or brain$ or vertebrobasilar).ti,ab. (254849)
27 (infarct$ or isch?emi$ or thrombo$ or emboli$).ti,ab. (21925)
28 26 and 27 (10063)
29 (cerebral or intracerebral or intracranial or parenchymal).ti,ab. (57829)
30 (brain or intraventricular or brainstem or cerebellar).ti,ab. (219455)
31 (infratentorial or supratentorial or subarachnoid).ti,ab. (1871)
32 29 or 30 or 31 (253456)
33 (haemorrhage or hemorrhage or haematoma or hematoma).ti,ab. (4490)
34 (bleed$ or aneurysm).ti,ab. (2582)
35 33 or 34 (6515)
36 32 and 35 (4133)
37 23 or 24 or 25 or 28 or 36 (36753)
38 22 and 37 (79)
39 exp cardiovascular disorders/ (46341)
40 (cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar$ or angina or isch?emi$).ti,ab. (78141)

41 39 or 40 (99044)
42 22 and 41 (387)
43 38 or 42 (401)
44 limit 43 to up=20140526-20150427 (22)

ASSIA via Proquest (1987 – current)
Searched on: 7th May 2015
Records retrieved: 59

(SU.EXACT("Loneliness") OR SU.EXACT.EXPLODE("Isolation" OR "Purdah" OR "Seclusion") OR SU.EXACT("Alienation") OR SU.EXACT.EXPLODE("Computer based social support" OR "Perceived social support" OR "Social support") OR SU.EXACT("Interpersonal networks") OR SU.EXACT("Social distance") OR SU.EXACT("Interpersonal relationships") OR SU.EXACT.EXPLODE("Close friends" OR "Companions" OR "Confidants" OR "Friends") OR (SU.EXACT("Close friendships") OR SU.EXACT("Friendships")) OR SU.EXACT("Social deprivation") OR SU.EXACT("Social participation") OR (ti((lonely OR loneliness OR solitude)) OR ab((lonely OR loneliness OR solitude))) OR ti(((social* OR societ* OR perce* OR person*) NEAR/3 (isolation OR isolated OR alienation OR alienated OR relation* OR detachment OR detached OR contact OR link OR tie OR ties OR support* OR network* OR participation OR activ* OR engage* OR connect* OR disconnect* OR cohesion OR cohesive OR embedded* OR vulnerab* OR interact*))) OR ti((social wellbeing OR social well-being OR social health OR social capital))) AND (SU.EXACT.EXPLODE("Cohort analysis" OR "Longitudinal studies") OR (ti(cohort*) OR ab(cohort*)) OR SU.EXACT("Epidemiology") OR SU.EXACT("Case controlled studies") OR (case* and control*))

Limited by publication date: 01 January 2014 to 07 May 2015

As records retrieved with the original strategy were low, the search terms to narrow results to coronary heart disease or stroke where not applied in the ASSIA update search.

Science Citation Index via Web of Science, Thomson Reuters (1900 – 2015-05-06)
Date searched: 7th May 2015
Records retrieved: 38

# 28	38	#27 OR #25 Indexes=SCI-EXPANDED Timespan=2014-2015
# 27	34	#26 AND #10 Indexes=SCI-EXPANDED Timespan=2014-2015
# 26	117,070	TS=(cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar* or angina or isch$emi*) Indexes=SCI-EXPANDED Timespan=2014-2015
# 25	11	#24 AND #10 Indexes=SCI-EXPANDED Timespan=2014-2015
# 24	33,888	#23 OR #15 OR #12 OR #11 Indexes=SCI-EXPANDED Timespan=2014-2015
# 23	6,851	#22 AND #19 Indexes=SCI-EXPANDED Timespan=2014-2015
# 22	24,276	#21 OR #20 Indexes=SCI-EXPANDED Timespan=2014-2015
# 21	15,687	TS=(bleed* or aneurysm) Indexes=SCI-EXPANDED Timespan=2014-2015
# 20	11,515	TS=(haemorrhage or hemorrhage or haematoma or hematoma) Indexes=SCI-EXPANDED Timespan=2014-2015
# 19	89,300	#18 OR #17 OR #16 Indexes=SCI-EXPANDED Timespan=2014-2015
# 18	2,561	TS=(infratentorial or supratentorial or subarachnoid) Indexes=SCI-EXPANDED Timespan=2014-2015
# 17	74,975	TS=(brain or intraventricular or brainstem or cerebellar) Indexes=SCI-EXPANDED Timespan=2014-2015
# 16	27,277	TS=(cerebral or intracerebral or intracranial or parenchymal) Indexes=SCI-EXPANDED Timespan=2014-2015
# 15	10,739	#14 AND #13 Indexes=SCI-EXPANDED Timespan=2014-2015
# 14	58,443	TS=(infarct* or isch$emi* or thrombo* or emboli*) Indexes=SCI-EXPANDED Timespan=2014-2015
# 13	84,106	TS=(cerebral or cerebellar or brain* or vertebrobasilar) Indexes=SCI-EXPANDED Timespan=2014-2015
# 12	4,569	TS=(cerebrovasc* or "cerebral vascular" or CVA* or poststroke) Indexes=SCI-EXPANDED Timespan=2014-2015
# 11	22,678	TS=stroke* Indexes=SCI-EXPANDED Timespan=2014-2015
# 10	329	#8 AND #4 Indexes=SCI-EXPANDED Timespan=2014-2015

# 9	1,794	#8 AND #4 Indexes=SCI-EXPANDED Timespan=All years
# 8	856,437	#7 OR #6 OR #5 Indexes=SCI-EXPANDED Timespan=All years
# 7	363,501	TS=(case$ and control$) Indexes=SCI-EXPANDED Timespan=All years
# 6	212,870	TS=longitudinal Indexes=SCI-EXPANDED Timespan=All years
# 5	329,586	TS=cohort$ Indexes=SCI-EXPANDED Timespan=All years
# 4	29,296	#3 OR #2 OR #1 Indexes=SCI-EXPANDED Timespan=All years
# 3	6,745	TI=(social wellbeing or social well-being or social health or social capital) Indexes=SCI-EXPANDED Timespan=All years
# 2	21,310	TI=((social* or societ* or perce* or person*) NEAR/3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or ctive* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)) Indexes=SCI-EXPANDED Timespan=All years
# 1	2,656	TS=(lonely or loneliness or solitude) Indexes=SCI-EXPANDED Timespan=All years

The Cochrane Library via Wiley

- Cochrane Database of Systematic Reviews (CDSR Issue 5 of 12, May 2015)
- Database of Abstracts of Reviews of Effects (DARE) Issue 2 of 4, April 2015
- Health Technology Assessment Database (HTA) Issue 2 of 4, April 2015
- NHS Economic Evaluations Database (NHSEED) Issue 2 of 4, April 2015
- Cochrane Central Register of Controlled Trials (CENTRAL) Issue 4 of 12, April 2015

Date searched: 7th May 2015
Records retrieved: 14 in total – CDSR = 0, DARE = 2, HTA = 0, NHSEED = 0, CENTRAL = 12

#1 MeSH descriptor: [Loneliness] this term only 56
#2 MeSH descriptor: [Social Isolation] this term only 141
#3 MeSH descriptor: [Social Alienation] this term only 17
#4 MeSH descriptor: [Social Support] this term only 2467
#5 MeSH descriptor: [Community Networks] this term only 133
#6 MeSH descriptor: [Social Distance] this term only 71
#7 MeSH descriptor: [Interpersonal Relations] this term only 1584
#8 MeSH descriptor: [Friends] this term only 89
#9 MeSH descriptor: [Psychosocial Deprivation] this term only 48
#10 MeSH descriptor: [Social Participation] this term only 20
#11 (lonely or loneliness or solitude):ti,ab,kw 174
#12 ((social* or societ* or perce* or person*) near/3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)):ti 1160
#13 (social wellbeing or social well-being or social health or social capital):ti 252
#14 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 5308
#15 MeSH descriptor: [Cerebrovascular Disorders] explode all trees 10092
#16 stroke*:ti,ab,kw 26204
#17 (cerebrovasc* or cerebral vascular or CVA* or poststroke):ti,ab,kw 7892
#18 (cerebral or cerebellar or brain* or vertebrobasilar):ti,ab,kw 31220
#19 (infarct* or isch*emi* or thrombo* or emboli*):ti,ab,kw 57171
#20 #18 and #19 7388
#21 (cerebral or intracerebral or intracranial or parenchymal):ti,ab,kw 16115
#22 (brain or intraventricular or brainstem or cerebellar):ti,ab,kw 23398
#23 (infratentorial or supratentorial or subarachnoid):ti,ab,kw 2296
#24 #21 or #22 or #23 34717
#25 (haemorrhage or hemorrhage or haematoma or hematoma):ti,ab,kw 15955
#26 (bleed* or aneurysm):ti,ab,kw 19819
#27 #25 or #26 29070
#28 #24 and #27 5256
#29 #15 or #16 or #17 or #20 or #28 38176
#30 #14 and #29 109
#31 MeSH descriptor: [Cardiovascular Diseases] explode all trees 77112
#32 (cardiovascular or cardio-vascular or heart or myocardial or myocardium or myocardiac or cardiac or coronar* or angina or isch*emi*):ti,ab,kw 125419
#33 #31 or #32 152270
#34 #14 and #33 403
#35 #30 or #34 435
#36 #30 or #34 Publication Year from 2014 to 2015 14

Ovid Social Policy and Practice <201503>
Date searched: 7th May 2015
Records retrieved: 15
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1 (lonely or loneliness or solitude).ti,ab. (976)
2 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (3118)
3 (social wellbeing or social well-being or social health or social capital).ti. (491)
4 or/1-3 (4439)
5 cohort$.tw. (3331)
6 (case$ and control$).tw. (1914)
7 longitudinal.tw. (5191)
8 or/5-7 (9737)
9 4 and 8 (257)
10 limit 9 to yr="2014 - 2015" (15)

As records retrieved with the original strategy where low, the search terms to narrow results to coronary heart disease or stroke where not applied in the Social Policy and Practice update search.

Grey literature searches:

Ovid HMIC Health Management Information Consortium <1979 to March 2015>
Date searched: 7th May 2015
Records retrieved: 2

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1 Loneliness/ (96)
2 social isolation/ (173)
3 social alienation/ (48)
4 social support/ (471)
5 exp Social networks/ (738)
6 interpersonal relations/ (553)
7 Friends/ (43)
8 participation/ (686)
9 (lonely or loneliness or solitude).ti,ab. (285)
10 ((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or tie or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti. (961)
11 (social wellbeing or social well-being or social health or social capital).ti. (229)
12 or/1-11 (3274)
13 exp cohort studies/ (1129)
14 cohort$.tw. (6873)
15 case control studies/ (146)
16 (case$ and control$).tw. (4227)
17 or/13-16 (10742)
18 12 and 17 (98)
19 limit 18 to yr="2014 -Current" (2)

As records retrieved with the original strategy where low, the search terms to narrow results to coronary heart disease or stroke where not applied in the HMIC update search.

The following sources of grey literature were searched using the terms loneliness or "social isolation" on May 7th 2015. Results were restricted to material published during the period 2014-2015.

National Database of Ageing Research (NDAR)
(http://www.cpa.org.uk/research/ndar_about.html)
No records retrieved.

Open Grey
http://www.opengrey.eu
No records retrieved.

The British Library electronic theses database (ETHOS)
http://ethos.bl.uk/Home.do
2 records retrieved.

The Networked Digital Library of Theses and Dissertations (NDLTD)
http://www.ndltd.org
search by Nicole

NHS Evidence
https://www.evidence.nhs.uk/
289 records retrieved and scanned for relevance. 5 relevant records found.

Social Care Institute for Excellence (SCIE)
http://www.scie.org.uk/
No records retrieved.

National Institute for Health and Social Care (NICE)
http://www.nice.org.uk/
22 records retrieved.

Search results

Database	Results	After deduplication	Custom 4 field
MEDLINE	82	70	MEDLINE Ovid update 05/05/15 MH
MEDLINE In-Process	6	6	MEDLINE in process Ovid update 05/05/15 MH
EMBASE	266	228	EMBASE Ovid update 06/05/15 MH
CINAHL	33	20	CINAHL via EBSCO update 07/05/15 MH
PsycInfo	22	18	PsycINFO Ovid update 06/05/15 MH
ASSIA	59	58	ASSIA Proquest update 07/05/15 MH
Sciences Citation Index (SCI)	38	21	Science Citation Index update 07/05/15 MH
Cochrane Database of Systematic Reviews (CDSR)	0	0	n/a
Database of Abstracts of Reviews of Effects (DARE)	2	2	DARE via Wiley Cochrane Library update 07/05/15 MH
Health Technology Assessment Database	0	0	n/a
NHS EED	0	0	n/a
CENTRAL	12	8	CENTRAL via Wiley Cochrane Library update 07/05/15 MH
Social Policy and Practice	15	15	Social Policy & Practice Ovid update 07/05/15 MH
HMIC	2	2	HMIC Ovid update 07/05/15 MH
Opengrey	0	0	n/a
NDLTD			*To be searched by Nicole*
NDAR	0	0	n/a
ETHOS	2	2	EThOS update 07/05/15 MH
NHS Evidence	5	5	NHS Evidence update 08/05/15 MH
Social Care Institute for Excellence (SCIE)	0	0	n/a
NICE	22	22	NICE website update 07/05/15 MH
Total	2929	2929	

Appendix 5.4 Measurement and prevalence of loneliness and social isolation in the studies included in the review

Studies are grouped according to the dimension of social relationships they investigated (loneliness, social isolation or a combination of both); the measure of social relationships used (e.g. studies using the Berkman-Syme Social Network Index are grouped together); and the datasets used (i.e. studies reporting data from the same dataset, e.g. the Established Populations for the Epidemiologic Studies of the Elderly Study, are grouped together).

Record ID (first author & year)	Term used in the paper	Measurement	Number of items	Scoring and categorisation	Prevalence of loneliness or isolation	Comments re. reliability, validity, responsiveness and/or interpretability	How many times were social relation-ships measured?	Effect estimates re. incident CHD and/or stroke
Loneliness								
André-Petersson, 2006	Social support	Combination of 3 sets of questions: a) questions on the availability of emotional support: - Do you have any friends or relatives who you like very much and who like you very much? - Do you have any really close friends with whom you feel intimate and with whom you can discuss anything? - If you have continued to work, is it because you want to feel that you are a valuable and important person? - When you have personal problems of any kind, do you have any close friend or relative to whom you can turn to discuss your problems? , b) questions on the adequacy of emotional support: - How often do you feel lonely? - Do you have the feeling that people appreciate what you do? - Do you have enough good friends to be with? - Do you think that you see your children too often or too rarely? c) questions about access to informal and material support: - Is there anyone in your neighbourhood from whom you can borrow things or exchange services? - Is there anyone in your neighbourhood from whom you can get help if you fall ill? - If you need help with something for 24hr, do you have anyone you can ask? (other than wife) - Do you know anyone who can help you to write an official letter or to appeal against a decision made by some authority? - Do you know where to go in order to get help to write an official letter or to appeal against a decision made	13	For each set of questions, answers were dichotomised based on a cut-off set at approximately the lowest 30th percentile. Subjects who scored low in any of the three domains (availability, adequacy or access) were considered to have an unsatisfactory level of social support; 2 categories: satisfactory v. unsatisfactory social support.	22.5% of subjects were classed as having unsatisfactory levels of social support, i.e. they scored low in one domain. 8.2% scored low in 2 domains, 3.4% scored low in 3 domains.	Hanson & Östergren (1987) reported that answers were generally skewed toward the positive side. Re. interpretability, note that subjects were classed as having social support if they scored low in one domain, regardless how they scored in the other domains. It was therefore possible for subjects reporting high access to support to be classed as having low social support because of scoring low in the adequacy domain, making the distinction between satisfactory and unsatisfactory levels of support difficult to interpret.	Once, at baseline	Comparing subjects with un-satisfactory (lonely) versus (v.) satisfactory social support (not lonely), hazard ratio (HR) for incident CHD: 1.19, 95% CI: 0.64 to 2.22

Eaker, 1992	Loneliness	‘Are you lonely during the day?’ Answer: yes or no	1	Subjects who answered yes to the loneliness question were classed as lonely; 2 categories: lonely v. not lonely.	Not reported	Direct question may deter participants from admitting to a socially stigmatised feeling, although there is evidence of similar questions correlating with the complex UCLA Loneliness Scale (Russell et al., 1978).	Once, at baseline	Comparing lonely v. not lonely subjects, HR for incident CHD: 4.0, 95% CI: 1.8 to 9.2
Thurston, 2009	Loneliness	Question taken from the Centre for Epidemiologic Studies of Depression scale: participants were asked to rate the statement: “I feel lonely” on a 4-point scale: Rarely or none of the time (<1 day), some or a little of the time (1–2 days), occasionally or a moderate amount of the time (3–4 days), or most of the time (5-7 days) in the past week.	1	Scores were categorized as low (<1 day), medium (1–2 days), and high (3–7 days). The CESD was administered a second time, and answers were used with the baseline responses to characterize loneliness across the two time points. Subjects reporting low loneliness at both interviews were classed as low loneliness, those reporting high loneliness at either interview were classed as high loneliness, and the remainder were classed as having moderate levels of loneliness. Two analyses were performed: one where loneliness was split into three categories, and one where the loneliness score was treated as a continuous variable.	. 241 subjects (9.2%) were classed as having high levels of loneliness, 409 (15.6%) as medium and 1,966 (75.2%) as low	Direct question may deter participants from admitting to a socially stigmatised feeling, although there is evidence of similar questions correlating with the complex UCLA Loneliness Scale (Russell et al., 1978). The 'medium loneliness' category is difficult to interpret given that it includes subjects with moderate levels of loneliness at both time points as well as individuals who fluctuated from high to low loneliness, or vice versa.	Twice, second time on average 8.2 years after baseline (SD = 0.6; range = 6.7–9.7)	Comparing subjects with high v. low levels of loneliness, HR for incident CHD: 1.53, 95% CI 1.07 to 2.21. Comparing men with high v. low levels of loneliness, HR for incident CHD: 0.88, 95% CI: 0.43 to 1.78. : Comparing women with high v. low levels of loneliness, HR for incident CHD: 1.81, 95% CI: 1.20 to 2.94

Social isolation								
Avendano, 2006	Social network	Social Networks Index (SNI) developed by Berkman and Syme: 1) Have you ever been married? If so, are you now married, separated, divorced or widowed? 2) How many close friends do you have? How many relatives do you have that you feel close to? How many of these friends or relatives do you see at least once a month? 3) 'Do you belong to any of these kinds of groups? Church/social or recreational group/labour union, commercial group or professional association/a group concerned with children/a group concerned with community betterment, charity or service/any other group.	6 (covering 4 domains: marriage, close friends and relatives, church membership, group membership)	People who scored 1 or less on the social network index were compared with those who scored higher; 2 categories: isolated v. not isolated	Not reported	No information re. reliability and validity in this study. Berkman (1977) acknowledged that the extent to which the social network and participation questions measure the relationships and kinds of participation in which respondents are really involved is unknown. Data from Sykes (2002), see below, suggests a degree of validity and reliability.	Once, at baseline	Among people aged 65 to 74, comparing people who scored 1 or less v. scoring higher on the social network index, HR for incident stroke: 2.03, 95% CI: 0.96 to4.28. Among those aged 75 and over, comparing people who scored 1 or less v. scoring higher on the social network index, HR for incident stroke: 1.36, 95% CI: 0.48 to
Colantonio 1992	Social network	Berkman-Syme SNI, see above	6 (covering 4 domains: marriage, close friends and relatives, church membership, group membership)	The index was scored on a scale from 1 to 12, with the lowest score given to the most isolated subjects; the index scores were dichotomized on the basis of the mean number of networks (x = 3.6)	1,372 subjects (57.2%) had few networks (1-3); 1,178 had larger networks (4+)	No information re. reliability and validity in this study. Berkman (1977) acknowledged that the extent to which the social network and participation questions measure the relationships and kinds of participation in which respondents are really involved is unknown. Data from Sykes (2002), see below, suggests a degree	Once, at baseline	When the social network variable was added to a Cox proportional hazards multivariate model looking at incident stroke, X2= 0.15, df=1, p-value=0.6995.
Eng, 2002	Social ties	Berkman-Syme SNI, see above	(covering 4 domains: marriage, close friends and relatives, church membership, group membership)	The authors reported that 'The index has four levels: low, medium, medium-high, and high (respectively, I, II, III, and IV). Persons with low levels of social ties can be characterized as unmarried, having few friends or relatives, and not being involved in community groups.'	6 % of the study population was socially isolated (level I of the social network index); 51.3% of subjects were well integrated (level IV).	No information re. reliability and validity in this study. Berkman (1977) acknowledged that the extent to which the social network and participation questions measure the relationships and kinds of participation in which respondents are really involved is unknown. Data from Sykes (2002), see below, suggests a degree of validity and reliability.	Twice, 8 years part - but only the measure-ment from 1988 was used in the analyses re. disease incidence	Comparing subjects with a low v. high level of social network, total coronary heart disease HR: 0.99, 95% CI: 0.81 to 1.20; nonfatal myocardial infarction HR: 1.11, 95% CI: 0.80 to 1.53; fatal coronary heart disease HR: 1.82, 95% CI: 1.02 to 3.23; sudden cardiac death HR: 0.71, 95% CI: 0.28 to 1.81.

Kawachi, 1996	Social network	Berkman-Syme SNI, see above	6 (covering 4 domains: marriage, close friends and relatives, church membership, group membership)	Responses to the index were categorised into four levels of social connection: low networks (individuals with low intimate contacts – not married, fewer than 6 friends or relatives – and no membership in either church or community groups), medium networks, medium-high networks and high networks	5.8% of the study population were socially isolated, 23.6% had medium levels of social network, 19.1% had medium-high network levels and 51.5% were socially integrated.	No information re. reliability and validity in this study. Berkman (1977) acknowledged that the extent to which the social network and participation questions measure the relationships and kinds of participation in which respondents are really involved is unknown. Data from Sykes (2002), see below, suggests a degree of validity and reliability.	Once, at baseline	Comparing subjects with a low v. high level of social network, HR for total stroke: 2.02, 95% CI: 1.00 to 4.08; HR for fatal stroke (age-adjusted model only): 3.64, 95% CI: 0.78 to 16.9; HR for nonfatal stroke: 1.86, 95% CI: 0.85 to 4.06; HR for total CHD: 1.14, 95% CI: 0.74 to 1.73; HR for fatal CHD: 1.42, 95% CI: 0.72 to 2.81; HR for nonfatal CHD: 1.00, 95% CI: 0.58 to 1.71; HR for sudden cardiac death: 0.68, 95% CI: 0.16 to 2.96; HR for non-sudden cardiac death: 1.89, 95% CI: 0.87 to 4.13.
Gafarov, 2013	Social support	Berkman-Syme SNI, see above	6 (covering 4 domains: marriage, close friends and relatives, church membership, group membership)	2 indices: one across all contacts (4 categories: high, average-1, average-2, low) and one re. close contacts only (3 categories: high, average, low).	Across social contacts: 77.7% had low levels of social network; 19.8% had an average social network; 2.5% had high levels of social network. Re. close contacts, 57.1% had low levels of contact, 37.3% had average levels of contact, and 5.7% had high levels of contact.	No information re. reliability and validity in this study. Berkman (1977) acknowledged that the extent to which the social network and participation questions measure the relationships and kinds of participation in which respondents are really involved is unknown. Data from Sykes (2002), see below, suggests a degree of validity and reliability.	Once, at baseline	with low v. higher levels of social network across the whole sample, HR for myocardial infarction: 2.92, 95% CI 1.040 to 8.208; HR for stroke: 2.72, 95% CI 1.094 to 6.763. Comparing subjects with low v. higher levels of social network in the 55-64 age group: HR for myocardial infarction: 5.9, 95% CI: 1.534 to 22.947. Comparing subjects with low v. higher levels of *close* social network, HR for myocardial infarction : 4.9, 95% CI: 1.108 to 21.762; HR for stroke: 4.1, 95% CI: 1.193 to 14.055. [unadjusted]
Sykes, 2002	Social support	Berkman-Syme SNI, see above	(covering 4 domains: marriage, close friends and relatives, church membership, group membership)	Each item of social support was measured on a scale 0-7, for a final range of 0-28. The score was treated as a continuous predictor variable for analysis.	Not reported	Cronbach's alpha: 0.84. Re. validity, authors reported negative co-variation between social support and hostility ($\phi = -0.35$), and between social support and depression ($\phi = -0.31$).	Once, at baseline	Logistic regression. Hard CHD, full model: X2 = 7.389, df = 5, p-value: not significant. Total angina pectoris, full model: X2 = 16.242, df = 5, p = 0.006. The authors report that the social network variable did not contributed to this effect.

