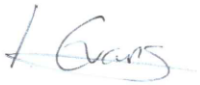
Social connections, cognitive reserve, and cognitive function in later life

Submitted by Isobel. E. M. Evans to the University of Exeter as a thesis for the degree of Doctor of Philosophy in Psychology, September 2018.

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.



Acknowledgements

I would not have been able to complete this PhD without the support of many people and I would like to express my gratitude to all of them.

First, I am grateful to my supervisors. I am thankful to Linda; her knowledge and enthusiasm for research has inspired me and she has guided and supported me throughout my journey. I am thankful to David for his patience, consistent encouragement, and for helping me to have confidence in my abilities. I am thankful to Carol for her insightful comments, motivation, and immense knowledge. You have all helped me to grow as a researcher and your contributions have been invaluable.

I am thankful to numerous people who have extended their help to me at various phases throughout my work. I am thankful to Anthony Martyr for his expertise and guidance in meta-analyses and for always being approachable whenever I have a question, to Rachel Collins for her contributions to the systematic review, to Bob Woods for his valuable suggestions, to Obi Ukoumunne for his guidance and support in statistical analysis, and to the REACH team for always being there to answer my questions and for their kind words of encouragement.

I am forever grateful to my Mum and Dad who are always there for me and have always encouraged me to do my best. Their love and support has motivated me to succeed and they have helped me to grow into the person that I am today. I am thankful to all of my friends and family who always provide a welcome escape from my studies. I am extremely grateful to Dan, who has always been there to listen to me moan about my struggles and has encouraged me to persevere and do the best that I can. You really are an inspiration to me and I have no idea what I would do without you. Thank you to my sister Olivia, and to Maddie, Ally, Charlotte, Jem, Lora, Kat, Emma, Beth, Katy, Sally, Soph, Cat, and Sharnie, for your unconditional friendship and support. You have all been incredible over the years and really are the best of friends I could ever wish for. I thank you all for maintaining my happiness!

Abstract

Background: Good social connections have been identified as a factor that may be associated with healthy cognitive function in later life. In line with cognitive reserve theory, good social connections may provide mental stimulation through complex interaction with others and hence build cognitive reserve and maintain healthy cognitive function. However, there is considerable inconsistency in findings reported by studies that examine this association. Inconsistency in findings may be attributed to the heterogeneity of concepts potentially associated with social connections and to the variation in approaches to measuring and defining these concepts.

Aims: To assess the association between aspects of social connections and cognitive function in later life. This thesis introduces a novel element by considering the moderating role of cognitive reserve in this association.

Method: A scoping review was conducted to establish which concepts are used within the literature to describe social connections and how these are measured and defined. Next, a systematic review and meta-analysis was conducted to identify evidence regarding the association between social isolation and cognitive function in published studies. Empirical work was conducted using cross-sectional and longitudinal data from the Cognitive Function and Ageing Study–Wales (CFAS-Wales) to determine the associations between social isolation, cognitive reserve, and cognitive function in healthy older people. Extending this approach further, these associations were examined in two groups potentially at risk of social isolation: older people with depression or anxiety and older people living alone. Finally, empirical work was completed using the Platform for Research Online to investigate Genetics and Cognition in Ageing (PROTECT) to assess how satisfaction with social contact may be associated with cognitive function compared to a structural measure of isolation.

Results: A lack of social connections was associated with poor cognitive function in later life. For people with depression or anxiety, these associations may be better explained by mood-related symptoms than social connections. People who live alone in later life were at no greater risk of poor cognitive function compared to those living with others. Satisfaction with social contact was associated with poor cognitive function but a structural measure of social isolation was not.

Conclusions: Social connections play an important role in building cognitive reserve and protecting people against poor cognitive function in later life. People who are vulnerable to social isolation have different needs to those who are less vulnerable. Satisfaction with social contact is often neglected in measures that assess structural aspects of social connections but may be a better predictor of cognitive function.

Table of contents

List of tables

List of figures

List of appendices

Chapter 1: Introduction

1.1 Ageing and cognitive function

Life expectancy worldwide is increasing by at least two years every decade (Mathers, Stevens, Boerma, White & Tobias, 2015). Projections suggest that the percentage of the population over the age of 60 will increase from 12% (around 800 million) in 2016 to 21% (more than 2 billion) in 2050 (United Nations, 2015). The number of older people is expected to exceed the number of children worldwide by 2047 (United Nations, 2015; Wasay, Grisold, Carroll & Shakir, 2016). While this increase in life expectancy is positive and suggests that many people remain healthy and happy in later life (Spijker & MacInnes, 2013) it also presents many challenges.

As people age, they are more likely to live with disability, complex co-morbidities, and chronic health conditions (Murad et al. 2015; Wolff, Starfield & Anderson, 2002). Cognitive decline is the single most feared aspect of ageing (Martin, 2004). Poor cognitive function and dementia account for a significant proportion of healthcare costs and place high economic and social burden on healthcare services (Milne, 2010; Prince et al. 2015; Prince, Comas-Herrera, Knapp, Guerchet & Karagiannidou, 2016; World Health Organization, 2015). It was estimated that the cost of dementia worldwide was US $604 billion in 2010 and this figure is expected to rise to $1 trillion in 2030 (Wimo et al. 2017). Cognitive decline is associated with a reduction in quality of life and more advanced decline or dementia is associated with a loss of independence and inability to complete daily tasks (Harada, Love & Triebel, 2013; Hendrie et al. 2006; Jekel et al. 2015; National Research Council, 2000; Nishiguchi et al. 2013; Seshadri et al. 2011; Wilson, De Leon et al. 2002). Such unprecedented rise in the ageing population and the negative implications of cognitive decline for individuals, families, and the wider society has led to research on preventing poor cognitive function to become a research priority (Fillit et al. 2002; National Research Council, 2000; Peel, Bartlett & McClure, 2004; Wilson, Beckett et al. 2002; World Health Organization, 2015; Zunzunegui, Alvarado, Del Ser & Otero, 2003).

Cognitive health is an important aspect of healthy ageing (Rowe & Khan, 1997). Cognition refers to the set of mental abilities and processes related to knowledge, attention, memory, judgement, decision making, language, and comprehension (Hendrie et al. 2006). Some people maintain good cognitive function in later life whereas others experience significant decline. Cognitive decline can be viewed as a continuum with healthy cognitive ageing, or age-related cognitive decline, on one end of the spectrum and dementia on the other (Deary et al. 2009). Cognitive ageing or age-related cognitive decline refer to the changes people experience in their cognitive abilities with older age (Liverman, Yaffe & Blazer, 2015). Some cognitive domains are more associated with age-related change, such as processing speed, executive functions, memory, and reasoning, which show a decline from middle age onwards, whereas others are less affected by age, such as verbal ability and general knowledge (Christensen, 2001; Deary et al. 2009; Hedden & Gabrieli, 2004; Park & Reuter-

Lorenz, 2009). On the other end of the spectrum, dementia is characterised by more severe decline in cognitive ability that interferes with an individual's ability to live and function independently (DSM-5; McKhann et al. 2011; Seshadri et al. 2011).

Cognitive decline has been described in several ways and multiple constructs have been put forward to capture the stage between healthy cognitive ageing and dementia (Brayne, 2007; Flicker, Ferris & Reisberg, 1991; Petersen et al. 2009; Stephan et al. 2010; Unverzagt et al. 2001). Cognitive impairment no dementia (CIND) refers to cognitive decline that is greater than expected for an individual's age and educational level but does not meet the threshold for dementia (Gauthier et al. 2006). Significant deviation of cognitive function from age- and education- based population norms may result in a diagnosis of mild cognitive impairment (MCI) or dementia (Petersen, Doody et al. 2001). One of the main differences between the criteria for CIND and MCI is that CIND requires either self- or informant- reported cognitive complaints, or impaired neuropsychological test performance (Plassman et al. 2008), whereas MCI requires both (Winblad et al. 2004).

MCI is the most enduring term to describe the stage between healthy cognitive ageing and dementia and has been investigated from a range of perspectives including clinical, imaging, genetic, pathological, and epidemiological (Petersen et al. 2014; Reisberg et al. 1988). MCI is widely understood as an intermediate stage of cognitive impairment between healthy cognitive ageing and dementia that for some individuals represents a transitional phase (Matthews, Stephan, McKeith, Bond & Brayne, 2008; Petersen et al. 2014; Seshadri et al. 2011). Although definitions have developed considerably since the concept was first introduced there is still considerable debate surrounding MCI. One important issue is that the concept is applied differently in research and clinical contexts (Petersen et al. 2014). In this thesis, the focus is on the research context, where MCI is used as a non-clinical description applied according to certain criteria, including moderate cognitive deficits (not dementia), self-reported cognitive complaints, impairment in neuropsychological tests, and preserved basic activities of daily living (ADLs) and instrumental functions (Portet et al. 2006; Winblad et al. 2004).

There is considerable variability observed in the cognitive trajectories of older people and while some retain a high level of cognitive and mental ability from mid- to late- life, others experience decline (Deary et al. 2009; Gow, Pattie, Whiteman, Whalley & Deary, 2007; Jagger et al. 2009; Lindeboom & Weinstein, 2004; Lopez et al. 2007; Wilson, Beckett et al. 2002). For many people an initial decline in cognition does not progress further, and some recover their cognitive ability over time (Gauthier et al. 2006; Mitchell & Shiri-Feshki, 2009; Wilson, Beckett et al. 2002). Changes in cognitive function may be observed in single or multiple domains, and vary in severity (Petersen,

Doody et al. 2001), and there are considerable individual differences in the timing and speed of decline (Christensen, 2001; Deary et al. 2007; Park, O'Connell & Thomson, 2003). The variability observed among trajectories of cognitive ageing and decline provides evidence that significant cognitive decline is not an inevitable part of ageing (Gow et al. 2007).

The nature and trajectory of a progression from cognitive ageing, through to MCI or CIND, to dementia is unclear and the process may not be sequential in all cases (Paúl, Ribeiro & Santos, 2010). People with CIND may progress to dementia at a higher rate than people who are cognitively normal (10-15% per year vs 1-2.5% per year respectively: Edland, Rocca, Petersen, Cha & Kokmen, 2002; Petersen, 2004; Petersen, Stevens et al. 2001). Some estimates suggest that approximately 5-46% of people with MCI will progress to dementia compared to 3% of age-matched individuals without MCI (Gauthier et al. 2006; Mitchell & Shiri-Feshki, 2009; Petersen, Doody et al. 2001; Petersen et al. 2009; Tschanz et al. 2006). One study has suggested that 83% of people with incident dementia received a diagnosis of MCI two years prior to their dementia diagnosis (Aerts et al. 2017). Both people with stable MCI and people who had experienced some reversion in symptoms of MCI were at increased risk of progression to dementia compared to people without MCI at baseline, although this risk was higher in people with stable MCI (Aerts et al. 2017). However, other studies suggest that having MCI does not predict subsequent progression to dementia, and cognitive function improves in many cases (Hong, Zarit & Johansson, 2003; Lindeboom & Weinstein, 2004; Pandya, Clem, Silva & Woon, 2016; Wilson, Beckett et al. 2002).

There are several possible reasons for the variation observed in progression rates from MCI to dementia. One explanation may relate to the criteria used to define MCI. A recent meta-analysis found that 6.7% of people with MCI progressed to dementia annually. However, when different criteria for MCI were considered this rose to 10% per year (Mitchell & Shiri-Feshki, 2009). This reflects how variation in definitions of MCI can account for the disparate findings relating to progression. Intra- and inter- individual variation in the manifestation of cognitive ageing and cognitive decline may be partly associated with differences in experiences across the lifespan (Liverman et al. 2015). Individuals who have higher cognitive ability in early life are more likely to have higher cognitive ability in later life. Early life cognitive ability has been suggested to account for approximately 50% of the variance in late life cognitive ability (Deary, Whalley, Lemmon, Crawford & Starr, 2000; Deary, Whiteman, Starr, Whalley & Fox, 2004). The remaining 50% of the variance is likely to reflect other factors that may also influence cognitive function across the lifespan. These factors may include genetic, demographic, or lifestyle factors. There are several modifiable lifestyle factors that may predict conversion from MCI to dementia, such as diabetes, diet, neuropsychiatric symptoms, educational level, and depression (Cooper, Sommerland, Lyketsos & Livingston, 2015).

Studies often do not account for differences in these factors across individuals and hence variation in the rate of cognitive trajectories may be heterogeneous across study samples. This thesis will investigate factors that may account for the variation in cognitive function in later life and will focus on poor cognitive function rather than dementia risk. Cognitive reserve is a theoretical concept that can account for the role of lifestyle factors and how they may be associated with cognitive outcomes in later life and will be the focus of this thesis.

1.2 Cognitive reserve theory

Cognitive reserve theory suggests that individuals differ in the degree of resilience against age-related brain pathology and hence may show differences in cognitive function at an equivalent level of pathology (Stern 2002, 2012). In Alzheimer's disease, brain pathology may predate any clinical symptoms by up to a decade or more (Hardy & Selkoe, 2002). Cognitive reserve theory was proposed following the observation that cognitively healthy older people were discovered to have advanced Alzheimer's pathology at death (Katzman et al. 1988). The theory proposes that reserve can account for the discontinuity between brain pathology and clinical outcome (Stern, 2012).

Cognitive reserve is discussed in terms of two theoretical models: active and passive. The passive model suggests that individual differences in brain structure may increase tolerance to pathology (Stern, 2012). This model is based around the theory of brain reserve capacity (Satz, 1993) and suggests that individuals with higher brain reserve, or large brain size, are able to sustain more neuropathology or damage to the brain before symptoms of cognitive impairment can be clinically observed. Having greater brain reserve capacity may protect individuals against poor cognitive function because sufficient neural substrate is maintained to ensue normal cognitive function, despite pathology, compared to an individual with smaller brain reserve capacity (Satz, 1993). The passive model recognises that there are individual differences in brain reserve capacity in relation to brain size and neuronal count (Katzman, 1993). This model does not account for differences in cognitive ability and assumes that there is a fixed threshold at which damage will result in clinically observable symptoms of poor cognitive function (Stern, 2002). There is an assumption that a depletion of synapses or type of damage to the brain will have the same effect on each individual. Individual differences only occur in overall brain reserve capacity and damage or pathology to the brain must meet a critical threshold to deplete brain reserve capacity and result in cognitive impairment (Stern, 2009).

The active model suggests that differences in cognitive function are linked to the capacity of an individual to utilize protective mechanisms associated with cognitive abilities built up over the lifespan, and actively compensate for damage caused by pathology (Stern, 2009). Unlike the passive

model, the active model suggests the brain attempts to cope with damage by using cognitive or compensatory processes, or 'cognitive reserve'. Two individuals may have the same amount of brain reserve capacity, but an individual with more cognitive reserve may tolerate more pathology before poor cognitive function is apparent than an individual with less cognitive reserve (Stern, 2002). The active model focuses on the processes that allow an individual to actively maintain function despite damage to the brain. Hence unlike the passive model, the active model does not assume there is some fixed critical threshold at which poor cognitive function may be clinically observed (Stern, 2009).

Cognitive reserve can be built up through a combination of experiences across the lifespan, such as physical exercise, educational level, occupational complexity, and participation in social and cognitively stimulating activities (Baumgart et al. 2015; Clare et al. 2017). These experiences may create a buffer against cognitive decline by enhancing neural connectivity and hence cognitive ability. This can help to protect the individual against the effects of disease pathology in the first instance, but also helps the brain to compensate for damage and recruit alternative neural pathways when required (Siedlecki et al. 2009). This may reduce or delay the manifestations of cognitive impairment and protect against the effects of pathological processes (Siedlecki et al. 2009). Some lifestyle factors have been associated with higher or lower risk of developing cognitive impairment and dementia in later life. For example, smoking is associated with an increased risk (Anstey, von Sanden, Salim & O'Kearney, 2007), whereas regular exercise (Beydoun et al. 2014; Plassman, Williams, Burke, Holsinger, & Benjamin, 2010), a healthy diet, moderate alcohol consumption (Kim et al. 2012), and engaging in cognitive and social activities (Bennett, Arnold, Valenzuela , Brayne & Schneider, 2014; Kuiper et al. 2016) are associated with a lower risk of cognitive impairment and dementia (Di Marco et al. 2014). Increasing protective factors and reducing risk factors should enhance cognitive reserve and make people more resilient in terms of their cognitive health (Fratiglioni & Wang, 2007).

As cognitive reserve is a theoretical construct and cannot be measured directly, proxy measures are often used to represent experiences that may build reserve across the lifespan. Educational level can be used to represent early-life cognitive activity (Stern, Alexander, Prohovnik & Mayeux, 1992; Stern et al. 1994), occupational complexity can represent mid-life cognitive activity (Richards & Sacker, 2003; Stern et al. 1994), and engagement in cognitively stimulating activity can represent late-life cognitive activity (Wilson, De Leon et al. 2002). The use of individual proxy measures to index cognitive reserve has been criticised as these indicators typically relate to a specific period of life. Cognitive reserve is built up through a combination of experiences across the lifespan rather than one fixed experience (Nucci, Mapelli, & Mondini, 2012; Rodríguez, Torrellas, Martín, & Fernandez,

2011). Although individual proxy measures may be related to some extent, their contribution to building reserve across the lifespan may be unique and each is likely to accrue collectively and contribute to reserve (Fratiglioni & Wang, 2007; Tucker & Stern, 2011). Measures that combine proxy measures of cognitive reserve relevant across the lifespan are preferable as they can account for the variance in reserve built at different stages of life (Nucci et al. 2012; Tucker & Stern, 2011; Valenzuela & Sachdev, 2007). This approach is taken in the measure of cognitive reserve used in this thesis.

Understanding how the lifestyle factors that build cognitive reserve may account for people transitioning from healthy cognitive ageing, to MCI, or dementia is necessary to develop interventions to prevent people from crossing the threshold to unhealthy cognitive decline (Gow et al. 2007). The advantage of this approach is that if successfully implemented, interventions may reduce risk factors and enhance protective factors within an individual's lifestyle. This should maintain good cognitive function and may prevent or delay the onset of cognitive problems in later life (Gow et al. 2007; Wirth, Haase, Villeneuve, Vogel & Jagust, 2014). One modifiable lifestyle factor that may build cognitive reserve and contribute to healthy cognitive function in later life is social connections. The nature of social connections in later life are discussed in the following section.

1.3 Social connections in later life

There is a range of concepts associated with social connections including structural, functional, and appraisal aspects (Antonucci, 1990; Victor, Scambler, Bond & Bowling, 2000). Each of these concepts are examined in more detail in Chapter 3, a scoping review of the concepts used to assess social connections in the literature. Briefly, marital status and living situation are basic socio-demographic indicators that can provide information regarding an individual's social context (Gow, Corley, Starr & Deary, 2013; Paúl et al. 2010). Social network refers to the number of people, including family and friends, within the social network (Wilson et al. 2015; Zunzunegui et al. 2003), while social activity and social isolation relate to the level of engagement in social activities and with others in the wider community to maintain social relationships (Nicholson Jr, 2009; Paillard-Borg, Fratiglioni, Winblad & Wang, 2009). Social support relates to the support that can be obtained from contacts within the social network (Ellwardt, Aartsen, Deeg & Steverink, 2013; Li & Zhang, 2015) and loneliness relates to individuals' levels of satisfaction with their social connections (Victor, Scambler, Bowling & Bond 2005).

Maintaining social connections has been identified as an important aspect of healthy ageing (Rowe & Khan, 1997). Having poor social connections has been associated with a range of negative outcomes, including premature death (Holt-Lunstad & Smith, 2012; Holt-Lunstad, Smith & Layton,

2010; Steptoe, Shankar, Demakakos & Wardle, 2013), greater vulnerability to physical health conditions (Boden-Albala, Litwak, Elkind, Rundek & Sacco 2005; Cornwell & Waite, 2009; Ertel, Glymour & Berkman 2008; Tomaka, Thompson & Palacios, 2006; Uchino, 2006; Umberson & Montez, 2010), lower wellbeing (Adams, Leibbrandt & Moon, 2011; Olesen & Berry, 2011; Tomaszewski, 2013), poorer quality of life (Bowling, 2005; Scharf, Phillipson & Smith, 2004), and reduced independence (Jekel et al. 2015; Liverman et al. 2015). There is also some evidence that social isolation is associated with poorer cognitive function (Fratiglioni, Paillard-Borg & Winblad 2004). Given the influence of social connections on various health outcomes, ensuring that older people remain well-connected in later life is important for promoting healthy ageing.

Although maintaining social connections in later life may benefit health outcomes, people face changes in their social environments as they get older, and the nature of social relationships change with age (George, 1996; Wenger, 1997). Social network size typically reduces with older age (Glass, De Leon, Seeman & Berkman, 1997; Turner & Marino, 1994; Zunzunegui et al. 2003). This may be the result of life course transitions, such as the death of a spouse or other relatives and friends, adult children moving away, retirement, or residential changes (Bordone & Weber, 2012; Carstensen, 1992; Cornwell, 2009; Cornwell & Waite 2009; de Jong Gierveld & Havens, 2004; Donnelly & Hinterlong, 2009; Litwin & Stoeckel, 2013; Perry & Pescosolido, 2012; Schafer, 2013). This may reduce the number of people within the social network and limit opportunities for social contact, and hence the possibility of social isolation and feelings of loneliness may increase (Carstensen, 1992; van Tilburg, 1995). Poor health and mobility may limit an individual's ability to engage with others (Cattell et al. 2001). The prevalence of social isolation and loneliness has been found to change over time (Wenger & Burholt, 2004). Increasing age, retirement migration, deterioration in health, childlessness, caring for a spouse, and the death of a spouse or other close family members were some factors identified as increasing social isolation and feelings of loneliness in later life (Wenger & Burholt, 2004). These changes to social networks may have a negative impact on quality of life, wellbeing, and physical and mental health (Adams et al. 2011; Cornwell & Laumann, 2015; Scharf et al. 2004).

Several social-psychological theories have been proposed to account for the reduction in social network size in later life. Many of these theories, such as social exchange theory, stipulate that individuals will only continue to engage in social exchanges with others if the benefits of interaction are not outweighed by the costs (Dowd, 1975). This is reiterated by socioemotional selectivity theory which posits that individuals become more selective with age and therefore will invest more time in emotionally meaningful goals and activities in order to maximise social and emotional gains and minimise risk (Carstensen, 1992; Fredrickson & Carstensen, 1990). Likewise, selective optimisation

and compensation theory suggests that individuals are less able to maintain competence in all types of social activities in older age and therefore must selectively narrow their range of activities and interactions to achieve optimal social contact (Baltes & Baltes, 1990; Freund & Baltes, 1998). Together, these theories suggest that individuals will selectively maintain social relationships that are rewarding and optimise or enrich their lives, yet will diminish interactions with people in peripheral networks (Carstensen, Fung & Charles, 2003).

Although social networks tend to decrease in size with age, there is some evidence to suggest that people are more satisfied with their social connections in later life and find the interactions they have with their social contacts more rewarding (Fingerman, Hay, & Birditt, 2004; Lansford, Sherman, & Antonucci, 1998). For example, older people report experiencing more positive feelings and interactions with their spouse than reported by younger people (Charles & Piazza, 2007). People also report less frequent negative social exchanges with age (Fingerman et al. 2004; Rook, 2003). This can be accounted for by an increase in selectivity for social relationships to achieve optimal social contact (Carstensen et al. 2003; Dowd, 1975; Freund & Baltes, 1998). Although people do experience the loss of close social contacts, for many people the number of close confidants and level of social support received remains the same with age (Ertel, Glymour, & Berkman, 2009; Field & Minkler, 1988; Schnittker, 2007). Older people gain new social ties and close confidants, and this has been associated with improvements in physical and mental health (Cornwell & Laumann, 2015). Furthermore, the loss of ties from social networks is associated with physical, but not psychological wellbeing (Cornwell & Laumann, 2015). People may expect changes in their social networks to occur as they grow older and hence may be more prepared to deal with them (Achenbaum & Bengstom, 1994; Cornwell & Waite, 2009). For example, it has been suggested that older people are able to adjust their levels of social interaction or their personal expectations about the types of social relationships that are feasible (Burholt & Scharf, 2013; Peplau & Caldwell, 1978; Wenger, Davies, Shahtahmasebi & Scott, 1996). Hence, a reduction in social network size may not necessarily lead to social isolation and feelings of loneliness (Cornwell & Waite, 2009).

Social connections may influence health through several mechanisms. One mechanism may be the diffusion of knowledge regarding healthy lifestyles and behaviours through social networks. Social networks provide social influence, which refers to the mechanism through which an individual can obtain guidance about health related behavioural norms through comparisons with others in their social network (Marsden & Friedkin, 1994). The dissemination of this information through social networks can influence lifestyle choices that are maintained through informal social control and may protect against poor cognitive function (Berkman, 1985; Berkman & Glass, 2000; Cassel, 1976). However, social networks may also promote unhealthy lifestyle behaviours and risk factors for poor

health, such as smoking, high alcohol consumption, or an unhealthy diet (Christakis & Fowler, 2007). An alternative mechanism may be that having plentiful social connections and being well-integrated with the wider community may evoke positive psychological states, such as a sense of security, purpose, belonging, and acknowledgement of self-worth (Cohen, Underwood & Gottlieb, 2000). Subsequently, these positive psychological states may benefit health and cognitive outcomes, due to an increased motivation for self-care (e.g. regular exercise, not smoking, moderate alcohol consumption), higher feelings of wellbeing, and greater perceived quality of life which have been associated with cognitive function (Cohen et al. 2000). It is also possible that good social connections may be an indicator of a healthy lifestyle in general, which may be linked with better cognitive function (Fratiglioni et al. 2004). Furthermore, being integrated with the wider community and engaging in frequent social contact may enhance the perception of being able to access social support (Lin, Ye & Ensel, 1999). Higher perceived availability of social support may reduce undesirable emotional, behavioural, and physiological responses to adverse life events (Lin et al. 1999). This may reduce the stress response to undesirable events, which has also been associated with an increased risk of poor cognitive function (Cacioppo & Hawkley, 2009; Wilson et al. 2003). Finally, cognitive reserve theory suggests that social connections may enhance cognitive reserve and benefit cognitive function. This thesis focuses on cognitive reserve as a possible mechanism and the next section outlines how social connections may be associated with cognitive reserve and cognitive function.

1.4 Social connections, cognitive reserve, and cognition in later life

Based on cognitive reserve theory, good social connections may build cognitive reserve both directly and indirectly through a number of mechanisms. Maintaining a social network requires constant monitoring of the interactions and reciprocal exchanges with each person in the social network, along with the cognitive skills and strategies used to create, maintain, and modify these contacts (Watson & Andrews, 2002). Having a social network requires memory capacity, as maintenance of a large number of social contacts requires memory for the nature of each relationship (Byrne & Whitten, 1989; Jolly, 1996). A larger number of social ties, including friends, family, and neighbours, and frequent engagement with these ties across the lifespan, and particularly in later life, increases the complexity of the social network and the level of mental stimulation. These processes are cognitively effortful and provide mental stimulation and hence may build reserve through the development of alternative cognitive strategies, or increases in neural growth and synaptic density, thus buffering against pathological processes (Bennett, Schneider, Tang, Arnold & Wilson, 2006; Fratiglioni et al. 2004; Fratiglioni, Wang, Ericsson, Maytan & Winblad, 2000). In addition, social connections may influence cognitive function and cognitive reserve indirectly through the type of

activities engaged in during social contact. For example, if an individual chooses to engage in cognitively stimulating activity during a social interaction, such as visiting a museum or playing a game, this may indirectly contribute to building reserve and protect against poor cognitive function (Aartsen, Smits, van Tilburg, Knipscheer & Deeg, 2002; Toepoel, 2013).

In support of cognitive reserve theory, evidence from large observational cohort studies suggests that people with poor social connections in later life have poor cognitive function (Barnes, De Leon, Wilson, Bienias & Evans, 2004; Barnes et al. 2007; Bassuk, Glass & Berkman, 1999; Béland, Zunzunegui et al. 2003; Bennet et al. 2006; Conroy, Golden, Jeffares, O'Neill & McGee, 2010; Crooks, Lubben, Petitti, Little & Chiu, 2008; DiNapoli, Wu & Scogin, 2014; Glei et al. 2005; Golden, Conroy & Lawlor, 2009; Haslam, Cruwys & Haslam, 2014; Holwerda et al. 2012; Hughes, Flatt, Fu, Chang & Ganguli, 2013; James, Wilson, Barnes & Bennett, 2011; Niti, Yap, Kua, Tan & Ng, 2008; Paillard-Borg et al. 2009; Shankar, Hamer, McMunn & Steptoe, 2013; Singh-Manoux, Richards & Marmot, 2003; Wilson, Krueger et al. 2007; Yaffe et al. 2009; Zunzunegui et al. 2003). However, there is some inconsistency in findings and some studies report no association between social connections and late-life cognitive function (Albert et al. 1995; Bosma et al. 2002; Elwood et al. 1999; Glei et al. 2005; Golden et al. 2009; Gow et al. 2007; Ho, Woo, Sham, Chan & Ashley, 2001; Holwerda et al. 2012; Hsu, 2007; Karp et al. 2005; O'Luanaigh et al. 2012; Paúl et al. 2010; Saczynski et al. 2006; Simning, Conwell & van Wijngaarden, 2014; Wang, He & Dong, 2015; Wilson, Krueger et al. 2007). This thesis will explore the association between social connections, cognitive reserve, and cognitive function in later life using a large observational cohort study, and will consider the reasons for conflicting findings in existing empirical work.

Evidence from imaging studies provides further support to suggest that social connections may enhance cognitive reserve. Empirical work using voxel-based morphometry, gross stereological analysis, and magnetic resonance imaging has found that larger and more complex social networks are associated with larger volume of the amygdala and the orbitofrontal cortex (Bickart, Wright, Dautoff, Dickerson, & Barrett, 2011; Bickart, Hollenbeck, Barrett & Dickerson, 2012; Hampton, Unger, Von Der Heide & Olson, 2016; Kanai, Bahrami, Roylance & Rees, 2011; Lewis, Rezaie, Browne, Roberts, & Dunbar, 2011; Powell, Lewis, Roberts, García-Fiñana, & Dunbar 2012; Von Der Heide, Vyas & Olson, 2014; Zou et al. 2016). A higher number of white matter lesions are observed in the brains of people who engage in less social activity (Bickart et al. 2011; Kwak, Joo, Youm & Chey, 2018). Larger grey matter density in other brain regions that are implicated in adaptive social behaviours have also been associated with larger social networks, such as the subgenual anterior cingulate cortex (Bickart et al. 2011) and ventromedial prefrontal cortex (Lewis et al. 2011). Together

these findings suggest that good social connections may be associated with greater brain reserve capacity, and thus implicates a role for cognitive reserve.

Findings from randomized controlled trials also support that social connections may contribute to building cognitive reserve (Wang, Xu & Pei, 2012; Yaffe & Hoang, 2013). Several trials that aimed to enhance social connections in community dwelling people have reported beneficial effects on cognitive function and an increase in brain volume for people in intervention compared to control groups (Dodge et al. 2015; Mortimer al. 2012; Pitkala, Routasalo, Kautiainen, Sintonen & Tilvis, 2011). This suggests that interventions to enhance social connections may contribute to build cognitive reserve and hence may benefit cognitive function. However, another randomized controlled trial reported no beneficial effect of an intervention to enhance social connections on cognitive function, although only five participants were allocated to the social intervention and so findings are likely to be underpowered and should be treated with caution (Park et al. 2014). It has been suggested that interventions focusing on physical and cognitive activity are more effective for enhancing cognitive function than social interventions (Mortimer al. 2012; Pitkala et al. 2011). However, it is possible that interventions to enhance physical and cognitive activity also involve social contact although this may not be the primary aim. The interventions in Mortimer et al. (2012) and Pitkala et al. (2011) involved exercising with others and engaging in games with others to enhance physical and cognitive activity. It is possible that the social elements of these interventions contributed to improvements in cognitive function (Aartsen et al. 2002; Toepoel, 2013). This reflects the difficulty of disentangling the specific contributions of lifestyle factors to cognitive function (Global Council on Brain Health, 2017) and suggests that other lifestyle factors may be implicated in the association between social connections, cognitive reserve, and cognitive function.

There are several methodological issues that may account for the discrepancy in findings across studies that assess the association between social connections and late-life cognitive function in observational cohort studies. Firstly, there are a wide range of concepts associated with social connections that range from structural (e.g. marital status, living situation, social networks, social isolation, social engagement), functional (social support), and appraisal (loneliness) aspects (Antonucci, 1990). Many of these concepts have distinct definitions yet are used interchangeably across studies. Approaches to defining and measuring these concepts varies considerably across studies which may further contribute to conflicting findings (Courtin & Knapp, 2017; Victor et al. 2000). It may be that each concept is differentially associated with cognitive function. These issues are discussed further in Chapter 3 which outlines each of the different concepts associated with social connections and how these concepts are measured and defined.

An additional methodological issue is reverse causation; the possibility that poor social connections are observed as a result of prodromal cognitive symptoms that have been reported in the early stages of dementia (Berger, Small, Forsell, Winblad & Bäckman, 1998; Cloutier, Chertkow, Kergoat, Gauthier & Belleville, 2015; Masliah & Salmon, 2016; Small, Fratiglioni, Viitanen, Winblad & Bäckman, 2000). Cognitive problems may result in difficulty maintaining social connections (Zunzunegui et al. 2003) and this is particularly important given that abnormal cognitive function has been reported between five (Gauthier et al. 2006) and nine (Amieva et al. 2005; Mahncke, Bronstone & Merzenich, 2006) years prior to diagnosis of Alzheimer's disease. Many studies attempt to control for this by excluding people with poor cognitive function or dementia at baseline (e.g. Barnes et al. 2004; James, Wilson et al. 2011; Shouse, Rowe & Mast, 2013; Zunzunegui et al. 2003). However, these attempts can be criticised, as the earliest baseline assessments are usually completed around the age of 65 years. This may be insufficient if cognitive decline is already apparent by the first assessment (Phillipson, Magee, Jones, Reis & Skaldzien, 2015; Ross et al. 1997). Likewise, the follow-up period in longitudinal studies must be sufficient to reduce the possibility of reverse causation (Deary et al. 2009). The empirical work in this thesis accounts for the possibility of reverse causation by excluding people with cognitive impairment or dementia at baseline.

In addition to these methodological issues, there are several other factors that may be implicated in the association between social connections and cognitive function. This thesis will consider some of these factors, specifically depression or anxiety, living situation, and satisfaction with social contact, and aims to determine whether accounting for these factors may reduce the variance in reported findings.

1.5 Factors that may influence the association between social connections and cognitive function

There are numerous factors that may be associated with social connections and cognitive function. For example, social factors, such as a low socioeconomic status, lack of money, poor transportation links, lack of opportunity and facilities in the community for social engagement, living alone or in rural areas, and geographical distance from family and friends (Bowling & Stafford, 2007; Findlay, 2003; Rosso, Taylor, Tabb & Michael, 2013; Wen, Hawkley & Cacioppo, 2006), health factors, such as poor mental or physical health (Angermeyer & Matschinger, 2003; Oliveira, Esteves & Carvalho, 2015), and person-level factors, such as personality and individual differences in preference for social contact (Bolger & Eckenrode, 1991; Finch & Graziano, 2001; Suurmeijer et al. 2005), may influence social connections and hence cognitive function. Equally, these factors may be independently associated with cognitive function. The research presented in this thesis will consider how depression or anxiety, living situation, and satisfaction with social contact may influence the association between social connections, cognitive reserve, and cognitive function in later life.

Depression and anxiety

Depression is a mood disorder that is common amongst older people and is characterised by symptoms of sadness, loss of interest, negative self-regard, and changes in thinking, sleep, appetite, and energy levels. Symptoms must manifest for more than two weeks and interfere with daily living before a clinical diagnosis can be made (DSM-5). Late-life depression has a huge societal impact, given its association with a range of medical conditions, including an increased risk of mortality and accelerated cognitive and functional decline (Alexopolous, 2005; Almeida, Alfonso, Hankey & Flicker, 2010; Austin et al. 1992; McDermott & Ebmeier, 2009). Poor cognitive function is common in late-life depression and often persists after the remission of mood-related symptoms (Alexopoulos, Meyers, Young, Mattis, & Kakuma, 1993; Alexopoulos, Young & Meyers, 1993; Bhalla et al. 2006). Depression is associated with poor function in specific cognitive domains, such as working memory, information processing speed, attention and inhibition, executive function, and visuospatial memory (Butters et al. 2000; Butters et al. 2004; Nebes et al. 2001; Nebes et al. 2002), and may be a risk factor for cognitive impairment and Alzheimer's disease (Diniz, Butters, Albert, Dew & Reynolds, 2013; Goveas, Espeland, Woods, Wassertheil-Smoller & Kotchen, 2011; Gulpers et al. 2016; Ownby, Crocco, Acevedo, John & Loewenstein, 2006; Rapp et al. 2006). However, findings are inconsistent and some studies report that depression may accompany poor cognitive function, but does not necessarily precede poor cognitive function (Panza et al. 2008; Richard et al. 2013; Wilson, Schneider et al. 2007).

Generalised anxiety disorder is another common mental health condition in later life and is characterised by at least six months of excessive worry that is difficult to control, irritability, difficulty concentrating, restlessness, and sleep disturbances (Aggarwal, Kunik, & Asghar-Ali, 2017; DSM-5). Anxiety has been associated with poor function in specific cognitive domains, including executive function and memory (Beaudreau & O'hara, 2009; Pietrzak et al. 2012; Yochim, Mueller & Segal, 2013) and an increased risk of cognitive decline and dementia (Burton, Campbell, Jordan, Strauss & Mallen, 2012; Gallacher et al. 2009; Palmer et al. 2007; Potvin, Forget, Grenier, Préville & Hudon, 2011; Sinoff & Werner, 2003; Wilson, Begeny, Boyle, Schnieder & Bennet, 2011). However, results are inconclusive and not all studies report this association (Andreescu et al. 2014; Bunce, Batterham, Mackinnon & Christensen, 2012; Okereke & Grodstein, 2013; Potvin et al. 2012; Potvin et al. 2013).

The finding that depression and anxiety may be risk factors for poor cognitive function has important implications for public health. It has been estimated that a reduction in the prevalence of depression by 10% could result in 68,000 fewer cases of Alzheimer's disease in the USA, and up to 326,000 fewer cases worldwide (Barnes & Yaffe, 2011). It is therefore important to consider psychosocial

factors that may contribute to maintaining symptoms of depression and anxiety and that may also be associated with cognitive function.

Being socially well-connected is one factor that may reduce symptoms of depression or anxiety (Diener & Seligman, 2004; Kawachi & Berkman, 2001; Kuchibhatla, Fillenbaum, Hybels & Blazer, 2012; Santini, Koyanagi, Tyrovolas, Mason & Haro, 2015; Sonnenberg et al. 2013). A lack of social contact, close social relationships, or a trusted confidant has been associated with lower well-being, poorer life satisfaction, and higher levels of depression or anxiety (Antonucci, Lansford & Akiyama, 2001; Baumeister & Leary, 1995; Cacioppo, Hawkley & Thisted, 2010; Diener & Seligman, 2004; García-Peña et al. 2013; Litwin, 2012; Prince, Harwood, Blizard, Thomas, & Mann, 1997; Segrin, 2000; Trivedi, Morris, Pan, Grannemann & Rush, 2005). People with depression or anxiety may have poorer social relationships and interactions compared to people without depression or anxiety due to symptoms of, or underlying reasons for, illness (Luanaigh & Lawlor, 2008; Segrin, 2000). Evidence suggests that people with depression or anxiety may perceive their relationships more negatively and hold negative expectations for social interaction which may reduce the amount of social contact they engage in (Cacioppo & Hawkley, 2009; Granerud & Severinsson, 2006). Engaging in less social contact may exacerbate social isolation and feelings of loneliness (Domènech-Abella et al. 2017; Luanaigh & Lawlor, 2008; Yaacob, Juhari, Talib & Uba, 2017). Therefore, people with depression or anxiety may be more vulnerable to experiencing feelings of social isolation and loneliness.

The relationship between social connections, cognitive function, and depression or anxiety is complex as poor social connections (Barnes et al. 2007; Fratiglioni et al. 2004; Kuiper et al. 2016; Zunzunegui et al. 2003) and symptoms of depression or anxiety (Aggarwal et al. 2017; Andreescu et al. 2014; Okereke & Grodstein, 2013; Pietrzak et al. 2012; Potvin et al. 2011; Potvin et al. 2013; Richard et al. 2013; Yochim et al. 2013) are independently associated with poor cognitive function. People with depression or anxiety may already be at greater risk of poor cognitive function due to their mental health, and this risk may be enhanced by the possibility of being more vulnerable to social isolation due to mood-related symptoms. The research presented in this thesis aims to consider how the association between social connections and cognitive function may be influenced by depression or anxiety. People who live alone may also be at greater risk of poor social connections and this is considered in the following section.

Living situation

Living alone is a common experience for many people in later life and recent estimates suggest that 31% of those aged 65-74, and 50% of those over 75 years, live alone (Evandrou, Falkingham, Rake & Scott, 2001; Office for National Statistics, 2018; Victor et al. 2000). Living alone is also more common

for women than men (Office for National Statistics, 2018; Victor et al. 2000). The number of people living alone in the UK is expected to increase due to the ageing population, decreased family sizes, and policies that promote ageing at home rather than institutional care (Genet et al. 2011; Hays, 2002; Murphy & Grundy, 2003; The New Policy Institute, 2006). Living alone may present challenges in later life, including poor physical or mental health (Buber & Engelhardt, 2008; Kharicha et al. 2007), social relationships (Victor, Scambler & Bond, 2000), or cognitive function (van Gelder et al. 2006).

Living alone in later life has been associated with an increased risk of poor cognitive function (Gow et al. 2007; Gow et al. 2013; van Gelder et al. 2006; Yaffe et al. 2009) and dementia (Fratiglioni et al. 2000; Holwerda et al. 2012). For people who live alone, the risk of cognitive decline is twofold compared to those who live with others and this risk is reported to be is 3.5 times higher for men who live alone in both mid- and late- life (van Gelder et al. 2006). In contrast, living with others, such as a spouse or adult children, has been associated with maintained cognitive function in later life (Bordone & Weber, 2012; Gow et al. 2007; Gow et al. 2013; van Gelder et al. 2006). Living alone may also influence social relationships and has been associated with increased feelings of loneliness (Newall, Chipperfield & Bailis, 2014; Victor et al. 2005) and social isolation (de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Havens, Hall, Sylvestre & Jivan, 2004; Kobayashi, Cloutier-Fisher & Roth, 2009). Social isolation and feelings of loneliness have also been associated with poor cognitive outcomes (DiNapoli et al. 2014; Holwerda et al. 2012; Wilson, Krueger et al. 2007). Hence, people who live alone in later life may be more vulnerable to social isolation and feelings of loneliness which may exacerbate the risk of poor cognitive function.

From a cognitive reserve perspective, living with others may enhance cognitive function through frequent interaction with others (van Gelder et al. 2006). Social interaction is cognitively stimulating and requires input from complex cognitive processes and therefore may contribute to maintaining cognitive function (Barnes et al. 2004; Bassuk et al. 1999; Berkman, Glass, Brissette & Seeman, 2000; Fratilgioni et al. 2004; Zunzunegui et al. 2003). People who live alone and particularly in later life may have less opportunity for social contact and hence may receive less cognitive stimulation from engaging in social interaction with others (Gow et al. 2007). Findings relating to the association between living alone and cognitive function are conflicting (Conroy et al. 2010; Gow et al. 2007; Gow et al. 2013; Mahoney, Einser, Havinghurt, Gray & Palta, 2000; Mazzuco, Meggiolaro, Ongaro & Toffolutti, 2016; van Gelder et al. 2006; Wang et al. 2015; Yaffe et al. 2009; Yeh & Liu, 2003) and do not consider the role of underlying mechanisms in this association. Therefore, this thesis aims to examine the association between living situation (alone or with others), cognitive reserve, and cognitive function. Satisfaction with social contact is another factor that may be implicated in the

association between social connections and cognitive function and is discussed in the following section.

Satisfaction with social connections

Individuals may differ in their preferences for the level of social activity and contact they engage in. Structural measures of social connections typically assess the quantity and frequency of social contact and social activity (Hawkley et al. 2008). A detailed consideration of the different approaches to assessing social concepts is presented in Chapters 3 and 4. Briefly, measures typically assume that a larger social network and frequent engagement in a range of social activities is beneficial to cognitive function (Fratiglioni et al. 2004; Zunzunegui et al. 2003). However, some individuals may function better and be satisfied with fewer social contacts and less engagement in social activity. These individuals may be identified as having poor social connections by structural measures which use cut-scores to determine how well-integrated an individual is based on a count of structural indicators. Yet this level of integration may be satisfactory for the individual and sufficient to provide cognitive stimulation comparable to an individual who may prefer to have a wider social network and engage in more social activity.

Several factors may explain why some people have a preference for less social contact. This may be due to personal factors, such as a preference for smaller social groups, or due to differences in an individual's aims and expectations for engaging in social activity. This may result in the same activity involving greater social demands for one individual compared to another (Aartsen et al. 2002; Toepoel, 2013). Personality may also influence preferences for social contact (Tov, Nai & Lee, 2016). Evidence suggests that extraverts may have larger social networks and interact with a wider range of social contacts (Suurmeijer et al. 2005) than people with neurotic personalities, or who are less extraverted (Bolger & Eckenrode, 1991; Finch & Graziano, 2001). Differences in personality type may therefore influence social connections and hence may indirectly influence cognitive function. People with depression or anxiety may also have differences in preference for social contact. Too much social integration may exacerbate symptoms of depression or anxiety as a result of experiencing, or perceiving, labelling and stigma from others which may heighten hypervigilance to social threats and negative rumination following social interactions (Angermeyer & Matschinger, 2003; Cacioppo & Hawkley, 2009; Granerud & Severinsson, 2006; Kashdan & Roberts, 2007; Oliveira et al. 2015; Wai & Bond, 2004). In such cases, attempting to increase level of social connectedness may be harmful to the individual, and could lead to a deterioration of mental health or accelerated cognitive decline, rather than have a positive impact on the individual.

Previous research has found that an individual's perceptions of their social context are important and may be associated with health outcomes. DiNapoli et al. (2014) assessed the relationship between social isolation and cognitive function and reported that a measure of satisfaction with social contact accounted for nearly double the variance in cognitive function compared to a structural measure of social isolation. Higher levels of satisfaction with social contact have also been associated with better cognitive function (Hughes, Andel, Small, Borenstein & Mortimer, 2008; Yeh & Liu, 2003). Infrequent social contact may not necessarily increase the risk of poor cognitive function if the individual rates this level of social contact as satisfying (Fratiglioni et al. 2000; Gow et al. 2013). This further supports the view that perceptions of social contexts may influence cognitive function in later life. Failing to account for satisfaction with social contact may partly account for the inconsistency in findings relating to the association between structural measures of social connections and cognitive function. This thesis aims to examine this possibility.

1.6 Research questions

The research evidence summarised advocates that maintaining cognitive function is an important aspect of healthy ageing. Cognitive reserve theory suggests that a range of lifestyle factors across the lifespan may cumulatively build reserve and contribute to maintaining good cognitive function. Being socially well-connected is another important aspect of healthy ageing and may enhance cognitive reserve and benefit cognitive function. However, findings regarding the association between social connections and cognitive function are conflicting. This may be due to the wide range of concepts associated with social connections. In addition, there are several other factors, such as depression or anxiety, living situation, and satisfaction with social contact, which may be associated with social connections and hence may influence the association with cognitive function. The research presented in this thesis aims to assess the association between social connections and cognitive function in later life, and extends previous work by examining the moderating role of cognitive reserve in this relationship. It also considers how depression or anxiety, living situation, and satisfaction with social contact may influence these associations, which has not been explored in previous work. This will be achieved through the following research questions:

1. How are concepts associated with social connections conceptualised and measured in the literature relating to cognitive function in later life?
2. What is the association between social isolation, cognitive reserve, and cognitive function in healthy older people?
3. Does the association between social isolation, cognitive reserve, and cognitive function differ for older people who are more at risk of social isolation (i.e. people with depression or anxiety and people who live alone)?