Nagayoshi 2014	**Social network**	**10-item Lubben Social Network Scale: 1. How many relatives do you see or hear from at least once a month? 2. Tell me about the relative with whom you have the most contact: How often do you see or hear from that person? 3. How many relatives do you feel close to? That is how many of them do you feel at ease with, can talk about private matters or can call for help? 4. Do you have any close friends? That is do you have any friends with whom you feel at ease can talk to about private matters or can call on for help? If so how many? 5. How many of these friends do you see or hear from at least once a month? 6. Tell me about the friend with whom you have the most contact. How often do you see or hear from that person? 7. When you have an important decision to make do you have someone you can talk to about it? 8. When other people you know have an important decision to make do they talk to you about it? 9a.Does anybody rely on you to something for them each day? 9b. Do you help anybody with something each day? 10. Do you live alone or with other people?**	**6 (covering 4 domains: marriage, close friends and relatives, church membership, group membership)**	**Scores range from 0 to 50 - the higher the score, the larger the social network; 4 categories: score ≤20=small social network; 21 to 25=moderate small social network; 26 to 30=moderate large social network; and ≥31=large social network.'**	**2.8% subjects had a small social network, 5.7% had a moderately small network, 13.9% a moderately large network, 77.6% a large network**	**Note that Nagayoshi's study does not focus on people aged 65+, the population for which the Lubben Social Network Scale was developed.**	**Once, at baseline**	**Comparing subjects with small v. large network, HR of stroke: 1.44, 95% CI: 1.02 to 2.04; HR of ischemic stroke: 1.41, 95% CI: 0.98 to 2.03.**
Player, 2007	**Social network**	**10-item Lubben Social Network Scale, see Nagayoshi 2014**	**10**	**Scores range from 0 to 50 - the higher the score, the larger the social network; 3 categories: the cohort was divided into tertiles (0 to 35, 36 to 39, 40 to 50.**	**30.3% had low social networks, 31.2% had moderate networks, 38.5% had high social network levels**	**Note that Player's study does not focus on people aged 65+, the population for which the Lubben Social Network Scale was developed.**	**Once, at baseline**	**χ2 analysis. P-value associated with χ2 in bivariate analysis re. social networks = 0.220**

Rosengren 2004	**Social integration**	**Same as Orth-Gomer 1993, see below.**	**6**	**Response alternatives were scored from 1 to 6. Scores were divided into quartiles and the variable was categorised into 3 levels of social integration: first quartile: low integration; second and third quartile: moderate integration, last quartile: high integration**	**The quartile of subjects with lowest scores were classed as having a low level of social integration**	**According to Unden 1989, internal consistency: Cronbach's alpha = 0.66; split-half reliability: Cronbach's alpha = 0.59.**	**Once, at baseline**	**Comparing subjects with high v. low levels of integration, HR for CHD: 0.45, 95% CI: 0.24-0.84.**
Orth-Gomer, 1993	**Social integration**	**1. Number of people met during an ordinary week. 2. Number of people with whom respondent shares interests. 3. Number of friends who at any time would come and visit respondent's home and wouldn't be embarrassed if it were untidy. 4. Number of friends or family members with whom respondent can talk frankly. 5. Someone available whom respondent can ask small favors. 6. Someone available—apart from family—to whom respondent can turn in times of difficulties.**	**6**	**Responses to items 1-4 were classified into 6 categories, from 0 to more than 15. All other items were coded yes/no and study subjects were divided into quartiles.**	**157 subjects (21.3%) were in the lower quartile.**	**According to Unden 1989, internal consistency: Cronbach's alpha = 0.66; split-half reliability: Cronbach's alpha = 0.59.**	**Once, at baseline**	**Comparing subjects in the lower v. upper quartiles of social integration, odds ratio (OR) for CHD: 3.8, 95% CI: 1.1 to 13.9.**
Kuper, 2006	**Social support**	**1. How many people do you know who share the same interests as you (including people from work and those you meet in your spare time)? 2. How many do you meet and speak with (not counting those who you only meet briefly and/or will not probably meet again)? 3. How many can drop by your home anytime without warning? (For instance, neither you nor they mind if the house is messy, or if you are in the middle of a meal; do not include close relatives). 4. How many can you speak openly with? 5. Apart from your family, can you turn to other people when in trouble? 6. How many people in your surrounding can you ask for favors if necessary?**	**6**	**The study population was divided into tertiles based on the responses across all of the women.**	**15,240 subjects (31.9%) had low social support; 15,807 subjects (33.1%) had intermediary social support; 16,666 subjects (34.9%) had high social support**	**No information re. validity**	**Once, at baseline**	**Comparing subjects with the highest v. lowest social support, HR for myocardial infarction: 1.3, 95% CI: 0.9-1.8.**

Ikeda, 2008	Social support	Perceived social support was measured combining questions re.: a) perceived emotional support: “Do you have someone that you can share your intimate feelings and secrets with? (no or yes)”; “Do you have someone that you feel safe and comfortable with? (no or yes)”; “Do you have someone who is supportive of your opinions and actions? (no or yes)”. b) social isolation, defined as not having a friend whom the respondent knew well enough to meet at least once per week: “How many friends do you meet at least once per week: none, 1 to 3 friends, more than 4 friends?”	4	The 4 questions were combined into an overall index of social support. Subjects were categorized into 4 levels based on the distribution of the combined index: low support (scores 0-1), medium (2-3), high (4), very high (5).	10% subjects had low social support, 19% had medium support, 42% had high support, 29% had very high support.	Internal consistency: Cronbach alpha = 0.75.	Once, at baseline	Non-fatal myocardial infarction: comparing subjects with low v. very high levels of support, HR: 0.90, 95% CI: 0.60 to 1.35; comparing men with low v. very high levels of support, HR: 1.06, 95% CI: 0.68 to 1.67; comparing women with low v. very high levels of support, HR: 0.55, 95% CI: 0.19 to 1.57. Fatal MI: comparing subjects with low v. very high levels of support, HR: 1.00, 95% CI: 0.61 to 1.63; comparing men with low v. very high levels of support, HR: 1.12, 95% CI: 0.65 to 1.94; comparing women with low v. very high levels of support, HR: 0.58, 95% CI: 0.17 to 1.99. Nonfatal stroke: comparing subjects with low v. very high level of support, HR: 1.11, 95% CI: 0.89 to 1.37; comparing men with low v. very high level of support, HR: 1.09, 95% CI: 0.84 to 1.43; comparing women with low v. very high level of support, HR: 1.22, 95% CI: 0.85 to 1.74. Fatal stroke: comparing subjects with low v. very high level of support, HR: 1.45, 95% CI: 1.00 to 2.10; comparing men with low v. very high level of support, HR: 1.59, 95% CI: 1.01 to 2.51; comparing women with low v. very high level of support, HR: 1.25, 95% CI: 0.63 to 2.46.
Reed, 1983	Social network	Two measures were used: 1) One ‘conceptual’ tool combining 9 items re: geographical proximity of parents; of wife’s parents; marital status; number of living children; number of persons in the household; frequency of social activities; frequency of discussing serious problems; frequency of attendance of religious services; number of social organizations attended regularly; 2) and one tool combining the first 5 items listed above (these items were selected based on factor analysis).	9 and 5	Men were divided into quartiles of the two different scores.	Subjects in the lower quartile were classed as having low levels of social network.	Authors acknowledge that the tool has not been validated, justifying their choice based on items used in similar studies.	Once, at baseline	Multiple logistic regression: coefficients associated with social network scores, CHD: beta = -0.0836, p-value > 0.5 nonfatal MI: beta = -0 0576, p-value > 0.5 fatal MI: beta = -0 0505, p-value > 0.5 angina: beta = -0.1348 , p-value > 0.5.

Reed, 1984	Social network	Questionnaire focusing on more intimate ties with relatives and household members: marital status; number of living children; number of persons in the household; geographic closeness of parents.	4	Men were grouped into quartiles based on their social networks summary score.	Subjects in the lower quartile were classed as having low levels of social network.	Authors acknowledge that the tool has not been validated, justifying their choice based on items used in similar studies.	Once, at baseline	Multiple logistic regression analysis. CHD: comparing subjects with low v. high networks, p-value ≤ 0.05. Stroke: comparing subjects with low v. high networks, p-value >0.05.
Rutledge, 2008	Social network	Social Network Index - The SNI collects information on 12 types of social relationships, including friends, employment, neighbours, marriage partners, belonging to a church, children, parents, in-laws, other relatives, class attendance (e.g., university), volunteer work, and group memberships.	12	Scoring of the SNI produces a measure of social network diversity based on the presence or absence of each of the 12 relationship domains over a 2-week period, with scores ranging from 0 to 12; 2 categories: a dichotomy between high and low scorers was operated based on a cut-off score of 6.	188 (30%) had low social network levels and 441 had high social network levels	No information re. validity or reliability was reported in this study.	Once, at baseline	Comparing subjects with low v. high social network index scores, HR for stroke: 2.7, 95% CI: 1.1 to 6.5.
Vogt, 1992	Social network - scope, size and frequenc y	Three indices were created: 1) scope of network, 2) size of network, and 3) frequency of contact within and across network sectors.	15	1) Network scope is the unweighted sum of the number of network domains in which respondents reported one or more relationships. 2) Network size is the combined number of family members, friends, work associates, and neighbours comprising the network. 3) Network frequency is a summed score derived from answers to questions about the frequency with which respondents interacted or participated in activities with others; for each measure, 3 categories: measures were divided into approximate tertiles to the degree that distributions of scores permitted.	Network measures were divided into approximate tertiles to the degree that distributions of scores permitted. For network scope, the mean score was 9.31 (SD = 1.72, range 2-12). The network frequency mean was 13.0 (SD = 3.59, range 0-22). The network size mean was 23.2 (SD = 6.31, range 3-47).	No information reported in this study. Maxwell (1985) reported that the 3 social network indices had low reliability (Cronbach's alpha ranged from .30 for network size to approximately .43 for network scope).	Once, at baseline	Comparing subjects in the low v. high tertiles of social network size: HR for CHD: 1.2, 95% CI: 0.9 to 1.6; HR for stroke: 0.9, 95% CI: 0.6 to 1.3, p-value = 0.58.

Barefoot, 2005	Social network/ social support	Participants were asked to indicate how frequently they had contact with persons in the following categories: parents, children, other family members, a spouse or partner, colleagues from work (after work), neighbors, and friends. Response options were ‘‘daily,’’ ‘‘weekly,’’ ‘‘monthly,’’ ‘‘rarely,’’ ‘‘never,’’ and ‘‘no one available.’’	7	The responses of ‘‘no one available,’’ ‘‘rarely,’’ and ‘‘never’’ were combined into a ‘‘no contact’’ category. Responses of ‘‘daily,’’ ‘‘weekly,’’ and ‘‘monthly’’ were grouped into one category indicating that contact was present. 2 diversity indices were created by summing responses across multiple classes of contacts. 1) One index was based on all contact sources, with scores ranging from 0 to 7. 2) A second index focused on relationships with parents, children, family, and friends, with scores ranging from 0 to 5. For each measure, there were 6 categories.	Diversity index based on all relationships: mean score on the scale was 3.6 (of a possible score of 7), with 7.5% of participants reporting 1 contact or no contacts and 9.9% reporting 6+ sources of contact. Re. contacts with intimate relationships: The mean score on this index was 2.9 (of a possible score of 5), with 195 (2%) of the participants reporting no contacts and 799 (8%) reporting contacts in all categories.	No data re. reliabilit y or validity were reported in this study.	Once, at baseline	Comparing people with 6-7 contacts to 0-1 contacts, HR for CHD: 0.67, 95% CI: 0.33 to 1.39. Comparing people with 5 intimate contacts to no contact, HR for CHD: 0.39, 95% CI: 0.14 to 1.06.
Hedblad, 1992	Contact frequenc y	Quantitative measure of how often the individual meets with children, kin, neighbours, friends and workmates.	5	A score was calculated by assigning one point to each questionnaire item, i.e. minimum score 0, maximum 6 points. 2 categories: total scores were dichotomised, with low frequency of contact defined as scoring 0-1 point	Not reported.	No data re. reliabilit y or validity were reported in this study.	Once, at baseline	Comparing subjects with low v. high contact frequency, relative risk (RR) for CHD: 1.2, 95% CI: 0.3 to 4.9; regression coefficient = 0.193, SE = 0.713.

Loneliness and social isolation measure combined								
Strodl, 2003	Social support	Duke Social Support Index (DSSI), 11-items. This is a shortened version of the DSSI. The index comprises two subscales: social interaction (i.e., frequency of interactions) and subjective support (i.e., satisfaction with emotional support provided).	11	The scores on the 11 items were combined and categorized as low-fair (score ≤26), high (score 27–29), and very high (score 30–33).	Low to fair social support: 1,579 (17%); high: 3,044; very high: 3,136	Cronbach alpha for this study: 0.62. The authors report that the 11-item DSSI has been validated with an Australian population and found to have reasonable test-retest reliability, concurrent validity, and construct validity (Goodger, Byles, & Higginbotham, 1999).	Once, at baseline	Comparing subjects with low to fair v. very high social support, OR for CHD: 1.41, 95% CI 1.11 to 1.79. [unadjusted]
Strodl, 2008	Social support	Duke Social Support Index (DSSI), 11-items. This is a shortened version of the DSSI. The index comprises two subscales: social interaction (i.e., frequency of interactions) and subjective support (i.e., satisfaction with emotional support provided). The scores on the 11 items were combined and categorized as low-fair (score ≤26), high (score 27–29), and very high (score 30–33).	11	The scores on the 11 items were combined and categorized as low-fair (score ≤26), high (score 27–29), and very high (score 30–33).	Low-fair social support: 3,613 (41%); high: 3,497; very high: 1,797.	Cronbach alpha for this study: 0.62. The authors report that the 11-item DSSI has been validated with an Australian population and found to have reasonable test-retest reliability, concurrent validity, and construct validity (Goodger, Byles, & Higginbotham, 1999).	Once, at baseline	Comparing subjects with low to fair v. very high social support, OR for stroke: 0.88, 95% CI: 0.62 to 1.25. [unadjusted]

Appendix 6.1 Study protocol: analyses of loneliness and social isolation over time, and associations with cardiovascular outcomes

Introduction

This protocol outlines the rationale for the proposed longitudinal observational study, and the methods that will be used for it. The purpose of specifying how the study will be conducted a priori is to: minimise bias, promote transparency, reduce the risk of duplication, and enable peer review (Light and Pillemer, 1984; Williams et al., 2010). Every effort will be made to adhere to the predetermined protocol. If changes are required to adapt to unanticipated circumstances, these will not be undertaken without consulting my supervisors. Protocol amendments will be documented in a protocol addendum and in the final report of the study.

Background

Adults with fewer social contacts (social isolation) or who feel unhappy about their social relationships (loneliness) are at increased risk of mortality and morbidity. A meta-analysis encompassing 70 longitudinal studies, with 48,673 participants averaging 66 years of age at initial evaluation and followed for an average of 7 years, found that weaker social relationships predicted premature mortality (Holt-Lunstad et al., 2015). In a review of longitudinal studies set in high-income countries, we found that deficiencies in social relationships were associated with an increased risk of developing stroke (RR: 1.32, 95% CI: 1.04 -1.68) and coronary heart disease (RR: 1.29, 95% CI: 1.04-1.59) (Valtorta et al., 2015, currently under review). Results from individual studies suggest that social relationships have implications for a range of health outcomes, including depression (Cacioppo et al., 2006b), cognitive decline (James et al., 2011), dementia (Fratiglioni et al., 2000), disability onset (Lund et al., 2010) and sleep disturbance (Cacioppo et al., 2002).

The influence of social relationships is comparable with other known risk factors for mortality and morbidity, such as physical activity, obesity, anxiety or job-strain (Holt-Lunstad et al., 2010). Yet compared with our understanding of these risk factors, we know much less about the link between social relationships and health. Researchers have identified three main pathways through which loneliness and social isolation may have an effect on health: behavioural (e.g. physical inactivity or smoking), psychological (via self-efficacy or self-esteem, for example) and physiological mechanisms (e.g. defective immune functioning or high blood pressure) (Berkman and Glass, 2000; Hawkley and Cacioppo, 2010). Because few studies to date have looked at loneliness and social isolation simultaneously, it is not clear whether certain pathways are more relevant to loneliness or to social isolation, and how the influences of these two experiences might differ. The dynamic nature of loneliness and social isolation has often been ignored, with many studies in this field relying on a cross-sectional design, or a longitudinal design in which social relationships were only captured once, most often at baseline. It is unclear which factors might act as effect modifiers, and whether certain groups could be particularly at risk of experiencing ill-health due to deficiencies in social relationships.

Current uncertainties about how loneliness and social isolation affect health are problematic because they limit our understanding of the mechanisms involved, and of how we might intervene to prevent and minimise adverse effects. I propose to reduce these uncertainties by carrying out a longitudinal observational study, to explore trajectories of loneliness and social isolation over time, and their association with health. The hypothesis underlying the proposed study is that persistent loneliness and social isolation may be especially detrimental for health.

Study objectives

Primary aim: To investigate the relationship between trajectories of loneliness and social isolation, and health.

Secondary aims:

- To investigate the pathways through which loneliness and social isolation might affect health;
- To explore whether certain population subgroups are at increased risk of experiencing the adverse health consequences of deficiencies in social relationships.

Participants and methods

Study design

General design

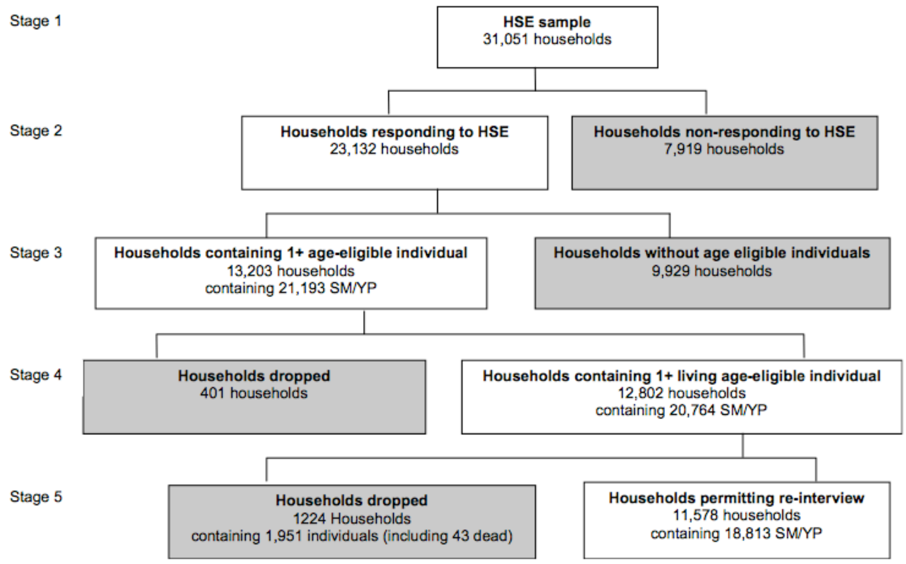
The proposed study is a secondary analysis of longitudinal data, using the English Longitudinal Study of Aging (Steptoe et al., 2013a). ELSA is a panel study of a cohort of people and their partners aged 50+, living in private households in England.

Sample design

ELSA began in 2002, drawing its initial sample from individuals who took part in the Health Survey for England (HSE), an annual cross-sectional survey designed to monitor the population's general health (Mindell et al., 2012). HSE employs a multi-stage stratified probability sampling design, in order for every address on the small users Postcode Address File (PAF) in England to have an equal chance of inclusion (Taylor et al., 2007).[19] Postcode sectors stratified by health authority and the proportion of households in the non-manual socio-economic groups are selected with probability proportional to their size. A fixed number of addresses are then selected systematically from each postcode sector. Households are identified for each address, and up to three households are randomly selected. Eligible individuals are asked to participate in a personal interview, followed by a nurse visit.

The HSE years 1998, 1999 and 2001 were chosen as the sampling frame for ELSA because they were recent and could provide a sufficiently large sample size. Taking these three HSE years together, a total of 31,051 households were sampled. Figure 1 summarises the ensuing sample selection process for ELSA's first wave.
Figure 1 ELSA sample definition for Wave 1 (http://www.ifs.org.uk/elsa/report03/w1_tech.pdf, p.10)

[19] NB: The use of the PAF as a sampling frame means that a very small percentage of households (less than 1%) will not have a chance of being included, a 'coverage' problem which affects all PAF-based surveys. In spite of this limitation, the PAF is generally accepted as having the best coverage for surveys of private households in the UK Taylor, R, Conway, L, Calderwood, L, Lessof, C, Cheshire, H, Cox, K & Scholes, S 2007, *Health, wealth and lifestyles of the older population in England: the 2002 English Longitudinal Study of Ageing - technical report, wave 1*, National Centre for Social Research, UK.



Only those households that responded to HSE were eligible for inclusion in Wave 1 of ELSA (Stage 2). To be issued to field, these households had to include at least one age–eligible individual (Stage 3) who was alive according to administrative records (Stage 4) and gave permission to be re-contacted in future (Stage 5). Alongside the target sample, partners aged under 50 and partners who had joined the household since HSE were invited for interview. As a result of this process, a sample of 11,578 households containing 18,813 core members and partners were eventually issued for ELSA. The Wave 1 fieldwork produced 12,100 productive individual interviews: 11,392 with core members (of which 204 were partial responses and 158 were proxy responses), 636 with younger partners and 72 with new partners.

To maintain ELSA's representativeness of all age groups over 50, its sample has been refreshed at three waves of data collection - waves 3, 4 and 6. The Wave 3 refreshment sample included people aged between 50 and 53 selected from HSE 2001-2004. In Wave 4, a sample of individuals aged 50 to 74 and their partners was added using data from HSE 2006. The Wave 6 refreshment sample included respondents from HSE 2009, 2010 or 2011, aged between 50 and 55.

Data collection

Waves of data collection take place every 2 years. Data are collected using computer-assisted personal interviews and self-completion questionnaires, with additional nurse visits every 4 years (waves 2, 4 and 6) for the assessment of biomarkers.

Comparison groups

For the proposed study, I am interested in comparing participants with different trajectories of loneliness and social isolation.

Loneliness

Loneliness is measured in waves 2,3,4,5, and 6 using two methods:

Using the three-item UCLA Loneliness measure:

- how often do you feel you lack companionship?
- how often do you feel left out?
- how often do you feel isolated from others?

Possible answers: Hardly ever or never(1)/some of the time(2)/often(3). Scores on the scale are summed to provide a loneliness score ranging from 3 to 9, with a higher score indicating greater loneliness.

Using a direct single item question:

How often do you feel lonely?

Possible answers: Hardly ever or never(1)/some of the time(2)/often(3).

In the initial exploratory phase of my work on ELSA, I will look at both measures and compare answers to single-item and the three-item tools. This will provide an insight into how the two measures correlate, both cross-sectionally and over time.

Social isolation

Reminder of definitions: social isolation is understood as a 'more objective' measure of the absence of relationships, ties or contacts with other people. Social relationships: 'exist between two people when each person influences the other's thoughts, feelings, and or behavior. In other words, a relationship exists when people are at least minimally interdependent' (Clark, 2001, p.14423) .

To operationalize this, I will use two separate variables:

- one variable re. frequency of contact with friends and family, via telephone/text messages/face to face/writing and existence of other ties such as work colleagues and members of community groups;

- one variable re. 'closeness' with family and friends – with no judgment as to how the respondent feels about this;

Trajectories

Trajectories of loneliness and social isolation will be investigated by looking at changes across the time period covered, i.e. 10 years/five waves for loneliness and 12 years/six waves for social isolation.

Depending on the amount and patterns of missing data, it may be that certain tools prove more adequate than others for subsequently analyzing the links between social relationships and health.

Outcomes variables

The outcomes that I can look at are:

- heart problem;

- stroke;
- memory problems;
- emotional, nervous or psychiatric problems;
- mortality;
- self-rated health;
- cancer;
- lung disease;
- arthritis.

I will begin by looking at associations with heart problems and stroke, to follow on from my systematic review.

Subject Selection

Inclusion Criteria

All core members of ELSA will be included in the analyses.

Exclusion Criteria

Partners (i.e. 'partners' and 'young partners') will not be included in my analyses (ELSA user guides make clear that partners are not part of the core sample and should not be included in all analyses. Their information has been collected to make it possible to carry out an analysis of a representative sample of couples where at least one spouse is 50 or older.)

Study Procedures

ELSA data files and accompanying materials (including dictionaries, user guides and technical reports) are available for download from the Economic and Social Data Service: https://discover.ukdataservice.ac.uk/series/?sn=200011 .

The data files that are of relevance to my study are:
Core data files for waves 1, 2, 3, 4, 5 and 6;
Nurse data files for waves 2,4 and 6;
Harmonised file for waves 1 to 6.

I have listed the variables to be extracted from these files in an excel file (see attached file named 'ELSA variables for my analyses 21.10.15.xlsx). These can broadly be categorized as follows:
- sociodemographic variables, including: age, gender, ethnicity, education, income, wealth, labour force status;

- social relationships: marital/partnership status, number of children, number of living siblings, number of living parents, number of grandchildren, number of people living in the household, whether respondent has any friends, membership of an organization or society, caring duties, frequency of contact with family and friends, quality of the relationship with family and friends, loneliness;

- morbidity and mortality: heart disease, stroke, memory problems, self-reported health, depression, emotional/nervous/psychiatric problem, quality of life, diabetes, cancer, lung disease, arthritis, mortality;

- biological and physiological variables, e.g. blood pressure, cholesterol;

- health-related behaviours: physical activity, alcohol consumption, fruit and vegetable consumption, smoking;

- functional limitations: ADLs and IADLs; BMI.

Using Stata/SE 14.1, all variables of interest will be extracted for each wave and collated into a single, wide format file. A long file version will be then created, to perform longitudinal analyses.

Statistical Plan

Statistical Methods

Descriptive statistics

For each wave, descriptive statistics will be produced for all variables extracted. For continuous variables (e.g. age, income and wealth), mean $\pm$ SD, median and ranges will be presented. For categorical variables (e.g. gender, ethnicity, education), percentages will be tabulated.

Once I have produced cross-sectional descriptive statistics, I will explore patterns across the six waves for:

- all variables relating to social relationships (e.g. loneliness, frequency of contact with family and friends);

- all variables relating to health (e.g. stroke, heart problems).

I will produce graphs to illustrate patterns of social relationships over time, i.e.:

- to look at how loneliness within individuals evolves over time;

- to look at how social isolation within individuals evolves over time;

- to look at whether loneliness and social isolation follow similar patterns over time;

- to explore whether trajectories of loneliness correlate with trajectories of social isolation over time.

NB: How I operationalise loneliness and social isolation in my subsequent analyses will depend on the amount of missing data across waves for different measuring instruments. I am keen to treat loneliness and social isolation as time-varying (unless descriptive statistics show that people report the same levels of loneliness and/or isolation across waves, but exploratory work by Victor suggests that this will not be the case) (Victor et al., Date unknown).

Analysing the links between loneliness or social isolation and health over time

The criteria guiding my choice of methods to analyse health outcomes in relation to prior trajectories are:
the structure of the dataset: many cases (n=17,981) and few periods (t=6);
the type of outcome variable studied: all outcomes currently considered for analyses are categorical;
the causal model I wish to investigate.

I anticipate using two statistical approaches:

1) Linear models for binary outcomes – to explore whether changes in loneliness and social isolation predict disease incidence/mortality;

2) Survival analysis – to explore the effect of time spent feeling lonely/being socially isolated, and disease incidence/mortality.

To control for potential confounders, explore potential mediators of the effect of poor relationships on health outcomes, and explore potential effect modifiers, I will create a series of models:

Loneliness

- model 1:loneliness, age, gender and socio-economic status (to adjust for potential confounders);

- model 2: model 1 + physiological/biological/behavioural variables, (i.e. potential confounders and/or on the causal pathway);

- model 3: model 2 + interaction terms to assess potential moderator effects, e.g. with socio-economic status

Social isolation

- model 1: social isolation (3 variables), age, gender and socio-economic status (to adjust for potential confounders);

- model 2: model 1 + physiological/biological/behavioural variables, (i.e. potential confounders and/or on the causal pathway);

- model 3: model 2 + interaction terms to assess potential moderator effects, e.g. with socio-economic status

Dealing with missing data

How I treat missing data will depend on the amount of missing data in my dataset (Menard, 2002):
- if nonresponse rates are low: I will conduct analyses using weighted data, to help minimize the bias from differential non-response among key sub-groups. Note that this scenario is the less likely one, given that the ELSA questions on social relationships were predominantly asked as part of a self-completion questionnaire;

- if nonresponse rates are high (over 30% reference Menard): I will try to explore patterns and mechanisms of missingness using the available data, and adopt an appropriate strategy (e.g. multiple imputation).

Addendum

Analyses of outcomes other than incident non-fatal heart disease and stroke were dropped, due to limited resources. I plan to repeat the analyses I performed on other outcomes in future.

The items available in ELSA were used to calculate the Framingham score for each participant and use this in the main statistical models, rather than entering each variable separately. The intention was to reflect assessment of cardiovascular risk by practitioners.

Variables other than potential confounders and items in the Framingham Score (e.g. physical activity, fruit and vegetable consumption) were dropped from analyses, either because they were not measured at baseline wave or because they could be both on the causal pathway and potential confounders.

Linear analyses were dropped, in favour of survival analyses only. Linear analyses would not have added any further information to the survival analyses.

Appendix 6.2 Annotated Stata do file for Chapter 6

The Stata commands used for the analyses presented in Chapter 6 are listed below. Outputs that were referred to but not provided in the main text (e.g. table A6.7) are presented here, immediately after the command(s) that generated them.

```
use "/Users/nicole/Google_Drive/Doctoral Fellowship
years/Longitudinal_data
analyses/ELSA/My_files/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta"

set more off

* Number of core participants at each wave, with details of which
cohort they belong to:

tab finstat1 // Repeat with finstat2, finstat3 finstat4, finstat5 and
finstat6.

* To generate long file:
reshape long finstat scfeela scfeelb scfeelc scfeeld scfeele uclalonel
rflone scscc siindex close closebis, i(idauniq) j(wave)
drop if finstat=="C1YP"
drop if finstat==""
tsset idauniq wave
xtdes, patterns (60)
```

* Table A6.7 Patterns of panel participation, waves 1 to 6. NB: In the pattern column, '1' means participation and '.' means non-participation.

Frequency	Percent	Cumulative percent	Pattern
4844	30.69	30.69	111111
1970	12.48	43.17	1.....
1722	10.91	54.08	...111
1207	7.65	61.73	11....
906	5.74	67.47	111...
826	5.23	72.70	1
699	4.43	77.13	..1111
612	3.88	81.01	1111..
554	3.51	84.52	11111.
305	1.93	86.45	...1..
201	1.27	87.73	..1...
190	1.20	88.93	...11.
170	1.08	90.01	111.11
139	0.88	90.89	11.111
117	0.74	91.63	1.1111
109	0.69	92.32	1.1...
95	0.60	92.92	1111.1
87	0.55	93.47	..11..
82	0.52	93.99	1...11
81	0.51	94.51	1..111
77	0.49	94.99	11..11
74	0.47	95.46	...1.1
65	0.41	95.88	..111.
64	0.41	96.28	..1.11
63	0.40	96.68	111.1.
56	0.35	97.03	11.1..
50	0.32	97.35	111..1
48	0.30	97.66	1..1..
45	0.29	97.94	11..1.
38	0.24	98.18	1.11..
35	0.22	98.40	11.11.
32	0.20	98.61	1...1.
32	0.20	98.81	1.111.
30	0.19	99.00	..11.1
30	0.19	99.19	1..11.
20	0.13	99.32	1.1.11
18	0.11	99.43	1....1
17	0.11	99.54	..1.1.
12	0.08	99.61	1..1.1
12	0.08	99.69	1.1.1.
12	0.08	99.77	11...1
12	0.08	99.84	11.1.1
9	0.06	99.90	..1..1
9	0.06	99.96	1.11.1
7	0.04	100.00	1.1..1
15783	100.00		XXXXXX

```
save "/Users/nicole/Google Drive/Doctoral Fellowship
years/Longitudinal data analyses/ELSA/My files/Chapter 6 analyses/Long
file LSI in ELSA.dta"

*Socio-demographic characteristics, for each wave:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear
```

```
*NB: This file includes core members only.
*103 participants who were core members from wave 3 onwards took part
in waves 1 & 2 as young partners. To drop them from analyses of waves
1 & 2, the following command needs to be applied:
drop if finstat1=="C1YP"
*Alternatively, where commands support 'if' options, care needs to be
taken to add 'if finstat1=="C1CM"'.

summarize ragey1 ragey2 ragey3 ragey4 ragey5 ragey6
tab ragender1 // repeat for ragender2, ragender3, ragender4,
ragender5, ragender6
tab raracem if finstat1=="C1CM" // repeat with finstat2=="C1CM",
finstat3!="", finstat4!="", finstat5!="" and finstat6!=""
xtile quint1=hatotb1, nq(5) // repeat for hatotb2, hatotb3, hatotb4
and hatotb5
sum hatotb1   hatotb1 if finstat1=="C1CM" //repeat for hatotob2 &
finstat2=="C1CM", hatotb3, hatotb4 and hatotb5
tab rlbrf_e1 // repeat for rlbrf_e2, rlbrf_e3, rlbrf_e4, rlbrf_e5 and
rlbrf_e6
tab rshlt1 if finstat1=="C1CM"// repeat for rshlt2, rshlt4, rshlt5 and
rshlt6
tab rshlta3
tab limitill1 if finstat1=="C1CM"// repeat for limitill2, limitill3,
limitill4, limitill5 and limitill6

*Loneliness:

*Direct single-item question about loneliness in general:
tab scfeele3 // repeat for scfeele4, scfeele5 and scfeele6
tab scfeele4 if finstat4=="C1CM"
tab scfeele5 if finstat5=="C1CM"
tab scfeele6 if finstat6=="C1CM"

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6 analyses/Long file LSI in
ELSA.dta", clear

gen lscfeele = l.scfeele
tab lscfeele scfeele, row

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear
replace scfeele3=. if scfeele3==.s | scfeele3==.a | scfeele3==.n //
repeat for scfeele4, scfeele5 and scfeele6
egen str_scfeele = concat(scfeele3 scfeele4 scfeele5 scfeele6)
egen nscfeele = rownonmiss(scfeele*)
tab str_scfeele
tab nscfeele
keep if nscfeele>1
sample 0.3
reshape long finstat scfeele, i(idauniq) j(wave)
drop if finstat=="C1YP"
scatter scfeele wave, by(idauniq)

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear

replace scfeele3=. if scfeele3==.s | scfeele3==.a | scfeele3==.n //
repeat for scfeele4, scfeele5 and scfeele6
egen str_scfeele = concat(scfeele3 scfeele4 scfeele5 scfeele6)
```

```
egen nscfeele = rownonmiss(scfeele*)
tab str_scfeele
tab nscfeele
tab str_scfeele if nscfeele==4
```

*Table A6.12 Patterns of answers to the direct question about loneliness in general among individuals who took part in all four waves

Sequence of answers (reminder: 1 = hardly ever/never lonely; 2 = lonely some of the time; 3 = often lonely)	Frequency	Percent	Cumulative percent
1111	2,169	52.68	52.68
1112	161	3.91	56.59
1113	12	0.29	56.89
1121	106	2.57	59.46
1122	65	1.58	61.04
1123	11	0.27	61.31
1131	6	0.15	61.45
1132	12	0.29	61.74
1133	13	0.32	62.06
1211	128	3.11	65.17
1212	35	0.85	66.02
1213	1	0.02	66.04
1221	51	1.24	67.28
1222	66	1.60	68.89
1223	12	0.29	69.18
1231	1	0.02	69.20
1232	10	0.24	69.44
1233	2	0.05	69.49
1311	10	0.24	69.74
1312	1	0.02	69.76
1321	3	0.07	69.83
1322	5	0.12	69.95
1323	2	0.05	70.00
1332	8	0.19	70.20
1333	7	0.17	70.37
2111	171	4.15	74.52
2112	51	1.24	75.76
2113	3	0.07	75.83
2121	47	1.14	76.97
2122	54	1.31	78.29
2123	6	0.15	78.43
2132	7	0.17	78.60
2133	3	0.07	78.67
2211	65	1.58	80.25
2212	67	1.63	81.88
2213	6	0.15	82.03
2221	72	1.75	83.77
2222	233	5.66	89.43
2223	19	0.46	89.90
2231	2	0.05	89.94
2232	22	0.53	90.48
2233	19	0.46	90.94
2311	7	0.17	91.11
2312	5	0.12	91.23
2313	1	0.02	91.26
2321	7	0.17	91.43
2322	36	0.87	92.30
2323	18	0.44	92.74
2331	3	0.07	92.81

2332	11	0.27	93.08
2333	17	0.41	93.49
3111	6	0.15	93.64
3112	2	0.05	93.68
3121	5	0.12	93.81
3122	3	0.07	93.88
3123	3	0.07	93.95
3131	1	0.02	93.98
3133	3	0.07	94.05
3211	5	0.12	94.17
3212	6	0.15	94.32
3213	1	0.02	94.34
3221	8	0.19	94.53
3222	37	0.90	95.43
3223	12	0.29	95.73
3232	10	0.24	95.97
3233	19	0.46	96.43
3311	1	0.02	96.45
3312	2	0.05	96.50
3321	6	0.15	96.65
3322	23	0.56	97.21
3323	15	0.36	97.57
3331	4	0.10	97.67
3332	19	0.46	98.13
3333	77	1.87	100.00
Total	4,117	100.00	

```
keep if nscfeele==4
codebook str_scfeele

*Table A6.13 Number of different sequences of answers to the direct
question about loneliness in general, among people who replied at all
four waves
```

```
----------------------------------------------------------------------
Codebook for the string variable capturing the sequence of responses
to the question about loneliness in general
----------------------------------------------------------------------

                  type:  string (str4)

         unique values:  74                        missing "":  0/4,117

              examples:  "1111"
                         "1111"
                         "1122"
                         "2211"
```

```
tab str_scfeele if ragey3>79
tab str_scfeele if ragey3<80
tab str_scfeele if rmstat3==7
tab str_scfeele if rmstat3!=7 & rmstat3!=.
xtile quint = hatotb3, nq(5)
tab str_scfeele if quint==1
tab str_scfeele if quint!=1 & quint!=.
tab str_scfeele if limitill3==1
tab str_scfeele if limitill3==0
```

*Table A6.14 Number of different sequences of answers to the direct question about loneliness in general, among people who replied at all four waves - subgroup analyses

	Number of different sequences
Younger than 80 (n=3,915)	72
Aged 80+ (n=202)	41
Widowed (n=521)	52
Not widowed (n=3,596)	70
Lowest wealth quintile (n=810)	66
Higher wealth quintiles (n=3,232)	69
Limiting longstanding illness (n=1,152)	66
No limiting longstanding illness	70

```
use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal data analyses/ELSA/My files/Chapter 6 analyses/ELSA_core_members_harmonised_&_non-harmonised_variables_for_analyses_only.dta", clear

generate timescfeele=.
replace timescfeele=4 if scfeele3+scfeele4+scfeele5+scfeele6==12
replace timescfeele=3 if scfeele3+scfeele4+scfeele5==9 & scfeele6!=3
replace timescfeele=3 if scfeele3+scfeele4+scfeele6==9 & scfeele5!=3
replace timescfeele=3 if scfeele5+scfeele4+scfeele6==9 & scfeele3!=3
replace timescfeele=3 if scfeele5+scfeele3+scfeele6==9 & scfeele4!=3
replace timescfeele=2 if scfeele3+scfeele4==6 & timescfeele==.
replace timescfeele=2 if scfeele3+scfeele5==6 & timescfeele==.
replace timescfeele=2 if scfeele3+scfeele6==6 & timescfeele==.
replace timescfeele=2 if scfeele4+scfeele6==6 & timescfeele==.
replace timescfeele=2 if scfeele5+scfeele6==6 & timescfeele==.
replace timescfeele=2 if scfeele5+scfeele4==6 & timescfeele==.
replace timescfeele=1 if scfeele3==3 & timescfeele==.
replace timescfeele=1 if scfeele4==3 & timescfeele==.
replace timescfeele=1 if scfeele5==3 & timescfeele==.
replace timescfeele=1 if scfeele6==3 & timescfeele==.
replace timescfeele=0 if timescfeele==.
tab timescfeele

egen nscfeele = rownonmiss(scfeele*)
tab nscfeele

tab timescfeele if nscfeele==3
```

*Table A6.15 Frequency of 'frequent loneliness' among people who replied in three waves

	Number of people	Percent
Never 'often lonely'	2,553	84.90
Once 'often lonely'	271	9.01
Twice 'often loneley'	99	3.29
Three times 'often lonely'	84	2.79
Total	3,007	

*Subgroup analyses:

```
gen aged=.
replace aged=1 if ragey3>79
replace aged=0 if aged==.
tab aged timescfeele, row col chi
```

```
gen widow=.
replace widow=1 if rmstat3==7
replace widow=0 if rmstat3!=7 & rmstat3!=.
tab widow timescfeele, row col chi

xtile quint = hatotb3, nq(5)
gen wealth=.
replace  wealth=1 if quint==1
replace  wealth=0 if wealth==. & hatotb3!=.
tab wealth timescfeele, row col chi

tab limitill3 timescfeele, row col chi

*CESD loneliness question:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear
tab rflone1 if finstat1=="C1CM" // repeat for rflone2 with
finstat2=="C1CM" option, then for rflone3, rflone4, rflone5 and
rflone6

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6 analyses/Long file LSI in
ELSA.dta", clear

gen lrflone = l.rflone
tab lrflone rflone, row

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear
replace rflone1=. if rflone1==.d | rflone1==.m | rflone1==.p |
rflone1==.r // repeat for rflone2, rflone3, rflone4, rflone5 and
rflone6
egen str_rflone = concat(rflone1 rflone2 rflone3 rflone4 rflone5
rflone6)
egen nrflone = rownonmiss(rflone*)
tab str_rflone
tab nrflone
keep if nrflone>1
sample 0.2
reshape long finstat rflone, i(idauniq) j(wave)
drop if finstat=="C1YP"
scatter scfeele wave, by(idauniq)

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear

replace rflone1=. if rflone1==.d | rflone1==.m | rflone1==.p |
rflone1==.r // repeat for rflone2, rflone3, rflone4, rflone5 and
rflone6
egen str_rflone = concat(rflone1 rflone2 rflone3 rflone4 rflone5
rflone6)
egen nrflone = rownonmiss(rflone*)
tab str_rflone
tab nrflone
tab str_rflone if nrflone==6
```

*Table A6.19 Patterns of answers to the direct question about loneliness in the past week among individuals who took part in all six waves

Sequence of answers (reminder: 0 = not often lonely much in the past week, 1 = lonely much in the past week)	Freq.	Percent	Cumulative percent
000000	3,170	69.73	69.73
000001	105	2.31	72.04
000010	98	2.16	74.20
000011	51	1.12	75.32
000100	79	1.74	77.06
000101	22	0.48	77.54
000110	35	0.77	78.31
000111	20	0.44	78.75
001000	94	2.07	80.82
001001	10	0.22	81.04
001010	19	0.42	81.46
001011	14	0.31	81.76
001100	21	0.46	82.23
001101	9	0.20	82.42
001110	18	0.40	82.82
001111	11	0.24	83.06
010000	104	2.29	85.35
010001	15	0.33	85.68
010010	14	0.31	85.99
010011	9	0.20	86.19
010100	17	0.37	86.56
010101	1	0.02	86.58
010110	8	0.18	86.76
010111	9	0.20	86.96
011000	28	0.62	87.57
011001	9	0.20	87.77
011010	9	0.20	87.97
011011	6	0.13	88.10
011100	13	0.29	88.39
011101	3	0.07	88.45
011110	18	0.40	88.85
011111	23	0.51	89.35
100000	114	2.51	91.86
100001	11	0.24	92.10
100010	10	0.22	92.32
100011	8	0.18	92.50
100100	16	0.35	92.85
100101	2	0.04	92.89
100110	5	0.11	93.00
100111	3	0.07	93.07
101000	15	0.33	93.40
101001	4	0.09	93.49
101010	5	0.11	93.60
101011	4	0.09	93.69
101100	6	0.13	93.82
101101	9	0.20	94.02
101110	13	0.29	94.30
101111	18	0.40	94.70
110000	27	0.59	95.29
110001	6	0.13	95.42
110010	8	0.18	95.60
110011	8	0.18	95.78
110100	10	0.22	96.00
110101	4	0.09	96.08

110110	2	0.04	96.13
110111	19	0.42	96.55
111000	19	0.42	96.96
111001	11	0.24	97.21
111010	10	0.22	97.43
111011	10	0.22	97.65
111100	9	0.20	97.84
111101	12	0.26	98.11
111110	21	0.46	98.57
111111	65	1.43	100.00
Total	4,546	100.00	

```
egen timesrflone=rowtotal (rflone1 rflone2 rflone3 rflone4 rflone5
rflone6)
tab timesrflone if nrflone==6 & finstat1!="C1YP"

*Table A6.20 Frequency of 'lonely much in the past week' reports among
people who replied at all six waves
```

Number of 'lonely much in the past week reports	Freq.	Percent	Cumulative percent
0	3,115	69.64	69.64
1	581	12.99	82.63
2	309	6.91	89.54
3	181	4.05	93.58
4	119	2.66	96.24
5	103	2.30	98.55
6	65	1.45	100.00
Total	4,473	100.00	

```
tab timesrflone if nrflone==5 & finstat1!="C1YP"
tab timesrflone if nrflone==4 & finstat1!="C1YP"
tab timesrflone if nrflone==3 & finstat1!="C1YP"


*Table A6.21 Frequency of 'lonely much in the past week' reports among
people who replied in five, four or three waves
```

	Five waves		Four waves		Three waves	
Times lonely much in the past week	Freq.	Percent	Freq.	Percent	Freq.	Percent
0	695	64.35	1,097	67.72	2,239	74.61
1	164	15.19	241	14.88	401	13.36
2	94	8.70	134	8.27	223	7.43
3	51	4.72	82	5.06	138	4.60
4	48	4.44	66	4.07	NA	NA
5	28	2.59	NA	NA	NA	NA
Total	1,080		1,620		3,001	

```
keep if nrflone==6

*Subgroup analyses:

gen aged=.
replace aged=1 if ragey1>79
replace aged=0 if aged==.
tab aged timesrflone, row col chi
```

```
gen widow=.
replace widow=1 if rmstat1==7
replace widow=0 if rmstat1!=7 & rmstat1!=.
tab widow timesrflone, row col chi

xtile quint = hatotb1, nq(5)
gen wealth=.
replace  wealth=1 if quint==1
replace  wealth=0 if wealth==. & hatotb1!=.
tab wealth timesrflone, row col chi

tab limitill1 timesrflone, row col chi

*Relationship between the direct question about loneliness in general
and the CESD question:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6 analyses/Long file LSI in
ELSA.dta", clear

svyset idauniq
tabulate scfeele rflone
svy: tabulate scfeele rflone, col row

*Three-item UCLA Loneliness Scale:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear

tab uclalonel2 if finstat2=="C1CM" // repeat without the if condition
for uclalonel3, uclalonel4, uclalonel5 and uclalonel6
tab scfeela2 if finstat2=="C1CM" // repeat without the if condition
for scfeela3, scfeela4, scfeela5 and scfeela6
tab scfeelb2 if finstat2=="C1CM" // repeat without the if condition
for scfeelb3, scfeelb4, scfeelb5 and scfeelb6
tab scfeelc2 if finstat2=="C1CM" // repeat without the if condition
for scfeelc3, scfeelc4, scfeelc5 and scfeelc6

egen str_uclalonel = concat(uclalonel2 uclalonel3 uclalonel4
uclalonel5 uclalonel6)
egen nuclalonel = rownonmiss(uclalonel*)
tab str_uclalonel
tab nuclalonel
keep if nuclalonel>1
sample 0.2
reshape long finstat uclalonel, i(idauniq) j(wave)
drop if finstat=="C1YP"
scatter uclalonel wave, by(idauniq)

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear

egen str_uclalonel = concat(uclalonel2 uclalonel3 uclalonel4
uclalonel5 uclalonel6)
egen nuclalonel = rownonmiss(uclalonel*)
tab str_uclalonel
tab nuclalonel
tab str_uclalonel if nuclalonel==5 //NB: this generates a list of
1,085 patterns, not reproduced here due to length/space constraints.
The most common pattern was scoring 3 (i.e. lowest score) across the
five waves (n=983, i.e. 30% of sample).
```

```
gen timesucla=.
replace timesucla=1 if uclalonel2==8 | uclalonel3==8 | uclalonel4==8 |
uclalonel5==8 | uclalonel6==8
replace timesucla=1 if uclalonel2==9 | uclalonel3==9 | uclalonel4==9 |
uclalonel5==9 | uclalonel6==9
replace timesucla=0 if timesucla==.

*Subgroup analyses:

gen aged=.
replace aged=1 if ragey2>79
replace aged=0 if aged==.
tab aged timesucla, row col chi

gen widow=.
replace widow=1 if rmstat2==7
replace widow=0 if rmstat2!=7 & rmstat2!=.
tab widow timesucla, row col chi

xtile quint = hatotb2, nq(5)
gen wealth=.
replace  wealth=1 if quint==1
replace  wealth=0 if wealth==. & hatotb2!=.
tab wealth timesucla, row col chi

tab limitill2 timesucla, row col chi

*Relationship between the direct question about loneliness in general
and the CESD question:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6 analyses/Long file LSI in
ELSA.dta", clear

svyset idauniq
tabulate scfeele uclalonel
svy: tabulate scfeele uclalonel, col row

*Social isolation:

*Index of social contacts:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear

tab sizehh1 if finstat1=="C1CM" // repeat for sizehh2 with
finstat2=="C1CM" option, then sizehh3, sizehh4, sizehh5 and sizehh6
tab contactCHILD1 if finstat1=="C1CM" // repeat for contactCHILD2 with
finstat2=="C1CM" option, then contactCHILD3, contactCHILD4,
contactCHILD5 and contactCHILD6
tab contactFAM1 if finstat1=="C1CM" // repeat for contactFAM2 with
finstat2=="C1CM" option, then contactFAM3, contactFAM4, contactFAM5
and contactFAM6
tab contactFRIEND1 if finstat1=="C1CM" // repeat for contactFRIEND2
with finstat2=="C1CM" option, then contactFRIEND3, contactFRIEND4,
contactFRIEND5 and contactFRIEND6
tab jobstatus1 if finstat1=="C1CM" // repeat for jobstatus2 with
finstat2=="C1CM" option, then jobstatus3, jobstatus4, jobstatus5 and
jobstatus6
tab scorgi1 if finstat1=="C1CM" // repeat for scorgi2 with
finstat2=="C1CM" option, then scorgi3, scorgi4, scorgi5 and scorgi6
```

```
tab siindex1 if finstat1=="C1CM" // repeat for siindex2 with
finstat2=="C1CM" option, then siindex3, siindex4, siindex5 and
siindex6

egen str_siindex = concat(siindex1 siindex2 siindex3 siindex4 siindex5
siindex6)
egen nsiindex = rownonmiss(siindex*)
tab str_siindex
tab nsiindex
keep if nsiindex>1
sample 0.2
reshape long finstat siindex, i(idauniq) j(wave)
drop if finstat=="C1YP"
scatter siindex wave, by(idauniq)

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear

egen str_siindex = concat(siindex1 siindex2 siindex3 siindex4 siindex5
siindex6)
egen nsiindex = rownonmiss(siindex*)
tab str_siindex
tab nsiindex
tab str_siindex if nsiindex==6 //NB: this generates a list of 757
patterns, not reproduced here due to length/space constraints.

gen timesiindex=.
replace timesiindex=1 if siindex1==5 | siindex2==5 | siindex3==5 |
siindex4==5 | siindex5==5 | siindex6==5
replace timesiindex=1 if siindex1==6 | siindex2==6 | siindex3==6 |
siindex4==6 | siindex5==6 | siindex6==6
replace timesiindex=0 if timesiindex==.
tab timesindex if nsiindex==6
tab timesindex if nsiindex==5
tab timesindex if nsiindex==4

*Subgroup analyses:

gen aged=.
replace aged=1 if ragey1>79
replace aged=0 if aged==.
tab aged timesindex, row col exact

gen widow=.
replace widow=1 if rmstat1==7
replace widow=0 if rmstat1!=7 & rmstat1!=.
tab widow timesindex, row col chi

xtile quint = hatotb1, nq(5)
gen wealth=.
replace  wealth=1 if quint==1
replace  wealth=0 if wealth==. & hatotb1!=.
tab wealth timesindex, row col chi

tab limitill1 timesindex, row col chi

*Index of close relationships:

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6
analyses/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear
```

```
tab scptrg1 if finstat1=="C1CM" // repeat for scptrg2 with
finstat2=="C1CM" option, then scptrg3, scptrg4, scptrg5 and scptrg6
sum scchdm1 if finstat1=="C1CM" // repeat for scchdm2 with
finstat2=="C1CM" option, then scchdm3, scchdm4, scchdm5 and scchdm6
tab scchdm1 if finstat1=="C1CM" // repeat for scchdm2 with
finstat2=="C1CM" option, then scchdm3, scchdm4, scchdm5 and scchdm6
sum scfamm1 if finstat1=="C1CM" // repeat for scfamm2 with
finstat2=="C1CM" option, then scfamm3, scfamm4, scfamm5 and scfamm6
tab scfamm1 if finstat1=="C1CM" // repeat for scfamm2 with
finstat2=="C1CM" option, then scfamm3, scfamm4, scfamm5 and scfamm6
sum scfrdm1 if finstat1=="C1CM" // repeat for scfrdm2 with
finstat2=="C1CM" option, then scfrdm3, scfrdm4, scfrdm5 and scfrdm6
tab scfrdm1 if finstat1=="C1CM" // repeat for scfrdm2 with
finstat2=="C1CM" option, then scfrdm3, scfrdm4, scfrdm5 and scfrdm6

sum close1 if finstat1=="C1CM" // repeat for close2 with
finstat2=="C1CM" option, then close3, close4, close5 and close6
tab close1 if finstat1=="C1CM" // repeat for close2 with
finstat2=="C1CM" option, then close3, close4, close5 and close6

hist close 1 if finstat1=="C1CM", freq // repeat for close2 with
finstat2=="C1CM" option, then close3, close4, close5 and close6

gen isolclose1=. //repeat for isolclose2, isolclose3, isolclose4,
isolclose5 and isolclose6
replace isolclose1=1 if close1<2 //repeat for isolclose2, isolclose3,
isolclose4, isolclose5 and isolclose6
replace isolclose1=0 if close1>1 & close1!=. //repeat for isolclose2,
isolclose3, isolclose4, isolclose5 and isolclose6
tab isolclose1 if finstat1=="C1CM" // //repeat for isolclose2 with
finstat2=="C1CM" option, then for isolclose3, isolclose4, isolclose5
and isolclose6

*Table A6.33 - Frequency of social isolation as measured using the
Index of Close Relationships in waves 1 to 6

                      | Wave 1| Wave 2| Wave 3| Wave 4| Wave 5| Wave 6|
----------------------+-------+-------+-------+-------+-------+-------+
Number of isolated    |   250 |   141 |   121 |   167 |  147  |  169  |
individuals (%)       |   (3) |   (2) |   (2) |   (2) |  (2)  |  (97) |
----------------------+-------+-------+-------+-------+-------+-------+
Number of non-isolated| 8,160 | 6,074 | 6,023 | 6,948 | 6,403 | 6,342 |
individuals (%)       |  (97) |  (98) |  (98) |  (98) |  (98) |  (97) |
----------------------+-------+-------+-------+-------+-------+-------+
Total                 | 8.410 | 6,215 | 6,144 | 7,110 | 6,550 | 6,511 |


use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6 analyses/Long file LSI in
ELSA.dta", clear

xtsum close
```