4. Are structural measures of social isolation consistent with measures of satisfaction with social contact and what is their association with cognitive function in later life?

1.7 Structure of the thesis

This thesis consists of this general introduction followed by eight chapters: a chapter outlining methodological details, a scoping review, a systematic review and meta-analysis, four empirical papers, and the general discussion. Versions of Chapters 4–8 are based on journal articles that have been published or have been submitted for publication. These have been reformatted for inclusion in the thesis but are similar to the published or submitted versions. A summary of the content of each chapter follows below.

Chapter 2: Methodology

This chapter presents an overview of the methodology of the two large cohort studies from which data used in the research presented in the thesis have been taken: the Cognitive Function and Ageing Study–Wales (CFAS-Wales) and the Platform for Research Online to investigate Genetics and Cognition in Ageing (PROTECT). It includes details of the design, participants and recruitment, study procedures, interviews, data access and management, and statistical methods used in the thesis.

Chapter 3: Social connections and cognition in later life: a scoping review

This chapter presents a scoping review and concept analysis focusing on social connections and cognitive function in later life. This was conducted because initial reading of the literature revealed there are numerous concepts relating to social connections used in the literature and approaches to defining and measuring these concepts appeared inconsistent across studies. The purpose of the scoping review was to clarify definitions of social concepts and examine methodological approaches to the assessment of structural, functional, and appraisal aspects of social connections. Studies are included that assess aspects of social contexts and the relationship with cognitive function. One limitation of approaches to assessing structural concepts was that the measures neglected to consider satisfaction with social contact which may be differentially associated with cognitive outcomes. Having conducted this review, I decided that the focus for the thesis would be social isolation, as findings relating to this concept and the association with cognitive function were less well established compared to other concepts.

Chapter 4: Social isolation and cognitive function in later life: a systematic review and meta-analysis

Having decided that social isolation would be the focus of this thesis, the next step was to review existing evidence about the relationship between social isolation and cognitive function in later life.

Chapter 4 presents a systematic review and meta-analysis of longitudinal cohort studies that assess this association. The review builds on the scoping review in Chapter 3 by quantifying the association between social isolation and cognitive function and summarising different methods of assessing social isolation in greater depth. The review also assesses the contribution of specific indicators of social isolation on cognitive function. The review suggested that there were conflicting findings among included studies, but overall social isolation was associated with poor cognitive function in later life. Few of the studies identified by the systematic review used standardised measures of social isolation or considered potential mechanisms underpinning the association. Measures also used standardised cut-points to determine whether an individual is isolated or not which cannot account for individual differences in preference for social contact. Hence the nature of the association between social isolation and cognitive function, along with potential mechanisms and other associated factors, is investigated further in Chapters 5–8.

Chapter 5: Social isolation, cognitive reserve, and cognition in later life

This chapter presents an empirical paper that assesses the association between social isolation and cognitive function using cross-sectional and longitudinal data from CFAS-Wales, a population-representative cohort of people over the age of 65. Using the CFAS-Wales cohort is a particular strength of the empirical work in this thesis and can provide robust findings that may improve on existing evidence. This study builds on previous research by considering the role of cognitive reserve in this association. These associations were first assessed in a group of community-dwelling older people without cognitive impairment, dementia or depression, to determine how social isolation may influence cognitive function in a relatively 'healthy' sample.

The next two chapters consider these associations in groups of people who may be more vulnerable to social isolation and in particular people with depression or anxiety and people who live alone. These people may experience social connections differently which may increase their risk of being isolated. Given that social isolation was found to be associated with poor cognitive function in Chapters 4 and 5, this greater vulnerability to being socially isolated may also increase their risk for poor cognitive function and hence warrants further investigation.

Chapter 6: Social isolation, cognitive reserve, and cognitive function in older people with depression or anxiety

Chapter 6 presents an empirical paper based on the same theoretical model used in Chapter 5 but applied to a sample of people from the CFAS-Wales cohort experiencing depression or anxiety, who may be at greater risk of social isolation. This study uses cross-sectional and longitudinal data to

determine whether the associations between social isolation, cognitive reserve, and cognitive function are the same as in the 'healthy' older sample examined in Chapter 5. This work is novel as these associations have not been considered in people with depression or anxiety before.

Chapter 7: Living alone and cognitive function in later life

Chapter 7 is an empirical study also based on the same theoretical model used in Chapter 5 but applied to compare the associations between living situation, cognitive reserve, and cognitive function in cross-sectional and longitudinal data from the CFAS-Wales cohort. People who live alone may also be at greater risk of social isolation and hence this may increase the risk of poor cognitive function. Previous work has produced conflicting findings and the analyses in this thesis are novel as they consider the moderating role of cognitive reserve in the association between living alone and cognitive function.

The findings from Chapters 5–7 provide insight into how social isolation may be associated with cognitive function in 'healthy' older people and in specific groups of people who are more vulnerable to social isolation. These chapters are novel as they consider the role of cognitive reserve in this relationship. However several questions remain unanswered and are addressed in Chapter 8.

Chapter 8: Social isolation, satisfaction with social contact, and cognitive function

One limitation identified in Chapters 3 and 4 was that measures of social isolation are often based on the assessment of structural features and use standardised cut-points to determine whether an individual is isolated or not. This approach does not take into account an individuals' level of satisfaction with their social contact. Therefore, Chapter 8 presents an exploration of how scores on measures that assess social isolation using structural measures compare to scores on measures of satisfaction with social contact. This chapter also considers how these measures may differ in their prediction of cognitive function.

Chapter 9: Discussion

The final chapter synthesises the findings from the research presented in this thesis. Findings are discussed in the context of the research questions and consider the nature of the relationship between social connections, cognitive reserve, and cognitive function in later life. This chapter also critically considers methodological issues of the research findings, discusses the implications of the work, and suggests future research directions.

1.8 Dissemination of findings

Dissemination through publication

The systematic review and empirical studies presented in this thesis have been submitted for publication in peer-reviewed academic journals. To date, the following chapters have been submitted or accepted for publication:

Evans, I. E. M., Martyr, A., Collins, R., Brayne, C., & Clare, L. (in press). Social isolation and cognitive function in later life: a systematic review and meta-analysis. *Journal of Alzheimer's Disease.*

Evans, I. E. M., Llewellyn, D. J., Matthews, F. M., Woods, R. T., Brayne, C., & Clare, L. (2018). Social isolation, cognitive reserve, and cognition in healthy older people. *PLoS One, 13,* e0201008.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. M., Woods, R. T., Brayne, C., & Clare, L. (in press). Social isolation, cognitive reserve, and cognition in older people with depression and anxiety. *Aging & Mental Health.*

Evans, I. E. M., Llewellyn, D. J., Matthews, F. M., Woods, R. T., Brayne, C., & Clare, L. (in press). Living alone and cognitive function in later life. *Archives of Gerontology and Geriatrics*.

Dissemination through published abstracts

Evans, I. E. M., Wu, Y. T., Brayne, C., Matthews, F. M., Woods, R. T., & Clare, L. (2017). Social isolation, cognitive reserve, and cognition in later life. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 13*, P869.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne. C., & Clare, L. (2018). Social isolation, cognitive reserve, and cognitive function in older people with mental health problems. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association,* 14, P1509-P1510.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne. C., & Clare, L. (2018). Living alone and cognitive function in later life. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, 14, P1379-P1380.

Dissemination through academic presentations

Several scientific presentations have been made based on the findings from this thesis:

Evans, I. E. M. (October 2016). *Social isolation, cognitive reserve, and cognitive function in later life: preliminary findings.* Oral presentation at the Cognitive Function and Ageing Studies (CFAS) scientific meeting, University of Cambridge.

Evans, I. E. M. (January 2017). *Social connections, cognitive reserve, and cognitive function in later life.* Oral presentation at the University of Exeter School of Psychology Think Tank Series, Exeter.

Evans, I. E. M., Brayne, C., Matthews, F. M., Woods, R. T., & Clare, L. (May 2017). *Social isolation, cognitive reserve, and cognitive function in later life.* Poster presented at the Alzheimer's Society conference, London.

Evans, I. E. M. (July 2017). *Social connections and cognition in later life: a scoping review.* Oral presentation at the British Society of Gerontology 46th annual conference, Swansea.

Evans, I. E. M., Wu, Y. T., Brayne, C., Matthews, F. M., Woods, R. T., & Clare, L. (July 2017). *Social isolation, cognitive reserve, and cognitive function in later life.* Poster presented at the Alzheimer's Association International Conference, London.

Evans, I. E. M. (October 2017). *Social connections and cognitive function in later life.* Oral presentation at the Cognitive Function and Ageing Studies (CFAS) scientific meeting, University of Newcastle.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne. C., & Clare, L. (May 2018). *Living alone and cognitive function in later life.* Poster presented at the Alzheimer's Society conference, London.

Evans, I. E. M. (May 2018). *Social connections, cognitive reserve, and cognitive function in later life.* Oral presentation at the postgraduate research showcase, University of Exeter.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne. C., & Clare, L. (May 2018). *Living alone and cognitive function in later life.* Poster presented at the postgraduate research showcase, University of Exeter.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne. C., & Clare, L. (July 2018). *Social isolation, cognitive reserve, and cognitive function in older people with depression or anxiety.* Poster presented at the Alzheimer's Association International Conference, Chicago.

Evans, I. E. M., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne. C., & Clare, L. (July 2018). *Living alone and cognitive function in later life.* Poster presented at the Alzheimer's Association International Conference, Chicago.

Evans, I. E. M. (September 2018). *Social connections, cognitive reserve, and cognitive function in later life: a summary of the findings.* Oral presentation at the Cognitive Function and Ageing Studies (CFAS) scientific meeting, London.

Dissemination through lay presentations/communication

Some of the findings in this thesis have been disseminated to lay audiences through public engagement events and articles:

- Britain needs scientists, University of Exeter. (March 2016).
- Healthy and active ageing, Beacon Heath community centre, Exeter. (May 2016).
- Alzheimer's Society Care and Cure magazine, issue 7. (July 2016). Accessed 01/08/2016 https://www.alzheimers.org.uk/download/downloads/id/3042/care_and_cure_magazine_-_issue_7_summer_2016.pdf
- Alzheimer's Society memory walk, Plymouth. (October 2016).
- Alzheimer's Society memory walk, Exeter. (September 2017).
- Sidmouth Science Festival, Sidmouth. (October 2017).

1.9 Conclusion

Social connections have been identified as a modifiable lifestyle factor that may be associated with poor cognitive function in later life. Based on cognitive reserve theory, having good social connections may help to build cognitive reserve which may protect individuals against poor cognitive function. This thesis aims to develop a greater understanding of the relationship between social connections and cognitive function, and to extend previous work by considering the moderating role of cognitive reserve as an underlying mechanism in this relationship. This thesis will also consider additional factors that may be implicated in the association between social connections and cognitive function, including depression or anxiety, living situation, and satisfaction with social contact. The next chapter outlines the methodology of the two large cohort studies used for the analyses in this thesis.

Chapter 2: Methodology

2.1 Summary

This chapter provides an overview of the methodological approaches used in the empirical studies included in this thesis. Chapter 3 is a scoping review and Chapter 4 is a systematic review and meta-analysis and each of these chapters contains a detailed outline of the methodological procedures used and therefore these are not outlined in this section. Chapters 5–8 use secondary data from two longitudinal cohort studies: the Cognitive Function and Ageing Study–Wales (CFAS-Wales) and the Platform for Research Online to investigate Genetics and Cognition in Ageing (PROTECT). Data from CFAS-Wales is drawn upon to answer questions about the relationship between social connections, cognitive reserve, and cognitive function in later life in Chapters 5–7. Data from PROTECT is used in Chapter 8 to answer questions about the relationship between structural measures of social isolation and satisfaction with social contact, and the association of both of these measures with cognitive function in later life. The present chapter includes information about each of these two longitudinal cohort studies, covering design, participants, data collection procedures, details of included measures, approaches to accessing and managing data, and preparing data for analysis.

2.2 Cognitive Function and Ageing Study–Wales (CFAS-Wales)

Empirical work presented in this thesis is primarily based on data from CFAS-Wales, a longitudinal population-based study of people over the age of 65 years living in Wales. The study was funded by the Economic and Social Research Council and the Higher Education Funding Council for Wales, and built on the design of two previous successful studies from the Medical Research Council's (MRC) Cognitive Function and Ageing Study (CFAS) collaboration (MRC-CFAS and CFAS-II). The CFAS cohorts are population-representative and can provide useful information about the prevalence of poor cognitive function and dementia in the UK.

MRC-CFAS was the original CFAS study and began in 1989. Data were collected from over 18,000 people over the age of 65 years across six sites in England and Wales (Cambridge, Liverpool, Newcastle, Nottingham, Oxford, and Gwynedd) using standardised interviews with participants and informants at several time points. Blood and saliva samples were collected and participants were asked if they would be willing to consider brain donation. Further information on MRC-CFAS can be found on the CFAS website: http://www.cfas.ac.uk/cfas-i/

Data for CFAS-II were collected across three sites in England (Cambridge, Newcastle, and Nottingham) and used a similar design to MRC-CFAS. Recruitment and baseline interviews were conducted between 2008 and 2011 and participants completed follow-up interviews two years later between 2010 and 2013. Further information on CFAS-II can be found on the CFAS-II website: http://www.cfas.ac.uk/cfas-ii/

CFAS-Wales was a parallel study to CFAS-II conducted in two areas of Wales (Gwynedd/ Ynys Môn and Neath Port Talbot). CFAS Wales used the same design as CFAS-II, with the inclusion of additional psychological and social measures. The inclusion of these additional measures provides a richer and more extensive dataset with the availability of a wider range of psychological variables to analyse. CFAS-Wales aimed to address questions regarding ageing in the 21st century, including factors that may affect health and cognitive function in older people, such as activity, participation, lifestyle, and environmental factors. Ethical approval for CFAS-Wales was granted by the National Health Service (NHS) North Wales - West Research Ethics Committee (REC Ref No: 10/WNo01/37; IRAS Project No: 40092).

2.2.1 Design

CFAS-Wales is a population based longitudinal cohort study of older people conducted across two locations in Wales. Interview data were collected at baseline and again at two year follow-up.

2.2.2 Participants

The study aimed to recruit 4,000 participants over the age of 65 across the two locations in Wales; one rural area (Gwynedd and Ynys Môn) and one urban area (Neath Port Talbot). Participants were recruited from general practice records and eligible participants were randomly selected from these lists between 2011 and 2013. General practitioners (GPs) were asked to update practice records for people who had died or moved out of the study locations. To account for the expectation that around 15% of individuals may be ineligible or incorrectly registered, and that there would be an 80% response rate, oversampling was used. Participants were stratified by age into two equal groups to ensure a representative sample of participants across the two age groups (65-74 and ≥75 years).

Recruitment for participants in CFAS-Wales began in 2011. Interview data were collected at baseline between 2011 and 2013, and follow-up data were collected two years later between 2013 and 2015. A representative sample of 3,593 participants completed interviews at baseline and 2,236 participants completed interviews at two year follow-up.

2.2.3 Procedure

Individuals identified as potential participants from GP lists, following checks by the GP, were sent a letter containing further information about the study and invited to participate. Participants who expressed interest then received a home visit from an interviewer, usually within a week of receiving the letter, to discuss the study further and address any questions. Individuals who agreed to participate completed a consent form and an appointment was made for the interviewer to return and conduct the interview.

2.2.4 Interviews

Participants were usually interviewed in their own homes and could choose to complete the interview in English or Welsh. All interviews were conducted by research assistants who had received training provided by the CFAS co-ordinating centre at the University of Cambridge. To ensure standardisation of interviewers, regular meetings and further training were conducted at each centre. Interviews took around two hours to complete and included the following components:

- Demographic information: including age, gender, educational level, employment history, social class, socioeconomic group, marital status, residential status, and intellectual activity (questions adapted from the European Prospective Investigation into Cancer and Nutrition Protocol: EPIC; Riboli, 1992).
- Social support, social capital, social networks, and social isolation (including the Lubben Social Network Scale–6: LSNS-6), care needs, and receipt of informal care (Lubben, 1988; Wenger, 1989).

- Depression, dementia, and anxiety, calculated using the Geriatric Mental State Automated Geriatric Examination Assisted Taxonomy (GMS-AGECAT; Copeland, Dewey & Griffiths-Jones 1986).
- Lifestyle factors: including history of smoking and alcohol consumption, diet, sleep, and physical activity (questions adapted from EPIC; Riboli, 1992).
- Social and civic participation, loneliness, and activity level (de Jong Gierveld & Kamphuis, 1985).
- Cognitive function: the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and extended items for CFAS (including executive function and verbal fluency), the Cambridge Cognitive Examination (CAMCOG; Huppert, Brayne, Gill, Paykel & Beardsall, 1995; Roth et al. 1986).
- Wellbeing (the Satisfaction with Life Scale; Diener, Emmons, Larsen & Griffin, 1985).
- Personality, resilience, self-esteem, interpersonal control, and self-efficacy (Windle, Markland & Woods, 2008).
- Use of Welsh and other languages.
- Health status: including self-reported chronic conditions (heart disease, diabetes, angina, stroke, epilepsy, Parkinson's disease, and meningitis), self-perceived health, medication history, and family history of medical problems (Chen, Dewey & Avery, 2001; Rose, 1962).
- Objective measures of visual impairment and hearing.
- Functional limitation, disability, extended activities of daily living (ADLs), and objective assessment of physical function (Bond & Carstairs, 1982).
- Use and receipt of health and social services and housing or disability benefits (questions adapted from the CFAS Resource Implication Study, 1992-1994).
- Interviewer's observations and ratings of the participant (including the Residential Environment Assessment Tool; Dunstan et al. 2005).
- Saliva sample for DNA acquisition.
- 10% of the sample provided a blood sample for vitamin B12 analysis.
- Participants were asked for permission to access health and social care records and to flag for death notification at the Office of National Statistics.

CFAS-Wales questionnaires are available online at: http://cfaswales.bangor.ac.uk/research-information.php.en?menu=1&catid=8832&subid=0

An informant interview was completed for 20% of participants, weighted towards those with functional and cognitive impairment. The informant interview collected information about the

respondent, including demographic information, health conditions, functional limitation, disability, ADLs, help received, service usage, language, medication, smoking and alcohol history, social support and networks, loneliness, resilience, self-efficacy, life satisfaction, family medical history, and questions from the GMS and History Aetiology Scale that is used by AGECAT and provides the Diagnostic and Statistical Manual of Mental Disorders–IV (DSM-IV) and the International Classification of Diseases–10 (ICD-10) classification of organic and mood disorders.

The informant interview for CFAS-Wales is available online at:
http://cfaswales.bangor.ac.uk/research-information.php.en?menu=1&catid=8832&subid=0

2.2.5 Data access procedures

Data were accessed from the co-ordinating centre at the University of Cambridge. A data access form was completed and included research questions, variables requested, and analytical plans (Appendix A). Once approved, a data agreement was completed (Appendix B) and anonymised data were transmitted using encrypted files.

2.2.6 Data management

Data were cleaned by the study co-ordinators at the University of Cambridge and scores were generated for several key variables, including the AGECAT, MMSE, CAMCOG, and LSNS-6. All items relevant to the thesis were inspected on receipt and data were further cleaned as appropriate. For questions that were unanswered during the interview, interviewers could record the response as either 'don't know', 'no answer', or 'not asked'. These responses were recoded as missing data for variables used in the thesis.

2.2.7 Variables from CFAS-Wales used in this thesis

Several key variables used in this thesis require further explanation of their development, scoring, and meaning. This section provides an overview of the key variables and how they were created and used.

Geriatric Mental State Automated Geriatric Assisted Taxonomy

The Geriatric Mental State Automated Geriatric Assisted Taxonomy (GMS-AGECAT) was used to assess whether participants have a diagnosis of either dementia, depression, anxiety, or no diagnosis (Copeland et al. 1986). The GMS-AGECAT was designed specifically for use with older people. The GMS is a semi-structured interview designed to assess the presence or absence of symptoms associated with organic and psychiatric disorders in older people. The AGECAT is a computerized diagnostic system that uses an algorithm to provide a classification of either dementia, anxiety, depression, or no illness based on the presence or absence of symptoms. Individuals are categorised

according to diagnosis and level of severity, which can range from zero (no or few symptoms) to four or five (severe symptoms). A score of zero or one indicates no illness, a score of two indicates that some borderline symptoms are present, and a score of three or above indicates a clinically significant case. The algorithm assigns only one diagnosis, such that if a participant has symptoms of more than one illness, the participant is classified as having the illness in which they present the most symptoms. Symptoms are assessed under eight syndrome clusters. For the organic cluster, symptoms include (a) mistakes in memory, object identification, and subjective memory complaints, (b) minor observational items and interviewer's judgement of memory impairment, and (c) disorientation and gross cognitive impairment. For the depression and anxiety cluster, symptoms assessed include (a) expressed and observed mood, (b) symptoms associated with depression such as loss of concentration and interest, irritability, low energy, and insomnia, (c) negative thoughts about the future and suicidal thoughts, (d) change in personality or weight and eating habits, (e) psychotic symptoms, mood swings, hallucinations, and delusions. The GMS-AGECAT has good agreement with clinical diagnoses made by psychiatrists (Cohen's Kappa = .84: Copeland et al. 1986; Copeland et al. 2002).

Scores for the AGECAT were calculated and provided by the data manager at the co-ordinating centre in Cambridge. For participants with missing data where an AGECAT score could not be calculated, the principal investigator Professor Carol Brayne reviewed the participant's available data and informant's responses and made a diagnosis.

The AGECAT was used in Chapters 5–7 to exclude people with a diagnosis of dementia from analyses to reduce the risk of reverse causation (Hultsch, Hertzog, Small & Dixon, 1999) and in Chapters 5 and 7 to exclude people with a diagnosis of depression as depression is associated with poor cognitive function (Rock, Roiser, Riedel & Blackwell, 2014). The AGECAT was used in Chapter 6 to identify people with anxiety, depression, or no diagnosis and compare these groups on a number of variables.

Mini-Mental State Examination

The Mini-Mental State Examination (MMSE; Folstein et al. 1975) consists of 22 items that assess orientation, language, registration, memory, spelling backward, and construction. Scores range from 0-30 and scores of ≤25 are typically considered to indicate cognitive impairment (Folstein, Folstein, McHugh & Fanjiang, 2001). MMSE scores are highly influenced by educational level, social class, age, and ethnicity which may complicate the interpretation of scores (Black et al., 1999; Bravo & Hébert, 1997; Ng, Niti, Chiam & Kua, 2007). The MMSE score was calculated by the data manager at the co-

ordinating centre at the University of Cambridge. Participants with a score of ≤25 were excluded from analyses in Chapters 5–7 to reduce the risk of reverse causation (Hultsch et al. 1999).

Cambridge Cognitive Examination

The Cambridge Cognitive Examination (CAMCOG; Roth et al. 1986) is a standardised measure of cognitive function that consists of 67 items. The measure assesses cognitive function along eight subscales, including orientation, language (comprehension and expression), memory (remote, recent, and learning), praxis, attention, abstract thinking, perception, and calculation. Total scores range from 0–107 and a lower score indicates impairment. Each of the sub-domains can be scored separately. Total scores and scores for specific sub-domains on the CAMCOG at baseline and follow-up were calculated by the data manager at the co-ordinating centre in Cambridge. CAMCOG scores were used as a measure of cognitive function in Chapters 5–7. For cross-sectional analyses, raw baseline scores were used to indicate cognitive function. For longitudinal analyses, a cognitive change score was calculated by subtracting the baseline score from the score at two year follow-up. Each participant's change score was then standardised using the standard deviation of the baseline CAMCOG score. This formula is outlined below:

Cognitive change score = CAMCOG score at two year follow-up – CAMCOG score baseline

Standardised change score = cognitive change score/ standard deviation of baseline CAMCOG score

Cognitive Reserve Score

A cognitive reserve score was created to assess level of cognitive reserve based on proxy measures. The cognitive reserve score was originally developed in CFAS based on the Lifetime of Experiences Questionnaire (LEQ: Valenzuela, Brayne, Sachdev, Wilcock & Matthews, 2011; Valenzuela & Sachdev, 2007). The LEQ asks detailed information about an individual's educational level, occupational complexity, and social and cognitive activity in early-, mid-, and late- life. CFAS does not assess these domains in as much detail as the LEQ and so a simplified proxy for the LEQ was created using measures from CFAS. The cognitive reserve score in CFAS includes measures of educational level, occupational complexity, and social engagement. While there was no index of cognitive activity in CFAS, relevant questions were included in CFAS-II and CFAS-Wales. A cognitive reserve score including cognitive activity was developed in CFAS-II (Opdebeeck et al. 2018). The cognitive reserve score in CFAS correlates highly with the total LEQ score (r = .60, p <.001, n = 70: Valenzuela & Sachdev, 2007; Valenzuela et al. 2011). This thesis assesses aspects of social connections as an independent variable in Chapters 5–7 therefore social engagement was not included in the cognitive

reserve score in this thesis. The cognitive reserve score used in Chapters 5–7 combined educational level, occupational complexity, and cognitive activity.