*Table A6.34 - Variation in number of close relationships reported across waves 1 to 6

```
Variable         |      Mean   Std. Dev.       Min        Max |    Observations
-----------------+--------------------------------------------+----------------
Number    overall|  8.429384     5.8643          0        133 |     N =   40940
of close  between|             5.144131          0        105 |     n =   13655
relations within |             3.620458  -47.57062   87.22938 | T-bar = 2.99817
```

```
use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal data analyses/ELSA/My files/Chapter 6 analyses/ELSA_core_members_harmonised_&_non-harmonised_variables_for_analyses_only.dta", clear

drop closebis1 // repeat for closebis2, closebis3, closebis4, closebis5 and closebis6
egen nclose = rownonmiss(close*)
tab nclose
keep if nclose>1
sample 0.2
reshape long finstat close, i(idauniq) j(wave)
drop if finstat=="C1YP"
scatter close wave, by(idauniq)

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal data analyses/ELSA/My files/Chapter 6 analyses/ELSA_core_members_harmonised_&_non-harmonised_variables_for_analyses_only.dta", clear

gen isolclose1=. //repeat for isolclose2, isolclose3, isolclose4, isolclose5 and isolclose6
replace isolclose1=1 if close1<2 //repeat for isolclose2, isolclose3, isolclose4, isolclose5 and isolclose6
replace isolclose1=0 if close1>1 & close1!=. //repeat for isolclose2, isolclose3, isolclose4, isolclose5 and isolclose6
egen timesisolclose=rowtotal (isolclose1 isolclose2 isolclose3 isolclose4 isolclose5 isolclose6)
drop closebis1 // repeat for closebis2, closebis3, closebis4, closebis5 and closebis6
egen nclose = rownonmiss(close*)
tab nclose
tab timesisolclose if nclose==6 & finstat1!="C1YP" // repeat with nclose5 and nclose4
```

* Table A6.35 - Frequency of social isolation measured using the Index of Close Relationships

Reporting no or one close relationship	Six waves of data n(%)	Five waves of data n(%)	Four waves of data n(%)
Never	1,624 (94)	1,460 (95)	1,513 (94)
Once	56 (3)	52 (3)	57 (4)
Twice	17 (1)	11 (1)	21 (1)
Three times	11 (1)	5 (0.3)	7 (0.4)
Four times	6 (0.3)	7 (0.5)	7 (0.4)
Five times	5 (0.3)	5 (0.3)	NA
Six times	3 (0.2)	NA	NA
Total	1,722	1,540	1,605

```
*Subgroup analyses:

gen aged=.
replace aged=1 if ragey1>79
replace aged=0 if aged==.
tab aged timesisolclose, row col exact

gen widow=.
replace widow=1 if rmstat1==7
replace widow=0 if rmstat1!=7 & rmstat1!=.
tab widow timesisolclose, row col chi

xtile quint = hatotb1, nq(5)
gen wealth=.
replace  wealth=1 if quint==1
replace  wealth=0 if wealth==. & hatotb1!=.
tab wealth timesisolclose, row col chi

tab limitill1 timesisolclose, row col chi

*Relationship between the two measures of social isolation:

graph bar close1 if finstat1=="C1CM", over(siindex1) // repeat for
close2 with the finstat2=="C1CM" option, then with close3, close4,
close5 and close6

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/Chapter 6 analyses/Long file LSI in
ELSA.dta", clear

svyset idauniq
gen isolclose=.
replace isolclose=1 if close<2
replace isolclose=0 if close>1 & close!=.
gen isolsiindex=.
replace isolsiindex=1 if siindex==5 | siindex==6
replace isolsiindex=0 if siindex <5
tabulate isolsiindex isolclose
svy: tabulate isolsiindex isolclose, row

*Relationship between loneliness and social isolation:

tabulate scfeele isolsiindex
svy: tabulate scfeele isolsiindex, row
tabulate rflone isolsiindex
svy: tabulate rflone isolsiindex, row
tabulate uclalonel isolsiindex
svy: tabulate uclalonel isolsiindex, row

tabulate scfeele isolclose
svy: tabulate scfeele isolclose, row
tabulate rflone isolclose
svy: tabulate rflone isolclose, row
tabulate uclalonel isolclose
svy: tabulate uclalonel isolclose, row
```

Appendix 7.1 Annotated Stata do file for Chapter 7

The Stata commands used for the analyses presented in Chapter 7 are listed below. Outputs that were referred to but not provided in the main text (e.g. table A7.4) are presented here, immediately after the command(s) that generated them.

```
* I open the wide file with data from the 6 ELSA waves, including
nursing interviews.

use "/Users/nicole/Google Drive/Doctoral Fellowship years/Longitudinal
data analyses/ELSA/My files/ELSA_core_members_harmonised_&_non-
harmonised_variables_for_analyses_only.dta", clear
set more off

*I have a social isolation index variable in my data, but not a social
isolation variable - i.e. a variable dichotomised based on whether
participants have one or no social ties/contacts/relationships, v. 2
or more.  I generate this variable for the four waves of interest
(i.e. wave 2 is my baseline wave, and the last wave of interest re.
predictors is wave 5, since I want to know what variables in that wave
mean for wave 6):

generate isol1=.
replace isol1=1 if siindex2==5
replace isol1=1 if siindex2==6
replace isol1=0 if siindex2<5
generate isol2=.
replace isol2=1 if siindex3==5
replace isol2=1 if siindex3==6
replace isol2=0 if siindex3<5
generate isol3=.
replace isol3=1 if siindex4==5
replace isol3=1 if siindex4==6
replace isol3=0 if siindex4<5
generate isol4=.
replace isol4=1 if siindex5==5
replace isol4=1 if siindex5==6
replace isol4=0 if siindex5<5

*The loneliness variables already exist, but they need recoding to
match the timeframe (i.e. wave 2 is baseline). Also, to avoid
confusion, I drop loneliness at waves 1 and 6, since they would not be
contributing to my analyses:

drop rflone1 rflone6
rename rflone2 rflone1
rename rflone3 rflone2
rename rflone4 rflone3
rename rflone5 rflone4

drop uclalonel6
rename uclalonel2 uclalonel1
rename uclalonel3 uclalonel2
rename uclalonel4 uclalonel3
rename uclalonel5 uclalonel4

*Stata does not impute values where these are coded as . followed by a
letter. So I replace all mising values for the loneliness variable
with '.':

replace rflone1=. if rflone1==.d
```

```
replace rflone1=. if rflone1==.m
replace rflone1=. if rflone1==.r
replace rflone1=. if rflone1==.p

replace rflone2=. if rflone2==.d
replace rflone2=. if rflone2==.m
replace rflone2=. if rflone2==.r
replace rflone2=. if rflone2==.p

replace rflone3=. if rflone3==.d
replace rflone3=. if rflone3==.m
replace rflone3=. if rflone3==.r
replace rflone3=. if rflone3==.p

replace rflone4=. if rflone4==.d
replace rflone4=. if rflone4==.m
replace rflone4=. if rflone4==.r
replace rflone4=. if rflone4==.p

*I am not interested in participants who are not core members, so I
drop them:
keep if finstat2=="C1CM"

* People have to have taken part in the self-completion and the
nursing visit:

drop if nurwt2==.
drop if inwsc2==0

*I exclude people who have already had an event prior to baseline:

drop if myheartever2==1
drop if mystrokever==1

* I drop proxy interviews (should not be necessary...):

drop if rproxy2==1 //not strictly necessary as the two lines above
should mean no proxy interviewees in wave 2 are left (which is the
case when I check using tab rproxy2)
drop if rproxy3==1
drop if rproxy4==1
drop if rproxy5==1
drop if rproxy6==1

* I generate a wealth quintile variable:

xtile quint1=hatotb2, nq(5)

* To check whether loneliness or isolation at baseline predict
attrition:

generate attrition=.
replace attrition=1 if finstat3=="" & finstat4=="" & finstat5=="" &
finstat6==""
replace attrition=1 if finstat4=="" & finstat5=="" & finstat6==""
replace attrition=1 if finstat5=="" & finstat6==""
replace attrition=1 if finstat6==""
replace attrition=0 if attrition==.

logit attrition isol1 rflone1 raeduc_e quint1 ragey2 limitill2
```

*Table A7.4 Results of logistic model predicting likelihood of attrition

Attrition	Coefficient	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Isolation	.2653148	.1793781	1.48	0.139	-.0862598	.6168893
Loneliness	-.0199226	.120986	-0.16	0.869	-.2570509	.2172056
Education	-.0041499	.0212646	-0.20	0.845	-.0458279	.037528
Wealth quint.	-.1878768	.0289819	-6.48	0.000	-.2446802	-.1310733
Age	.0479907	.0044562	10.77	0.000	.0392567	.0567248
Illness	.2289536	.0836672	2.74	0.006	.0649689	.3929383
_cons	-3.584849	.3105352	-11.54	0.000	-4.193486	-2.976211

```
* I check missing data frequency and patterns for the baseline
variables:

misstable summarize quint1 ragey2 ragender risk10 rflone1 isol1
sysval2 hemdabis2 smokebis2 diab2 hdlmg2 cholmg2

misstable patterns quint1 ragey2 ragender risk10 rflone1 isol1

* To check the missing data frequency and patterns re. the loneliness
and social isolation variables over time, and to pursue with survival
analyses, I need the data in person-period format.

* To generate time-to-event data:

egen str_cvdevent = concat(cvdeventever2 cvdevent3 cvdevent4 cvdevent5
cvdevent6)
tab str_cvdevent
generate dur=.

* I code the duration of follow-up for people who experience a first
CVD event during the study period:

replace dur=1 if cvdevent3==1
replace dur=1 if cvdevent3==2
replace dur=2 if cvdevent4==1 & cvdevent3==0 // I am interested in
first events only, hence the inclusion of cvdevent3==0 criteria here,
and below.
replace dur=2 if cvdevent4==2 & cvdevent3==0
replace dur=3 if cvdevent5==1 & cvdevent3==0 & cvdevent4==0
replace dur=3 if cvdevent5==2 & cvdevent3==0 & cvdevent4==0
replace dur=4 if cvdevent6==1 & cvdevent3==0 & cvdevent4==0
&cvdevent5==0
replace dur=4 if cvdevent6==2 & cvdevent3==0 & cvdevent4==0
&cvdevent5==0

* I code the duration of follow-up for people who are lost to follow-
up (censored) prior to the end of the study:

replace dur=1 if str_cvdevent=="0...." // NB: people with missing
values in between waves are classed as censored after the last wave
for which they have data.
replace dur=4 if str_cvdevent=="0...0"
replace dur=4 if str_cvdevent=="0..0."
replace dur=4 if str_cvdevent=="0..00"
replace dur=3 if str_cvdevent=="0.0.."
replace dur=4 if str_cvdevent=="0.0.0"
replace dur=4 if str_cvdevent=="0.00."
replace dur=4 if str_cvdevent=="0.000"
replace dur=2 if str_cvdevent=="00..."
replace dur=4 if str_cvdevent=="00..0"
replace dur=4 if str_cvdevent=="00.0."
replace dur=4 if str_cvdevent=="00.00"
```

```
replace dur=3 if str_cvdevent=="000.."
replace dur=4 if str_cvdevent=="000.0"
replace dur=4 if str_cvdevent=="0000."
replace dur=4 if str_cvdevent=="00000"

codebook dur
list str_cvdevent if dur==. // Follow-up is still missing for some
participants. They are the ones with missing data at some point prior
to an event.
* I code these as having an event in that wave - i.e. I assume that
the code is not reffering to an event in a prior wave for which data
were missing.

replace dur=2 if str_cvdevent=="0.1.0"
replace dur=2 if str_cvdevent=="0.10."
replace dur=2 if str_cvdevent=="0.100"
replace dur=2 if str_cvdevent=="0.1.."
replace dur=3 if str_cvdevent=="0.01."
replace dur=3 if str_cvdevent=="0.010"
replace dur=3 if str_cvdevent=="0..1."
replace dur=3 if str_cvdevent=="00.20"
replace dur=3 if str_cvdevent=="00.1."
replace dur=3 if str_cvdevent=="00.10"
replace dur=3 if str_cvdevent=="0..10"
replace dur=4 if str_cvdevent=="0.001"
replace dur=4 if str_cvdevent=="000.1"
replace dur=4 if str_cvdevent=="0.0.2"
replace dur=4 if str_cvdevent=="00.01"
replace dur=4 if str_cvdevent=="0.002"
replace dur=4 if str_cvdevent=="00..1"
replace dur=4 if str_cvdevent=="0...1"
replace dur=4 if str_cvdevent=="0..01"

codebook dur //to double-check whether any duration values are
missing. None are.

*I generate an event variable:

generate event=.
replace event=1 if cvdevent3==1 & dur==1 // the dur==1 is not strictly
necessary here, but is for cvdevent4 onwards. Since my event is
*first* CVD event, any other does not count.
replace event=1 if cvdevent3==2 & dur==1
replace event=1 if cvdevent4==1 & dur==2
replace event=1 if cvdevent4==2 & dur==2
replace event=1 if cvdevent5==1 & dur==3
replace event=1 if cvdevent5==2 & dur==3
replace event=1 if cvdevent6==1 & dur==4
replace event=1 if cvdevent6==2 & dur==4
replace event=0 if event==.

codebook event

*To generate a variable for new diagnosis of a heart condition:

generate event1=0
replace event1=1 if mynewheart3==1 & dur==1 & cvdevent3<2
replace event1=1 if mynewheart4==1 & dur==2 & cvdevent4<2
replace event1=1 if mynewheart5==1 & dur==3 & cvdevent5<2
replace event1=1 if mynewheart6==1 & dur==4 & cvdevent6<2

codebook event1

*To generate a variable for new stroke:
```

```
generate event2=0
replace event2=1 if mynewstroke3==1 & dur==1 & cvdevent3<2
replace event2=1 if mynewstroke4==1 & dur==2 & cvdevent4<2
replace event2=1 if mynewstroke5==1 & dur==3 & cvdevent5<2
replace event2=1 if mynewstroke6==1 & dur==4 & cvdevent6<2

codebook event2

*I double-check frequencies of events:

tab event
tab event1 event2 // We note that in 22 cases, a stroke and a heart
problem are reported in the same wave.
*Hence the discrepancy between number of events using event, and
number of events using event1+event2.

* I generate survival tables and look at mean follow-up:

ltable dur event, noadjust
ltable dur event, hazard noadjust

sum dur // NB: dur is in waves, so for years I need to multiply by
two.
display 3.34*2

* I recode missing variables to . so that they are eligible for
imputation:

replace smokebis2=. if smokebis2==.d
replace smokebis2=. if smokebis2==.m
replace sysval2=. if sysval2==.j

* I drop the risk10 variable, since this will be recalculated post
imputation:

drop risk10

*For imputation:

generate heart=0
replace heart=1 if mynewheart3==1
replace heart=1 if mynewheart4==1
replace heart=1 if mynewheart5==1
replace heart=1 if mynewheart6==1

generate stroke=0
replace stroke=1 if mynewstroke3==1
replace stroke=1 if mynewstroke4==1
replace stroke=1 if mynewstroke5==1
replace stroke=1 if mynewstroke6==1

* I keep only the variables am interested in for my survival analyses:

keep idauniq heart stroke quint1 ragey2 ragender uclalonel1 uclalonel2
uclalonel3 uclalonel4 finstat1 finstat2 finstat3 finstat4 finstat5
finstat6 isol1 isol2 isol3 isol4 rflone1 rflone2 rflone3 rflone4
categrisk10 dur event event1 event2 diab2 sysval2 hdlmg2 cholmg2
hemdabis2 smokebis2

* Commands for multiple imputation by chained equations :

mi set flongsep phdimput // I use the flongsep format to allow me to
generate the Framingham CVD risk score variable post the mi impute
command
mi register imputed rflone1 rflone2 rflone3 rflone4 isol1 isol2 isol3
```

```
isol4 hemdabis2 smokebis2 diab2 sysval2 hdlmg2 cholmg2 quint1
uclalonel1 uclalonel2 uclalonel3 uclalonel4
mi register regular event event1 event2 ragey2 ragender dur heart
stroke
mi impute chained (truncreg, ll(80) ul(259)) sysval2 (truncreg, ll(19)
ul(139)) hdlmg2 (truncreg, ll(81) ul(476)) cholmg2 (ologit) quint1
uclalonel1 uclalonel2 uclalonel3 uclalonel4 (logit) hemdabis2
smokebis2 diab2 rflone1 rflone2 rflone3 rflone4 isol1 isol2 isol3
isol4 = ragey2 i.ragender i.heart i.stroke i.dur, add(25)

* To generate the new Framingham 10-year CVD risk score, I cannot use
straightforward commands to generate passive variables. So, in
accordance with the
* Stata help section re. generating passive variables, I proceed as
follows (NB: I tried using a loop but with no success).

mi copy newphdimput
do Framingham.do
save newphdimput, replace

use _1_newphdimput
do Framingham.do
save _1_newphdimput, replace // repeat for imputations 2 to 25


mi convert mlong // I change the mi format to a more efficient set up.

* I generate a categorical variable for the Framingham risk score,
where <10% is low, 10-19% is medium and over 20% is high risk:
mi passive: generate micategrisk10=.
mi passive: replace micategrisk=0 if risk10<0.10
mi passive: replace micategrisk10=1 if risk10>0.09 & risk10<0.20
mi passive: replace micategrisk10=2 if risk10>0.19 & risk10!=.

* I generate a variable for cumulative exposure to social isolation:

mi passive: generate sumis1=isol1
mi passive: generate sumis2=isol1+isol2
mi passive: generate sumis3=isol1+isol2+isol3
mi passive: generate sumis4=isol1+isol2+isol3+isol4

* I generate a variable for cumulative exposure to loneliness assessed
using the CESD single item:

mi passive: generate sumlone1=rflone1
mi passive: generate sumlone2=rflone1+rflone2
mi passive: generate sumlone3=rflone1+rflone2+rflone3
mi passive: generate sumlone4=rflone1+rflone2+rflone3+rflone4

* I generate a variable for cumulative exposure to loneliness assessed
using the ucla scale, dichotomised:

mi passive: generate dichotlonel1=.
mi passive: replace dichotlonel1=1 if uclalonel1==6 | uclalonel1==7 |
uclalonel1==8 | uclalonel1==9
mi passive: replace dichotlonel1=0 if uclalonel1<6
mi passive: generate dichotlonel2=.
mi passive: replace dichotlonel2=1 if uclalonel2==6 | uclalonel2==7 |
uclalonel2==8 | uclalonel2==9
mi passive: replace dichotlonel2=0 if uclalonel2<6
mi passive: generate dichotlonel3=.
mi passive: replace dichotlonel3=1 if uclalonel3==6 | uclalonel3==7 |
uclalonel3==8 | uclalonel3==9
mi passive: replace dichotlonel3=0 if uclalonel3<6
mi passive: generate dichotlonel4=.
```

```
mi passive: replace dichotlonel4=1 if uclalonel4==6 | uclalonel4==7 |
uclalonel4==8 | uclalonel4==9
mi passive: replace dichotlonel4=0 if uclalonel4<6

mi passive: generate sumdichotlonel1=dichotlonel1
mi passive: generate sumdichotlonel2=dichotlonel1+dichotlonel2
mi passive: generate
sumdichotlonel3=dichotlonel1+dichotlonel2+dichotlonel3
mi passive: generate
sumdichotlonel4=dichotlonel1+dichotlonel2+dichotlonel3+dichotlonel4

*I copy the baseline loneliness and social isolation variables so that
I don't 'lose' them when the data are expanded:

mi passive: generate baselone=rflone1
mi passive: generate baseisol=isol1

mi passive: generate baseucla=dichotlonel1

save "newphdimput.dta", replace

* Descriptive statistics for imputed and non-imputed datasets - to
check differences and uncover unexpected discrepancies:

mi estimate: mean ragey2
mi xeq 0: mean ragey2
mi estimate: proportion ragender
mi xeq 0: proportion ragender
mi estimate: proportion quint1
mi xeq 0: proportion quint1
mi estimate: mean risk10
mi xeq 0: mean risk10
mi estimate: proportion micategrisk10
mi xeq 0: proportion micategrisk10

mi estimate: mean sysval2
mi xeq 0: mean sysval2
mi xeq : generate sysval22 = sysval2*sysval2
mi estimate (sd : sqrt( _b[sysval22] - _b[sysval2]*_b[sysval2] ) ) :
svy : mean sysval2 sysval22

mi estimate: proportion hemdabis2
mi xeq 0: proportion hemdabis2
mi estimate: proportion smokebis2
mi xeq 0: proportion smokebis2
mi estimate: proportion diab2
mi xeq 0: proportion diab2
mi estimate: mean cholmg2
mi xeq 0: mean cholmg2
mi xeq : generate cholmg22 = cholmg2*cholmg2
mi estimate (sd : sqrt( _b[cholmg22] - _b[cholmg2]*_b[cholmg2] ) ) :
svy : mean cholmg2 cholmg22

mi estimate: mean hdlmg2
mi xeq 0: mean hdlmg2
mi xeq : generate hdlmg22 = hdlmg2*hdlmg2
mi estimate (sd : sqrt( _b[hdlmg22] - _b[hdlmg2]*_b[hdlmg2] ) ) : svy
: mean hdlmg2 hdlmg22

mi estimate: proportion sumlone4
mi xeq 0: proportion sumlone4
mi estimate: proportion sumis4
mi xeq 0: proportion sumis4

save "/Users/nicole/Google Drive/Doctoral Fellowship
```

```
years/Longitudinal data analyses/ELSA/My files/longnewphdimput.dta",
replace

mi register imputed baseucla baselone baseisol sumlone1 sumlone2
sumlone3 sumlone4 sumis1 sumis2 sumis3 sumis4 dichotlonel1
dichotlonel2 dichotlonel3 dichotlonel4 sumdichotlonel1 sumdichotlonel2
sumdichotlonel3 sumdichotlonel4

mi reshape long rflone isol uclalonel dichotlonel sumis sumlone
sumdichotlonel, i(idauniq) j(t)
drop if t>dur
mi update

* Missing data frequency and patterns:

mi xeq 0: misstable pattern ragender ragey2 risk10 quint1 rflone isol
mi xeq 0: codebook idauniq if rflone!=. & isol!=. & risk!=. &
quint1!=.

* Descriptive statistics re. loneliness UCLA score across waves:

mi estimate: mean uclalonel

* Generate event variable for analyses:

mi passive: generate y=0
mi passive: replace y=event if t==dur

mi passive: generate y1=0
mi passive: replace y1=1 if t==dur & event1==1

mi passive: generate y2=0
mi passive: replace y2=1 if t==dur & event2==1

mi tsset idauniq t

* Generate variable to assess frequency of loneliness and isolation
together, as well as separately:

mi passive: generate rels=.
mi passive: replace rels=1 if rflone==1 & isol==0
mi passive: replace rels=2 if isol==1 & rflone==0
mi passive: replace rels=3 if rflone==1 & isol==1
mi passive: replace rels=0 if rflone==0 & isol==0

save "/Users/nicole/Google Drive/Doctoral Fellowship
years/Longitudinal data analyses/ELSA/My files/longnewphdimput.dta",
replace

* Cross-sectional patterns of loneliness and social isolation
responses:

mi estimate: proportion rels
mi xeq 0 : proportion rels

* To check whether loneliness/isolation at one wave predicts
missigness in these variables at the next:

mi xeq 0: sort idauniq t; by idauniq: gen lrflone=l.rflone
mi xeq 0: sort idauniq t; by idauniq: gen lisol=l.isol
mi xeq 0: gen missingl=0
mi xeq 0: gen missingi=0
mi xeq 0: replace missingl=1 if rflone==.
mi xeq 0: replace missingi=1 if isol==.
```

mi xeq 0: sort idauniq t; xtreg missingl l.rflone, fe

*Table A7.6 Output relating to the fixed effect logit model with missing loneliness as the binary outcome and loneliness in the previous wave as the explanatory variable

```
Fixed-effects (within) regression               Number of obs     =     12,107
Group variable: idauniq                         Number of groups  =      4,723

R-sq:                                           Obs per group:
     within  = 0.0004                                         min =          1
     between = 0.0001                                         avg =        2.6
     overall = 0.0000                                         max =          3

                                                F(1,7383)         =       3.16
corr(u_i, Xb)  = -0.0261                        Prob > F          =     0.0755

------------------------------------------------------------------------------
    missingl |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rflone |
         L1. |   -.013811   .0077692    -1.78   0.076    -.0290409    .0014189
             |
       _cons |   .0368839   .0016095    22.92   0.000     .0337288     .040039
-------------+----------------------------------------------------------------
     sigma_u |  .18426268
     sigma_e |  .15267403
         rho |   .5929356   (fraction of variance due to u_i)
------------------------------------------------------------------------------
F test that all u_i=0: F(4722, 7383) = 2.20                  Prob > F = 0.0000
```

mi xeq 0: sort idauniq t; xtreg missingi l.isol, fe

*Table A7.7 Output relating to the fixed effect logit model with missing social isolation as the binary outcome and social isolation in the previous wave as the explanatory variable

```
Fixed-effects (within) regression               Number of obs     =      8,757
Group variable: idauniq                         Number of groups  =      4,141

R-sq:                                           Obs per group:
     within  = 0.0000                                         min =          1
     between = 0.0003                                         avg =        2.1
     overall = 0.0001                                         max =          3

                                                F(1,4615)         =       0.11
corr(u_i, Xb)  = -0.0183                        Prob > F          =     0.7452

------------------------------------------------------------------------------
    missingi |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        isol |
         L1. |  -.0125261   .0385486    -0.32   0.745    -.0880999    .0630477
             |
       _cons |   .2268181   .0039717    57.11   0.000     .2190318    .2346045
-------------+----------------------------------------------------------------
     sigma_u |  .39724391
     sigma_e |  .34443021
         rho |  .57084951   (fraction of variance due to u_i)
------------------------------------------------------------------------------
F test that all u_i=0: F(4140, 4615) = 2.01                  Prob > F = 0.0000
```