Educational level was recorded as the number of years in education. Participants' main occupation was determined as the occupation the participant had worked for the longest period. Occupational complexity was assessed using social class and the social economic grouping of the participant's main occupation; these two elements were combined using 14 categories ranging from highly professional high social class occupations (e.g. a doctor, or a lawyer) to less professional occupations typically associated with a lower class (e.g. a cleaner, or an advertising sign holder). An additional ranking of 15 was given to housewives as these participants did not receive a formal code in the UK social class ranking system. The classification scores were reversed to be in the same direction as educational level and cognitive activity. Cognitive activity was measured by seven questions about engagement in a range of activities (including listening to the radio, reading a newspaper, magazine, or book, playing games such as cards or chess, and completing crosswords or puzzles). Responses were recorded on a 5-point scale (once a year or less, several times a year, several times a month, several times a week, or every day/ almost every day). Lower scores indicated lower engagement in cognitive activity.

Scores for the three subscales were weighted based on the interquartile range to ensure that each component of the cognitive reserve score contributed equally to determining whether a person's cognitive lifestyle reflected low, medium, or high levels of activity. This gave the following formula: cognitive reserve score = (2.33 x educational level) + (1.4 x occupational complexity) + (1 x cognitive activity). A higher score indicates higher levels of cognitive reserve.

Social isolation

The Lubben Social Network Scale–6 (LSNS-6; Lubben et al. 2006) is a standardised measure of social isolation. The measure is constructed of six questions, three of which assess family ties and three comparable questions that assess non-kinship ties. Each set of three questions ask the participant about the number of relatives/ friends the participant sees or hears from at least once a month, could call on for help, and can speak with about private matters. Participants respond on a scale ranging from 0 (indicating no relatives/ friends available) to 5 (indicating nine or more relatives/ friends available). Total scores range from 0-30, with lower scores indicating social isolation. A score of ≤12 is typically used to indicate social isolation. Separate scores can be obtained for the family and friends subscales and these range from 0-15 and a lower score indicates social isolation. LSNS-6 scores were calculated by the data manager at the co-ordinating centre in Cambridge.

Living situation

Living situation was assessed in CFAS-Wales by asking participants 'does anyone else live here?' (yes/ no). If yes, the participant was required to specify their relationship to those they reside with from the following: spouse/ partner, parents, siblings, children, grandchildren, other relatives, friends, or other. More than one relationship option could be selected.

Social contact

Social contact was assessed by asking participants two questions about the frequency of contact with their family and friends. Participants could respond on a six point scale as follows: daily (5), 2-3 times a week (4), at least weekly (3), at least monthly (2), less often (1), or never/no relative (0). Scores for each question were summed, giving a possible range from 0-10, with zero indicating less social contact and ten indicating greater social contact.

Loneliness

The six-item de Jong Gierveld scale (de Jong Gierveld & van Tilburg, 2006) was used to assess loneliness in CFAS-Wales. The scale assesses social and emotional loneliness using two separate scales comprised of three questions each. Participants respond to questions on a three point scale: yes, more or less, or no. For the social and emotional loneliness subscales, scores range from 0-3 and a higher score indicates greater feelings of social or emotional loneliness. An overall loneliness score can be generated by summing scores from each of the subscales, with a range from 0-6, and a higher score indicates greater feelings of loneliness.

2.2.8 Statistical techniques

Chapters 5–7 contain detailed information regarding statistical approaches to analyses. In brief, all CFAS-Wales data were analysed in Stata version 15.0. Linear regression, logistic regression, and moderation analyses were used to assess the relationship between social connections, cognitive reserve, and cognitive function in later life. ANCOVAs, t-tests and chi squared tests were used to compare differences across groups.

2.3 Platform for Research Online to investigate Genetics and Cognition in Ageing (PROTECT)

PROTECT is an ongoing longitudinal cohort study of adults in the UK over the age of 50 and living in the community. This ten-year study aims to assess the association of genetic, lifestyle, and medical factors with cognitive function over a period of eight years. For this thesis, additional questionnaires focusing on social connections were administered to a sample of people who had agreed to be invited to participate in additional studies through the PROTECT platform.

2.3.1 Design

PROTECT is a longitudinal study of people aged ≥50 living in the community in the UK. Questionnaires are completed online using the PROTECT platform.

2.3.2 Participants

The study aimed to recruit 5,000 people over the age of 50 living in the UK. Participants were eligible to take part if they were living in the community, had access to a computer and the internet, speak English, and had no established diagnosis of cognitive impairment or dementia. Participants were recruited through several channels: (1) advertisement at King's College London, the University of Exeter, and the Royal Devon and Exeter NHS Trust, (2) invitation of participants in existing cohorts and completed trials who had indicated they would like to be contacted about future research, (3) advertisement on Join Dementia Research, and (4) information leaflets placed in GP surgeries and memory clinics. Recruitment began in 2013 and baseline assessment was completed in November 2015. A total of 20,000 participants were recruited to the study.

2.3.3 Procedure

People who expressed an interest in participating were directed to the PROTECT study website (http://www.protectstudy.org.uk/) where they could read the information sheet and sign a consent form online (http://www.protectstudy.org.uk/consent.aspx) if they wished to take part. Participants receive an email alerting them when questionnaires and assessments are available to complete and must click on a link to access a consent form which must be filled in before responding to the measures. Questionnaire data are collected online through the PROTECT platform and participants are able to save their progress and return to complete the assessment at their convenience. Email reminders are sent to prompt the participants to fill in any incomplete questionnaires. All participants completed a baseline assessment between November 2015 and August 2016 and are invited to complete a follow-up assessment by email yearly, for up to eight years. Participants can consent to being invited to participate in additional studies that are administered through the PROTECT platform that are not part of the annual follow-up assessment.

2.3.4 Questionnaires

All data are collected through the online PROTECT study platform, with the exception of genetic samples. The following information was collected at baseline and is collected annually at the follow-up assessment:

- Demographic characteristics: age, gender, ethnicity, marital status, educational level, employment, and NHS number.
- Medical history: existing medical conditions, prescriptions, weight, and height.

- Lifestyle: current amount and type of exercise, smoking status, diet, use of dietary supplements, use of technology, current use of cognitive training, and number of languages spoken.
- Mental health history: a series of validated mental health scales are completed to provide information about the participants' history and current status with regard to stress, depression, anxiety, mood, and psychosis. The test battery also includes items relating to childhood stress and alcohol and drug use.
- Mild behaviour impairment scale: a validated scale to detect early changes in behaviour in older adults.
- Pain interference scale (4-item short form): a validated scale to capture regular experience of pain in adults.
- St Mary's sleep questionnaire: a nine-item questionnaire that captures sleep quality in the last month.
- Menopause and fertility assessment (females only): a 17-item questionnaire to capture past and current information about female fertility and menopause to enable investigation of links with cognitive health.
- Validated measures of cognitive health are completed three times in one week at baseline and each annual assessment as follows:
    - Baddeley grammatical reasoning test: accuracy of grammatical statements about a presented picture.
    - Simple and choice reaction time: brief computerised test of reaction time.
    - Paired associate learning: verbal learning.
    - Spatial working memory: memory test involving recall.
    - Instrumental activities of daily living: to determine overall function in daily life.
    - Informant questionnaire on cognitive decline in the elderly (IQCODE): informant-rated measure of cognitive function (a self-rated version was included as an alternative if an informant was not available).
    - The Wesnes online cognitive testing system: a cognitive test battery that includes interactive assessment of reaction time, grammatical reasoning, picture recognition, and digit vigilance.

Before each assessment participants completed a brief mood questionnaire using the Bond-Lader visual analogue scale of mood and alertness (Bond & Lader, 1974) to give a real-time assessment of mood. Participants were asked for permission for the research team to request their medical notes from their GP to enable analysis of study outcomes against medical status. To obtain genetic

samples, two saliva sample kits were posted to each participant to self-administer in their home. A freepost envelope was provided to return samples to the National Institute of Health Research Bio-resource bank.

Following baseline assessment, contact was maintained with participants through the study website and will be until the end of the study. Participants receive a bi-annual email newsletter with updates from the study. Each participant will be asked to complete the measures listed above on an annual basis.

2.3.5 Procedure and questionnaires for 'social connections' study using PROTECT platform

To address the aims of this thesis, the PROTECT platform was used to administer questionnaires relating to social connections. A sub-sample of participants were recruited through the PROTECT platform to participate in a questionnaire survey relating to social connections in later life. Email invitations were sent to 7,000 people aged ≥60 who had completed cognitive and mental health assessments at the most recent annual follow-up assessment (wave three). The email contained an overview of the social connections study and a link to the participant information sheet (Appendix C) and consent form (Appendix D). If individuals wished to participate they could sign the online consent form and proceed to complete the questionnaires. The survey was stopped once the target of 5,000 participants was reached. Permission to complete this study was granted by the study co-ordinator and ethical approval was granted by the University of Exeter School of Psychology Ethics Committee (Appendix E and F).

For the social connections study, participants completed four questionnaires relating to social connections. The full questionnaire can be found in Appendix G and relevant variables are outlined in more detail in section 2.3.7 of this chapter.

2.3.6 Data access procedures

A data access form was completed and provided details of the research questions, variables requested, and planned analyses (Appendix H). A data agreement form was completed (Appendix I) and anonymised data were sent using encrypted files from the co-ordinating centre at King's College London.

2.3.7 Data management

Variables taken from the PROTECT annual assessment (wave three) were cleaned and scored by the study co-ordinators at King's College London. Variables relating to social connections generated from questionnaire responses from the social connections study were cleaned and scored on receipt.

2.3.8 Variables from PROTECT used in this thesis

Several variables from PROTECT are used in this thesis and this section outlines the measures and scoring.

Social isolation

Social isolation was assessed using the Lubben Social Network Scale–6 (LSNS-6: Lubben et al. 2006). The LSNS-6 is a standardised measure of social isolation, consisting of three sets of questions that assess family ties, and a set of three comparable questions assessing non-kinship ties. The three items assess the number of relatives/ friends the participant sees or hears from at least once a month, could call on for help, and can speak with about private matters. Responses are collected using a six category response set, in which the participant indicates the number of relatives/ friends available. Response scores range from 0 (no relatives/ friends) to 5 (nine or more relatives/ friends). Scores for each question are summed and range from 0-30, with 0 indicating social isolation and 30 no social isolation. A score of ≤12 indicates social isolation. Scores can be obtained for the family and friends subscales separately and range from 0-15 and lower scores indicate social isolation (Lubben et al. 2006).

Satisfaction with social contact

Satisfaction with social contact was assessed using a measure adopted from the Canadian Study of Health and Aging (Andrew & Rockwood, 2010). The measure consists of eight questions that assess whether the participant is satisfied with their level of social contact, relationships with family and friends, available support, and level of social engagement. Scores for dichotomous questions (yes/ no) are scored as zero if the social deficit is absent and one if present. Intermediate values are scored in equal increments from 0-1 (i.e. terrible = 1, unhappy = 0.83, mostly dissatisfied = 0.67, mixed = 0.5, mostly satisfied = 0.33, pleased = 0.17, and delighted = 0). Total scores range from 0-8 and higher scores indicate poor satisfaction with social contact.

Cognitive function

Cognitive function was assessed using a validated online cognitive test (Corbett et al. 2015) consisting of four tasks, including digit span to assess verbal working memory (Huntley, Hampshire, Bor, Owen & Howard, 2016), paired associate learning to assess visual episodic memory (Owen et al. 1993), self-ordered search to assess spatial working memory (Owen, Downes, Sahakian, Polkey & Robbins, 1990), and grammatical reasoning to assess verbal reasoning (Baddeley, 1968). Participants completed each of the cognitive tests up to three times over seven days as part of their annual

assessment at wave three. The mean score of the participant's performance over the three trials was taken as the score for cognitive function.

Depression

Depression was assessed using the Patient Health Questionnaire–9 (PHQ-9: Kroenke, Spitzer & Williams, 2001). This measure assesses how often the participant has been bothered by nine symptoms of depression over the past two weeks. Responses are recorded from not at all (0) to nearly every day (3). Scores range from 0-27 and scores of 0-4 indicate minimal depression, scores of 5-14 indicate mild to moderate depression, and scores of ≥15 indicate moderately severe to severe depression.

2.3.9 Statistical techniques

Chapter 8 contains detailed information regarding statistical approaches to analyses. In brief, the data were analysed in Stata version 15.0. Linear regression and moderation analyses were used to assess the associations between social isolation, satisfaction with social contact, cognitive function, and depression in later life. ANOVA was used to compare differences across groups.

2.4 Conclusion

This chapter has provided an overview of CFAS-Wales and the PROTECT study, including details regarding participants, procedures, data collection, and interviews. It has also provided an overview of the variables that are used in this thesis and how they were prepared and scored for analysis. The next chapter of the thesis is a scoping review and was completed in the early stages of the PhD as initial reading of the literature revealed there are numerous concepts relating to social connections and there is considerable inconsistency in approaches to defining and measuring these concepts. The scoping review aimed to provide an overview of the different social concepts that are used and was necessary to ensure that empirical work in this thesis was based on definitions and measures of social concepts that are reliable and valid.

Chapter 3: Social connections and cognitive function in later life: a scoping review

3.1 Summary

This chapter presents a scoping review and was completed at an early stage to inform the development of research presented in this thesis. The aim of the scoping review was to establish which terms are used in the literature to assess social connections in later life and the types of measures that are used to assess these concepts. This work led on to a more comprehensive systematic review and meta-analysis (Chapter 4) and has provided a foundation for my understanding of different social concepts that are assessed in empirical work (Chapters 5–8).

Background: Social connections have been implicated as an important factor for maintaining cognitive function in later life, although evidence is inconclusive. This inconsistency may be attributed to the range of concepts associated with social connections. This scoping review was conducted because initial reading of the literature suggested the need to clarify which social concepts are used and how they are defined and is a precursor to a systematic review which assesses the relationships between social connections and cognitive function.

Objective: To examine which concepts are available to assess social connections and how they are defined and measured in empirical studies. Given the implications for good social connections on late-life cognitive function there will be a particular focus on studies that assess cognitive function as an outcome.

Method: A scoping review was conducted using four online databases (PubMed, PsycInfo, AgeLine, and Web of Science) using the terms ("social isolation" OR "loneliness" OR "social network*") AND ("cognit*" OR "cognitive decline") AND ("later life" OR "older adults" OR "elderly").

Results and conclusions: Forty-two studies were identified for inclusion. Social concepts were divided into structural (marital status, living situation, social networks, social isolation, social engagement), functional (social support), and appraisal (loneliness) aspects of social contexts. There was considerable inconsistency across studies in approaches to defining and measuring social concepts and assessing cognitive function. This was reflected in the findings of studies, which were inconclusive in explaining the relationship between aspects of social connectedness and cognitive function in later life. Methodological limitations of the different approaches are discussed.

3.2 Introduction

The term 'cognition' encompasses several mental processes and abilities, such as attention, memory, decision making, and problem solving (Hendrie et al. 2006). Collectively, these domains of cognition are essential for maintaining an individual's sense of independence, identity, and ability to function successfully in daily life (Hendrie et al. 2006; Nishiguchi et al. 2013). Maintaining cognitive function in later life is key to ensuring quality of life (Jekel et al. 2015). Cognitive ageing is conceptualised as a life-long process of 'gradual, ongoing, yet highly variable change in cognitive functions that occur as people get older' and is a normal process in healthy ageing (Liverman et al. 2015). Cognitive ageing should not significantly influence an individual's ability to function independently (Liverman et al. 2015). Some people may experience more complex cognitive problems that influence their ability to function independently. Such change is not considered a normal consequence of healthy ageing and impairment may have a detrimental impact on daily living, such as a reduced ability to function independently, perform daily activities, and lower quality of life (Giebel et al. 2014; Jekel et al. 2015). Reported prevalence rates of people over the age of 65 experiencing symptoms of cognitive impairment range from 3–42% (Jagger et al. 2009; Ward, Arrighi, Michels & Cedarbaum, 2012). People who experience a significant deviation of cognitive function from population norms may receive a diagnosis of mild cognitive impairment (MCI) or dementia, which are associated with more serious symptoms of cognitive deficit (Petersen, Doody et al. 2001). Given such high prevalence rates and the associated economic and social burden (Prince et al. 2015), promoting the maintenance of cognitive function in later life is an important public health priority (Liverman et al. 2015; NHS England, 2015; World Health Organization, 2015).

One approach to maintaining cognitive function in later life is to identify modifiable lifestyle factors that are associated with cognitive function (Di Marco et al. 2014; Stern 2002, 2012). Several factors have been identified that may increase the risk of poor cognitive function, such as smoking (Anstey et al. 2007) and diabetes (Cheng, Huang, Deng & Wang, 2012). Some factors may reduce risk, such as physical activity (Beydoun et al. 2014; Plassman et al. 2010), cognitive activity (Bennett et al. 2014), or a healthy diet (Plassman et al. 2010). Having strong and plentiful social connections has been identified as an additional factor that may reduce risk of poor cognitive function (Fratiglioni et al. 2004). Evidence regarding the relationships between social connections and cognitive function is less clear than other risk factors, which may relate to the complexity of studying social concepts. For example, to assess smoking simply requires a comparison of people who do and do not smoke, or for physical activity, an activity intervention could be introduced to a randomised controlled trial to determine whether this effects cognitive function. Whereas assessing social connections is much more complex and difficult to isolate from other factors. For example, it is difficult to distinguish

specific social concepts from one another as all likely interact to contribute to an individual's social context (Victor et al. 2000). Additionally, social engagement often occurs when people are engaging in other activities that may provide cognitive stimulation and so it is difficult to determine which factor has the most beneficial contribution to cognitive function (Aartsen et al. 2002; Global Council on Brain Health, 2017; Toepoel, 2013).

Social connections have been associated with a range of positive health outcomes, including reduced mortality (Holt-Lunstad et al. 2010; Steptoe et al. 2013), better wellbeing (Adams et al. 2011), higher quality of life (Bowling, 2005; Scharf et al. 2004), and reduced risk for a range of health conditions (Cornwell & Waite, 2009; Tomaka et al. 2006). There is also evidence that a high level of social connections is associated with better cognitive function, although findings are less consistent. For example, in their review, Fratiglioni et al. (2004) found that a socially integrated lifestyle was associated with a reduced risk of Alzheimer's disease and other dementias. In a more recent review, Kuiper et al. (2016) found that both structural (including social activity and social network size) and functional (including social support, loneliness, and satisfaction with household members) aspects of social relationships were associated with cognitive decline. The authors also noted considerable heterogeneity in approaches to measuring social concepts, which created some discrepancies in conclusions regarding the relationships between social concepts and cognitive function across studies. A review focussing on loneliness and cognitive function in later life reported that loneliness appeared to be negatively correlated with cognitive function, although these findings were not significant after controlling for demographic and psychosocial factors (Boss, Kang & Branson, 2015). Notably, in each of these reviews a considerable number of studies were included that reported no relationship between aspects of social connections and cognitive function in later life. This inconsistency in findings reflects that compared to other lifestyle factors, less is known about whether there is an association between social connections and late-life cognitive function. Given that having good social connections may reduce the risk of poor cognitive function, it is important to identify whether this relationship is present and if so how social connections may serve to maintain cognitive function in later life.

One reason for the current limited understanding of how social connections may influence cognitive function may be that there are a range of concepts associated with social connections. Social connections is a broad term that encompasses several concepts relating to features of an individual's social context. These features can range from basic structural indicators, such as marital status or living situation (Gow et al. 2013; Paúl et al. 2010), to more complex indicators such as social network size and frequency of contact with others (Wilson et al. 2015; Zunzunegui et al. 2003). Social engagement and social isolation are two additional structural concepts that refer to

participation in social and community activities or sustaining meaningful and positive relationships with social contacts (Nicholson Jr, 2009; Paillard-Borg et al. 2009). Social networks can function to offer social resources such as emotional, instrumental, or informational support if required (Ellwardt et al. 2013; Li & Zhang, 2015). Furthermore, individuals may have positive or negative appraisals of their social contexts, and will inevitably make appraisals of their satisfaction with aspects of this social context. This may include the perceived availability of, and emotional closeness with, social contacts, and feelings of loneliness (Victor et al. 2005). Each of these concepts are unique and have distinct definitions, yet they are also related to some extent (Victor et al. 2000). Although many studies aim to assess one specific concept, measures vary in the social resources included, meaning that concepts are assessed in a non-distinctive way (Gow & Mortensen, 2016). This may explain why studies assessing the relationship between social connections and cognitive function are inconsistent.

Given the range of concepts associated with social connections and the possible benefits of having good social connections on cognitive function, we conducted a review to outline and conceptualise approaches to assessing social connections. In particular, this review focused on studies that assess the association between social connections and cognitive function in later life. The first aim was to explore which concepts have been used to reflect ideas about social connections within the literature and how frequently these concepts are used. The second aim was to examine how social concepts and cognitive function are defined and assessed in empirical studies, and in particular which standardised measures are used, and the extent to which measures are devised for specific studies. The final aim was to consider any methodological issues that emerge in relation to different approaches to assessing these concepts.

3.3 Method

A systematic literature search was undertaken. Key terms were identified by examining which terms are used in empirical papers and through discussion with other researchers in the field. Because social connections is a broad concept that captures a range of narrow concepts, several more specific terms were included. Search terms also included the target population (older people), and the outcome of interest (cognition). The final search terms are displayed in Table 3.1. These terms were broad enough to capture a wide scope of relevant literature. The search was conducted on the 08/02/2016 using four electronic databases: PubMed, PsycInfo, AgeLine, and Web of Science. No time limits were imposed. Reference lists of included studies were searched for additional relevant studies.

Table 3.1. *Search terms used in the review.*

Step	Terms
1	social* isolat* OR social* network* OR loneliness OR lonely
2	cognit* OR cognitive decline
3	late* life OR old* OR elder*
4	#1 AND #2 AND #3

To capture sufficient breadth, studies were selected for inclusion based the following predefined criteria: (i) article examined the relationship between social connections and cognition (either a measure of global cognitive function or any cognitive sub-domain) or dementia in later life, (ii) empirical study (i.e. not a review, editorial, or opinion piece), (iii) human participants, and (iv) written in English. Studies that reported findings based on cross-sectional and longitudinal data were included. Studies were excluded if they did not assess cognitive function as an outcome or were intervention studies.

3.4 Results and discussion

A flowchart showing the process of study selection is presented in Figure 3.1. Initial search results generated 897 references after duplicates were removed. Studies were screened by title, then by abstract, and finally full-text studies were retrieved and screened. Forty-six studies were retained for inclusion in the review. Relevant information from each article was extracted and entered into a table (Table 3.2).