* I now look at the first association of interest: baseline L and SI, and risk of event:

*Univariate analyses:
*Loneliness:
mi estimate, eform: cloglog y i.t i.baselone
*Social isolation:
mi estimate, eform: cloglog y i.t i.baseisol

```
* Multivariate analyses:
* Confounders:
mi estimate, eform: cloglog y i.t i.baselone i.baseisol c.ragey2
i.ragender i.quint1

*With CVD risk score:
mi estimate, eform: cloglog y i.t i.baselone i.micategrisk i.baseisol
c.ragey2 i.ragender i.quint1

*Check interactions with time:
mi estimate: cloglog y i.t##i.baselone i.ragender c.ragey2 i.baseisol
i.micategrisk i.quint1
mi test 2.t#1.baselone 3.t#1.baselone 4.t#1.baselone
mi estimate, eform: cloglog y i.t##i.baseisol i.baselone i.ragender
c.ragey2 i.micategrisk i.quint1
mi test 2.t#1.baseisol 3.t#1.baseisol 4.t#1.baseisol
mi estimate, eform: cloglog y i.t##c.ragey2 i.ragender i.baseisol
i.baselone i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi estimate, eform: cloglog y i.t##i.ragender c.ragey2 i.baseisol
i.baselone i.micategrisk i.quint1
mi test 2.t#1.ragender 3.t#1.ragender 4.t#1.ragender
mi estimate, eform: cloglog y i.t##i.quint1 i.ragender c.ragey2
i.baseisol i.baselone i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi estimate, eform: cloglog y i.t##i.micategrisk i.quint1 i.ragender
c.ragey2 i.baseisol i.baselone
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk

* Table A7.14 P-values associated with interaction terms between
baseline explanatory variables and time measured in waves,
successively entered into model D:

Interaction between time and... | P-value associated with Wald test
statistic
--------------------------------+------------------------------------
loneliness                      |  0.139
social isolation                |  0.726
age                             |  0.515
gender                          |  0.441
wealth quintile                 |  0.807
Framingham risk category        |  0.687


* Is there any evidence of significant interaction between loneliness
and isolation ?

mi estimate, eform: cloglog y i.t i.baselone##i.baseisol i.micategrisk
c.ragey2 i.ragender i.quint1

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y i.t i.baselone##c.ragey2 i.baseisol
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.baselone##i.ragender c.ragey2
i.baseisol i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.baselone##i.quint1 i.ragender
c.ragey2 i.baseisol i.micategrisk
mi test 1.baselone#2.quint1 1.baselone#3.quint1 1.baselone#4.quint1
```

```
1.baselone#5.quint1
mi estimate, eform: cloglog y i.t i.micategrisk##i.baselone i.baseisol
i.quint1 i.ragender c.ragey2
mi test 1.baselone#1.micategrisk 1.baselone#2.micategrisk

*Social isolation:
mi estimate, eform: cloglog y i.t i.baselone i.baseisol##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.baselone i.baseisol##i.ragender
c.ragey2  i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.baselone i.baseisol##i.quint1
i.ragender c.ragey2 i.micategrisk
mi test 1.baseisol#2.quint1 1.baseisol#3.quint1 1.baseisol#4.quint1
1.baseisol#5.quint1
mi estimate, eform: cloglog y i.t i.baselone i.baseisol##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.baselone#1.micategrisk 1.baseisol#2.micategrisk

* And repeat for each outcome:

*Heart:

*Univariate analyses:
*Loneliness:
mi estimate, eform: cloglog y1 i.t i.baselone
*Social isolation:
mi estimate, eform: cloglog y1 i.t i.baseisol

* Multivariate analyses:
* Confounders:
mi estimate, eform: cloglog y1 i.t i.baselone i.baseisol c.ragey2
i.ragender i.quint1

*With CVD risk score:
mi estimate, eform: cloglog y1 i.t i.baselone i.micategrisk i.baseisol
c.ragey2 i.ragender i.quint1

*Check interactions with time:
mi estimate, eform: cloglog y1 i.t##i.baselone i.ragender c.ragey2
i.baseisol i.micategrisk i.quint1
mi test 2.t#1.baselone 3.t#1.baselone 4.t#1.baselone
mi estimate, eform: cloglog y1 i.t##i.baseisol i.baselone i.ragender
c.ragey2 i.micategrisk i.quint1
mi test 2.t#1.baseisol 3.t#1.baseisol 4.t#1.baseisol
mi estimate, eform: cloglog y1 i.t##c.ragey2 i.ragender i.baseisol
i.baselone i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi estimate, eform: cloglog y1 i.t##i.ragender c.ragey2 i.baseisol
i.baselone i.micategrisk i.quint1
mi test 2.t#1.ragender 3.t#1.ragender 4.t#1.ragender
mi estimate, eform: cloglog y1 i.t##i.quint1 i.ragender c.ragey2
i.baseisol i.baselone i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi estimate, eform: cloglog y1 i.t##i.micategrisk i.quint1 i.ragender
c.ragey2 i.baseisol i.baselone
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk

* Is there any evidence of significant interaction between loneliness
and isolation ?

mi estimate, eform: cloglog y1 i.t i.baselone##i.baseisol
i.micategrisk c.ragey2 i.ragender i.quint1
```

```
*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y1 i.t i.baseisol i.baselone##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baseisol i.baselone##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baseisol i.baselone##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.baselone#2.quint1 1.baselone#3.quint1 1.baselone#4.quint1
1.baselone#5.quint1
mi estimate, eform: cloglog y1 i.t i.baseisol
i.baselone##i.micategrisk i.quint1 i.ragender c.ragey2
mi test 1.baselone#1.micategrisk 1.baselone#2.micategrisk

*Social isolation:
mi estimate, eform: cloglog y1 i.t i.baselone i.baseisol##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baselone i.baseisol##i.ragender
c.ragey2  i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baselone i.baseisol##i.quint1
i.ragender c.ragey2 i.micategrisk
mi test 1.baseisol#2.quint1 1.baseisol#3.quint1 1.baseisol#4.quint1
1.baseisol#5.quint1
mi estimate, eform: cloglog y1 i.t i.baselone
i.baseisol##i.micategrisk i.quint1 i.ragender c.ragey2
mi test 1.baseisol#1.micategrisk 1.baseisol#2.micategrisk

*Stroke (loneliness only):

*Univariate analyses:
*Loneliness:
mi estimate, eform: cloglog y2 i.t i.baselone

* Multivariate analyses:
* Confounders:
mi estimate, eform: cloglog y2 i.t i.baselone c.ragey2 i.ragender
i.quint1

*With CVD risk score:
mi estimate, eform: cloglog y2 i.t i.baselone i.micategrisk c.ragey2
i.ragender i.quint1

*Check interactions with time:
mi estimate, eform: cloglog y2 i.t##i.baselone i.ragender c.ragey2
i.micategrisk i.quint1
mi test 2.t#1.baselone 3.t#1.baselone 4.t#1.baselone
mi estimate, eform: cloglog y2 i.t##c.ragey2 i.ragender i.baselone
i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi estimate, eform: cloglog y2 i.t##i.ragender c.ragey2 i.baselone
i.micategrisk i.quint1
mi test 2.t#1.ragender 3.t#1.ragender 4.t#1.ragender
mi estimate, eform: cloglog y2 i.t##i.quint1 i.ragender c.ragey2
i.baselone i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi estimate, eform: cloglog y2 i.t##i.micategrisk i.quint1 i.ragender
c.ragey2 i.baselone
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk
```

```
*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y2 i.t i.baselone##c.ragey2 i.ragender
i.quint1 i.micategrisk
mi estimate, eform: cloglog y2 i.t i.baselone##i.ragender c.ragey2
i.quint1 i.micategrisk
mi estimate, eform: cloglog y2 i.t i.baselone##i.quint1 i.ragender
c.ragey2  i.micategrisk
mi test 1.baselone#2.quint1 1.baselone#3.quint1 1.baselone#4.quint1
1.baselone#5.quint1
mi estimate, eform: cloglog y2 i.t i.baselone##i.micategrisk i.quint1
i.ragender c.ragey2
mi test 1.baselone#1.micategrisk 1.baselone#2.micategrisk
```

* Table A7.15 Summary of P-values associated with interaction terms between baseline loneliness and social isolation, and all other covariates in model D:

	P-value associated with t or Wald test		
Interaction between...	Overall CVD	CHD	Stroke
loneliness and social isolation	0.885	0.818	NC, too few cases
loneliness and age	0.040	0.207	<0.001
loneliness and gender	0.397	0.134	0.204
loneliness and wealth quintile	0.450	0.283	0.528
loneliness and Framingham risk	0.017	0.407	0.003
social isolation and age	0.765	0.996	NC, too few cases
social isolation and gender	0.780	0.997	NC, too few cases
social isolation and wealth quintile	0.952	0.973	NC, too few cases
social isolation and Framingham risk	NC, too few cases	NC, too few cases	NC, too few cases

```
mi estimate, eform: cloglog y i.t i.baselone##c.ragey2
micategrisk##i.baselone i.baseisol i.ragender i.quint1
mi test 1.baselone#1.micategrisk 1.baselone#2.micategrisk
```

* Table A7.16 Output relating to model D with loneliness and age, and loneliness and Framingham risk category interaction terms. Outcome: overall CVD.

```
Multiple-imputation estimates                   Imputations       =         25
Complementary log-log regression                Number of obs     =     17,819
                                                Average RVI       =     0.0669
                                                Largest FMI       =     0.2590
DF adjustment:   Large sample                   DF:     min       =     369.19
                                                        avg       =   1.52e+09
                                                        max       =   1.73e+10
Model F test:       Equal FMI                   F(  16,85458.9)   =      12.13
Within VCE type:          OIM                   Prob > F          =     0.0000

--------------------------------------------------------------------------------
             y |     exp(b)   Std. Err.      t    P>|t|     [95% Conf. Interval]
---------------+----------------------------------------------------------------
             t |
             2 |   1.835386   .2125711     5.24   0.000     1.462658    2.303096
             3 |   2.066585   .2418646     6.20   0.000      1.64298    2.599408
             4 |   2.321809   .2750305     7.11   0.000     1.840761    2.928572
               |
    1.baselone |   4.775714   3.995371     1.87   0.062     .9266461     24.6129
        ragey2 |   1.046825   .0058882     8.14   0.000     1.035347    1.058431
               |
      baselone |
     #c.ragey2 |
             1 |   .9892779   .0130845    -0.82   0.415     .9639616    1.015259
               |
 micategrisk10 |
             1 |   1.481826   .2240065     2.60   0.009     1.101471    1.993524
             2 |   1.645636   .2849592     2.88   0.004     1.171607    2.311455
               |
 micategrisk10#|
     baselone**|
           1 1 |   .5244194   .1818109    -1.86   0.063     .2656939    1.035085
           2 1 |   .4542608   .1689721    -2.12   0.034     .2190662    .9419657
               |
    1.baseisol |   .6762122   .1601766    -1.65   0.099     .4244172     1.07739
               |
      ragender |
        1.male |   .9550571   .0913016    -0.48   0.631     .7918477    1.151906
               |
        quint1 |
             2 |   .9114639   .1105711    -0.76   0.445     .7185858    1.156113
             3 |   .8984381   .1098318    -0.88   0.381     .7070166    1.141686
             4 |    .931483    .113393    -0.58   0.560     .7337606    1.182484
             5 |   .9165186    .114995    -0.69   0.487     .7167032    1.172042
               |
         _cons |   .0008052   .0003056   -18.77   0.000     .0003827    .0016941
--------------------------------------------------------------------------------
**P-value associated with Wald test: 0.102
```

```
mi estimate, eform: cloglog y2 i.t i.baselone##c.ragey2
micategrisk##i.baselone i.ragender i.quint1
mi test 1.baselone#1.micategrisk 1.baselone#2.micategrisk
```

* Table A7.17 Output relating to model D with loneliness and age, and loneliness and Framingham risk category interaction terms. Outcome: stroke.

```
Multiple-imputation estimates                    Imputations       =         25
Complementary log-log regression                 Number of obs     =     17,819
                                                 Average RVI       =     0.0437
                                                 Largest FMI       =     0.1911
DF adjustment:   Large sample                    DF:     min       =     673.65
                                                         avg       =   7.16e+09
                                                         max       =   9.00e+10
Model F test:       Equal FMI                    F(  15,178919.7)  =       4.83
Within VCE type:          OIM                    Prob > F          =     0.0000

--------------------------------------------------------------------------------
            y2 |     exp(b)   Std. Err.      t    P>|t|     [95% Conf. Interval]
---------------+----------------------------------------------------------------
             t |
             2 |   2.182339   .5909106     2.88   0.004     1.283639    3.710236
             3 |   2.150919   .6049985     2.72   0.006     1.239375    3.732891
             4 |   1.875019   .5679923     2.08   0.038     1.035511    3.395134
               |
    1.baselone |   18.85643   38.59905     1.43   0.151     .3412135     1042.06
        ragey2 |   1.071838   .0141955     5.24   0.000      1.04437    1.100028
               |
      baselone |
        #c.ragey2 |
             1 |   .9814837   .0318543    -0.58   0.565     .9209933    1.045947
               |
 micategrisk10 |
             1 |   1.108146   .4513043     0.25   0.801     .4980952    2.465369
             2 |   1.536317   .6703033     0.98   0.325     .6525292    3.617109
               |
micategrisk10  |
   #baselone** |
           1 1 |   .1581886   .1299163    -2.25   0.025       .03159    .7921386
           2 1 |   .1379551   .1118583    -2.44   0.015     .0281475    .6761373
               |
      ragender |
        1.male |   1.038131   .2394738     0.16   0.871     .6604968    1.631674
               |
        quint1 |
             2 |    1.00869   .2814554     0.03   0.975     .5837764    1.742887
             3 |   1.003045   .2807712     0.01   0.991     .5794991    1.736152
             4 |   .9665583   .2748211    -0.12   0.905     .5536129    1.687524
                        5  |   .5981349   .2009688    -1.53   0.126     .3096005
1.155571
               |
         _cons |   .0000283   .0000261   -11.36   0.000     4.65e-06    .0001725
--------------------------------------------------------------------------------
**P-value associated with Wald test: 0.033
```

*UCLA Loneliness tool - repeat all fo the above:
*Univariate analyses:
*Loneliness:
mi estimate, eform: cloglog y i.t i.baseucla

* Table A7.18 Association between loneliness at baseline using the UCLA three-item measure (dichotomised at 6+) and overall CVD, univariate analysis

```
------------------------------------------------------------------------------
 Outcome: CVD|     exp(b)   Std. Err.      t    P>|t|     [95% Conf. Interval]
        event|
-------------+----------------------------------------------------------------
           t |
           2 |   1.791829   .2074673     5.04   0.000     1.428038    2.248294
           3 |    1.95891   .2289713     5.75   0.000      1.55783    2.463253
           4 |   2.118561   .2501823     6.36   0.000     1.680823      2.6703
             |
  Lonely at  |
  baseline   |   1.207596    .116964     1.95   0.051     .9987944    1.460048
             |
       _cons |   .0223482   .0020699   -41.04   0.000     .0186382    .0267967
------------------------------------------------------------------------------
```

```
*Social isolation:
mi estimate, eform: cloglog y i.t i.baseisol

* Multivariate analyses:

* Confounders:
mi estimate, eform: cloglog y i.t i.baseucla i.baseisol c.ragey2
i.ragender i.quint1

*With CVD risk score:
mi estimate, eform: cloglog y i.t i.baseucla i.micategrisk i.baseisol
c.ragey2 i.ragender i.quint1

* Table A7.19 Association between loneliness at baseline using the
UCLA three-item measure (dichotomised at 6+) and overall CVD, model D
```

Outcome: CVD event	exp(b)	Std. Err.	t	P>|t|	[95% Conf.	Interval]
t						
2	1.833291	.2123217	5.23	0.000	1.460999	2.30045
3	2.065474	.2417197	6.20	0.000	1.642119	2.597973
4	2.316103	.2743488	7.09	0.000	1.836245	2.92136
Lonely at baseline	1.178573	.11734	1.65	0.099	.9696341	1.432536
Framimgham risk category						
1	1.348975	.1854553	2.18	0.030	1.030039	1.766666
2	1.478451	.2393043	2.42	0.016	1.076116	2.03121
Isolated at baseline	.6703703	.1580507	-1.70	0.091	.4217014	1.065674
Age	1.045111	.0054487	8.46	0.000	1.034484	1.055847
Gender						
1.male	.9560474	.0909245	-0.47	0.637	.7934385	1.151982
Wealth quintile						
2	.9060248	.1099747	-0.81	0.416	.7141995	1.149372
3	.9030269	.1105283	-0.83	0.405	.7104186	1.147855
4	.9276101	.1129645	-0.62	0.537	.7306432	1.177675
5	.9161676	.1151678	-0.70	0.486	.7160961	1.172138
_cons	.0009785	.0003458	-19.61	0.000	.0004895	.001956

```
*Check interactions with time:
mi estimate, eform: cloglog y i.t##i.baseucla i.ragender c.ragey2
i.baseisol i.micategrisk i.quint1
mi test 2.t#1.baseucla 3.t#1.baseucla 4.t#1.baseucla
mi estimate, eform: cloglog y i.t##i.baseisol i.baseucla i.ragender
c.ragey2 i.micategrisk i.quint1
mi test 2.t#1.baseucla 3.t#1.baseucla 4.t#1.baseucla
mi estimate, eform: cloglog y i.t##c.ragey2 i.ragender i.baseisol
i.baseucla i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi estimate, eform: cloglog y i.t##i.ragender c.ragey2 i.baseisol
i.baseucla i.micategrisk i.quint1
mi test 2.t#1.ragender 3.t#1.ragender 4.t#1.ragender
mi estimate, eform: cloglog y i.t##i.quint1 i.ragender c.ragey2
i.baseisol i.baseucla i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi estimate, eform: cloglog y i.t##i.micategrisk i.quint1 i.ragender
c.ragey2 i.baseisol i.baseucla
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk
```

```
* Is there any evidence of significant interaction between loneliness
and isolation ?

mi estimate, eform: cloglog y i.t i.baseisol##i.baseucla i.micategrisk
c.ragey2 i.ragender i.quint1

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y i.t i.isol i.baseucla##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.isol i.baseucla##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.isol i.baseucla##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.baseucla#2.quint1 1.baseucla#3.quint1 1.baseucla#4.quint1
1.baseucla#5.quint1
mi estimate, eform: cloglog y i.t i.isol i.micategrisk##i.baseucla
i.quint1 i.ragender c.ragey2
mi test 1.baseucla#1.micategrisk 1.baseucla#2.micategrisk

*Social isolation:
mi estimate, eform: cloglog y i.t i.baseucla i.baseisol##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.baseucla i.baseisol##i.ragender
c.ragey2  i.quint1 i.micategrisk
mi estimate, eform: cloglog y i.t i.baseucla i.baseisol##i.quint1
i.ragender c.ragey2 i.micategrisk
mi test 1.baseisol#2.quint1 1.baseisol#3.quint1 1.baseisol#4.quint1
1.baseisol#5.quint1
mi estimate, eform: cloglog y i.t i.baseucla i.baseisol##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.baseisol#1.micategrisk 1.baseisol#2.micategrisk

* And repeat for each outcome:

*Heart:

*Univariate analyses:
*Loneliness:
mi estimate, eform: cloglog y1 i.t i.baseucla
*Social isolation:
mi estimate, eform: cloglog y1 i.t i.baseisol

* Multivariate analyses:
* Confounders:
mi estimate, eform: cloglog y1 i.t i.baseucla i.baseisol c.ragey2
i.ragender i.quint1

*With CVD risk score:
mi estimate, eform: cloglog y1 i.t i.baseucla i.micategrisk i.baseisol
c.ragey2 i.ragender i.quint1

*Check interactions with time:
mi estimate, eform: cloglog y1 i.t##i.baseucla i.ragender c.ragey2
i.baseisol i.micategrisk i.quint1
mi test 2.t#1.baseucla 3.t#1.baseucla 4.t#1.baseucla
mi estimate, eform: cloglog y1 i.t##i.baseisol i.baseucla i.ragender
c.ragey2 i.micategrisk i.quint1
mi test 2.t#1.baseisol 3.t#1.baseisol 4.t#1.baseisol
mi estimate, eform: cloglog y1 i.t##c.ragey2 i.ragender i.baseisol
i.baseucla i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi estimate, eform: cloglog y1 i.t##i.ragender c.ragey2 i.baseisol
```

```
i.baseucla i.micategrisk i.quint1
mi test 2.t#1.ragender 3.t#1.ragender 4.t#1.ragender
mi estimate, eform: cloglog y1 i.t##i.quint1 i.ragender c.ragey2
i.baseisol i.baseucla i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi estimate, eform: cloglog y1 i.t##i.micategrisk i.quint1 i.ragender
c.ragey2 i.baseisol i.baseucla
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk

* Is there any evidence of significant interaction between loneliness
and isolation ?

mi estimate, eform: cloglog y1 i.t i.baseisol##i.baseucla
i.micategrisk c.ragey2 i.ragender i.quint1

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y1 i.t i.baseisol i.baseucla##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baseisol i.baseucla##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baseisol i.baseucla##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.baseucla#2.quint1 1.baseucla#3.quint1 1.baseucla#4.quint1
1.baseucla#5.quint1
mi estimate, eform: cloglog y1 i.t i.baseisol
i.baselone##i.micategrisk i.quint1 i.ragender c.ragey2
mi test 1.baseucla#1.micategrisk 1.baseucla#2.micategrisk

*Social isolation:
mi estimate, eform: cloglog y1 i.t i.baseucla i.baseisol##c.ragey2
i.ragender i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baseucla i.baseisol##i.ragender
c.ragey2  i.quint1 i.micategrisk
mi estimate, eform: cloglog y1 i.t i.baseucla i.baseisol##i.quint1
i.ragender c.ragey2 i.micategrisk
mi test 1.baseisol#2.quint1 1.baseisol#3.quint1 1.baseisol#4.quint1
1.baseisol#5.quint1
mi estimate, eform: cloglog y1 i.t i.baseucla
i.baseisol##i.micategrisk i.quint1 i.ragender c.ragey2
mi test 1.baseisol#1.micategrisk 1.baseisol#2.micategrisk

*Stroke (loneliness only):

*Univariate analyses:
*Loneliness:
mi estimate, eform: cloglog y2 i.t i.baseucla

* Multivariate analyses:
* Confounders:
mi estimate, eform: cloglog y2 i.t i.baseucla c.ragey2 i.ragender
i.quint1

*With CVD risk score:
mi estimate, eform: cloglog y2 i.t i.baseucla i.micategrisk c.ragey2
i.ragender i.quint1

*Check interactions with time:
mi estimate, eform: cloglog y2 i.t##i.baseucla i.ragender c.ragey2
i.micategrisk i.quint1
```

```
mi test 2.t#1.baseucla 3.t#1.baseucla 4.t#1.baseucla
mi estimate, eform: cloglog y2 i.t##c.ragey2 i.ragender i.baseucla
i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi estimate, eform: cloglog y2 i.t##i.ragender c.ragey2 i.baseucla
i.micategrisk i.quint1
mi test 2.t#1.ragender 3.t#1.ragender 4.t#1.ragender
mi estimate, eform: cloglog y2 i.t##i.quint1 i.ragender c.ragey2
i.baseucla i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi estimate, eform: cloglog y2 i.t##i.micategrisk i.quint1 i.ragender
c.ragey2 i.baseucla
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y2 i.t i.baseucla##c.ragey2 i.ragender
i.quint1 i.micategrisk
mi estimate, eform: cloglog y2 i.t i.baseucla##i.ragender c.ragey2
i.quint1 i.micategrisk
mi estimate, eform: cloglog y2 i.t i.baseucla##i.quint1 i.ragender
c.ragey2  i.micategrisk
mi test 1.baseucla#2.quint1 1.baseucla#3.quint1 1.baseucla#4.quint1
1.baseucla#5.quint1
mi estimate, eform: cloglog y2 i.t i.baseucla##i.micategrisk i.quint1
i.ragender c.ragey2
mi test 1.baseucla#1.micategrisk 1.baseucla#2.micategrisk

* Framingham score items entered separately:

mi estimate, eform: cloglog y i.t i.quint1 c.ragey2 i.ragender
i.baselone i.baseisol i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2
c.hdlmg2 c.sysval2
```