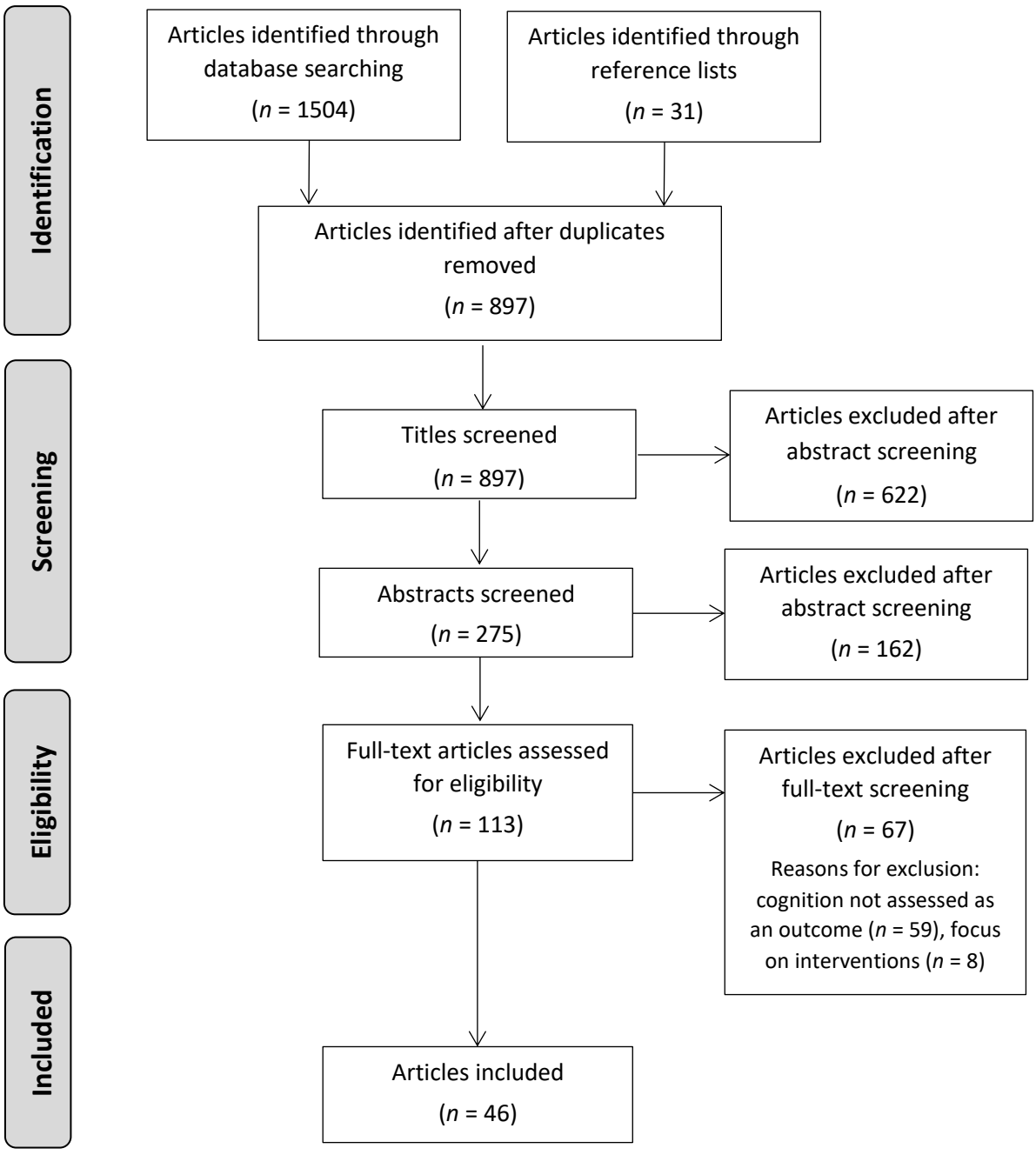


Figure 3.1. Screening process for including articles in the scoping review.

Concepts identified

A range of concepts relating to social connections were identified. Many of these concepts were related to some extent and captured similar features of social contexts. For example, some concepts captured quantitative and structural aspects of social contexts, whereas other concepts captured more complex features of social contexts, such as the function of, or the individual's perceptions of, their social network. To help organise discussion of the results, the concepts that emerged were divided into three key themes of structural, functional, and appraisal aspects of social connections (Antonucci, 1990). The first theme focused on structural aspects of social connections and considered objective and quantitative features of social contexts. This included socio-demographic information, such as marital status and living situation, in addition to details about social networks, including the number of contacts within the network, and the type of contacts, such as a spouse, family, or friends. Level of social isolation and engagement also provide structural information as these concepts provide an index of integration with social contacts and the wider community. The functional theme considered the availability of, and the type of, social support that can be obtained from contacts within the social network. Finally, the appraisal theme considered the perceived satisfaction with aspects of the social network. This included the availability of social contacts, emotional closeness and ties with other people, and feelings of loneliness.

Categorising measures of social connections under each of these themes was challenging as many studies considered more than one concept in social measures. Definitions of concepts varied across studies and some provided no definition. Consequently, there was variation in approaches to assessing each social concept. Some studies were non-specific in their assessment of social concepts and conflated several other social concepts that were not directly related to the concept being assessed. For example, some measures that were created to assess social networks included questions that assessed marital status, living situation, social engagement, or availability of social support (Barnes et al. 2007; Fratiglioni et al. 2000; Green, Rebok & Lyketsos, 2008; Stoykova, Matharan, Dartigues & Amieva, 2011; Wang et al. 2015). This complicates the interpretation of the measure and further complicates classifying the measure into a category. For the purposes of the review, the concept identified by the authors within the studies aims was used to organise and discuss studies under the relevant theme.

Table 3.2. *Summary of included studies assessing the relationship between social connections and cognition in later life*.

Reference	Country	*N* in analysis	Follow-up (years)	Age at baseline	Social concept and assessment	Cognitive domain and assessment	Reported findings
Aartsen et al. (2005)	Netherlands	1144	6	≥60	**Marital status**: marital status, length of widowhood.	**Memory:** Immediate and delayed recall.	Widowed people had greater memory decline than married people. Length of widowhood did not predict cognitive function.
Albert et al. (1995)	USA	1115	2	≥70	**Emotional support:** received from friends and relatives. **Social networks: c**ount of the number of friends and relatives one feels close to.	**Language:** Boston naming test. **Spatial recognition:** delayed recognition span test. **Verbal memory:** recall of the naming items. **Conceptualisation:** Similarities subtest of WAIS-R. **Visuospatial ability:** figure copying.	Emotional support and social networks were not associated with cognitive decline.
Andrew & Rockwood (2010)	Canada	2468	5	≥70	**Social vulnerability index:** 40 items assessing language ability, living situation, social support, socially oriented ADLs, leisure activities, experiences in relationships, feelings about social relationships and activities, and SES.	**Global cognition:** combination of sub-domains: immediate and remote memory, orientation, attention and concentration, language and naming, verbal fluency, and executive function. **Dementia diagnosis:** 3MS and the DSM-III-R.	Increased social vulnerability was associated with increased odds of cognitive decline and dementia (but this relationship did not remain significant when controlling for age, gender, frailty, and baseline 3MS).
Armstrong et al. (2015)	USA	2959	6	≥71	**Social vulnerability index:** 18 variables assessing living situation, social networks, and marital status.	**Global cognition:** CASI.	A higher score on the social vulnerability index was associated with cognitive decline.
Barnes et al. (2004)	USA	3899	5	≥65	**Social networks:** number of children, relatives and friends seen at least once and month. **Social engagement:** participation in social and productive activities (e.g. religious services/ groups, museum, activities or groups outside the home, part/ full time job).	**Global cognition:** MMSE. **Episodic memory:** immediate and delayed recall of the East Boston story. **Perceptual speed:** Symbol digit modalities test.	A higher number of social ties and social engagement was associated with reduced cognitive decline.
Barnes et al. (2007)	USA	9704	15	≥65	**Social network:** LSNS-6.	**Global cognition:** 3MS.	Cognitive decline was associated with a poor social network score.
Bassuk et al. (1999)	USA	756	12	≥65	**Social disengagement:** six indicators of social engagement including presence of a spouse, monthly visual contact with three or more relatives or close friends, yearly nonvisual contact with 10 or more relatives or close friends, monthly attendance at religious services, group membership, and regular participation in recreational social activities. **Emotional support:** availability of social contacts to provide support, talk over problems, help make a difficult decision, and satisfaction with available support.	**Global cognition:** SPMSQ.	Level of social disengagement was significantly associated with increased risk of cognitive decline. Those with no ties had twice the odds of experiencing cognitive decline than those with 5-6 ties.
Béland et al. (2005)	Spain	1165	6	≥65	**Social networks:** number of relatives seen monthly, presence of friends, number of children, frequency of contact, and living distance from ties.	**Global cognition:** PCL	A higher number of family ties and social engagement with relatives was associated with better cognitive function up until 80 years of age. After 80, the difference diminished.

					Social engagement: how often the participant feels they help, are useful to, and play an important role, in their children's, families, or friends lives. **Social integration:** membership in a community association, monthly attendance of religious services, community centre with recreational activities for seniors, and a public square or outdoor meeting place.		
Bennett et al. (2006)	USA	89	Not reported	≥80	**Social network:** number of children, family, and friends the participant feels close to, at ease with, and can talk to about private matters, and frequency of interaction.	**Global cognition:** combination of sub-domains: episodic memory, semantic memory, working memory, perceptual speed, visuospatial ability, and a brain autopsy.	Social network size modified the association between pathology and cognitive function. At more severe levels of global disease pathology, cognitive function remained higher for people with larger network sizes (effects most pronounced for semantic and working memory).
Bosma et al. (2002)	Netherlands	830	3	≥50	**Social engagement:** organizational memberships (e.g. clubs).	**Global cognition:** MMSE **Perceptual speed:** Stroop colour word test **Verbal learning:** verbal learning test, letter digit coding test, and word fluency.	Social engagement was significantly associated with verbal learning, but not perceptual speed or the MMSE.
Conroy et al. (2010)	Ireland	802	Cross-sectional	≥65	**Social support:** availability of a person who made the participant feel loved and appreciated, a close confidante, and a person who would provide practical help. **Loneliness:** 'How often in the past 12 months have you been bothered by loneliness?' **Living situation** **Marital status**	**Global cognition:** AMT.	Living alone and social support was not associated with poorer cognitive function, but reduced social activity was associated poorer cognitive scores.
Crooks et al. (2008)	USA	1340	4	≥78	**Social network:** LSNS-6 and self-report of satisfaction with the amount of contact with family and friends.	**Global cognition:** TICS-M. **Dementia:** TDQ and medical records.	A larger social network characterised by greater social support and daily social contact was associated with lower risk of dementia and poor cognitive function.
DiNapoli et al. (2014)	USA	267	Cross-sectional	≥70	**Social isolation:** LSNS-6. **Perceived social isolation:** perceptions of support network, e.g. how many relatives/friends do you feel close to such that you could call on them for help? and perceived confidence in network e.g. how many relatives/friends do you feel at ease with whom you can talk about private matters? **Social disconnections:** social network size and monthly contact.	**Memory:** recall and recognition. **Executive functioning:** trail making test B and the controlled oral word association test. **Attention:** trail making test A. **Language ability:** Boston naming test.	Social isolation, perceived social isolation, and social disconnectedness were associated with poorer cognitive function across all four cognitive domains.
Ellwardt et al. (2015)	Netherlands	2959	19	≥54	**Network complexity:** count of social contacts, frequency of contact, type of relationships, Cohen's Social Network Index.	**Global cognition:** MMSE.	More complex social networks were associated with better cognitive function. This was not explained by the size of the network, or by the presence of specific relationship types.
Ellwardt et al. (2013)	Netherlands	2255	3, 6	≥55	**Social support:** participants name nine people with whom they have regular, socially active contacts and are asked how much emotional and instrumental support is received. **Loneliness:** de Jong Gierveld Loneliness Scale.	**Global cognition:** MMSE. **Information processing speed: c**oding task. **Non-verbal and abstract reasoning:** Raven coloured progressive matrices.	Higher levels of emotional and instrumental support were associated with better cognitive performance indirectly through reduced feelings of loneliness, but were unrelated to changes in loneliness and cognitive functioning independently.
Elwood et al. (1999)	UK	1870	Cross-sectional	≥66	**Social contact:** number of persons, family and friends, with whom there was meaningful daily contact.	**Global cognition:** CAMCOG and MMSE. **Intelligence:** AH4	Social leisure activities were not associated with cognitive performance (but intellectual and physical

					Leisure activity: frequency of participation under the following four categories: social (dances, social events, spectator at sports events, visiting a public house or club, playing darts, snooker), cultural (participation in music or drama, concerts, theatre, cinema, church, community or voluntary work), intellectual (attending lectures, classes, libraries, museums, games, creative arts), physical (gardening, walking, jogging, ball games, household jobs).	**Reaction time:** choice reaction time.	leisure activities were). Associations between social contact and cognition were weak.
Ertel et al. (2008)	USA	16638	6	≥51	**Social integration:** marital status, volunteer activity (at least one hour in the past year), frequency of contact with children, parents, and neighbours (phone, in person, or mail).	**Memory:** Immediate and delayed recall.	Higher baseline social integration predicted slower memory decline.
Fratiglioni et al. (2000)	Sweden	1368	3	≥75	**Social network:** marital status, living arrangement, having children, having close social ties, frequency of, and availability of, social contacts, satisfaction with social contact and support.	**Dementia diagnosis:** DSM-III-R.	Individuals living alone and with no friends or relatives had an increased risk of developing dementia (but this was non-significant after adjusting for covariates). Infrequent contact did not increase dementia risk if such contacts were experienced as satisfying.
Fung et al. (2011)	China	476	Cross-sectional	≥60	**Leisure activity:** variety and frequency of leisure activities undertaken (divided into: cognitive, social, recreational, and physical). **Loneliness:** de Jong Gierveld Loneliness Scale.	**Global cognition:** C-MMSE. **Dementia:** C-CDR.	Greater feelings of loneliness were associated with poorer cognitive function.
Gerst-Emerson et al. (2014)	USA	1079	Cross-sectional	≥80	**Loneliness:** UCLA-3 loneliness scale.	**Global cognition:** MMSE.	Lower levels of loneliness were associated with better cognitive functioning.
Glei et al. (2005)	Taiwan	2387	13	≥60	**Social network:** marital status, living situation, weekly contact with relatives, friends, and neighbours. **Social participation:** frequency of participation in activities.	**Global cognition:** SPMSQ.	Greater engagement in social activities was associated with lower risk of cognitive impairment. Social network was not significantly related to cognitive decline.
Golden et al. (2009)	Ireland	1334	Cross-sectional	≥65	**Social network:** Wenger's network typology (classifies networks into five types, based on eight items which assess availability of close local family, level of involvement of family, friends and neighbours, and level of interaction with community and voluntary groups).	**Global cognition:** MMSE.	Distance to nearest child and relative, and frequency of contact with relatives was not associated with poor cognition. Attendance at religious and other meetings, and contact with friends and neighbours was associated with poor cognition.
Gow et al. (2007)	UK	488	69	≥80	**Social support:** The significant others scale which assesses the availability of, and perceived satisfaction with, the support network. **Living situation** **Loneliness:** rate current loneliness and whether availability of people to talk to about problems.	**Mental ability:** MHT administered at ages 11 and 79. Raw MHT scores converted into IQ scores.	A greater number of people in the support network was not associated with better cognitive function. Being married was associated with better cognitive ability. Living alone was associated with poorer cognitive function.
Gow et al. (2013)	UK	1091	59	≥70	**Marital status** **Living arrangement** **Social contact:** frequency of social contact (face-to-face, phone, letter) in the past two weeks. **Loneliness:** 'at the present moment do you feel lonely?' **Social support:** 'how often are there people you can really count on to be dependable when you needed help?' and the level of satisfaction with support.	**Mental ability:** MHT administered at ages 11 and 79. Raw MHT scores converted into IQ scores. **Intelligence:** WAIS-R memory **Reaction and inspection time:** reaction and inspection time.	Receiving more social support was associated with better cognitive performance (although there was no association with memory). Marital status and the number of social contacts were not associated with cognitive function. A higher level of loneliness was associated with lower general cognitive ability, whereas not living alone and higher social support were independently associated

							with faster processing speed (but not after controlling for depression).
Graves et al. (1999)	USA	1604	2	≥65	**Social support:** modified interpersonal support evaluation list.	**Global cognition:** CASI.	Social support was not related to cognitive decline.
Green et al. (2008)	USA	874	23	≥40	**Social network:** number of relatives, friends, neighbours, frequency of interaction on the phone or face-to-face visits, and availability of emotional support.	**General cognitive function:** MMSE. **Delayed recall:** delayed recall task.	Larger social networks and greater availability of emotional support was associated with better scores of the MMSE and delayed recall task. Frequency of social contact was not associated with cognitive scores.
Håkansson et al. (2009)	Finland	1449	21	≥65	**Marital status:** married/ cohabiting, separated/ divorced, single, or widowed.	**Dementia diagnosis:** DSM-IV **General cognition:** MMSE.	Mid-life marital status was associated with late-life cognitive function. People without a partner had twice the risk of developing cognitive impairment or Alzheimer's disease compared to those living with a partner.
Haslam et al. (2014)	UK	3413	8	≥50	**Social contacts:** number of close relationships with children, immediate family, and friends, frequency of contact, and the quality of social contacts. **Loneliness:** "how often do you feel you lack companionship?" **Social engagement:** number of group memberships (e.g. sports, church, social clubs, neighbourhood watch, education, arts, music), community activities (e.g. day trips, holidays, hobbies, using the internet, reading), and participation in cultural activities (e.g. cinema, restaurants, theatre, concert, opera).	**Orientation:** give day, month, and year. **Immediate and delayed memory:** list recall. **Prospective memory:** carry out a previously presented instruction later in the session. **Verbal fluency:** category recall.	Group engagement was associated with better cognitive function. There was a significant interaction between group engagement and age, indicating that these group relationships are most important when people are older.
Ho et al. (2001)	Chinese	988	3	≥70	**Marital status** **Social support:** contact with friends, relatives, neighbours, and participation in community or religious activities.	**Orientation:** Clifton Assessment Procedure for the elderly.	Among men, being divorced and having poor social support increased the risk of cognitive impairment.
Holmén et al. (2000)	Sweden	589	Cross-sectional	≥75	**Loneliness:** (emotional) 'do you experience loneliness?' (social) 'do you often feel lonely?'	**General cognition:** MMSE. **Dementia diagnosis:** DSM-III-R. **Dementia severity rating** CDR.	Social loneliness was associated with dementia status. Emotional loneliness was not associated with dementia status.
Holtzman et al. (2004)	USA	354	12	≥50	**Social network:** number of relatives, family members, friends, and neighbours kept in touch with by phone or visits, and frequency of contact. **Emotional support:** how much respondents believed spouse or partners, relatives, and friends cared about them, could rely on them for help for a serious problem, and could relax/ be themselves around.	**Global cognition:** MMSE.	A larger social network was associated with less cognitive decline. There was no association found for the benefits of emotional support on cognition.
Holwerda et al. (2012)	Netherlands	2173	3	≥65	**Social isolation:** living alone, unmarried, poor social support. **Loneliness:** 'Do you feel lonely or do you feel very lonely?'	**Global cognition:** CAMDEX and MMSE. **Dementia diagnosis:** GMS-AGECAT.	People living alone and those not or no longer married, and those experiencing feelings of loneliness had an increased risk of dementia. Not having social support was associated with a lower risk of dementia.
Hsu, (2007)	Taiwan	2310	6	≥60	**Social participation:** paid or unpaid work and attending meetings of social groups/ clubs (e.g. religious, union or occupational organization, political group, community action or service group, clan association, elderly club)	**General cognition:** SPMSQ.	Compared to those who did not work at all, having paid work did not affect cognitive function, whereas doing unpaid work at baseline was associated with a higher probability of poorer cognitive function. Participation in social groups was not associated with cognitive function.

Hughes et al. (2008)	USA	217	5	≥65	**Social network:** number of contacts, frequency of contact, and number of close relatives and friends, negative social interactions (how often in the past month others placed demands, were critical, pried into affairs, and took advantage). **Social support:** emotional support (frequency of others providing support and comfort in difficult times, listening or talking about feelings, and showing interest or concern), instrumental support (frequency of others providing transportation, help with housework, chores, and help with shopping), informational support (frequency of others suggesting action to solve a problem, making a difficult situation easier to understand, and sharing what they did in a similar stressful situation), and satisfaction with support.	**General cognition:** 3MS. **Attention:** Stroop test. **Perceptual speed:** trail making test (A & B). **Episodic memory: d**elayed free recall, cued recall, and recognition.	Baseline satisfaction with support and social network were associated with better cognitive performance. Receiving less emotional, instrumental, or informational support was not associated with cognitive function. Reporting more negative social interactions was associated with better general cognitive ability.
Hughes et al. (2013)	USA	816	3	≥65	**Social activity:** variety and frequency of participation in activities (e.g. religious attendance, attending a special family occasion, visiting friends/ family, senior centre, clubs, restaurants, lodge, bar, and working/ volunteering.	**Global cognition:** MMSE.	More frequent engagement in a variety of social activities in persons with MCI was associated with a lower risk of poor cognitive function.
James, Wilson et al. (2011)	USA	1138	5	≥65	**Social activity:** frequency of participation in social activities in the past year (e.g. restaurants, sporting events, bingo, trips, volunteer work, visits to relatives or friends houses, participation in groups, such as senior centres, religious attendance).	**Global cognition:** combination of sub-domains: episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability.	Global cognitive decline (and decline across each individual cognitive domain) was reduced by an average of 70% in those who were frequently socially active compared to infrequently.
Karp et al. (2005)	Sweden	776	3	≥75	**Social activity:** frequency of participation in activities classified as low (handicraft, exhibitions, museums, walking, gardening, cooking, writing), moderate (visiting a summerhouse, attending courses, theatre, concert, sport, travelling, outdoor activities, playing music, singing), and high (playing chess or cards, political or cultural interests, meeting friends, participating in groups, attending church, bingo) social component.	**Dementia diagnosis:** DSM-III-R	Greater engagement with social activity was not associated with lower risk of dementia.
Li & Zhang (2015)	China	4190	7	≥64	**Social network:** marital status and number of close children. **Social participation:** frequency of playing cards/ mah-jong, and attending organized social activities. **Functional support:** availability of three contacts they rely on to 'talk most frequently in daily life', 'talk to first when you need to share your thoughts?', and 'ask for help when you have problems/ difficulties?'	**General cognition:** C-MMSE.	People with family-focused or restricted network types tended to have poorer cognitive function.
Lindstrom et al. (2005)	USA	466	Cross-sectional	≥61	**Social activity:** frequency of listening to music, attending social clubs, talking on the phone, visiting with others, religious attendance.	**Dementia diagnosis:** neuropsychological, laboratory and neurological examinations.	Participation in social activities reduced the risk of developing Alzheimer's disease.
Niti et al. (2008)	China	1635	1	≥55	**Social activity:** number and frequency of participation in religious services, cinema, restaurants, sports events, day or excursion trips, playing cards or games, senior citizen clubs, group recreational activities (e.g. karaoke/ dancing).	**General cognition:** MMSE.	Participation in social activities was associated with a lower risk of cognitive decline.