*Table A7.20 Model D with all Framingham risk score items entered separately

Outcome: CVD event	exp(b)	Std. Err.	t	P>|t|	[95% Conf.	Interval]
t						
2	1.838166	.2128972	5.26	0.000	1.464867	2.306594
3	2.072427	.2425568	6.23	0.000	1.647611	2.606777
4	2.329078	.2759297	7.14	0.000	1.846464	2.937834
Wealth quintile						
2	.9141477	.1114979	-0.74	0.462	.7197729	1.161014
3	.9155245	.1128101	-0.72	0.474	.7190909	1.165618
4	.9423154	.1163265	-0.48	0.630	.7398037	1.200262
5	.9638997	.1234835	-0.29	0.774	.7498655	1.239026
Age	1.04834	.0047403	10.44	0.000	1.03909	1.057673
Gender						
1.male	.9956809	.0862809	-0.05	0.960	.8401484	1.180006
Loneliness	1.208998	.1385961	1.66	0.098	.9657082	1.513579
Isolation	.6803045	.1615599	-1.62	0.106	.4264911	1.085167
Diabetes	.9974025	.1446134	-0.02	0.986	.7506774	1.325219
Hypertension medication	1.289082	.1312255	2.49	0.013	1.055918	1.573732
Smoking	1.051086	.1251997	0.42	0.676	.8322381	1.327483
Total cholesterol	1.000688	.0011151	0.62	0.537	.9984988	1.002883
Hdl cholesterol	.991991	.0035653	-2.24	0.026	.985009	.9990224
Systolic blood pressure	1.005298	.0022422	2.37	0.018	1.00091	1.009704
_cons	.0006511	.0003194	-14.95	0.000	.0002488	.0017038

```
mi estimate, eform: cloglog y1 i.t i.quint1 c.ragey2 i.ragender
i.baselone i.baseisol i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2
c.hdlmg2 c.sysval2
mi estimate, eform: cloglog y2 i.t i.quint1 c.ragey2 i.ragender
i.baselone i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2 c.hdlmg2
c.sysval2

* Repeat with full cases analyses:

*CVD:
mi xeq 0: cloglog y i.t i.baselone, eform
mi xeq 0: cloglog y i.t i.baseisol, eform
mi xeq 0: cloglog y i.t i.baselone i.baseisol c.ragey2 i.ragender
i.quint1, eform
mi xeq 0: cloglog y i.t i.baselone i.baseisol c.ragey2 i.ragender
i.quint1 i.micategrisk, eform

*Interaction with time?

mi xeq 0: cloglog y i.t##i.baselone i.ragender c.ragey2 i.baseisol
i.micategrisk i.quint1, eform
mi test 2.t#1.baselone 3.t#1.baselone 4.t#1.baselone
mi xeq 0: cloglog y i.t##i.baseisol i.baselone i.ragender c.ragey2
i.micategrisk i.quint1
mi test 2.t#1.baseisol 3.t#1.baseisol 4.t#1.baseisol
mi xeq 0: cloglog y i.t##c.ragey2 i.ragender i.baseisol i.baselone
i.micategrisk i.quint1
mi test 2.t#c.ragey2 3.t#c.ragey2 4.t#c.ragey2
mi xeq 0: cloglog y i.t##i.ragender c.ragey2 i.baseisol i.baselone
i.micategrisk i.quint1
mi xeq 0: cloglog y i.t##i.quint1 i.ragender c.ragey2 i.baseisol
i.baselone i.micategrisk
mi test 2.t#2.quint1 2.t#3.quint1 2.t#4.quint1 2.t#5.quint1
```

```
3.t#2.quint1 3.t#3.quint1 3.t#4.quint1 3.t#5.quint1 4.t#2.quint1
4.t#3.quint1 4.t#4.quint1 4.t#5.quint1
mi xeq 0:cloglog y i.t##i.micategrisk i.quint1 i.ragender c.ragey2
i.baseisol i.baselone
mi test 2.t#1.micategrisk 2.t#2.micategrisk 3.t#1.micategrisk
3.t#2.micategrisk 4.t#1.micategrisk 4.t#2.micategrisk

*Heart:
mi xeq 0: cloglog y1 i.t i.baselone, eform
mi xeq 0: cloglog y1 i.t i.baseisol, eform
mi xeq 0: cloglog y1 i.t i.baselone i.baseisol c.ragey2 i.ragender
i.quint1, eform
mi xeq 0: cloglog y1 i.t i.baselone i.baseisol c.ragey2 i.ragender
i.quint1 i.micategrisk, eform

*Stroke:
mi xeq 0: cloglog y2 i.t i.baselone, eform
mi xeq 0: cloglog y2 i.t i.baselone c.ragey2 i.ragender i.quint1 ,
eform
mi xeq 0: cloglog y2 i.t i.baselone c.ragey2 i.ragender i.quint1
i.micategrisk, eform

*Second aspect of my analyses: cumulative/repeated exposure:

mi estimate, eform: cloglog y i.t ib1.sumlone
mi estimate, eform: cloglog y i.t ib1.sumis
mi estimate, eform: cloglog y i.t i.quint1 ib1.sumlone ib1.sumis
i.ragender c.ragey2
mi estimate, eform: cloglog y i.t i.quint1 ib1.sumlone ib1.sumis
i.ragender c.ragey2 i.micategrisk10

*What about at least once...?

mi passive: generate atleastoncelonel=sumlone
mi passive: replace atleastoncelonel=1 if sumlone==1 | sumlone==2 |
sumlone==3 | sumlone==4
mi passive: generate atleastonceisol=sumis
mi passive: replace atleastonceisol=1 if sumis==1 | sumis==2 |
sumis==3 | sumis==4


mi estimate, eform: cloglog y i.t i.atleastoncelonel
mi estimate, eform: cloglog y i.t i.atleastonceisol
mi estimate, eform: cloglog y i.t i.quint1 i.atleastoncelonel
i.atleastonceisol i.ragender c.ragey2
mi estimate, eform: cloglog y i.t i.quint1 i.atleastoncelonel
i.atleastonceisol i.ragender c.ragey2 i.micategrisk10

* Is there any evidence of significant interaction between loneliness
and isolation ?

mi estimate, eform: cloglog y i.t i.sumlone##i.sumis i.micategrisk
c.ragey2 i.ragender i.quint1

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y i.t i.sumis ib1.sumlone##c.ragey2
i.ragender i.quint1 i.micategrisk
mi test 0.sumlone#c.ragey2 2.sumlone#c.ragey2 3.sumlone#c.ragey2
4.sumlone#c.ragey2
mi estimate, eform: cloglog y i.t i.sumis i.sumlone##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi test 1.sumlone#1.ragender 2.sumlone#1.ragender 3.sumlone#1.ragender
```

```
4.sumlone#1.ragender
mi estimate, eform: cloglog y i.t i.sumis i.sumlone##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.sumlone#2.quint1 1.sumlone#3.quint1 1.sumlone#4.quint1
1.sumlone#5.quint1 2.sumlone#2.quint1 2.sumlone#3.quint1
2.sumlone#4.quint1 2.sumlone#5.quint1 3.sumlone#2.quint1
3.sumlone#3.quint1 3.sumlone#4.quint1 3.sumlone#5.quint1
4.sumlone#2.quint1 4.sumlone#3.quint1 4.sumlone#4.quint1
4.sumlone#5.quint1
mi estimate, eform: cloglog y i.t i.sumis i.sumlone##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.sumlone#1.micategrisk 2.sumlone#1.micategrisk
3.sumlone#1.micategrisk 4.sumlone#1.micategrisk
1.sumlone#2.micategrisk 2.sumlone#2.micategrisk
3.sumlone#2.micategrisk 4.sumlone#2.micategrisk

*Social isolation:
mi estimate, eform: cloglog y i.t i.sumlone i.sumis##c.ragey2
i.ragender i.quint1 i.micategrisk
mi test 1.sumis#c.ragey 2.sumis#c.ragey 3.sumis#c.ragey
4.sumis#c.ragey
mi estimate, eform: cloglog y i.t i.sumlone i.sumis##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi test 1.sumis#1.ragender 2.sumis#1.ragender 3.sumis#1.ragender
4.sumis#1.ragender
mi estimate, eform: cloglog y i.t i.sumlone i.sumis##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.sumis#2.quint1 1.sumis#3.quint1 1.sumis#4.quint1
1.sumis#5.quint1 2.sumis#2.quint1 2.sumis#3.quint1 2.sumis#4.quint1
2.sumis#5.quint1 3.sumis#2.quint1 3.sumis#3.quint1 3.sumis#4.quint1
3.sumis#5.quint1 4.sumis#2.quint1 4.sumis#3.quint1 4.sumis#4.quint1
4.sumis#5.quint1
mi estimate, eform: cloglog y i.t i.sumlone i.sumis##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.sumis#1.micategrisk 2.sumis#1.micategrisk
3.sumis#1.micategrisk 4.sumis#1.micategrisk 1.sumis#2.micategrisk
2.sumis#2.micategrisk 3.sumis#2.micategrisk 4.sumis#2.micategrisk

*Heart disease only:

mi estimate, eform: cloglog y1 i.t ib1.sumlone
mi estimate, eform: cloglog y1 i.t ib1.sumis
mi estimate, eform: cloglog y1 i.t i.quint1 ib1.sumlone ib1.sumis
i.ragender c.ragey2
mi estimate, eform: cloglog y1 i.t i.quint1 ib1.sumlone ib1.sumis
i.ragender c.ragey2 i.micategrisk10

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y1 i.t i.sumis i.sumlone##c.ragey2
i.ragender i.quint1 i.micategrisk
mi test 1.sumlone#c.ragey 2.sumlone#c.ragey 3.sumlone#c.ragey
4.sumlone#c.ragey
mi estimate, eform: cloglog y1 i.t i.sumis i.sumlone##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi test 1.sumlone#1.ragender 2.sumlone#1.ragender 3.sumlone#1.ragender
4.sumlone#1.ragender
mi estimate, eform: cloglog y1 i.t i.sumis i.sumlone##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.sumlone#2.quint1 1.sumlone#3.quint1 1.sumlone#4.quint1
1.sumlone#5.quint1 2.sumlone#2.quint1 2.sumlone#3.quint1
2.sumlone#4.quint1 2.sumlone#5.quint1 3.sumlone#2.quint1
3.sumlone#3.quint1 3.sumlone#4.quint1 3.sumlone#5.quint1
```

```
4.sumlone#2.quint1 4.sumlone#3.quint1 4.sumlone#4.quint1
4.sumlone#5.quint1
mi estimate, eform: cloglog y1 i.t i.sumis i.sumlone##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.sumlone#1.micategrisk 2.sumlone#1.micategrisk
3.sumlone#1.micategrisk 4.sumlone#1.micategrisk
1.sumlone#2.micategrisk 2.sumlone#2.micategrisk
3.sumlone#2.micategrisk 4.sumlone#2.micategrisk

*Social isolation:
mi estimate, eform: cloglog y1 i.t i.sumlone i.sumis##c.ragey2
i.ragender i.quint1 i.micategrisk
mi test 1.sumis#c.ragey 2.sumis#c.ragey 3.sumis#c.ragey
4.sumis#c.ragey
mi estimate, eform: cloglog y1 i.t i.sumlone i.sumis##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi test 1.sumis#1.ragender 2.sumis#1.ragender 3.sumis#1.ragender
4.sumis#1.ragender
mi estimate, eform: cloglog y1 i.t i.sumlone i.sumis##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.sumis#2.quint1 1.sumis#3.quint1 1.sumis#4.quint1
1.sumis#5.quint1 2.sumis#2.quint1 2.sumis#3.quint1 2.sumis#4.quint1
2.sumis#5.quint1 3.sumis#2.quint1 3.sumis#3.quint1 3.sumis#4.quint1
3.sumis#5.quint1 4.sumis#2.quint1 4.sumis#3.quint1 4.sumis#4.quint1
4.sumis#5.quint1
mi estimate, eform: cloglog y1 i.t i.sumlone i.sumis##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.sumis#1.micategrisk 2.sumis#1.micategrisk
3.sumis#1.micategrisk 4.sumis#1.micategrisk 1.sumis#2.micategrisk
2.sumis#2.micategrisk 3.sumis#2.micategrisk 4.sumis#2.micategrisk

*Stroke only:

mi estimate, eform: cloglog y2 i.t ib1.sumlone
mi estimate, eform: cloglog y2 i.t ib1.sumis
mi estimate, eform: cloglog y2 i.t i.quint1 ib1.sumlone i.ragender
c.ragey2
mi estimate, eform: cloglog y2 i.t i.quint1 ib1.sumlone i.ragender
c.ragey2 i.micategrisk10

*Checking for evidence of interaction with age, gender, wealth or
Framingham risk score:

*Loneliness:
mi estimate, eform: cloglog y2 i.t i.sumis i.sumlone##c.ragey2
i.ragender i.quint1 i.micategrisk
mi test 1.sumlone#c.ragey 2.sumlone#c.ragey 3.sumlone#c.ragey
4.sumlone#c.ragey
mi estimate, eform: cloglog y2 i.t i.sumis i.sumlone##i.ragender
c.ragey2 i.quint1 i.micategrisk
mi test 1.sumlone#1.ragender 2.sumlone#1.ragender 3.sumlone#1.ragender
4.sumlone#1.ragender
mi estimate, eform: cloglog y2 i.t i.sumis i.sumlone##i.quint1
i.ragender c.ragey2  i.micategrisk
mi test 1.sumlone#2.quint1 1.sumlone#3.quint1 1.sumlone#4.quint1
1.sumlone#5.quint1 2.sumlone#2.quint1 2.sumlone#3.quint1
2.sumlone#4.quint1 2.sumlone#5.quint1 3.sumlone#2.quint1
3.sumlone#3.quint1 3.sumlone#4.quint1 3.sumlone#5.quint1
4.sumlone#2.quint1 4.sumlone#3.quint1 4.sumlone#4.quint1
4.sumlone#5.quint1
mi estimate, eform: cloglog y2 i.t i.sumis i.sumlone##i.micategrisk
i.quint1 i.ragender c.ragey2
mi test 1.sumlone#1.micategrisk 2.sumlone#1.micategrisk
3.sumlone#1.micategrisk 4.sumlone#1.micategrisk
1.sumlone#2.micategrisk 2.sumlone#2.micategrisk
```

```
3.sumlone#2.micategrisk 4.sumlone#2.micategrisk
```

* Table A7.22 Summary of P-values associated with interaction terms between loneliness and social isolation, and all other covariates in model D:

Interaction between...	P-value associated with t or Wald test: Overall CVD	CHD	Stroke
loneliness and social isolation	NC**	NC	NC
loneliness and age	0.005	0.020	NC
loneliness and gender	0.753	0.738	NC
loneliness and wealth quintile	NC	NC	NC
loneliness and Framingham risk	NC	NC	NC
social isolation and age	0.460	0.586	NC
social isolation and gender	NC	NC	NC
social isolation and wealth quintile	NC	NC	NC
social isolation and Framingham risk	NC	NC	NC

** NC: Not calculated, due to too few cases.

*With the Framingham items entered separately:

```
mi estimate, eform: cloglog y i.t i.quint1 ib1.sumlone ib1.sumis
i.ragender c.ragey2 i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2 c.hdlmg2
c.sysval2
```

*Table A7.23 Model D with the Framingham score items entered separately and all first CVD events as the outcome

```
------------------------------------------------------------------------------
           y |     exp(b)   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
           t |
           2 |   1.830278   .2142511     5.16   0.000     1.455043     2.30228
           3 |   2.081465   .2472951     6.17   0.000     1.649071    2.627234
           4 |   2.310127   .2813369     6.88   0.000     1.819587     2.93291
             |
      quint1 |
           2 |   .9133457   .1114842    -0.74   0.458     .7190116    1.160204
           3 |   .9191903   .1133802    -0.68   0.495     .7217884     1.17058
           4 |   .9402446   .1162363    -0.50   0.618     .7379234    1.198037
           5 |   .9688694   .1247358    -0.25   0.806     .7527936    1.246966
             |
     sumlone |
           0 |   .7447302   .0861369    -2.55   0.011     .5936612    .9342419
           2 |   .9064729   .1835744    -0.48   0.628     .6094201     1.34832
           3 |   .9263838   .2629438    -0.27   0.788     .5310532    1.616009
           4 |   1.317036   .4973102     0.73   0.466     .6283259    2.760645
             |
       sumis |
           0 |   1.670102   .4533591     1.89   0.061     .9764532    2.856502
           2 |   1.258275   .5292977     0.55   0.586     .5486807    2.885571
           3 |   .7620291   .5386347    -0.38   0.701      .189355    3.066665
           4 |   .8040427   .6968608    -0.25   0.801     .1465269    4.412055
             |
    ragender |
      1.male |   1.014945   .0881823     0.17   0.864     .8560201    1.203375
      ragey2 |   1.048906   .0047837    10.47   0.000     1.039572    1.058324
     1.diab2 |   .9962137    .144557    -0.03   0.979     .7496114    1.323942
 1.hemdabis2 |   1.295014   .1319904     2.54   0.011     1.060518    1.581359
 1.smokebis2 |   1.055106   .1260651     0.45   0.653     .8348211    1.333517
     cholmg2 |   1.000717   .0011132     0.64   0.520     .9985311    1.002907
      hdlmg2 |   .9920367   .0035458    -2.24   0.026     .9850939    .9990284
     sysval2 |   1.005481   .0022526     2.44   0.015     1.001073    1.009908
       _cons |   .0004765   .0002768   -13.17   0.000     .0001524    .0014898
------------------------------------------------------------------------------
```

```
mi estimate, eform: cloglog y i.t i.quint1 i.sumlone##c.ragey2
ib1.sumis i.ragender i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2
c.hdlmg2 c.sysval2
mi test 1.sumlone#c.ragey 2.sumlone#c.ragey 3.sumlone#c.ragey
4.sumlone#c.ragey
```

*Heart outcomes only:

mi estimate, eform: cloglog y1 i.t i.quint1 i.sumlone ib1.sumis i.ragender c.ragey2 i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2 c.hdlmg2 c.sysval2

*Table A7.24 Model D with the Framingham score items entered separately and all first heart disease events as the outcome

```
------------------------------------------------------------------------------
          y1 |     exp(b)   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
           t |
          2  |    1.73144     .22697     4.19   0.000     1.339139    2.238667
          3  |   2.020201    .266803     5.32   0.000     1.559475    2.617042
          4  |   2.273799   .3064422     6.10   0.000     1.745962    2.961211
             |
      quint1 |
          2  |    .878916   .1203702    -0.94   0.346     .6720046    1.149536
          3  |    .885207   .1224642    -0.88   0.378     .6749683    1.160931
          4  |     .92078   .1272154    -0.60   0.550     .7023477    1.207145
          5  |   1.007141   .1428068     0.05   0.960     .7627668    1.329808
             |
     sumlone |
          1  |   1.286211   .1691839     1.91   0.056     .9938868    1.664515
          2  |   1.256053   .2536023     1.13   0.259     .8454182    1.866139
          3  |   1.433627   .4015533     1.29   0.198     .8279285    2.482443
          4  |   1.887917   .7442747     1.61   0.107     .8717921    4.088396
             |
       sumis |
          0  |   1.459156   .3891073     1.42   0.158     .8630504     2.46699
          2  |   1.156031    .499013     0.34   0.737       .49456    2.702216
          3  |   .8621451   .5935491    -0.22   0.830     .2226115    3.338975
          4  |   .8895586    .758315    -0.14   0.891     .1669475      4.7399
             |
    ragender |
      1.male |   .9862655   .0960522    -0.14   0.887     .8148742    1.193705
      ragey2 |   1.043766   .0053204     8.40   0.000      1.03339    1.054246
     1.diab2 |   1.073694   .1702658     0.45   0.654     .7868582    1.465092
 1.hemdabis2 |    1.36612   .1535485     2.78   0.006     1.096014    1.702793
 1.smokebis2 |   .9384778   .1288185    -0.46   0.644     .7171091    1.228182
     cholmg2 |   1.001148   .0012172     0.94   0.346     .9987598    1.003542
      hdlmg2 |   .9915658   .0039975    -2.10   0.036     .9837389     .999455
     sysval2 |   1.003693   .0024938     1.48   0.138     .9988153    1.008594
       _cons |   .0005621   .0003591   -11.71   0.000     .0001604    .0019697
------------------------------------------------------------------------------
```

mi estimate, eform: cloglog y1 i.t i.quint1 ib1.sumlone##c.ragey2 ib1.sumis i.ragender i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2 c.hdlmg2 c.sysval2
mi test 0.sumlone#c.ragey 2.sumlone#c.ragey 3.sumlone#c.ragey 4.sumlone#c.ragey

mi estimate, eform: cloglog y2 i.t i.quint1 i.sumlone i.ragender c.ragey2 i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2 c.hdlmg2 c.sysval2
mi estimate, eform: cloglog y2 i.t i.quint1 ib1.sumlone##c.ragey2 i.ragender i.diab2 i.hemdabis2 i.smokebis2 c.cholmg2 c.hdlmg2 c.sysval2
mi test 0.sumlone#c.ragey 2.sumlone#c.ragey 3.sumlone#c.ragey 4.sumlone#c.ragey

*With the UCLA score:

mi estimate, eform: cloglog y i.t ib1.sumdichotlone
mi estimate, eform: cloglog y i.t i.quint1 ib1.sumdichotlone i.sumis i.ragender c.ragey2
mi estimate, eform: cloglog y i.t i.quint1 ib1.sumdichotlone i.sumis i.ragender c.ragey2 i.micategrisk10

*Table A7.25 Model D with the three-item UCLA score dichotomised and all first CVD events as the outcome

y	exp(b)	Std. Err.	t	P>|t|	[95% Conf.	Interval]
t						
2	1.810502	.2132798	5.04	0.000	1.43723	2.28072
3	2.028144	.2437207	5.88	0.000	1.602545	2.566771
4	2.254235	.2781815	6.59	0.000	1.769936	2.871051
quint1						
2	.8997081	.109274	-0.87	0.384	.7091182	1.141523
3	.897742	.1099368	-0.88	0.378	.7061755	1.141275
4	.9190961	.1121802	-0.69	0.489	.723547	1.167495
5	.9107501	.1149281	-0.74	0.459	.7111859	1.166314
sumdichotlone1						
0	.8715603	.0990326	-1.21	0.226	.6975018	1.089054
2	1.039623	.1865906	0.22	0.829	.7310626	1.478417
3	1.2208	.2592478	0.94	0.348	.8050525	1.85125
4	1.249882	.3722542	0.75	0.454	.6971495	2.240848
sumis						
1	.5979106	.1618432	-1.90	0.059	.3501349	1.021027
2	.7497363	.2354115	-0.92	0.359	.4045258	1.389539
3	.4585464	.3044919	-1.17	0.241	.1240166	1.695457
4	.4899899	.3925241	-0.89	0.373	.1018041	2.358353
ragender						
1.male	.968613	.0927118	-0.33	0.739	.802899	1.168529
ragey2	1.046038	.0054774	8.60	0.000	1.035355	1.056831
micategrisk10						
1	1.349534	.1849462	2.19	0.029	1.031365	1.765855
2	1.479943	.2393264	2.42	0.016	1.077521	2.032658
_cons	.001065	.0003877	-18.80	0.000	.0005217	.0021739

```
mi estimate, eform: cloglog y i.t i.quint1 i.sumdichotlone##c.ragey2
i.sumis i.ragender i.micategrisk10
mi test 1.sumdichotlone#c.ragey 2.sumdichotlone#c.ragey
3.sumdichotlone#c.ragey 4.sumdichotlone#c.ragey

*Lagged values of sumis and sumlone:

mi tsset idauniq t
mi xeq: sort idauniq t; by idauniq: gen lagsumlone = l.sumlone
mi xeq: sort idauniq t; by idauniq: gen lagsumis = l.sumis

mi estimate, eform: cloglog y i.t ib1.lagsumlone
mi estimate, eform: cloglog y i.t ib1.lagsumis
mi estimate, eform: cloglog y i.t i.quint1 ib1.lagsumlone ib1.lagsumis
i.ragender c.ragey2
mi estimate, eform: cloglog y i.t i.quint1 ib1.lagsumlone ib1.lagsumis
i.ragender c.ragey2 i.micategrisk10
mi estimate, eform: cloglog y i.t i.quint1 ib1.lagsumlone##c.ragey2
ib1.lagsumis i.ragender i.micategrisk10
mi test 0.lagsumlone#c.ragey 2.lagsumlone#c.ragey 3.lagsumlone#c.ragey
```

*Table 7A.26 Association between cumulative loneliness or social isolation and CVD incidence, omitting the wave immediately prior to the event

Explanatory variable	Hazard ratio	95% CI	P-value
Model A: loneliness only			
Never lonely	0.80	0.61 to 1.03	0.082
Once lonely	1.00 (reference)		
Twice lonely	1.01	0.62 to 1.66	0.958
Three times lonely	1.41	0.69 to 2.86	0.344
Model B: social isolation only			
Never isolated	1.08	0.62 to 1.88	0.789
Once isolated	1.00 (reference)		
Twice isolated	1.61	0.66 to 3.94	0.296
Three times isolated	0.84	0.17 to 4.22	0.832
Model C: Relationships and potential confounders			
Never lonely	0.86	0.66 to 1.13	0.277
Once lonely	1.00 (reference)		
Twice lonely	0.96	0.58 to 1.56	0.855
Three times lonely	1.25	0.61 to 2.55	0.538
Never isolated	1.54	0.88 to 2.71	0.131
Once isolated	1.00 (reference)		
Twice isolated	1.53	0.62 to 3.75	0.352
Three times isolated	0.74	0.15 to 3.71	0.711
Model D: Relationships, CVD risk and potential confounders			
Never lonely	0.86	0.66 to 1.13	0.280
Once lonely	1.00 (reference)		
Twice lonely	0.95	0.58 to 1.55	0.824
Three times lonely	1.23	0.60 to 2.51	0.565
Never isolated	1.54	0.88 to 2.69	0.132
Once isolated	1.00 (reference)		
Twice isolated	1.53	0.62 to 3.76	0.354
Three times isolated	0.73	0.14 to 3.69	0.704

```
* Comparing at least once versus never lonely or isolated:

mi passive: generate dichotlagsumlon=lagsumlone
mi passive: replace dichotlagsumlon=1 if lagsumlone==2
mi passive: replace dichotlagsumlon=1 if lagsumlone==3

mi estimate, eform: cloglog y i.t i.quint1 i.dichotlagsumlon
ib1.lagsumis i.ragender c.ragey2 i.micategrisk10

* Repeat with full cases analyses:

*CVD:
mi xeq 0: cloglog y i.t ib1.sumlone, eform
mi xeq 0: cloglog y i.t ib1.sumis, eform
mi xeq 0: cloglog y i.t ib1.sumlone ib1.sumis c.ragey2 i.ragender
i.quint1, eform
mi xeq 0: cloglog y i.t ib1.sumlone ib1.sumis c.ragey2 i.ragender
i.quint1 i.micategrisk, eform

*Heart:
mi xeq 0: cloglog y1 i.t ib1.sumlone, eform
mi xeq 0: cloglog y1 i.t ib1.sumis, eform
mi xeq 0: cloglog y1 i.t ib1.sumlone ib1.sumis c.ragey2 i.ragender
i.quint1, eform
mi xeq 0: cloglog y1 i.t ib1.sumlone ib1.sumis c.ragey2 i.ragender
i.quint1 i.micategrisk, eform
```

```
*Stroke:
mi xeq 0: cloglog y2 i.t ib1.sumlone, eform
mi xeq 0: cloglog y2 i.t ib1.sumlone c.ragey2 i.ragender i.quint1 ,
eform
mi xeq 0: cloglog y2 i.t ib1.sumlone c.ragey2 i.ragender i.quint1
i.micategrisk, eform

*What about at least once lonely/isolated?

mi xeq 0: cloglog y i.t atleastoncelonel atleastonceisol c.ragey2
i.ragender i.quint1 i.micategrisk, eform
mi xeq 0: cloglog y1 i.t atleastoncelonel atleastonceisol c.ragey2
i.ragender i.quint1 i.micategrisk, eform
mi xeq 0: cloglog y2 i.t atleastoncelonel atleastonceisol c.ragey2
i.ragender i.quint1 i.micategrisk, eform

*Posthoc examination of the prevalence of loneliness and social
isolation according to ethnicity:

tab rflone1 raracem, chi col

*Table A7.27 Prevalence of loneliness according to ethnicity in the
ELSA subsample used for my survival analyses:

+-------------------+
| Key               |
|-------------------|
|     frequency     |
| column percentage |
+-------------------+

                   |   raracem: r race -
  r2flone:w2 CESD: |        masked
       Felt lonely |   1.white  4.non-whi |     Total
-------------------+----------------------+----------
              0.no |     4,681         43 |     4,724 
                   |     89.03      72.88 |     88.85 
-------------------+----------------------+----------
             1.yes |       577         16 |       593 
                   |     10.97      27.12 |     11.15 
-------------------+----------------------+----------
             Total |     5,258         59 |     5,317 
                   |    100.00     100.00 |    100.00 

          Pearson chi2(1) =  15.3478   Pr = 0.000



. tab isol1 raracem, chi col
```

*Table A7.28 Prevalence of loneliness according to ethnicity in the ELSA subsample used for my survival analyses:

```
+-------------------+
| Key               |
|-------------------|
|     frequency     |
| column percentage |
+-------------------+
```

isol1	raracem: r race - masked 1.white	4.non-whi	Total
0	3,644	35	3,679
	96.05	97.22	96.06
1	150	1	151
	3.95	2.78	3.94
Total	3,794	36	3,830
	100.00	100.00	100.00

Pearson chi2(1) = 0.1302 Pr = 0.718

Appendix 7.2 Results of analyses using listwise deletion

A) Association between loneliness and social isolation at baseline (ELSA wave 2), and CVD incidence between waves 2 and 6 – listwise deletion

	Total cardiovascular disease			Heart disease			Stroke		
Explanatory variable	**Hazard Ratio**	**95% Confidence**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Model A1 : Loneliness only									
Loneliness	1.39	1.12-1.73	0.003	1.43	1.12-1.82	0.004	1.45	0.87-2.43	0.158
Model B1 : Social isolation only									
Social isolation	0.88	0.53-1.45	0.610	1.02	0.61-1.71	0.933	NC*	NC	NC
Model C1 : Loneliness, social isolation, age, gender and wealth									
Loneliness	1.22	0.93-1.59	0.164	1.24	0.92-1.67	0.159	1.11	0.66-1.88	0.690
Social isolation	0.59	0.35-0.98	0.040	0.71	0.42-1.21	0.209	NC	NC	NC
Age (one year increase)	1.06	1.05-1.07	<0.001	1.05	1.04-1.06	<0.001	1.07	1.05-1.09	<0.001
Gender (male)	1.20	1.00-1.44	0.047	1.14	0.94-1.40	0.186	1.13	0.78-1.63	0.525
Wealth									
First (lowest)	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Second quintile	0.81	0.60-1.08	0.153	0.81	0.58-1.12	0.209	0.99	0.57-1.71	0.957
Third quintile	0.88	0.66-1.17	0.394	0.88	0.64-1.22	0.446	1.01	0.58-1.75	0.979
Fourth quintile	0.90	0.68-1.18	0.446	0.93	0.68-1.27	0.643	0.95	0.55-1.66	0.861
Fifth quintile	0.81	0.61-1.08	0.150	0.88	0.64-1.21	0.437	0.59	0.31-1.14	0.113
Model D1: Loneliness, social isolation, age, gender, wealth and CVD risk score									
Loneliness	1.35	0.99-1.85	0.058	1.31	0.92-1.85	0.130	1.48	0.82-2.68	0.189
Social isolation	0.81	0.46-1.43	0.468	1.04	0.59-1.85	0.885	NC	NC	NC
One year increase in age	1.05	1.04-1.07	<0.001	1.05	1.04-1.07	<0.001	1.06	1.03-1.09	<0.001
Gender (male)	1.13	0.87-1.46	0.367	1.06	0.80-1.42	0.669	1.05	0.62-1.77	0.848
Wealth									
First (lowest)	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Second quintile	0.67	0.47-0.9 5	0.025	0.64	0.43-0.95	0.029	0.96	0.50-1.85	0.899
Third quintile	0.78	0.56-1.10	0.158	0.73	0.50-1.06	0.102	0.93	0.48-1.79	0.824
Fourth quintile	0.79	0.57-1.09	0.148	0.76	0.53-1.10	0.145	0.90	0.46-1.74	0.745
Fifth quintile	0.71	0.50-1.00	0.048	0.76	0.52-1.11	0.150	0.50	0.22-1.13	0.095
Framingham score									
Low	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Medium	1.34	0.94 - 1.91	0.102	1.56	1.05-2.31	0.027	0.76	0.38-1.55	0.454
High	1.34	0.88-2.05	0.170	1.35	0.84-2.17	0.218	1.10	0.49-2.47	0.809

* NC: Not Calculated, due to insufficient numbers of strokes among isolated individuals.

B) Association between loneliness and social isolation in waves 2 to 5, and CVD incidence between waves 2 and 6 – listwise deletion

Explanatory variable	Total cardiovascular disease			Heart disease			Stroke		
	Hazard Ratio (HR)	95% Confidence Interval (CI)	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Model A2 : Loneliness only									
Loneliness									
Never	0.67	0.54-0.84	0.001	0.71	0.55-0.92	0.009	0.53	0.32-0.86	0.010
Once	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Twice	0.91	0.61-1.36	0645	0.98	0.63-1.53	0.927	0.61	0.23-1.62	0.320
Three times	1.06	0.60-1.87	0.845	1.28	0.70-2.32	0.426	0.36	0.05-2.68	0.316
Four times	1.06	0.78-3.42	0.190	1.82	0.82-4.01	0.141	1.16	0.15-8.98	0.888
Model B2 : Social isolation only									
Social isolation									
Never	1.29	0.66-2.50	0.454	1.05	0.54-2.04	0.892		NC*	
Once	1.00 (reference)			1.00 (reference)					
Twice	1.93	0.71-5.19	0.195	1.37	0.46-4.10	0.573			
Three times	0.68	0.09-5.36	0.711	0.70	0.09-5.53	0.733			
Four times	1.70	0.21-1356	0.618	1.65	0.21-13.24	0.636			
Model C2 : Loneliness, social isolation, age, gender and wealth									
Loneliness									
Never	0.81	0.57-1.13	0.218	0.85	0.58-1.25	0.402	0.65	0.39-1.07	0.088
Once	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Twice	1.04	0.57-1.89	0.910	1.10	0.56-2.16	0.776	0.54	0.20-1.44	0.218
Three times	0.95	0.37-2.44	0.911	1.35	0.52-3.54	0.539	0.27	0.04-2.07	0.209
Four times	1.93	0.57-6.47	0288	2.54	0.74-8.73	0.138	0.88	0.11-6.84	0.903
Social isolation									
Never	2.29	1.12-4.66	0.023	1.72	0.84-3.53	0.138		NC	
Once	1.00 (reference)			1.00 (reference)					
Twice	2.14	0.77-5.93	0.145	1.46	0.47-4.50	0.508			
Three times	0.68	0.08-5.50	0.715	0.65	0.08-5.32	0.689			
Four times	1.67	0.20-13.69	0.635	1.53	0.18-12.66	0.695			
Model D2: Loneliness, social isolation, age, gender, wealth and CVD risk score									
Loneliness									
Never	0.83	0.55-1.27	0.391	0.86	0.54-1.37	0.524	0.66	0.36-1.21	0.181
Once	1.00 (reference)			1.00 (reference)			1.00 (reference)		
Twice	1.14	0.56-2.33	0.725	1.03	0.45-2.34	0.949	0.84	0.30-2.37	0.737
Three times	1.46	0.54-3.90	0.456	1.84	0.67-5.07	0.237	1 (empty)		
Four times	2.55	0.58-11.28	0.216	3.30	0.73-14.98	0.122	1.47	0.18-11.95	0.719
Social isolation									
Never	2.84	1.05-7.73	0.040	2.18	0.80-5.96	0.127		NC	
Once	1.00 (reference)			1.00 (reference)					
Twice	3.44	0.96-12.33	0.057	2.85	0.76-10.77	0.122			
Three times	1 (empty)			1 (empty)					
Four times	4.44	0.474-1.57	0.192	4.01	0.42-38.39	0.228			

* NC: Not Calculated. Because social isolation was rare, and there were few strokes, not all frequencies of social isolation were associated with at least one event (i.e. there were empty cells in tabulations). Frequency of social isolation was therefore not included in the models where stroke was the sole outcome.

Appendix 8.1 Papers published based on the work presented in this thesis

A) Loneliness, social isolation and social relationships: what are we measuring? A novel framework for classifying and comparing tools

Authors: Nicole K Valtorta, Mona Kanaan, Simon Gilbody, Barbara Hanratty
Journal and year: *BMJ Open*, 2016

ABSTRACT

Objectives: We present a novel way of classifying and comparing measures of social relationships, to help readers interpret the growing literature on loneliness and social isolation, and to provide researchers with a starting point to guide their choice of measuring tool.

Methods: Measures of social relationships used in epidemiological studies were identified from two systematic reviews – one review on the association between social relationships and health and social care service use, and a second review on the association between social relationships and health. Questions from each measure were retrieved and tabulated, to derive a classification of social relationship measures.

Results: We present a classification of measures according to two dimensions: 1) whether instruments cover structural or functional aspects of social relationships and 2) the degree of subjectivity asked of respondents. We explain how this classification can be used to clarify the remit of the many questionnaires used in the literature, and to compare them.

Conclusions: Different dimensions of social relationships are likely to have different implications for health. Our classification of social relationship measures transcends disciplinary and conceptual boundaries, allowing researchers to compare tools that developed from different theoretical perspectives. Careful choice of measures is essential to further our understanding of the links between social relationships and health, to identify people in need of help, and to design appropriate prevention and intervention strategies.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- We systematically searched for tools measuring social relationships, following the Centre for Reviews and Disseminations guidelines.
- We classified measures in a way that transcends disciplinary and conceptual boundaries, allowing us to compare tools developed from different theoretical perspectives.
- As well as providing an easy interpretation of existing research for researchers, policymakers and practitioners, the classification we present can help guide researchers' choice of measure in future studies.
- Other factors that need to be taken into account when choosing tools, and that are not covered in this paper, include psychometrics, study population, and study hypothesis.

INTRODUCTION

Social relationships 'exist between two people when each person influences the other's thoughts, feelings, and or behaviour, [i.e.] when people are at least minimally interdependent'.[1] Their influence on health is attracting growing interest from policy makers and practitioners, amidst concern about the wellbeing of certain groups, in particular older adults, in increasingly fragmented industrialised societies.[2-4] We know from reviews of the research evidence that people with weaker social relationships are at greater risk of premature mortality.[5] What we do not know is whether some aspects of relationships (e.g. their quality or quantity; subjectively v. objectively assessed availability) are more problematic than others, and for whom.

One of the main reasons why we know little about the comparative effects of different social relationship dimensions is the inconsistent use of terminology. In the absence of a comprehensive framework, investigators from a range of disciplines, including sociology, psychology, demography, and epidemiology, have suggested definitions of concepts that cannot always easy be reconciled. For example, House and Khan proposed to distinguish between two dimensions of social relationships: social network and social support [6]. They defined social network as the structural dimension of social relationships, encompassing aspects such as the density, duration, dispersion, reciprocity and homogeneity of relationships. Social support was defined as the functional aspect of relationships (i.e. covering aspects such as the provision or receipt of information, instrumental help, emotional support or advice). In contrast, O'Reilly suggested instead that social network be used as the main concept, with social support as a subsidiary concept covering the qualitative and behavioural aspects of the social network [7].

Approaches to operationalising tools have been similarly heterogeneous, so that it is often unclear how different measurement tools differ or overlap, making comparison difficult. This raises a number of questions: how do researchers choose their measure? Are these measures relevant to the population under study? Do questionnaires capture what they purport to measure? In this study, we propose a new way of classifying measures of social relationships. Our aim is to provide a transparent and accessible way of reviewing tools, to help readers understand and interpret the existing evidence.

Rationale for developing a classification of measurement tools

There are many instruments available for assessing different aspects of social relationships: the Berkman-Syme Social Network Index,[8] the Lubben Social Network Scale,[9] the de Jong Gierveld Loneliness Scale,[10] the UCLA Loneliness Scale,[11] the Interview Schedule for Social Interaction,[12] for example. Exactly what these tools are designed to measure is often unclear. Researchers have tended to use terms including social integration, social ties or social isolation loosely and interchangeably, so that labels such as 'measure of social support' or 'social interaction scale' are not reliable indicators. For example, in an article reporting results from the Prospective Epidemiological Study of Myocardial Infarction, we read that '*social support*' was measured using the Berkman-Syme *Social Network* Index.[13] In a systematic review of observational studies on psychosocial factors and coronary heart disease, 'social support' was understood to encompass a range of situations and measurement tools, including 'high love and support from wife', 'social network index' and 'social isolation'.[14]

An important reason for clarifying the literature is that different domains of social relationships might have different implications for health. Unfortunately, most epidemiological studies focus on only one measure of social relationships, precluding direct comparisons. Evidence from the few studies that do include measures of objective as well as subjective aspects of social relationships suggests that the two dimensions are weakly correlated, and that they have independent effects on health-related outcomes.[15-17] A single approach to measuring social relationships is therefore unlikely to be appropriate for all purposes, and investigators need to choose measurement tools carefully, basing their choice on clear hypotheses of how and why social relationships might influence particular health outcomes.[18]

To overcome the lack of conceptual clarity in the literature and to help researchers choose measurement tools tailored to their needs and objectives, we propose a way of classifying instruments that allows comparison across disciplinary boundaries. Our classification builds upon a distinction frequently referred to in the literature, the difference between functional (qualitative) and the structural (quantitative) aspects of social relationships,[19] and takes into account a second, important, dimension: the way in which questionnaire items are phrased, which informs us about the degree of subjectivity asked of respondents.

METHODS

We developed a classification in two stages. First, we systematically searched for studies on the association between social relationships and health and social care service use among adults aged 65 and over. Searches were tailored to eight electronic databases (MEDLINE, EMBASE, Scopus, Web of Science, CINAHL Plus, the Cochrane Library, the Centre for Reviews and Disseminations database and PsycINFO) using a combination of index headings (e.g. 'Loneliness', 'Social isolation', 'Social support') and free text terms (see Appendix 1 for the search strategy used in MEDLINE), and were last updated in October 2015. The reference lists of relevant studies were screened for further eligible records. The 32,205 records identified were screened by two researchers who selected studies which included a measure of the quantity and/or quality of individuals' social relationships. We applied no study design, language, publication type or date restrictions. For each study, we retrieved the questions used to assess social relationships and grouped them according to how they were formulated. Through this process we identified two ways in which questions differed: 1) whether they were asking about the structure or the function of social relationships, and 2) whether respondents were being asked to report on: past and present contact with others; availability of relationships as they perceive it; adequacy of their relationships; feelings relating to social relationships.

In a second phase, we tested whether a framework based on these two dimensions could be used to classify the measures used in studies on social relationships and cardiovascular disease. To identify these studies, we searched sixteen electronic databases (MEDLINE, EMBASE, CINAHL Plus, PsycINFO, ASSIA, Web of Science, Cochrane Library, Social Policy and Practice, National Database of Ageing Research, Open Grey, HMIC, ETHOS, NDLTD, NHS Evidence, SCIE, and NICE), using a combination of thesaurus and free text terms including loneliness, social isolation, social relationships, social support, social network (search last updated in May 2015; for an example of the full electronic strategy used to search MEDLINE, see Appendix 2). The titles and abstracts of the 35, 925 records identified were independently screened by two researchers, who selected eligible studies based on whether they included a measure of the quality and/or quantity of individuals' social relationships.

RESULTS

Our systematic searches identified 54 instruments (see Appendix 3 for a full list, including references to the studies in which each tool was used, and references to the original article or report in which the tool was described). The number of questions in each tool ranged from one to thirty-two. Taking each question at a time, we considered its content and the way in which it was formulated. This allowed us to develop a classification based on a) whether the question was about the function or structure of social relationships and b) the degree of subjectivity which it required from respondents.

First dimension: structure versus function

Questions that touch on the structure of social relationships seek to find out who people share an interpersonal relationship with, and to assess the linkages between these individuals.[20] Structural characteristics of social relationships cover the number and type of people with whom a person interacts, the diversity, density and reciprocity of a person's social network, and frequency and duration of contact between individuals. Examples of questions concerned with structure include: 'Have you ever been married? If so, are you now married, separated, divorced or widowed?' (Berkman-Syme Social Network Index)[8] 'How many relatives do you see or hear from at least once a month?' (Lubben Social Network Scale).[9]

Questions on the functional aspects of social relationships target the qualitative and behavioural characteristics of interactions and exchanges between people.[20] These questions are about the purpose and nature of relationships, with much of the literature focusing on their beneficial functions, in particular receiving and providing social support. This can take the form of emotional help (e.g. expressions of love and caring), tangible aid (e.g. transport), information or companionship.[21] While much of the epidemiological literature has focused on social support as the mechanism through which social relationships affect health, we note that other functions are likely to affect health too, notably social influence and engagement, and opportunities for person-to-person contact.[18] Examples of questions to do with function include: 'At present, do you have someone you can share your most private feelings with (confide in) or not?' (Interview Schedule for Social Interaction)[12] 'How often is there someone available to take you to the doctor if you needed it?' (MOS Social Support Survey)[22]

Second dimension: the degree of subjectivity asked of respondents

All answers to self-report questionnaires involve a degree of subjectivity, nevertheless, when comparing questions on social relationships, we found that the degree of subjectivity expected of respondents varied, based on the way in which items were formulated. In the following section, we describe each of the four different formulations we identified, starting with the more objective questions, and progressively moving towards greater subjectivity.

1) Items assessing respondents' involvement in social relationships

A first type of question aims to capture people's access to social relationships using a relatively objective approach. These questions often, but not always, ask individuals to quantify their social relationships and require a numerical answer. For example: 'How many relatives do you see or hear from at least once a month?' (possible answers: 0, 1, 2, 3 or 4, 5 to 8, or 9+, Lubben Social Network Scale)[9]. Such questions attempt to gauge the size and range of social relationships in which a person is involved, although we note that answers could be telling us more about individuals' needs rather than access - i.e. people might not have engaged in certain social relationships because they did not feel the need to, rather than because they could not.

2) Items assessing the availability of social relationships as perceived by respondents

A second way of assessing access to social relationships is to ask people whether such relationships are available to them. For example, in a 4-item measure of social isolation used in the Japan Public Health Center-based Prospective Study II, participants were asked: 'Do you have someone who is supportive of your opinions and actions?'.[23] Questions are often phrased hypothetically, for example: 'Is there someone who would give you any help at all if you were sick or disabled, for example, your husband/wife, a member of your family, or a friend?' (OARS Social Resource Scale)[24] Such questions do not tell us about whether social relationships are actually available to individuals, but are a measure of availability as perceived by respondents.

3) Items assessing the adequacy of social relationships from respondents' perspective

A third type of question asks respondents to report on whether they are satisfied with the quality and/or quantity of their interaction with others. Examples of such items include: How satisfied are you with the kinds of relationships you have with your family and friends? (possible answers: Very dissatisfied, Somewhat dissatisfied, Satisfied, 11-item Duke Social Support Index);[25] 'I find my circle of friends and acquaintances too limited.' (possible answers: "yes!" "yes," "more or less," "no," and "no!" or "yes," "more or less," and "no", de Jong Gierveld Loneliness Scale).[10] Answering such questions requires participants to appraise their social relationships against their expectations.

4) Items where respondents are asked about their feelings relating to social relationships

A last type of question focuses on feelings associated with social relationships. For example, in the UCLA Loneliness Scale, respondents are asked whether they 'feel isolated from others', ‘feel left out’, or ‘feel completely alone’.[11] Questions can cover both positive and negative feelings, and ask how people feel about the quality as well as the quantity of their relationships.

Using the classification to clarify what each questionnaire is measuring

As we developed our classification, it became apparent that whilst the majority of questionnaires were designed with a total score in mind (i.e. no subscales), they often included more than one type of question. In Table 1 we list the 54 instruments identified from our systematic searches, and the dimensions they cover. Asterisks indicate that subscales are available for this questionnaire.

Table 1. Classification of social relationship measures.

Tool used	Number of items	Dimension 1: function v. structure		Dimension 2: degree of subjectivity			
		Structure	Function	Involve-ment in relation-ships	Perceived availabilit y	Perceived adequacy	Feeli ngs/ Emot ions
Berkman-Syme Social Network Index	4	X	X	X			
11-item de Jong Gierveld Loneliness Scale	11		X		X	X	X
35-item Duke Social Support Index	32	X	X	X	X	X	
11-item Duke Social Support Index	11	X	X	X	X	X	
4-item Duke Social Support Index	4	X	X	X	X		
Duke-UNC Functional Social Support Questionnaire	11	X	X			X	
ENRICHD Social Support Inventory (ESSI)	7	X	X	X	X	X	
Gijón Scale for the elderly’s social-family assessment, family and social relationships subscales	10	X		X			
12-item Interpersonal Support Evaluation List (ISEL)	12		X		X		
Interview Measure of Social Relationships	Data not found	X	X	X	X	X	

Litwin Support Network Types	7	X		X			
10-item Lubben Social Network Scale	10	X	X	X	X		
6-item Lubben Social Network Scale	6	X	X	X	X		
Medical Outcomes Study (MOS) Social Support Survey	20		X		X		
Multidimensional Scale of Perceived Social Support (MSPSS)	12		X		X		
Negative Affect Scale	5		X				X
Nottingham Health Profile Social Isolation subscale	5		X		X		X
Older Americans Research and Service Center (OARS) Social Resource Scale	7	X	X	X	X	X	X
Oslo-3 Social Support Scale	3		X		X		
Personal Resource Questionnaire (PRQ2000)	15		X		X	X	X
University of California, Los Angeles (UCLA) Loneliness Scale	20		X		X	X	X
Wenger Support Network Typology	8	X		X			
A measure of social isolation (LaVeist 1997)	2	X		X			
A measure of social network (Mechakra-Tahiri 2011)	4	X		X			
A measure of social anchorage (Rennemark 2009)	4		X				X
Questionnaire on social network (Rodriguez-Artalejo 2006)	4	X		X			
Question about the number of sources of support (Tennstedt 1993)	1	X	X	X			
An index of social support (Lai 2006)	5	X	X	X	X		
A measure of living arrangements and informal care (Crets 1996)	2	X		X			
A measure of satisfaction with	6		X		X	X	

social support (Feld 1994)							
A measure of social integration (Orth-Gomer 1996)	6	X	X	X	X		
A measure of social isolation (Cloutier-Fischer 2009)	2	X	X	X	X		
A measure of social network (Reed 1983)	9	X		X			
A measure of social network (Reed 1984)	4	X		X			
A measure of social support (Tran 1997)	5	X		X			
A measure of social support (André-Petersson 2006)	13		X		X	X	X
A measure of social support (Ikeda 2008)	4	X	X	X	X		
A measure of social support (Kuper 2006)	6	X		X	X		
An social network index (Rutledge 2008)	12	X		X			
Social network type (Coe 1984)	2	X		X		X	
Social network type - family (Coe 1985)	2	X		X		X	
Multi-item measures combining questions about frequency of contact with others and participation in activities	2 or more	X		X			
Question(s) about frequency of face to face and/or phone contact with family and/or friends and/or neighbours, e.g.: 'How many times during the past week did you spend some time with someone who does not live with you? ' (Hyduk 1996)	1 or more	X		X			
Question(s) about the geographical proximity of family and friends	1	X		X			
Question(s) about the number of close friends or	1 or more	X	X	X			

relatives, e.g. asking respondents for the 'number of friends [they] feel close to' (Lee 2008)							
Question(s) about participation in social activities such as going to the cinema, sport events, church attendance or volunteering, e.g. 'In the past two weeks, did you go to a show or movie, sports event, club meeting, classes or other group event?' (The Longitudinal Study of Aging, 1992)	1 or more	X					
Question(s) about the perceived availability of emotional, tangible, informational and/or other support, e.g. 'Is there someone who would give you any help at all if you were sick or disabled, for example your husband/wife, a member of your family, or a friend?' (Barresi, 1987)	1 or more		X		X		
Question(s) about received support, e.g. asking participants whether they received assistance during the past month with 7 tasks, including shopping, housework or going to the doctor	1 or more		X				
Question(s) about satisfaction with social relationships and/or participation, e.g. asking participants whether they believe their present level of	4		X			X	

social activities to be adequate							
Question(s) about the size of a person's network, e.g. number of friends and relatives outside the household	1 or more	X		X			
Question about time spent alone	1	X		X			
Single-item question about feeling lonely, e.g.: 'How often in the last 12 months have you been bothered by loneliness?’	1		X				X

*Subscales available.