Okabayashi et al. (2004)	Japan	2200	Cross-sectional	≥60	**Social support:** availability of social contacts to talk about your worries or problems and feeling loved and cared for. **Negative relations:** assessed how critical, demanding, or overly protective the participants spouse, children, relatives, and friends are.	**General cognition:** SPMSQ (Japanese version).	Social support was not associated with cognitive impairment. Greater support from children was associated with reduced cognitive impairment. Among those with a spouse, greater negative strain was correlated with a reduced level of cognitive impairment.
O'Luanaigh et al. (2012)	Ireland	466	Cross-sectional	≥70	**Marital status** **Loneliness:** 'Do you feel lonely?' **Social networks:** Wenger's Social Networks Typology (classifies social networks into local integrated, family-dependent, private, local self-contained and wider community focused).	**Pre-morbid intellect:** National Adult Reading Test (NART-2) **Psychomotor processing speed:** digit symbol coding **Verbal fluency:** category fluency **Visual memory:** Wechsler memory scale **Working memory:** letter number sequencing **Global cognition:** MMSE.	There was an association between loneliness and global cognition (and sub-domains psychomotor processing speed and visual memory). There was no significant relationship between social network or marital status and cognition.
Paillard-Borg et al. (2009)	Sweden	776	9	≥75	**Social activity:** number and frequency of social activities and other organizations, frequency and satisfaction of contact with friends, children, and relatives.	**Dementia diagnosis:** DSM-III-R **Global cognition:** MMSE	Social factors are protective against dementia risk.
Paúl et al. (2010)	Portugal	1268	Cross-sectional	≥50	**Social network:** LSNS-6 **Marital status:** single, married, or widowed. **Living arrangement:** with partner, children, or alone.	**Global cognition:** MMSE.	Widowers showed the highest percentage of cognitive impairment, followed by single people, and then married people. There was no association between cognitive impairment and social networks.
Saczynski et al. (2006)	USA	2513	4, 8	≥45	**Social engagement:** marital status, living arrangement, frequency of participation in social, political, or community groups, social events, number of face-to-face or telephone contacts with close friends per month, and the existence of a confidant relationship).	**Global cognition:** CASI. **Dementia diagnosis:** DSM-III-R, neuropsychological battery, neurologic examination, and a proxy interview including the IQCODE.	No association between midlife social engagement and cognitive function or dementia risk. Those with lower levels of late-life social engagement had a poorer cognitive function and higher dementia risk. Those with low social engagement in both midlife and late-life had a slightly higher risk of dementia than those with consistently high engagement.
Seeman et al. (2001)	UK	1145	7.5	≥70	**Marital status** **Social network:** number contacts (children, friends, and relatives). **Social participation:** monthly participation in religious or other groups. **Social support:** emotional support (availability of people at ease with and able to call on for help and listen about worries or problems, feelings loved and cared for), instrumental support (receiving help with daily tasks or giving advice). **Negative interactions:** frequency of negative interactions involving conflicts or excessive demands from others.	**Language:** Boston naming test. **Abstraction:** WAIS-R. **Spatial ability:** copying. **Recall:** incidental and delayed item recall.	More frequent emotional support, being unmarried, and experiencing more frequent conflict/ demands from relationships was associated with better cognitive function at baseline. Frequency of emotional support was associated with change in cognitive performance at follow-up.
Shankar et al. (2013)	UK	6034	4	≥50	**Social isolation:** marital status, living situation, contact with children, family, and friends, and engagement with organizations, religious groups, sports clubs or committees. **Loneliness:** UCLA Loneliness Scale.	**Memory:** immediate and delayed recall. **Verbal fluency:** category fluency.	Social isolation and loneliness were associated with poorer scores on verbal fluency and memory at baseline. Increasing isolation was associated with lower scores on verbal fluency and memory at follow-up. Loneliness was associated with lower scores on recall at follow-up but not with verbal fluency.

Simning et al. (2014)	USA	190	Cross-sectional	≥60	**Social isolation:** LSNS-6. **Social support:** multidimensional scale of perceived social support.	**Global cognition:** Mini-Cog.	Social isolation and social support were not associated with cognitive function.
Singh-Manoux et al. (2003)	UK	5352	Cross-sectional	≥50	**Social activity:** frequency of participation in social activities (e.g. visiting friends and relatives, going to pubs and social clubs, cultural visits, social games, positions of office, school governor, councillor, involvement in clubs or organisations).	**Verbal memory:** word recall. **Inductive reasoning:** the AH 4-I. **Verbal ability:** the mill hill vocabulary test. **Phonemic and semantic verbal fluency:** category naming.	Participation in social leisure activities was associated with better cognitive function.
Stessman et al. (2013)	Israel	2181	15	≥70	**Loneliness:** 'How often do you feel lonely?'	**Global cognition:** MMSE.	Baseline loneliness was not associated with cognitive impairment.
Stoykova et al. (2011)	France	2055	20	≥65	**Social index score:** social network size, satisfaction with social relationships, feeling understood by others, and participation in social activities.	**Global cognition:** MMSE. **Semantic verbal fluency:** Isaacs set test. **Abstract thinking:** similarities test. **Episodic memory and learning abilities:** Wechsler paired associate test. **Visual-perceptual speed:** digit symbol test. **Immediate visual memory:** Benton visual retention test.	People with higher social index scores had better semantic verbal fluency and episodic memory at baseline. There was no association between the social index score and any of the cognitive measures at follow-up.
Tilvis et al. (2004)	Finland	629	10	≥75	**Loneliness:** 'Do you ever suffer from loneliness?'	**Global cognition:** MMSE. **Dementia severity rating:** CDR.	Feelings of loneliness were strong predictors of cognitive decline.
van Gelder et al. (2006)	Finland, Netherlands, and Italy	1030	10	≥65	**Marital status:** married, divorced, separated, or widowed. **Living situation:** alone or with others.	**General cognition:** MMSE.	Being unmarried and living alone was associated with poor cognitive function.
Wang et al. (2002)	Sweden	732	7	≥75	**Social activity:** number and frequency of activities participated in (e.g. attending the theatre, concerts, or art exhibitions, traveling, playing cards or games, participating in social groups or a pension organization). **Social network:** marital status, living arrangement, parenthood, number of close social ties, frequency of contact, satisfaction with social network.	**Dementia diagnosis:** DSM-III-R	People who frequently engaged in social activity had a lower incidence of dementia.
Wang et al. (2015)	China	764	Cross-sectional	≥90	**Social networks:** marital status, living arrangement, number of children, close friends, and neighbours, frequency of face-to-face contact with, visits to, and visits from, family, friends, and neighbours, frequency of participation in collective activities in the community.	**General cognition:** MMSE.	Being single, having more close friends, and a high level of social contact were associated with better cognitive function. Number of children, living arrangements and ties with neighbours were not associated with cognitive function.
Wilson et al. (2007)	USA	791	4	≥70	**Loneliness:** de Jong-Gierveld Loneliness Scale. **Social isolation:** number of children, family, and friends, and frequency of interaction.	**General cognition:** MMSE **Episodic memory:** immediate and delayed recall. **Semantic memory:** verbal fluency test, the Boston naming test, and the national adult reading test. **Working memory:** digit span forward and backward and digit ordering.	Loneliness was associated with an increased risk of dementia. More frequent social activity was associated with reduced Alzheimer's disease risk. Social network size was not related to risk.

						Perceptual speed: number comparison, symbol digit modalities test, and Stroop test. **Visuospatial tests:** judgment of line orientation, standard progressive matrices.	
Wilson et al. (2015)	USA	529	4.8	≥70	**Negative social interaction:** frequency of experiencing neglect or rejection by others, unwanted intrusion or advice, failure by others to provide help, and unsympathetic or insensitive behaviour by others. **Social network:** number of children, family, and friends with regular contact. **Social activity:** frequency of participation in social activities (e.g. restaurants, sporting events, bingo, day or overnight trips, volunteer work, visiting relatives or friends, participating in groups, and religious attendance). **Loneliness:** de Jong Gierveld Loneliness Scale.	**Episodic memory:** immediate and delayed recall. **Semantic memory:** verbal fluency test, the Boston naming test, and the national adult reading test. **Working memory:** digit span forward and backward and digit ordering. **Perceptual speed:** number comparison, symbol digit modalities, and Stroop test. **Visuospatial tests:** judgment of line orientation, standard progressive matrices.	A higher level of negative social interactions was associated with higher incidence of MCI and more rapid cognitive decline.
Xu et al. (2015)	USA	841	15	≥60	**Marital experience:** positive marital experience (satisfaction with marriage, feeling loved and cared for by spouse, and how much partner listens to worries or problems) and negative marital experience (how bothered or upset participants feel about their marriage and the frequency of unpleasant disagreements or conflicts).	**Global cognition:** SPMSQ.	People with more frequent negative marital experiences had a slower decline in cognition over time compared to those with less frequent negative marital experiences. People who were divorced experienced a more rapid increase in cognitive limitations.
Yaffe et al. (2009)	USA	2509	8	≥70	**Social aspects:** paid or voluntary word, providing care for a spouse or child, frequent visits to family or friends, feeling a need for more social support, and living situation.	**General cognition:** 3MS.	People who worked or volunteered, were not taking care of a spouse or child, were receiving enough social support, and living with someone at baseline and were more likely to be cognitive maintainers than decliners. Major decliners were more likely to be older, less likely to work or volunteer, and less likely to receive support.
Yeh & Liu (2003)	Taiwan	4989	Cross-sectional	≥65	**Social support:** marital status, perceived positive support from friends, living alone, and loneliness.	**Global cognition:** SPMSQ.	Higher cognitive function was associated with increased social support. People that were unmarried had lower cognitive function than those who were married.
Zunzunegui et al. (2003)	Spain	964	4	≥65	**Social network:** number of monthly visual and phone contacts with friends and relatives (other than children). **Social integration:** membership in a community association, monthly religious attendance, and visits to a social centre with recreational activities for the elderly. **Social engagement:** feeling helpful, useful, and able to play an important role in children, family, and friends lives.	**Global cognition:** SPMSQ. **Orientation and memory:** the Barcelona test and story recall.	Small social networks, poor social integration, and lack of social engagement were associated with cognitive decline. Formal participation in social activities protects against cognitive decline.

Note: WAIS-R = the Wechsler Adult Intelligence Scale-Revised, ADLs = activities of daily living, SES = socioeconomic status, 3MS = Modified Mini-Mental State Examination, DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, third edition – revised, CASI = Cognitive Abilities Screening Instrument, MMSE = Mini-Mental State Examination, LSNS-6 = Lubben Social Network Scale-6, SPMSQ = Short Portable Mental Status Questionnaire, PCL = Legane´s' Cognitive Test (Prueba Cognitiva de Legane´s), AMT = Abbreviated Mental Test, TICS-M = Telephone Interview for Cognitive Status –modified, TDQ = The Telephone Dementia Questionnaire, CAMCOG = Cambridge Cognitive Examination, C-MMSE = Chinese version of the Mini-Mental State Examination, C-CDR = Chinese version of the Clinical Dementia Rating Scale, MHT = Moray House Test, IQ = intelligence quotient, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, fourth edition, CDR = Clinical Dementia Rating Scale, CAMDEX = Cambridge Mental Disorders of the Elderly Examination, GMS-AGECAT = The Geriatric Mental State Examination and the Automated Geriatric Examination for Computer Assisted Taxonomy, MCI = Mild Cognitive Impairment, IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly.

Structural

The structural dimension of social connections refers to objective and quantitative features of social contexts (Antonucci, 1990; Barnes et al. 2004). This includes socio-demographic features, such as marital status and living situation, and social networks, social isolation, and social engagement.

Marital status

As marital status is an objective demographic variable, there was little variation in its definition and assessment. Fourteen studies were identified that assessed the relationship between marital status and cognitive function, and several other studies used marital status as an indicator of other social concepts, such as social isolation, or social networks. Most measures asked participants to indicate their marital status based on response categories such as married, widowed, divorced, single, or cohabiting (Table 3.2: Gow et al. 2013; Håkansson et al. 2009; Li & Zhang, 2015; O'Luanaigh et al. 2012; Paúl et al. 2010; van Gelder et al. 2006). Some measures also considered the number of years married, widowed, or divorced (Aartsen, van Tilburg, Smits, Comijs & Knipscheer, 2005). Only one study assessed qualitative features of marriage and considered positive and negative interactions within the relationship (Xu, Thomas & Umberson, 2015).

Some of these studies concluded that being married is protective against poor cognitive function (Aartsen et al. 2005; Gow et al. 2007; Håkansson et al. 2009; van Gelder et al. 2006; Yeh & Liu, 2003), dementia (Holwerda et al. 2012) and Alzheimer's disease (Håkansson et al. 2009). One study found that the risk for developing cognitive impairment was twice as high for those without a partner at mid-life, and this risk was almost three times higher for those without a partner at both mid- and late- life (Håkansson et al. 2009). Length of widowhood has also been found to predict subsequent rate of cognitive decline (van Gelder et al. 2006); however findings are inconsistent (Aartsen et al. 2005). People who are widowed have been reported to have a higher rate of cognitive impairment (16.3%) than people who are single (12.1%) or married (6.1%: Paúl et al. 2010). Divorcees are reported to experience a more rapid decline in cognition following their divorce (Xu et al. 2015). Together, this evidence suggests that being married may benefit late-life cognition. However, some findings contradict this and report no association between marital status and cognitive function (Glei et al. 2005; Gow et al. 2013; Paúl et al. 2010; O'Luanaigh et al. 2012). Some evidence suggests that cognitive function is higher among those who are unmarried than those who are married (Seeman, Lusignolo, Albert & Berkman, 2001; Wang et al. 2015). This suggests that the relationship between marital status and cognition is complicated and other factors may be implicated.

Although marital status provides a useful perspective on wider social contexts, this is too simplistic as a stand-alone measure. The approach assumes that one close social relationship with a spouse is the optimal form of social contact to protect against cognitive decline, yet marriage is no longer necessarily the norm in every society. Many people remain single either for the majority of their lives, or at various phases of their lives. Rather than depending on a spouse or long-term partner, single people may substitute other social contacts to satisfy this role. Although these relationships are not intimate, they may be sufficient to provide a comparable level of social and emotional support. Furthermore, being socially connected encompasses more than interaction with one other individual. It may be the complexity of social networks and interactions, and the indirect benefits of social contact, that protect against cognitive decline. Social contact with one person does not seem sufficient to provide this; hence engagement with the wider social network must be considered (Berkman, 2000). The simplicity of the measure may account for the variance in reported findings relating to cognitive outcomes. However, if included in a measure assessing wider features of social contexts, marital status may provide useful information regarding social relationships (e.g. Armstrong et al. 2015; Ertel et al. 2008; Fratiglioni et al. 2000; Glei et al. 2005; Gow et al. 2013; Li & Zhang, 2015; Saczynski et al. 2006; Seeman et al. 2001; Wang, Karp, Winblad & Fratiglioni, 2002; Wang et al. 2015; Yeh & Liu, 2003).

Living situation

Like marital status, living situation is based on demographic information and can be objectively assessed, typically by asking about household composition and where the participant resides (Table 3.2: Gow et al. 2007; Gow et al. 2013; Paúl et al. 2010; van Gelder et al. 2006). Nine studies were identified that assessed the association between living situation and cognitive function, and the measures in these studies typically also assessed social networks.

Some of these studies found that living alone was associated with poor cognitive function (Gow et al. 2007; van Gelder et al. 2006; Yaffe et al. 2009) and elevated risk of dementia (Fratiglioni et al. 2000; Holwerda et al. 2012). Living alone has been associated with a twofold risk of cognitive decline compared to living with others and this risk may be 3.5 times higher for men living alone at both mid- and late- life (van Gelder et al. 2006). Conversely, some studies have found no association between living alone and cognitive function (Conroy et al. 2010; Glei et al. 2005; Gow et al. 2013; Wang et al. 2015). This inconsistency suggests that living situation is not the only factor that influences cognitive function and that the simplicity of living situation as an individual measure may not be sufficient to capture changes in cognitive function.

One issue with the literature on living situation in later life is that living situation represents a small aspect of an individual's complex social context. It is questionable whether living alone necessarily means an individual has less opportunity for engagement. If living situation is assessed alongside other aspects of social contexts, it may provide additional insight into the individual's social lifestyle (e.g. Andrew & Rockwood, 2010; Armstrong et al. 2015; Fratiglioni et al. 2000; Gerst-Emerson, Shovali & Markides, 2014; Holwerda et al. 2012; Saczynski et al. 2006; Wang et al. 2002; Wang et al. 2015; Yeh & Liu, 2003).

Social networks

Assessing the composition of social networks can provide insight into social connections. The term social network refers to the set of people with whom an individual has contact and shares a social bond (Dunbar, 1998; Zunzunegui et al. 2003). Social networks may be influenced by marital status and living situation, but these are not the only, or even necessarily the key, consideration. Networks can be further divided into family, friends, and acquaintances, according to the role these contacts hold within the network (Lubben et al. 2006; Phillipson, Bernard, Phillips & Ogg, 1998). Social networks were assessed by 22 studies in the review. The most common approach to assess social networks was a count of the number of contacts within the social network and the frequency of interaction with these contacts (Table 3.2: Albert et al. 1995; Barnes et al. 2004; Barnes et al. 2007; Béland et al. 2004; Bennett et al. 2004; Crooks et al. 2008; Ellwardt, van Tilburg & Aartsen, 2015; Elwood et al. 1999; Fratiglioni et al. 2000; Glei et al. 2005; Green et al. 2008; Holtzman et al. 2004; Hughes et al. 2008; Stoykova et al. 2011; Wang et al. 2015; Wilson et al. 2015; Zunzunegui et al. 2003). Some measures considered the geographical proximity of contacts (Barnes et al. 2004; Béland et al. 2005; Golden et al. 2009; Holtzman et al. 2004; Zunzunegui et al. 2003). Another approach was to use standardised measures that have been developed to assess social networks, such as the Lubben Social Network Scale (LSNS; Lubben, 1988) or the shortened six item version (LSNS-6; Lubben et al. 2006), or Wenger's social networks typology (Wenger, 1997). These measures also use a count of contacts and frequency of interaction, in addition to enquiring about the availability of social support and social engagement (Barnes et al. 2007; Crooks et al. 2008; Golden et al. 2009; Paúl et al. 2010; O'Luanaigh et al. 2012).

Findings suggest that a larger social network, containing a high number of social ties protects against cognitive decline (Barnes et al. 2004; Barnes et al. 2007; Bassuk et al. 1999; Béland et al. 2005; Bennet et al. 2006; Crooks et al. 2008; DiNapoli et al. 2014; Zunzunegui et al. 2003) and dementia (Crooks et al. 2008; Fratiglioni et al. 2000; Holtzman et al. 2004) in later life. Studies that reported this association were both cross-sectional and longitudinal, with a follow-up period of between two

(Béland et al. 2005) and twelve (Holtzman et al. 2004) years. It has been suggested that compared to an individual with one social tie, the rate of global cognitive decline was reduced by about 39% for those with 16 social ties (Barnes et al. 2004). Likewise, those with no social ties had twice the odds of experiencing cognitive decline than those with five or six ties (Bassuk et al. 1999). More specifically related to dementia risk, a limited social network has been suggested to increase the risk of dementia by 60% (Fratiglioni et al. 2000). However, there are some contradictory findings that suggest social networks are not associated with better cognitive function. (Albert et al. 1995; Elwood et al. 1999; Glei et al. 2005; Golden et al. 2009; Gow et al. 2007; O'Luanaigh et al. 2012; Paúl et al. 2010; Wang et al. 2015; Wilson, Krueger et al. 2007). Some studies have found the relationship between social networks and cognitive function to exist cross-sectionally, but not longitudinally (Ellwardt et al. 2015; Green et al. 2008; Stoykova et al. 2011). This has led some authors to conclude that social network characteristics and cognitive functioning are intertwined, but that the relationship may be mostly cross-sectional in nature (Ellwardt et al. 2015). This may mean that social networks tend to be larger in individuals that are more cognitively able, or conversely that social network size reduces for people with cognitive decline.

These approaches seem adequate to assess basic structural features of social networks and to indicate the frequency of interaction with these contacts. Many measures offer response categories covering a range of social contacts and frequencies of interaction. One issue with this approach is that these measures cannot capture the quality of relationships. Many people may have an extensive social network but typically rely on a few close social contacts (Hill & Dunbar, 2003). Measures that assess networks based on a count of contacts and frequency of interaction cannot capture these more complex features and thus may be insufficient to comprehensively define social contexts. Very few measures considered methods that did not involve face-to-face contact such as phone calls, email, or letters and no studies in this review considered video chat (Crooks et al. 2008; Green et al. 2008; Holtzman et al. 2004; Zunzunegui et al. 2003). These alternative methods of communication should not be disregarded when enquiring about social contact as we do not know how face-to-face contact compares to other forms of contact. Some measures ask additional questions to assess social networks; for example, questions regarding marital status and living situation (Ellwardt et al. 2015; Fratiglioni et al. 2000; Glei et al. 2005; Wang et al. 2015), social engagement (Ellwardt et al. 2015; Stoykova et al. 2011; Wang et al. 2015), and functional aspects of the social network, such as the availability of emotional support (Barnes et al. 2007; Bennett et al. 2004; Green et al. 2008; Stoykova et al. 2011). Although this information is useful, it is not as relevant for assessing network composition. Including these questions therefore reduces the specificity and validity of measures.

Social isolation

Social isolation can be defined as the absence of meaningful and sustained relationships with family and friends or disengagement from the wider community (Nicholson Jr, 2009). Some authors argue for a distinction between perceived social isolation and social disconnection (Cornwell & Waite, 2009). While social disconnectedness focuses on structural features such as a lack of social contacts and social inactivity, perceived isolation emphasises dissatisfaction with relationships rather than their absence (DiNapoli et al. 2014). Only three studies identified in this review considered social isolation and its relationship with cognitive function. Unlike other concepts, the assessment of social isolation was less clear. Many studies used a networks approach including standardised measures, such as the LSNS (Lubben, 1988), which can be justified based on consensus within the literature that isolation is defined as an absence of social contact (Table 3.2: Nicholson Jr, 2009). Some measures also consider perceived social isolation by enquiring about satisfaction with social networks and feelings of loneliness.

Findings regarding the relationship between social isolation and cognition are mixed. One study reported that higher levels of isolation were associated with poorer cognitive function at baseline and four year follow-up (Shankar et al. 2013). One further study supports this, finding that social isolation was associated with poorer overall cognitive functioning cross-sectionally (DiNapoli et al. 2014). Higher levels of perceived social isolation have been associated with a reduction in overall cognitive function, emphasising the importance of subjective appraisals of satisfaction with social contact. Conversely, one study reported no association between social isolation and cognitive function (Simning et al. 2014). The inconsistency across these few studies suggests that current evidence is insufficient to determine whether this relationship is present.

Several studies made inferences about the level of social isolation based on other features of social connections, such as the availability of social support (Holwerda et al. 2012), living situation, marital status (Holwerda et al. 2012; Wilson, Krueger et al. 2007), or social engagement (Holwerda et al. 2012; O'Luanaigh et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007). Including additional aspects such as living situation and geographical proximity to others can influence the identification of social isolation. For example, Scharf (2002) included living situation in a measure of social isolation and found that 79% of participants met the criteria for social isolation. In a revised measure not including living situation, only 2% of participants met the criteria for severe isolation, and 23% for moderate isolation (Scharf et al. 2004; Scharf & Smith, 2004). Evidently, including living arrangement and geographical proximity inflates the estimation of isolation. Excluding 'living alone' from measures of social isolation stabilises estimates of isolation to around 5-10% of older people (Victor

et al. 2008). This reflects that including additional concepts to assess isolation reduces the specificity of the measure and thus the validity. An additional issue with measures that assess social isolation and other structural social concepts is that authors determine a cut-point by which individuals are classified as isolated or not. This fails to capture individual differences in preference for level of contact with others (Burger, 1995). For example, some people may prefer to have smaller social networks and less frequent contact and are satisfied with this, whereas others may prefer a large social network and frequent contact. Measures that are based on structural aspects such as a count of the number of social contacts or frequency of interaction cannot capture how individuals' feel about their level of social contact which may be important to predict cognitive or other health outcomes. There is also considerable variation in defining social isolation. Some studies have defined isolation as having contact with less than 21 people per week (Townsend, 1957; Tunstall, 1966). Others suggest less than one direct contact per day (either face-to-face or over the phone) to indicate isolation, and three or more direct contacts per day to indicate high engagement (Lubben 1988; Lubben et al. 2006).

Social engagement

Social engagement can be defined as participation in socially meaningful or productive activity that contributes to the maintenance of social connections (Barnes et al. 2004; Zunzunegui et al. 2003). A high level of engagement can reinforce existing social relationships and provide a basis for developing new relationships, and hence may lead to a larger social network and reduce isolation (Bassuk et al. 1999). Social engagement was assessed in 21 studies identified in the scoping review. Participants were typically asked to indicate whether they participate in any social activities, the frequency of participation, and the type of activity engaged in (Barnes et al. 2004; Bassuk et al. 1999; Béland et al. 2005; Ertel et al. 2008; Glei et al. 2005; Hsu, 2007; Hughes et al. 2013; James, Wilson et al. 2011; Karp et al. 2005; Li & Zhang, 2015; Lindstrom et al. 2005; Niti et al. 2008; Paillard-Borg et al. 2009; Saczynski et al. 2006; Seeman et al. 2001; Wang et al. 2002; Wilson et al. 2015; Zunzunegui et al. 2003). Some studies incorporated additional concepts into measures of social engagement, such as marital status, living situation, social networks, and social support.