Using the classification to compare measures

Clarifying the remit of each instrument allows us to situate tools in relation to other available measures. In Figure 1, we have mapped the multi-item questionnaires developed as stand-alone tools onto a two-dimensional diagram. Questionnaires were placed on the diagram according to whether they contained questions focusing on the structural, functional or both aspects of relationships (vertical axis); and according to the degree of subjectivity asked of respondents (horizontal axis). Where questionnaires contained more than one type of question - e.g. the Duke Social Support Indices, where participants are asked about their involvement in relationships, as well as to report on the perceived availability and adequacy of relationships -, they were mapped accordingly i.e. spanning across these three types of questions. Similarly, where questionnaires included questions about structural as well as functional aspects, they were placed so as to straddle both areas of the diagram (e.g. the Lubben social Network Scales, the ENRICH Social Support Inventory, or the Duke-UNC Functional Social Support Questionnaire). For the purpose of clarity, we did not include single-item tools and tools that were developed for specific studies or datasets in our diagram.

Figure 1 here.

Figure 1 allows us to compare and contrast tools. For example, we observe that whilst they both explicitly target social support, the ENRICHD Social Support Inventory includes questions on the function as well as the structure of relationships, whereas the MOS Social Support Survey focuses on functional aspects only. The diagram also enables us to identify tools with similar foci, and questionnaires that might complement each other. As we might expect, tools explicitly designed for measuring loneliness (e.g the UCLA Loneliness Scale and the de Jong Gierveld Loneliness Scale) tend to be based on more subjective questions, whereas social network indices primarily use more objective measures. Perhaps less intuitively, given that loneliness is commonly defined as referring to the negative feeling associated with people perceiving the *quantity and quality* of their relationships to be deficient,[26] we note that tools explicitly designed to measure loneliness tend to focus exclusively on the functional aspects of relationships.

CONCLUSIONS

The classification described in this paper was designed to help readers interpret the existing literature on loneliness and isolation, and to help inform future epidemiological studies on social relationships. One of the ways in which it can be employed is by researchers who intend to review the literature, and who need to define which dimensions of social relationships they are interested in. Rather than rely on inconsistent conceptual terminology, they can use the classification to define the remit of their review (e.g. focus on functional or structural dimensions) and identify which measurement tools do and do not fit within their criteria.

Another important way in which the classification can contribute to future research is by helping to guide researchers' choice of measurement tool, since it provides an overview of some of the tools previously used in epidemiological studies, and allows investigators to compare instruments developed from different disciplines and theoretical perspectives. Once researchers have compared tools using our framework, they will be in a position to consider other factors of relevance, most importantly: psychometrics (has the tool been validated and shown to be reliable? What of its responsiveness and interpretability?); study population (is the tool adequate for the age group or the cultural context?); and whether the tool captures the most relevant dimensions of social relationships given the investigators' hypotheses about how relationships influence health. Careful choice of measures is essential if we are to further our understanding of how social relationships affect health, and to identify people in need of help. Only by being clear about what is measured and why can we design appropriate prevention and intervention strategies that target the areas of relationships most problematic for health and wellbeing.

What is already known on this subject

The influence of social relationships on morbidity is widely accepted. Dimensions including social support, social networks, social isolation and loneliness have all been linked to ill health and premature mortality. Because terms have been used interchangeably and loosely by researchers, it is not clear what aspects of social relationships are being measured. This study aims to clarify the literature by introducing a way of classifying the range of tools that exist to measure social relationships.

What this study adds

The classification of social relationship measures presented in this paper allows us to compare measures that have been developed from different theoretical and disciplinary perspectives. It provides researchers, policymakers and practitioners with a framework to understand and interpret existing research studies, as well as helping to guide researchers' choice of measure in future studies.

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Figure legend

Figure 1. Comparing multi-item questionnaires using a two-dimensional diagram.

B) Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies

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Journal and year: *Heart*, 2016

STRUCTURED ABSTRACT

Background: The influence of social relationships on morbidity is widely accepted, but the size of the risk to cardiovascular health is unclear.

Objective: We undertook a systematic review and meta-analysis to investigate the association between loneliness or social isolation and incident coronary heart disease (CHD) and stroke.

Methods: Sixteen electronic databases were systematically searched for longitudinal studies set in high-income countries and published up until May 2015. Two independent reviewers screened studies for inclusion and extracted data. We assessed quality using a component approach and pooled data for analysis using random effects models.

Results: Of the 35,925 records retrieved, twenty-three papers met inclusion criteria for the narrative review. They reported data from 16 longitudinal datasets, for a total of 4,628 CHD and 3,002 stroke events recorded over follow-up periods ranging from 3 to 21 years. Reports of eleven studies (CHD) and eight studies (stroke) provided data suitable for meta-analysis. Poor social relationships were associated with a 29% increase in risk of incident coronary heart disease (pooled relative risk: 1.29, 95% confidence interval: 1.04 to 1.59) and a 32% increase in risk of stroke (pooled relative risk: 1.32, 95% confidence interval: 1.04 to 1.68). Subgroup analyses did not identify any differences by gender.

Conclusion: Our findings suggest that deficiencies in social relationships are associated with an increased risk of developing CHD and stroke. Future studies are needed to investigate whether interventions targeting loneliness and social isolation can help to prevent two of the leading causes of death and disability in high-income countries.

Systematic review registration number: CRD42014010225 (PROSPERO International prospective register of systematic reviews).

Key questions

What is already known about this subject?
People with poorer social relationships are at increased risk of premature death. The implications of social relationships for disease onset are unclear.

What does this study add?
This systematic review of prospective longitudinal studies found that deficiencies in social relationships are associated with an increased risk of developing CHD and stroke of around 30%. This association is comparable in size to other recognised psychosocial risk factors, such as anxiety and job strain.

How might this impact on clinical practice?
Efforts to reduce cardiovascular disease incidence need to consider loneliness and social isolation.

INTRODUCTION

Adults who have few social contacts (i.e. who are socially isolated) or feel unhappy about their social relationships (i.e. who are lonely) are at increased risk of premature mortality.[1] The influence of social relationships on mortality is comparable with well-established risk factors, including physical activity and obesity.[2] Yet compared with our understanding of these risk factors, we know much less about the implications of loneliness and social isolation for disease aetiology.

Researchers have identified three main pathways through which social relationships may affect health: behavioural, psychological and physiological mechanisms.[3,4] Health-risk behaviours associated with loneliness and social isolation include physical inactivity and smoking.[5] Loneliness is linked to lower self-esteem and limited use of active coping methods,[6] while social isolation predicts decline in self-efficacy.[7] Feeling lonely or being socially isolated is associated with defective immune functioning and higher blood pressure.[8,9] This evidence suggests that loneliness and social isolation may be important risk factors for developing disease, and that addressing them would benefit public health and wellbeing.

The aim of this study was to investigate the size of the association between deficiencies in social relationships and incident CHD or stroke, the two greatest causes of burden of disease in high income countries.[10] We conducted a systematic review to answer the following primary question: are deficiencies in social relationships associated with developing CHD and stroke in high-income countries? Our secondary objectives included investigating whether loneliness or social isolation were differentially associated with incident heart disease and stroke, and whether the association between social relationships and disease incidence varied according to age, gender, marital status, socio-economic position, ethnicity and health.

METHODS

This study followed the Centre for Reviews and Dissemination's Guidance for undertaking reviews in healthcare.[11] A protocol was registered with the International Prospective Register of Systematic Reviews (registration number: CRD42014010225).[12]

Study eligibility criteria

To meet inclusion criteria, studies had to investigate new CHD and/or stroke diagnosis at the individual level as a function of loneliness and/or social isolation. We defined CHD as encompassing the diagnoses listed under codes l20-l25 of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), and stroke as ICD-10 codes I60–69. We excluded studies where CHD or stroke diagnosis was not the first instance of diagnosis among participants, except where analyses controlled for previous events. We applied no other exclusion criteria regarding study population. Measures of social relationships met inclusion criteria for loneliness if they were consistent with its definition as a subjective negative feeling associated with someone's perception that their relationships with others are deficient.[13] Measures of social isolation had to be consistent with its definition as a more objective measure of the absence of relationships, ties or contact with others.[14] We focussed on longitudinal studies in order to investigate the temporal relationships between loneliness or isolation and subsequent disease. Our purpose was to clarify the public health challenge posed by deficiencies in social relationships in high income countries, [15] so we excluded all other settings. We applied no language, publication type or date restrictions to inclusion.

Search strategy and selection criteria

We searched sixteen electronic databases for published and grey literature published up until May 2015: MEDLINE, EMBASE, CINAHL Plus, PsycINFO, ASSIA, Web of Science, Cochrane Library, Social Policy and Practice, National Database of Ageing Research, Open Grey, HMIC, ETHOS, NDLTD, NHS Evidence, SCIE, and NICE. Thesaurus and free text terms (e.g. loneliness, social isolation, social relationships, social support, social network) were combined with filters for observational study designs and tailored to each database. The search strategy included no health terms, as it aimed to capture all disease outcomes, rather than focus on CHD and stroke. For the full electronic strategy used to search MEDLINE, see Appendix 1.

To complement the electronic search, we screened reference lists, searched for citations in Scopus (the largest database of abstracts and citations) and contacted topic experts identified through the UK Campaign to End Loneliness' Research Hub.

After removing duplicates, two researchers independently screened titles and abstracts before assessing full records using a standardised screening sheet. Additional information was sought from authors when necessary (3 (60%) responded). When authors did not reply, we searched for information from related publications to inform our decision.

Data extraction and quality assessment

Data were extracted into a standardised form by one researcher, and checked by a second. Study authors were contacted to obtain missing data.

Based on the Agency for Healthcare Research and Quality framework and taxonomy of threats to validity and precision,[16] we selected the following domains as relevant for assessing studies : sampling bias, nonresponse bias, missing data, differential loss to follow-up, information error with regards to exposure and outcome measure, detection bias, confounding, and study size. We identified age, gender and socio-economic status as potential confounders (i.e. factors correlated with exposure, predictive of outcome and not on the causal pathway).[17,18] No studies were excluded due to quality; instead, subgroup and sensitivity analyses were performed, to test the stability of findings according to internal validity.

Quantitative synthesis

We hypothesised that social relationships were associated with disease incidence, and that this association may differ according to the dimension of relationships measured, and individual- and contextual-level factors. A preliminary synthesis was developed by grouping study characteristics and results according to their measure of relationships. The majority of papers reported relative hazards of new diagnosis, comparing people with higher versus lower levels of loneliness or social isolation. Since incidence of disease was low (<10%) in the three studies reporting odds ratios, these estimates were approximated to relative risks.[19] Where the lonely or isolated group was used as the reference, results were transformed to allow comparison across studies.

Patterns identified in the preliminary synthesis were formally investigated. Only papers for which an effect estimate and standard error or confidence interval were available (reported in the paper or provided by contacted authors), or could be calculated, contributed to this stage of the analysis. Where several papers reported results from the same cohort, we privileged the findings with the longest follow-up time. If a study included multiple measures of exposure and/or outcome, we selected the result relating to the most comprehensive measure. Where a study used statistical controls to calculate an effect size, we extracted data from the most complex model to minimize risk of confounding. All effect sizes were transformed to the natural log for analyses. Using Revman version 5.3,[20] CHD and stroke effect estimates were plotted in separate forest plots, and heterogeneity between studies was assessed using the I^2 statistic.

Potential sources of variation were explored with pre-specified subgroup analyses. Since heterogeneity could not be explained and removed based on these analyses, but we deemed studies sufficiently similar to warrant aggregation, we combined results using random effects models. This approach allows for between-study variation, and is consistent with our assumption that the effects estimated in the different studies were not identical, since they investigated different dimensions of social relationships and derived from different populations.

Finally, sensitivity analyses were performed to test whether our overall results were affected by internal study validity and small-study effects. Contour-enhanced funnel plots for asymmetry were drawn using STATA version 12.[21] The limited number and the heterogeneity of studies did not support the use of tests for funnel plot asymmetry.[22]

RESULTS

A total of 23 studies based on 16 cohorts were identified for inclusion in the review, after a two-stage process. See Figure 1 for a flow diagram of the study selection process. Eleven studies on CHD and 8 studies on stroke met inclusion criteria for the quantitative syntheses (i.e studies based on independent samples reporting data from which the natural log of the estimate and its standard error could derived).

Table 1 summarises the descriptive characteristics of the evidence included in our review (see appendix 2 for individual study characteristics).

Table 1. Characteristics of the included evidence.

Population characteristics across included studies	
Total number of participants	181,006
Age of participants	Aged 18 and over
Breakdown of the population according to world region	- Europe: 38% of participants - North America: 33% of participants - Asia (Japan and Asian Russia): 25% of participants - Australia: 5% of participants
Study characteristics	
Baseline data collection years, range	1965 to 1996
Length of follow-up, range	3 to 21 years
Size, range	Between 98 and 47,713 subjects
Gender	- All-male sample in 9 papers[23-31] - All-female sample in 6 papers[32-37] - Mixed sample in 8 papers[38-45]

Assessment of loneliness and social isolation

Prevalence of loneliness or social isolation ranged from 2.8%[42] to 77.2%.[33] Three papers measured loneliness,[23,32,44] 18 measured social isolation[24-31,33-35,38-43,45] and two papers used a measure combining both dimensions.[36,37] The three papers on loneliness used different tools: a direct question asking about loneliness feelings during the day,[32] a question on feelings of loneliness in the past week,[44] and a 13-item tool encompassing the perceived availability, adequacy or accessibility of social relationships.[23] Across the 18 studies on social isolation, 11 tools were used: six studies used the Berkman-Syme Social Network Index,[46] two studies used the 10-item Lubben Social Network Scale,[47] and the remainder used nine different tools on the availability and/or frequency of contacts. One cohort study used a measure combining social isolation and loneliness, the 11-item Duke Social Support Index, which asks about frequency of interaction and satisfaction with relationships.[48]

Loneliness and social isolation were predominantly treated as a categorical variable; two studies analysed them as continuous variables.[31,44] Only one study reported results based on measuring social relationships more than once.[44]

Ascertainment of CHD and stroke

A total of 4,628 CHD and 3,002 stroke events were recorded across the 23 papers. Eighteen studies measured incident CHD and 10 measured stroke (five studies reported on both outcomes). Diagnosis was ascertained from medical records, death certificates or national registers in all but 4 studies. Others used self-report,[36,37] or telephone interviews with a nurse or physician.[35] Two studies verified self-reported events against medical records.[31,38,40] The majority of studies with a measure of CHD focused on MI and/or CHD death (11/18). Four studies included angina pectoris within their measure of CHD, and two presented results for angina separately. The remit of the CHD measure was unclear in one study.[45]

Study validity

Figure 2 summarises risk of bias across the studies included in our review (see Appendix 3 for details of criteria). For many of the instruments assessing social relationships, information on reliability and validity was limited (Appendix 4 displays detailed information on the validity and reliability of tools). Four cohorts (6 articles) relied on subjects reporting new diagnosis for all or part of the outcomes measured, and were judged to be at greater risk of misclassification (see Appendix 2 for details of outcome assessment). Limited information on attrition and blinding of outcome assessment meant that susceptibility to differential loss to follow-up and detection bias was unclear. We note that the multiplicity of risk factors investigated and the differential length of follow-up suggest that outcome assessment is unlikely to have been influenced by knowledge of baseline information on social relationships.

The results reported in 12 papers were at lower risk of confounding, i.e. analyses controlled or accounted for age, gender and socio-economic status. [23,24,29,30,32,35,38,39,41,42,44,45] Four studies presented results from univariate analyses,[33,36,37,43] with a further study adjusting for age only.[28] The remaining eight reports did not control for socio-economic status, although in the case of the Health Professionals Follow-up Study the relative socio-economic homogeneity of the sample may limit the impact of this omission.[24,26]

Loneliness, social isolation and CHD

Across 11 studies (3,794 events; one study did not report numbers) based on independent samples, the average relative risk of new coronary heart disease when comparing high versus low loneliness or social isolation was 1.29 (95% confidence interval 1.04 to 1.59; see Figure 3). We found evidence of heterogeneity within this comparison (I^2=66%, χ^2=29.16, df=10, P=0.001) and explored whether this could be explained by social relationship domain (loneliness v. social isolation), gender, risk of confounding and higher risk of bias due to exposure measurement error. We found no evidence that effects differed according to each subgroup (see Appendix 5). We were not able to explore other potential sources of heterogeneity due to limited information and study numbers.

Social isolation and stroke

Across nine independent study samples (2,577 events; one study did not report numbers), the average relative risk of stroke incidence was 1.32 (95% confidence interval 1.04 to 1.68; see Figure 4). Following confirmation of heterogeneity (I^2=53%, χ^2=17.07 df=8, P=0.03) we performed subgroup analyses according to risk of confounding and risk of bias due to outcome measurement error (there were too few studies to perform any other analyses). There was no evidence of effects differing according to subgroup (see Appendix 6); we had insufficient information to explore other potential sources of heterogeneity.

Risk of bias across studies

To test whether our findings were sensitive to internal study validity, we compared results with and without studies at greater risk of bias. We found no evidence of a difference in the ratio of the relative risks for CHD and stroke according to study validity (see Table 2).

Table 2 Sensitivity analyses

	Pooled estimate of the relative risk, based on all studies (95% CI) (number of effect estimates)	**Without studies at greater risk of information bias (exposure)**	**Without studies at greater risk of information bias (outcome)**	**Without studies at greater risk of confounding**	**Without studies at greater risk of bias in at least one domain**
CHD	1.29 (1.04-1.59) (n=11)	1.34 (1.03, 1.74) (n=9)	1.28 (1.01, 1.63) (n=10)	1.34 (1.03, 1.76) (n=7)	1.42 (1.00, 2.01) (n=7)
Stroke	1.32 (1.04-1.68) (n=8)	1.42 (1.09, 1.85) (n=7)	1.30 (0.98, 1.71) (n=4)	1.34 (1.05, 1.73) (n=6)	1.30 (0.98, 1.71) (n=4)

Visual assessment of contour enhanced funnel plots suggested that studies might be missing in areas of statistical significance (see Figures 5 (a) and (b)). Comparing fixed- and random-effects estimates, we found the random-effects estimate to be more beneficial (CHD: RR, random-effects: 1.29, 95% CI: 1.04-1.59, compared with RR fixed-effects: 1.18, 95% CI: 1.06-1.31; stroke: RR, random-effects: 1.32, 95% CI: 1.04-1.68, compared with RR fixed-effects: 1.19, 95% CI: 1.03-1.36). This suggests the presence of small-study effects, which could be due to reporting bias. Although we found no evidence that study quality and true heterogeneity explained small-study effects in our review, these, along with chance, remain possible explanations.

Additional studies

Seven papers with a measure of social isolation were excluded from quantitative synthesis since they either did not report data in a format suitable for pooling and/or shared data with other studies.[25,27-29,31,40,43] Of the four papers that did not duplicate data from other studies, two reported results based on the Honolulu Heart Program: social isolation appeared to predict CHD but not stroke, in analyses adjusted for age, though the association disappeared in multivariate analysis.[28,29] In a univariate analysis of data from the Atherosclerosis Risk in Communities Study (USA) the Lubben Social Network score was not significantly associated with incident CHD among people with prehypertension.[43] A further study found no evidence of an association between social isolation and CHD among men in France and Northern Ireland,[31] although we note that this study controlled for depression, one of the possible pathways through which social isolation might lead to disease.

DISCUSSION

Summary of findings and comparison with other work

Our review found that poor social relationships were associated with a 29% increase in risk of incident coronary heart disease and a 32% increase in risk of stroke. This is the first systematic review to focus on the prospective association between loneliness or social isolation and first occurrence of CHD or stroke.

Earlier reviews reported that cardiovascular disease (CVD) prognosis is worse among people with poorer social relationships.[1,2] Narrative reviews on social support and CHD have described an association with prognosis as well as incidence, but the strength of evidence was low.[49,50] A recent review of seven papers linked loneliness and social isolation to occurrence of CHD,[51] but the effect on prognosis and incidence could not be disentangled.

We found an association between poor social relationships and incident cardiovascular disease comparable in size to other recognised psychosocial risk factors, such as anxiety[52] and job strain.[53] Our findings indicate that efforts to reduce the risk of CHD and stroke could benefit from taking both loneliness and social isolation into account, as we found no evidence to suggest that one was more strongly related to disease incidence than the other. This is in line with other research linking subjective and objective isolation to hypertension, a risk factor for both stroke and CHD.[8,9]

Strengths and limitations

Our focus on longitudinal studies allowed us to comment on the direction of the relationship between social relationships and health, and avoid the problem of reverse causation. Pooling results from studies of CHD that measured loneliness and isolation allowed us to answer the broader question of whether deficiencies in social relationships are associated with disease incidence. We anticipated and explored heterogeneity where possible but found no statistical evidence that components of internal validity were associated with effect estimates.

Subgroup analyses specified a priori showed no difference between the association of loneliness or social isolation with CHD incidence, and we found no evidence across studies of differences between men and women. We found insufficient data to explore the relative effects of the quantity and quality of relationships, or study effect modifiers in depth. Seven of the estimates included in our meta-analyses (5 CHD, 2 stroke) were extracted from studies where participants were of higher socio-economic status and in better health than the target population. The role of deficiencies in social relationships may be greater among individuals under stress,[54] and our results may underestimate the health-damaging implications of loneliness and social isolation among disadvantaged groups. Our review included some data collected from 1965; more recent strategies for CHD prevention may have modified the influence of loneliness and social isolation on disease incidence.

In common with other reviews of observational studies, we cannot infer causality from our findings; nor can we exclude confounding by unmeasured common causes, or reverse causation if deficiencies in social relationships are the result of subclinical disease. Publication bias is a concern in every review, and may lead us to overestimate the 'true' effect of poor social relationships. Conversely, our pooled effects could be a conservative estimate: most of the studies in this review statistically adjusted for factors that are likely to be on the causal pathway, such as depression or health-related behaviour.

Implications

The main finding of our review, that isolated individuals are at increased risk of developing

CHD and stroke, supports public health concerns over the implications of social relationships for health and wellbeing. Our work suggests that addressing loneliness and social isolation may have an important role in the prevention of two of the leading causes of morbidity in high-income countries.

A variety of interventions directed at loneliness and social isolation have been developed, ranging from group initiatives such as educational programmes and social activities, to one-to-one approaches including befriending and cognitive behavioral therapy. These have primarily focused on secondary prevention, targeting people identified as isolated or lonely, but their effectiveness is unclear. Evaluative research is needed to investigate their impact on a range of health outcomes. Addressing health-damaging behaviours is also likely to be important, with lonely and isolated people more likely to smoke and be physically inactive, for example [5] Primary prevention strategies, such as promoting social networks or developing resilience, have received limited attention to date. Risk factors for loneliness and social isolation such as gender, socio-economic position, bereavement and health status, are well established[14,18] and hold the key to identifying people who may benefit from intervention.

Our findings suggest that tackling loneliness and isolation may be a valuable addition to CHD and stroke prevention strategies. Health practitioners have an important role to play in acknowledging the importance of social relations to their patients.

Legends for figures:
Figure 1 PRISMA Flow diagram
Figure 2 Internal validity
Figure 3 Forest plot of studies investigating incident CHD
Figure 4 Forest plot of studies investigating incident stroke
Figure 5 (a) Contour-enhanced funnel plot, CHD studies
Figure 5 (b) Contour-enhanced funnel plot, stroke studies

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Transparency declaration: The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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C) Title: Solitude et isolement: le « problème » tel qu'il est appréhendé au Royaume-Uni.
In English : Loneliness and isolation: how the « problem » is being tackled in the United Kingdom

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Résumé : La solitude, entendue comme le sentiment négatif ressenti par ceux qui ne sont pas satisfaits de leurs relations sociales, et l'isolement social, caractérisé par l'absence relative de contact avec autrui, sont depuis peu reconnus comme étant un défi de santé publique au Royaume-Uni. Comment ce « problème » social est-il défini, quels sont les acteurs identifiés pour y faire face, et quelles sont les actions proposées ? C'est ce que nous explorons dans cet article, en prenant comme point de départ la représentation du problème tel qu'il est abordé dans le Livre Blanc de 2012 « *Caring for our Future: Reforming care and support* » . En adoptant une perspective de santé publique, nous invitons le lecteur à porter un regard critique sur cette représentation, qui aborde principalement la solitude et l'isolement social comme problèmes liés au grand âge, symptômes d'une société individualiste qui peine à prendre soin de ses aînés. Le but est notamment de comprendre quels sont les fondements, mais aussi d'entrevoir les limites, de l'approche d'intervention telle qu'elle est actuellement envisagée au Royaume-Uni.

Abstract : Loneliness, understood as the negative feeling experienced by those who perceive their social relationships to be deficient, and social isolation, characterised by the relative absence of contact with others, have recently been identified as a public health challenge in the United Kingdom. How is this social « problem » defined, who is expected to tackle it, and how? These are the questions we explore in our article, taking as our starting point the problem as it is represented in the 2012 White Paper « *Caring for our Future: Reforming care and support* ». Adopting a public health perspective, we invite the reader to take a critical look at a representation which primarily frames loneliness and social isolation as problems linked to older age, symptoms of an individualistic society that is struggling to take care of its elderly population. Our aim is to shed light on the foundations, as well as to identify certain limitations, of the intervention approach currently pursued in the United Kingdom.

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