Findings suggested that a higher level of social engagement was associated with a lower risk of poor cognitive function (Barnes et al. 2004; Bassuk et al. 1999; Béland et al. 2005; Conroy et al. 2010; Glei et al. 2005; Golden et al. 2009; Haslam et al. 2014; Hughes et al. 2013; James, Wilson et al. 2011; Niti et al. 2008; Paillard-Borg et al. 2009; Singh-Manoux et al. 2003; Yaffe et al. 2009; Zunzunegui et al. 2003) and dementia (Lindstrom et al. 2005; Wang et al. 2002; Wilson, Krueger et al. 2007) in later life. One study reported that compared to those who are infrequently socially active, risk of cognitive

decline was reduced by approximately 70% in socially active individuals (James, Wilson et al. 2011). Participation in social groups has been found to reduce the cognitive age of an 80-year-old by 9.5 years (Haslam et al. 2014). For those with MCI, higher frequency of engagement and a wider range of social activities slowed the progressive rate of decline over three years (Hughes et al. 2013). However, there is some evidence to suggest no association between social engagement and late-life cognitive function (Bosma et al. 2002; Elwood et al. 1999; Ho et al. 2001; Hsu, 2007; Karp et al. 2005; Saczynski et al. 2006). Again, this conflicting evidence limits understanding about the nature of this relationship.

There are some methodological challenges associated with the assessment of social engagement in later life. Many measures ask participants about engagement with a wide range of activities. Some of these activities may be more social than others, for example, visiting friends or attending an over 60s club may require greater social input than going to the theatre or participating in sport (Aartsen et al. 2002; Bassuk et al. 1999; Hultsch, Hammer & Small, 1993; Toepoel, 2013). Some studies account for this by grouping activities into categories based on the level of social input; however it is still difficult to determine the extent of social input the participant receives (Hsu, 2007; Karp et al. 2005; Paillard-Borg et al. 2009). For example, some older people may be more socially engaged while participating in a given activity than others. Likewise, many studies assessing social engagement ask participants about their leisure activities. Many leisure activities have social outcomes either as a main goal (e.g. visiting friends and family) or as a by-product of another primary goal (e.g. attending the theatre and group sports or games; Toepoel, 2013). It is therefore challenging to establish the extent of social input that contributes to cognitive function, as the leisure activity itself may provide cognitive stimulation and contribute to the maintenance of cognitive function (Global Council on Brain Health, 2017).

Functional

Social support

Unlike structural features of social connections, functional aspects consider how individuals' mobilise their social networks to gain support as required. Social support refers to the process through which support can be obtained from contacts within the social network in times of need (Williams, Barclay & Schmied, 2004). This concept can be further divided into emotional, instrumental, and informational support (Broadhead, Gehlbach & Kaplan, 1989; Dickens, Richards, Greaves & Campbell, 2011; Ellwardt et al. 2013; Holtzman et al. 2004; Hughes et al. 2008; Seeman & Berkman, 1988). Emotional support refers to support received when faced with difficult private matters. Instrumental support refers to practical support received for activities of daily living (e.g.

cooking, shopping, or transportation). Informational support refers to sharing information with contacts to solve a problem or understand a difficult situation (Ellwardt et al. 2013; Seeman et al. 2001). No single type of support emerges as consistently most effective. Effectiveness depends on the individual's situation, context, and requirements. Fourteen studies assessed social support and cognitive function. Some studies assessed social support in general (Conroy et al. 2010; Crooks et al. 2008; Gow et al. 2007; Gow et al. 2013; Graves et al. 1999; Ho et al. 2001; Holwerda et al. 2012; Okabayashi, Liang, Krause, Akiyama & Sugisawa, 2004; Simning et al. 2014; Yaffe et al. 2009; Yeh & Liu, 2003) and questions typically asked participants about the availability of, and satisfaction with, support. Other studies were more specific and aimed to assess one type of social support. For example, measures that assessed emotional support asked participants if they felt they could count on anyone to talk to about problems, or provide help when making difficult decisions (Albert et al. 1995; Bassuk et al. 1999; Ellwardt et al. 2013; Holtzman et al. 2004; Hughes et al. 2008; Li & Zhang, 2015; Seeman et al. 2001). Studies that assessed instrumental support asked participants if they had anyone that could provide practical help if needed, such as helping around the house or with shopping (Conroy et al. 2010; Ellwardt et al. 2013; Okabayashi et al. 2004; Seeman et al. 2001). Informational support was assessed by asking participants if they had someone they could gain information from to help solve a problem, make a difficult situation easier to understand, or to obtain advice (Ellwardt et al. 2013; Seeman et al. 2001). Some measures also assessed loneliness (Yeh & Liu, 2003), social contact, and social participation (Conroy et al. 2010; Ho et al. 2001; Yeh & Liu, 2003) as indicators of social support. Although these concepts may be associated with social support, they do not provide an indication of the level of support available and so including these additional indicators reduces the validity of such measures.

Studies that assessed social support have found that higher levels of support were associated with better cognitive function (Conroy et al. 2010; Crooks et al. 2008; Gow et al. 2013; Ho et al. 2001) and lower dementia risk (Crooks et al. 2008; Holwerda et al. 2012; Yaffe et al. 2009; Yeh & Liu, 2003). One study suggested that greater social support from children was associated with reduced cognitive impairment. This relationship was not found for support received from a spouse, friends, or neighbours (Okabayashi et al. 2004). However, some studies assessing the relationship between social support and cognition report no association (Gow et al. 2007; Graves et al. 1999; Simning et al. 2014). Studies that specifically assessed emotional support suggest that higher availability of emotional support was associated with better cognitive function (Ellwardt et al. 2013; Green et al. 2008; Seeman et al. 2001). However, some studies have not found this association (Albert et al. 1995; Bassuk et al. 1999; Holtzman et al. 2004). Studies that assessed the relationship between

instrumental (Ellwardt et al. 2013; Hughes et al. 2008) and informational support (Hughes et al. 2008) reported no association with late-life cognitive function.

One issue with the assessment of social support is that measures assume a unidirectional process of receiving support from others. None of the included studies consider that older people may provide support to others, which may be cognitively effortful and benefit cognitive function. Related research has reported that providing instrumental and emotional support to others significantly reduced mortality and that receiving support had no influence on mortality once giving support was taken into consideration (Brown, Nesse, Vinokur & Smith, 2003). This suggests that providing support has an important influence on health. Neglecting to assess an individual's role as a provider of support means that we cannot completely characterise the role of social support within networks (Bassuk et al. 1999). Another issue with the assessment of social support is the tendency to emphasise the social networks of older people are only useful to provide support. This emphasis problematizes normal aspects of social relationships and offers only a negative function for social networks. Older people draw upon their social networks for other reasons, such as engaging in social activities and having positive and meaningful interactions with friends and family. These experiences are likely to build relationships and thus increase reassurance that support is available if required. Failure to consider how these experiences may enhance perceptions of social support provides a limited perspective on the social contexts of older people.

Appraisal

Loneliness

The final dimension of social connections is appraisal. This refers to perceived satisfaction with aspects of the social network, such as the availability of social contacts or emotional closeness with other people (Grenade & Boldy, 2008; Routasalo, Tilvis, Kautiainen & Pitkala, 2009). Those who are not satisfied with their networks may express feelings of loneliness. Loneliness refers to a negative or unpleasant feeling of isolation, arising from the absence of, or dissatisfaction with, quality or quantity of existing relationships (Coyle & Dugan, 2012; de Jong Gierveld & Havens, 2004; Dickens et al. 2011; Victor et al. 2000). The experience of loneliness is subjective and can vary in frequency, intensity, and duration (Wenger & Burholt, 2004). While some individuals can live a solitary lifestyle and never experience feelings of loneliness, others may have extensive social networks but experience intense feelings of loneliness (Victor et al. 2005). There is an argument for dividing the concept into social and emotional loneliness (Holmén, Ericsson & Winblad, 2000; Peplau & Caldwell, 1978). Social loneliness refers to the negative feelings that arise as a result of an absence of meaningful relationships and lack of integration, whereas emotional loneliness refers to the

perceived lack of an attachment figure or confidant (van Baarsen, Snijders, Smit & van Duijn, 2001). Loneliness was assessed in 12 studies in this review. Given the subjective variation in the meaning of loneliness, assessing this concept operationally is challenging. Some studies assess social and emotional loneliness separately, whereas others assess loneliness as one concept (Table 3.2). Measures consistently assesses loneliness by asking participants to express current feelings of loneliness, or loneliness experienced within a specific temporal reference period (e.g. the past 12 months: Conroy et al. 2010; Gow et al. 2007; Gow et al. 2013; Holmén et al. 2000; Holwerda et al. 2012; O'Luanaigh et al. 2012; Stessman, Rottenberg, Shimshilashvili, Ein-Mor & Jacobs, 2013). Standardised measures of loneliness are available, such as the de Jong Gierveld Loneliness Scale which assesses social and emotional loneliness (de Jong Gierveld & Kamphuls, 1985), and the UCLA 3-item loneliness scale which assesses relational and social connections, and self-perceived isolation (Hughes, Waite, Hawkley, & Cacioppo, 2004). These measures were utilised in several studies (Ellwardt et al. 2013; Fung, Leung & Lam, 2011; Shankar et al. 2013; Wilson, Krueger et al. 2007; Wilson et al. 2015).

Collectively, studies have provided strong evidence that higher feelings of loneliness are associated with poorer cognitive function (Conroy et al. 2010; Ellwardt et al. 2013; Fung et al. 2011; Gerst-Emerson et al. 2014; Gow et al. 2013; O'Luanaigh et al. 2012; Shankar et al. 2013; Tilvis et al. 2004) and greater dementia risk (Holwerda et al. 2012; Wilson, Krueger et al. 2007). It has been reported that individuals who experience intense feelings of loneliness may be twice as likely to develop Alzheimer's disease and may have more rapid cognitive decline over four years compared to those with less intense feelings of loneliness (Wilson et al. 2007). Only one study in this review did not find an association between loneliness and cognition (Stessman et al. 2013).

Although loneliness is typically assessed by asking about current feelings of loneliness, it is difficult to establish the validity of this approach. Loneliness is an emotionally salient, complex, and subjective experience that is not static and can be challenging to operationalise (Victor et al. 2005). The meaning of loneliness is likely to vary considerably across individuals and cultures which may further influence the reliability of findings (Jylhä, 2004). Many studies use a single question which enables comparison across studies; however this is a simplistic approach and may not provide sufficient insight into the extent, nature, or meaning of loneliness, nor its causes and consequences. The use of a single item may increase the likelihood of generating a socially desirable response as it may be difficult for individuals to define their social context in terms of loneliness, especially to a researcher (Jylhä & Jokela, 1990). Single direct questions may be answered defensively by participants to avoid undermining their self-worth during interview (Victor et al. 2008).

Social index scores

Rather than focusing on one concept, some studies combine sets of questions that assess several social concepts, generating an overall 'social index' score. Four studies in the scoping review used this approach (Andrew & Rockwood, 2010; Armstrong et al. 2015; Conroy et al. 2010; Yaffe et al. 2009). Questions and concepts included in measures of social index scores have the potential to be very different. Although this provides a broader perspective covering several aspects of social contexts, the outcome score is not specific to any concept, meaning it is not possible to establish which concepts are most beneficial for maintaining cognitive function.

However, using a social index score may be more appropriate for assessing complex features of social contexts. While it is important to establish whether any specific social concepts have a greater influence on cognitive function than others, it could be argued that this approach provides an incomplete and compartmentalised perspective of social contexts. Social concepts have distinct definitions, but are correlated to some extent and operate dynamically to form unique social contexts for each individual (Victor et al. 2008). This raises questions about whether social concepts can be measured and understood in isolation. It may be more appropriate to use a social index score to consider multiple concepts and provide a comprehensive perspective of social connections and their relationship with cognitive function.

Measures of cognitive function

There is great variability of measures employed to assess cognitive function across studies. This inconsistency may further explain why findings assessing the relationship between social connections and cognitive function are so diverse. Many studies use measures of global cognition to assess cognitive function. However, a wide range of measures are available and there is considerable variation of measures employed across studies. The Mini-Mental State Examination (MMSE) was the most commonly used measure across studies in this review. Other measures included the Modified Mini-Mental State Examination (3MS), the Cambridge Cognitive Assessment (CAMCOG), the Cognitive Abilities Screening Instrument (CASI), the Short Portable Mental Status Questionnaire (SPMSQ), Legane's Cognitive Test (PCL), the Abbreviated Mental Test (AMT), the Telephone Interview for Cognitive Status–Modified (TICS-M), and the Mini-Cog. Global measures of cognitive function provide a single outcome score for overall cognitive function. However there are some global measures that can generate sub-scores for specific cognitive domains. Studies that assessed cognitive outcomes using the MMSE produced mixed findings and some reported a relationship between social concepts and cognitive function (Barnes et al. 2004; Ellwardt et al. 2015; Gerst-Emerson et al. 2014; Håkansson et al. 2009) while others reported no association (Bosma et al. 2002;

Elwood et al. 1999; Stessman et al. 2013). There were inconsistent findings across all social concepts, regardless of whether findings were cross-sectional or longitudinal, except for loneliness in which all studies using the MMSE reported a significant relationship (Gerst-Emerson et al. 2014; Holmén et al. 2000; Stessman et al. 2013; Tilvis et al. 2004; Wilson, Krueger et al. 2007). One advantage of using a standardised measure of global cognitive function is that they are well validated and cut-off scores for cognitive impairment are defined across a range of clinical settings so comparison of cognitive status across studies is possible. However, these measures are criticised and the adequacy of the sensitivity and specificity in detecting cognitive impairment is disputed (Lin, O'Connor, Rossom, Perdue & Eckstrom, 2013). Measures are often validated in samples of a specific age, educational level, or ethnic group which further complicates interpretation of scores (Black et al. 1999; Ng et al. 2007).

A further criticism is that many measures of global cognitive function provide only one score for global cognitive function. This does not allow full consideration of whether the assessed social concept affects overall cognition, or whether there are domain-specific effects. Some studies have accounted for this and have used measures that assess specific domains. This may have been in addition to the use of a measure of global cognition, or as an alternative. Some of these studies assessed only one specific domain or several domains, and others have utilised a large battery of measures that assess a wide range of domains. Many of these studies conducted analyses on the relationship between social constructs and each of these individual domains, and have then combined results from each of these domains to provide an overall outcome of global cognitive function. Unlike global measures, domain-specific assessments of cognitive function can determine whether social concepts are associated with impairment in specific cognitive domains. These associations are more likely to be missed by global measures of cognitive function. However, one issue with the assessment of specific cognitive domains is that there are a range of measures available to assess each domain and a range of cognitive domains that could potentially be assessed. This increases variation across studies, which may increase discrepancies in findings and create uncertainty regarding which cognitive domains are most affected by social constructs. A wide range of specific cognitive domains are assessed using a range of measures (Table 3.2). Domains assessed include language (DiNapoli et al. 2014), verbal fluency (O'Luanaigh et al. 2012), attention (Hughes et al. 2013), memory (Bennett et al. 2006; James, Wilson et al. 2011; Singh-Manoux et al. 2003; Stoykova et al. 2011; Wilson et al. 2015; Zunzunegui et al. 2003), orientation (Haslam et al. 2014), visuospatial ability (Seeman et al. 2001), perceptual speed (Hughes et al. 2008), and intelligence (Gow et al. 2007; Gow et al. 2013). Again findings for the association between social concepts and each cognitive domain were varied.

Rather than assessing cognitive function, some studies have assessed the relationship between social concepts and dementia diagnosis. Typically, these studies use the DSM diagnostic criteria (Andrew & Rockwood, 2010; Fratiglioni et al. 2000; Karp et al. 2005; Paillard-Borg et al. 2009), although other measures have been utilised, such as the Telephone Dementia Questionnaire (TDQ: Crooks et al. 2008), the Clinical Dementia Rating Scale (CDR: Fung et al. 2011; Tilvis et al. 2004), consulting medical records (Crooks et al. 2008; Lindstrom et al. 2005) and a combination of these approaches (Crooks et al. 2008). The use of dementia diagnosis rather than poor cognitive function creates further inconsistency across studies and may result in discrepancies in findings, especially given that social withdrawal may be a prodromal symptom of dementia (Saczynski et al. 2006).

3.5 Summary and conclusions

This review aimed to explore which concepts are used to reflect social connections and how these concepts are defined and assessed in the literature. A range of concepts were identified, including structural, functional, and appraisal aspects. Social networks and social engagement were the most frequently studied concepts. Marital status, social support, and loneliness were the next most frequently studied, followed by living situation, and finally social isolation which was only assessed in three of the studies identified. Fewer studies may focus on social isolation as the definition relates to numerous other concepts, such as social networks and social engagement, hence aspects of isolation may be captured by studies assessing these concepts (Nicholson Jr, 2009).

The consistency of approaches to defining and assessing concepts varied. For marital status and living situation, there was little disparity, given that each are demographic features of social contexts. For other concepts, many studies did not provide clear operationalised definitions and where definitions were provided there were differences across studies. Consequently, there were considerable differences in approaches to the assessment of concepts. One approach to assess social concepts was to use validated measures, yet such measures are not available for all concepts, and even if available, not all studies utilised these measures. Instead, many studies generated single questions, or sets of questions. These generated measures may be briefer and more targeted to the concept being assessed, which can provide more detail and increase validity of measures. However, this specificity narrows the perspective of the social context, meaning that relevant details may be missed. Likewise, the social resources assessed within these measures varied across studies, leading to a lack of specificity and high inconsistency in methodological approaches. The variation in methodological approaches needs to be addressed before the relationship between social connections and cognitive function in later life can be established. Given that each of these social concepts are distinct, it is likely that each concept has an independent influence on cognitive

function. It is therefore necessary for each social concept to be assessed distinctly to understand their complex relationships with cognitive function.

Given the variation in approaches to defining and measuring social concepts, it is unsurprising that there is inconsistency in reported findings relating to late-life cognitive outcomes. For structural and functional social concepts, this inconsistency means that it is not possible to draw conclusions regarding the nature of the association between social connections and cognitive function in later life. The only concept consistently associated with cognitive function was loneliness. This may reflect that loneliness is typically assessed using a standardised approach which may increase the reliability of findings (Conroy et al. 2010; Holwerda et al. 2012; O'Luanaigh et al. 2012). Loneliness is subjectively rated allowing the participant to reflect on their social context (Gerst-Emerson et al. 2014). Measures assessing structural and functional concepts do not allow for personal reflection of satisfaction and rely on cut-points of measures to determine whether the individual is socially connected or not. This operational approach fails to account for individual differences in preference for social contact or satisfaction with social contact which may account for the variation in reported findings (Burger, 1995). This approach also does not account for differences in personal circumstances; for example, people with small families and people who have no children are more likely to be classed as isolated. The consistency observed in findings for loneliness suggests that individual differences in preference for contact are important and may influence findings.

This review has several limitations. Although the review has aimed to provide an overview of how social concepts are reflected and assessed in the literature, the synthesised evidence is not comprehensive. This review was conducted to explore the nature of the evidence available in preparation for a more comprehensive systematic review which is presented in Chapter 4. Findings suggest that there is limited understanding and evidence that assesses social isolation and cognitive function in later life. Therefore a systematic review may consider studies assessing aspects of social isolation (e.g. social networks, social activity) in addition to measures designed to assess isolation. Publication bias was not assessed in the review as this was intended as a scoping exercise to clarify approaches to defining and measuring concepts associated with social connections in the literature. Publication bias is addressed in the systematic review and meta-analysis presented in Chapter 4.

This review has informed the development of the research presented in this thesis. It has outlined the approaches to defining and measuring concepts associated with social connections and has highlighted the inconsistency in these approaches across studies. This lack of consistency has resulted in uncertainty regarding how social connections may be associated with cognitive function in later life. In order to sufficiently understand these relationships, methodological limitations of

assessing social concepts should be addressed and greater consistency in approaches to assessing these concepts needs to be achieved.

Chapter 4: Social isolation and cognitive function in later life: a systematic review and meta-analysis

4.1 Summary

Findings from the scoping review (Chapter 3) suggest that there are a range of concepts associated with social connections and that the assessment of these concepts varies considerably across studies. These concepts may be associated with cognitive function in later life, however the scoping review suggests that findings across studies and relating to specific concepts are conflicting. Previous reviews have focused on the relationship between social networks, loneliness, social activity, and social support and cognitive function. No review has considered the association between social isolation and cognitive function. This chapter presents a systematic review and meta-analysis of studies that assess the association between social isolation and cognitive function.

Background: There is some evidence to suggest that social isolation may be associated with poor cognitive function in later life. However, findings are inconsistent and there is wide variation in the measures used to assess social isolation.

Objective: We conducted a systematic review and meta-analysis to investigate the association between social isolation and cognitive function in later life.

Methods: A search for longitudinal studies assessing the relationship between aspects of social isolation (including social activity and social networks) and cognitive function (including global measures of cognition, memory, and executive function) was conducted in PsycInfo, CINAHL, PubMed, and AgeLine. A random effects meta-analysis was conducted to assess the overall association between measures of social isolation and cognitive function. Sub-analyses investigated the association between different aspects of social isolation and each of the measures of cognitive function.

Results: Sixty-five articles were identified by the systematic review and 51 articles were included in the meta-analysis. Low levels of social isolation characterised by high engagement in social activity and large social networks were associated with better late-life cognitive function (r = .054, 95% CI: .043, .065). Sub-analyses suggested that the association between social isolation and measures of global cognitive function, memory, and executive function were similar and there was no difference according to gender or number of years follow-up.

Conclusions: Aspects of social isolation are associated with cognitive function in later life. There is wide variation in approaches to measuring social activity and social networks across studies which may contribute to inconsistencies in reported findings.

4.2 Introduction

Cognitive ageing refers to a process in which some decline in cognitive function is observed as a consequence of healthy ageing (Harada et al. 2013; Liverman et al. 2015; Rabbitt, Diggle, Smith, Holland & McInnes, 2001). Cognitive ageing is widely considered to be a normal part of healthy ageing whereas clinically significant changes in cognitive function are not (Christensen, 2001; Deary et al. 2007; Stephan, Matthews, McKeith, Bond & Brayne, 2007). The trajectory of cognitive ageing varies across older people. Some people experience major cognitive decline that may progress to dementia, whereas others experience subtle changes and minor cognitive impairment, consistent with cognitive ageing (Royall, Palmer, Chiodo & Polk, 2005; Salthouse, 2010a; Wilson, Beckett et al. 2002). Decline in some cognitive domains, such as memory and executive function, tends to be more age-related whereas decline in other domains, such as language and general knowledge, tends to be less affected by ageing (Deary et al. 2009; Ferreira, Owen, Mohan, Corbett & Ballard, 2015; Gunstad et al. 2006; Huntley et al. 2018).

In addition to differences in the trajectories of cognitive ageing, it has been observed that some older people have considerable brain pathology without exhibiting concomitant declines in cognition (Katzman et al. 1988; Mortimer, Snowdon & Markesbery, 2003; Wharton et al. 2011). Cognitive reserve theory accounts for this discrepancy and for variations in cognitive ageing by proposing that individuals with greater cognitive reserve are able to optimise cognitive performance by recruiting differential brain networks or using alternative cognitive strategies when faced with pathology (Stern, 2002; Valenzuela et al. 2012). Protective lifestyle factors have been identified that may contribute to increased cognitive reserve, such as physical exercise, educational level, occupational complexity, and engaging in cognitive activity (Anstey, Cherbuin & Herath, 2013; Opdebeeck, Martyr & Clare, 2016; Stern, 2009). As these lifestyle factors are modifiable, interventions aimed at reducing risk and enhancing modifiable protective factors may provide a basis to ameliorate poor cognitive function (Kulmala, Ngandu & Kivipelto, 2018; Tucker & Stern 2011). Good social connections may also increase cognitive reserve and protect against declining cognitive function (Atti et al. 2010). However, compared to other lifestyle factors, the association between social connections and cognitive function is less clear, with conflicting findings (Fratiglioni et al. 2004; Kuiper et al. 2016).

There are several reasons why the association between social connections and late-life cognitive function may be less well understood. Firstly, studying social concepts is more complex than assessing lifestyle factors such as physical activity or smoking which may be more readily observable and easier to quantify objectively using a standardised approach (Anstey et al. 2007; Beydoun et al. 2014). The nature of social connections is more challenging to specify and isolate; for example, social connectivity may occur during other activities that provide cognitive stimulation (Aartsen et al.

2002). It is therefore difficult to determine which factors or combination of factors are most beneficial to cognitive function (Aartsen et al. 2002).

There is a wide range of concepts associated with social connections (Holt-Lunstad et al. 2010). Some concepts focus on structural aspects, such as social networks, social isolation, and marital or living situation, whereas others, such as social support, are more related to functional aspects of social contexts, and yet others consider the appraisal of social situations and feelings of loneliness (Antonucci, 1990). It can be difficult to isolate specific social concepts as all are likely to interact or contribute to an individual's social context, yet each is conceptually distinct (Victor et al. 2000). Although studies often aim to assess one specific social concept, many create measures that combine questions assessing a range of concepts. For example, one study created a measure of social isolation that classified participants as isolated who were living alone, were unmarried, and had low levels of social support (Holwerda et al. 2012). This measure may not accurately reflect social isolation, as living alone and being unmarried do not necessarily mean an individual is isolated (Victor et al. 2000). Likewise, although social support can be useful in determining level of social isolation, both concepts have distinct definitions. Social isolation is defined as having few social contacts and low engagement or integration within a wider community (Nicholson Jr, 2009) whereas social support focuses more on the availability of social contacts on whom the individual can draw for support if required (Williams et al. 2004). Therefore, the extent to which this measure assesses social isolation could be disputed. Some studies aim to assess either social activity or social networks, but often create measures that assess both concepts and sometimes also include other social indicators, such as marital status or living situation (Hill, Burdette, Angel & Angel, 2006; Nelson, Noonan, Goldberg & Buchwald, 2013; Obisesan & Gillum, 2009; Santini et al. 2017; Van Ness & Kasl, 2003), social support (Li & Zhang, 2015), or perceptions of feeling understood (Stoykova et al. 2011). Indeed, measures described as assessing one particular concept may contain elements that assess other distinct social concepts. Therefore, measures may not assess social concepts in isolation which may account for between-study inconsistencies regarding the relationship between social connections and cognitive function (Gow & Mortensen, 2016).

Reverse causality is another methodological issue particularly for cross-sectional studies that assess the association between social connections and cognitive function (Hultsch et al. 1999). The nature of social relationships often changes in later life (Green et al. 2008; Wrzus, Hänel, Wagner & Neyer, 2013) and there is evidence to suggest that people who experience a decline in cognitive or physical health may be less able to maintain their social relationships (Aartsen, van Tilburg, Smits & Knipscheer, 2004; Cornwell & Waite 2009; Steptoe et al. 2013). Therefore, poor social relationships may be a consequence of cognitive decline rather than a cause (Rizzuto & Fratiglioni, 2014; Wang et

al. 2013; Zunzunegui et al. 2003). The risk of reverse causation can be reduced by using longitudinal data, and studies with a longer interval between the baseline assessment of social measures and follow-up of cognitive function are more reliable for inferring the direction of causality (Fratiglioni et al. 2004; Kuiper et al. 2016).

Several previous reviews have considered the relationship between various aspects of social connections and cognitive function, such as social networks (Fratiglioni et al. 2004), loneliness or perceived isolation (Boss et al. 2015; Cacioppo & Hawkley, 2009), social activity and engagement (Wang et al. 2012), marital status, social networks, and social support (Kelly et al. 2017; Kuiper et al. 2016; Wang et al. 2012; Williams, Plassman, Burke, Holsinger & Benjamin, 2010). Each of these reviews reports equivocal findings regarding the association between aspects of social connections and cognitive function from both cross-sectional and longitudinal studies. A recent review uniquely considered the methodological quality of studies, applied meta-analytic techniques, and also considered structural (social activity and size of social networks) and functional (social support, loneliness, and satisfaction with household members) aspects of social relationships (Kuiper et al. 2016). No previous review has focussed on social isolation and the association with cognitive function.

Social isolation is defined as a state in which an individual has a minimal number of social contacts and lacks engagement with others and the wider community (Nicholson Jr, 2009). Social isolation can be viewed as a continuum, with isolation and a high level of social participation as opposing extremes (de Jong Gierveld & Havens, 2004). Therefore, social isolation can be captured by studies that assess social networks and social activity or engagement (Nicholson Jr, 2009). Being socially isolated may be associated with having fewer social contacts, a smaller social network (Hultsch et al. 1999; Stern, 2002), and less engagement in social activity. In turn, this may be associated with fewer opportunities to make new social contacts, thus leading to a smaller social network and increased isolation (Victor et al. 2000). From a cognitive reserve perspective, engaging with people in the social network and participating in social activity is cognitively effortful and hence may contribute to building cognitive reserve and enhancing cognitive function (Fratiglioni et al. 2004; Zunzunegui et al. 2003).

Given that social isolation may be associated with poor cognitive function in later life, we aimed to investigate, through a systematic review and meta-analysis of data from longitudinal cohort studies, the relationship between aspects of social isolation (including social activity and social networks) and cognitive function in community-dwelling older people. We considered studies that assessed cognitive function using validated measures of global cognition, as these are frequently used, and

measures of memory and executive function, as change in these domains is central to the concept of cognitive ageing (Deary et al. 2009; Martyr & Clare, 2012). Finally, given the variation in approaches to measuring social isolation, we aimed to summarise methods used to assess this concept in articles identified by the review.

4.3 Method

Systematic search strategy

To identify longitudinal articles assessing the relationship between aspects of social isolation and cognitive function in later life, a systematic search was conducted in PsycInfo, CINAHL, PubMed, and AgeLine for English-language publications to 11th October 2016. No date restrictions were imposed. Search terms focused on three areas: (i) aspects of social isolation (e.g. social relationships, social contact, social activity, social engagement), (ii) cognitive function (e.g. cognition, cognitive decline, cognitive health), and (iii) later life (e.g. older, ageing). See Appendix J for full details of the search terms. An identical, updated search was conducted in the same databases on 8th January 2018.

Inclusion criteria

Articles were included if (i) the sample comprised people who were community-dwelling, aged ≥50 years at baseline, and with no cognitive impairment, (ii) measured social isolation in terms of social network/ contact and/ or social engagement/ activity, (iii) measured cognitive function, decline, or change using a standardised measure of global cognitive function, memory, or executive function, (iv) longitudinal with a minimum of one-year follow-up, providing an assessment of the relationship between social isolation and cognitive outcomes at follow-up, and (v) peer reviewed. Articles that assessed dementia status as an outcome were excluded as they related to dementia diagnosis rather than cognitive function.

Procedure

A flowchart showing how articles were identified is presented in Figure 4.1. Titles, abstracts, and full-text articles were screened by two independent reviewers (Isobel Evans and Rachel Collins). Disagreements were resolved in consensus meetings or resolved by reference to a third reviewer (Linda Clare). Reference lists of included articles and relevant reviews (Cacioppo & Hawkley 2009; Fratiglioni et al. 2004; Kelly et al. 2017; Kuiper et al. 2016; Wang et al. 2012; Williams et al. 2010) were screened to identify additional articles that were not retrieved in the initial searches. Data extraction included information about study population, assessment of social isolation and cognitive function, statistical methods, and results. References were managed using Endnote X7.

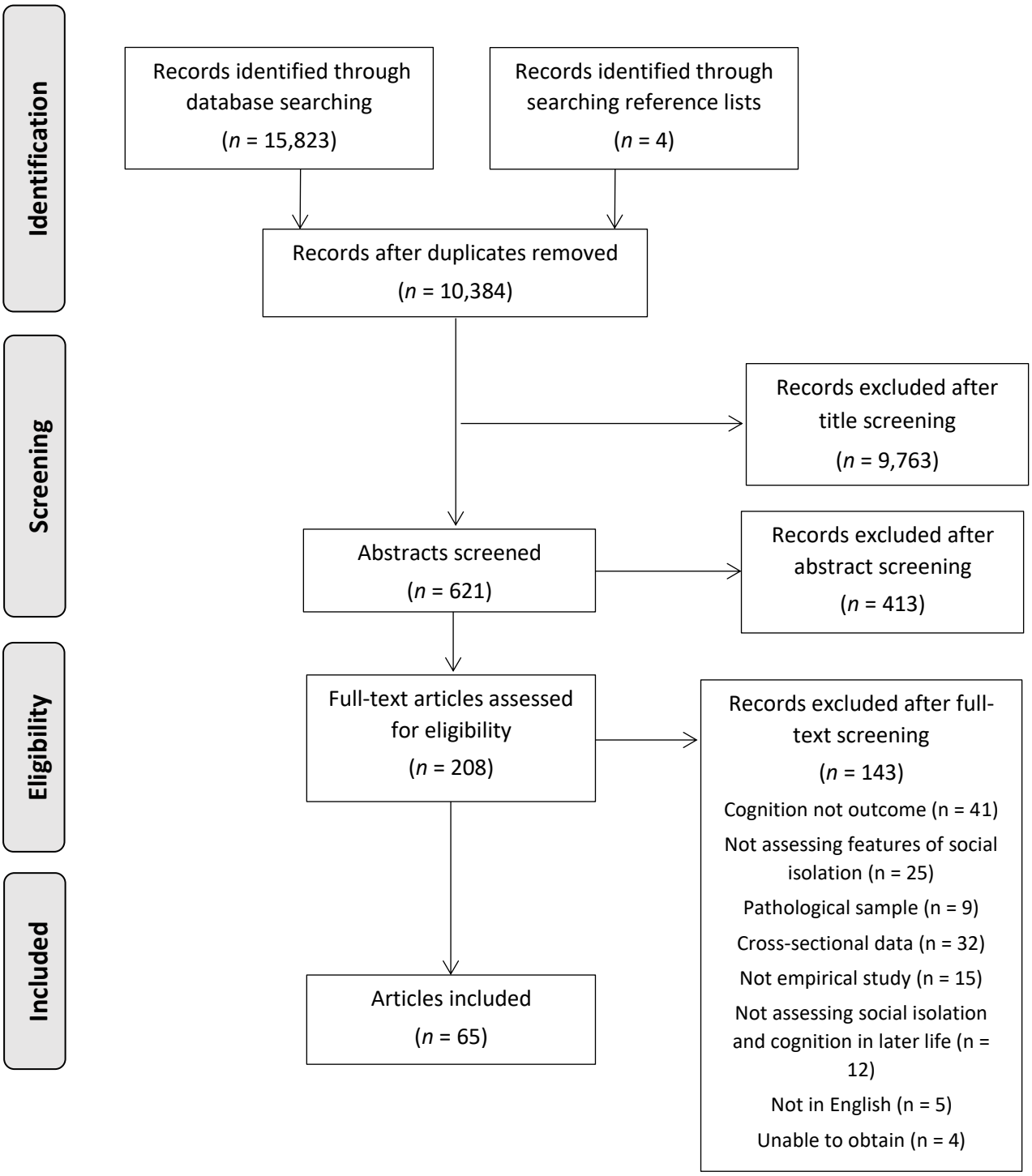


Figure 4.1. Screening process for including articles in the systematic review.

The methodological quality of included articles was assessed by a single reviewer (Isobel Evans) based on the critical appraisal skills programme (CASP, 2013) checklist for cohort studies and published guidelines (Downs & Black, 1998). The checklist comprised 14 items covering the following areas: study aims, population, method, measures, results, and analysis (see Appendix K). Each article received a score ranging from 1 (poor) to 3 (very good) for each item. Scores were summed to provide an overall quality rating for each article. Possible scores range from 14–42 with higher scores indicating greater methodological quality.

Statistical analysis

To investigate the association between social isolation and cognitive function a correlational random effects meta-analysis was conducted using Comprehensive Meta-Analysis 2 (Borenstein, Hedges, Higgins & Rothstein, 2005). A standardized correlation direction was used, and where necessary the direction was changed to facilitate cross-study comparisons. For articles where r was not reported, data were transformed into r. For articles that reported a specific p value with standardized or unstandardized coefficients, or odds or hazard ratios, the p value was used. For articles that reported unstandardized coefficients, but without reporting a specific p value (e.g. reported $p < .05$), the precise p value was calculated using the formula suggested by Altman and Bland (2011). Articles that reported standardized coefficients were converted into r using the formula suggested by Peterson and Brown (2005). For articles that reported odds or hazard ratios, but did not report a specific p value, an exact p value was calculated using the formula suggested by Altman and Bland (2011). For articles that used latent growth curve models, or made comparisons across groups (e.g. ANCOVA), specific p values reported in the article for these analyses were used. Where p values were given as a range of significance a cautious approach was used in which the value used to calculate the correlation was set at the upper limit of the range (e.g. for $p < .05$ the value was set at $p = .049$). Where exact non-significant p values were not given and there was insufficient information to calculate a p value, r was reported as 0.

Where multiple articles used data from the same cohort and reported findings based on the same social or cognitive measure, the data included in the meta-analysis were selected based on the following hierarchical criteria: (i) data could be extracted for meta-analysis, (ii) articles with the most comprehensive measures of social isolation, (iii) longest follow-up duration, and (iv) largest sample size. The software package was instructed to average the multiple within-article correlations to correct for violations of independence so that all available data could be included in the analysis.

Effect sizes were calculated using the random effects model as the included articles employed different methods of assessing social isolation and cognitive function and included heterogeneous

samples of older people. The random effects model estimates and incorporates the magnitude of heterogeneity into the overall estimated effect (DerSimonian & Kacker, 2007). Between-article heterogeneity was assessed using an index of inconsistency (I^2: Higgins, Thompson, Deeks & Altman, 2003). This calculates a percentage of heterogeneity resulting from study differences that is not due to chance; therefore larger values indicate greater heterogeneity.

Articles identified in the search were grouped based on social measures as assessing either social activity, social networks, or a combination of both, based on how the authors of each article described the social measure assessed. Cognitive measures were grouped as assessing either global cognitive function, memory, or executive function. Several analyses were conducted to assess the relationships between aspects of social isolation and cognitive function as follows:

a) All social measures and (i) all cognitive measures, (ii) measures of global cognition, (iii) memory, and (iv) executive function.
b) Social activity and (i) all cognitive measures, (ii) measures of global cognition, (iii) memory, and (iv) executive function.
c) Social networks and (i) all cognitive measures, (ii) measures of global cognition, and (iii) memory.
d) Measures that assess a combination of social activity and networks and (i) all cognitive measures, (ii) measures of global cognition, and (iii) memory.

Two further sub-analyses were conducted that considered all social and all cognitive measures and assessed:

e) Gender differences where articles reported findings for men and women separately.
f) Length of follow-up, divided into 2-3 years, 4-9 years, and 10-24 years follow-up.

We conducted further sub-analyses to assess how specific indicators of social activity and social networks were associated with cognitive function. Finally, sub-analyses were conducted to assess the association between measures of social activity/ social networks and specific measures of cognitive function (e.g. the Mini-Mental State Examination: MMSE).

4.4 Results

Identification of articles

The search identified 10,384 unique records, of which 621 abstracts were screened, and 208 full-text articles were examined, resulting in 65 articles meeting inclusion for the review. Table 4.1 summarises characteristics of each article. Fifty-one articles were included in the meta-analysis.

Table 4.1. *Characteristics and results of studies included in the review.*

			Population characteristics			Measures		
Author	**Country, *Study cohort***	**Study duration in years**	***N* in analysis**	**Age, *M* (SD), range in years**	**Women (%)**	**Social isolation measure**	**Cognitive measure**	**Study quality**
Aartsen et al. (2002)	Netherlands, *Longitudinal Aging Study Amsterdam*	6	1126	68.7 (8.3), 55-85	55	**Social activity**: church attendance, neighbourhood association, helping others	**Global cognition**: MMSE	39
Ellwardt et al. (2015)		Mean: 6 Maximum: 20	2201	67.7 (8.27), 54-85	54	**Social network**: social network size, number of social roles	**Global cognition**: MMSE	40
Klaming et al. (2017)		Maximum: 14	1966	76.2 (6.8), ≥65	54	**Social activity**: organisation membership, leisure activity	**Episodic memory**: Rey Auditory Verbal Learning Test	36
Albert et al. (1995)	USA, *Established Populations for Epidemiologic Studies of the Elderly*	Range 2-2.5	1192	74.3 (2.7), 70-79	55	**Social network**: number of contacts	Global cognition: composite measure of language (Boston naming test), nonverbal and verbal memory (delayed recognition span test), conceptualization (similarities subtest of the WAIS-R), and visuospatial ability (figure copying)	35
Bassuk et al. (1999)		12	710	NR, ≥65	63	**Social network and activity combined**: marital status, frequency of social contact, leisure activity, group membership	**Global cognition**: SPMSQ	36
Béland et al. (2005)*	Spain, *Aging in Legane's*	6	519	75.6 (6.9), 65-100	58	**Social network**: number of relatives, frequency of contact, living arrangement **Social activity**: group membership, leisure activity	**Global cognition**: PCL	41
Zunzunegui et al. (2003)		4	557	NR, ≥65	47	**Social network**: number of contacts, frequency of contact **Social activity**: group membership, social and leisure activity	**Global cognition**: composite measure of the SPMSQ, the Barcelona test, and short story recall	40
Bennett et al. (2006)	USA, *Rush Memory and Aging Project*	NR	89	84.3 (5.6)	55	**Social network**: number of contacts, frequency of interaction	**Global cognition**: composite measure of episodic memory (immediate and delayed recall, word list memory, recall, and recognition), semantic memory (Boston naming test, verbal fluency, reading test), working memory, (digit span forward and backward, digit ordering), perceptual speed (symbol digit modalities test, number comparison, Stroop test), and visuospatial ability (judgement line orientation and Raven's standard progressive matrices).	28
Boyle et al. (2010)*		Mean 4.0 (1.58) Range 1-7	698	80.4 (7.4)	75			35
James, Boyle et al. (2011)*		Mean: 4.5 Maximum: 8	954	78.4 (NR), ≥55	74			33
James, Wilson et al. (2011)		Mean: 5.2 Range 0.4-12.3	1138	79.6 (7.5), ≥65	74	**Social activity**: cultural and leisure activity		35
Bielak et al. (2014)	Australia, *Australian Longitudinal Study of Ageing*	Mean: 5.8 Maximum: 15	1321	77.46 (NR), 65-98	49	**Social activity**: group social activity, interaction with friends and family	**Immediate episodic memory**: Boston naming test **Delayed episodic memory**: Boston naming test	39
Giles et al. (2012)[2]		Maximum: 15	706	78.6 (5.7), ≥70	32	**Social network**: number of contact, living arrangement, frequency of contact, existence of confidant	**Episodic memory**: recall test	37

Brown et al. (2012)[1]	Canada, *Victoria Longitudinal Study*	Maximum 18	977	68.6 (6.7), 55-85	63	**Social activity**: leisure and cultural activity, volunteer work, visiting friends and relatives, organisation membership	**Memory**: list learning and recall **Executive function**: similarities fluency task	38
Brown et al. (2016)*		Maximum: 18	755	68.3 (7.0), NR	65			36
Small et al. (2012)*		Mean: 9.3 Maximum: 12	952	68.6 (6.7), 55-94	63		**Episodic memory**: word and story recall **Semantic memory**: fact recall and vocabulary	39
Ertel et al. (2008)*	USA, *Health and Retirement Study*	6	16638	64.5 (.08), 51-99	58	**Social network and activity combined**: marital status, volunteer work, visiting friends, family, and neighbours	**Memory**: immediate and delayed recall	38
Nelson et al. (2013)		Maximum: 12	203	NR, ≥50	59		**Memory**: TICS-M **Global cognition**: TICS-Mental status	35
Glei et al. (2005)	Taiwan, *Study of Health and Living Status of the Elderly in Taiwan*	Maximum: 7	2387	71.8 (5.2), 64-94	44	**Social network**: marital status, number of contacts, frequency of contact **Social activity**: volunteer work, leisure activities, visiting friends and relatives, organisation membership	**Global cognition**: SPMSQ	39
Hsu. (2007)		6	3302	NR, ≥60	44	**Social activity**: paid/unpaid work, organisation membership, social club	**Global cognition**: SPMSQ	35
Yen et al. (2010)		10	1142	69.8 (4.9), ≥64	59	**Social activity**: volunteer work, participating in group activity	**Global cognition**: SPMSQ	37
Haslam et al. (2014)	UK, *English Longitudinal Study of Ageing*	Maximum: 4	3413	62.6 (8.9), 50-99	57	**Social activity**: relationship quality, frequency of contact, number of close contacts **Social network**: cultural and leisure activities, group membership	**Global cognition**: composite measure of orientation (orientation measure from MMSE), immediate and delayed memory (immediate and delayed verbal learning task), prospective memory (remembering to carry out a previous instruction), and verbal fluency (category recall)	38
Shankar et al. (2013)		4	6034	65.6 (9.5), ≥50	55	**Social network and activity combined**: marital status, frequency of contact with family and friends, organisation membership, leisure activity	**Memory**: immediate and delayed word recall **Executive function**: verbal fluency test	40
Hill et al. (2006)	USA, *Hispanic Established Populations for Epidemiologic Study of the Elderly*	8	2472	72.3 (6.1), 65-107	58	**Social network and activity combined**: marital status, living arrangement, church attendance, frequency of contact with family	**Global cognition**: MMSE	37
Howrey et al. (2015)		Maximum: 18	2767	73.2 (6.5), ≥65	58	**Social activity**: church attendance	**Global cognition**: MMSE	38
Li & Zhang (2015)	China, *Chinese Longitudinal Healthy Longevity Survey*	7	4190	77.6 (9.4), 64-114	54	**Social network and activity combined**: marital status, number of close children, social support, leisure activity, social groups	**Global cognition**: MMSE	39
Zhang (2006) *		2	3867	83.8, 90-105	59	**Social network**: marital status, number of children who visit regularly	**Global cognition**: MMSE	38
Marioni et al. (2015)*	France, *PAQUID*	Maximum: 20	3653	75.3 (6.8), ≥65	58	**Social activity**: group membership, visits from family and friends	**Global cognition**: MMSE	38
Marioni et al. (2014)*		Maximum: 20	2854	77.0 (6.8)	59	**Social network**: number of contacts	**Global cognition**: MMSE	40

Stoykova et al. (2011)		Mean: 9.2 (6.6) Maximum: 20	2052	74.6 (6.66), ≥65	54	**Social network**: number of contacts, satisfaction with relationships, social group membership	**Global cognition**: MMSE	40
McHugh Power et al. (2018)	Ireland, *Irish Longitudinal Study of Ageing*	2	6985	63.5 (9.5), 50-80	54	**Social activity**: social and leisure activities	**Global cognition**: composite measure of immediate and delayed recall and MMSE	37
Santini et al. (2017)		Median: 2 years Range: 16-40 months	6098	6.3 (9.2), ≥50	52	**Social network and activity combined**: marital status, number of contacts, frequency of contact, church attendance, group membership	**Global cognition**: MMSE	39
Niti et al. (2008)	Singapore, *Singapore Longitudinal Aging Studies*	Median: 1.5 Range 1-2	1635	66.0 (7.3), 55-93	65	**Social activity**: cultural and leisure activities	**Global cognition**: MMSE	39
Schwingel et al. (2009)		2	1754	NR, ≥55	NR	**Social activity**: volunteering/paid work	**Global cognition**: MMSE	39
Thomas et al. (2011a)	USA, *American Changing Lives Survey*	3	1642	Men: 69.4, 60-92 Women: 70.4, 60-95	67	**Social activity**: frequency of social contact, volunteer work, group membership, church attendance	**Global cognition**: SPMSQ	39
Thomas et al. (2011b)*		Maximum: 16 Average: 2.6	1667	70.1 (NR), ≥60	67		**Global cognition**: SPMSQ	37
Barnes et al. (2004)	USA, *Chicago Health and Aging Project*	Mean: 5.3 Maximum: 6	3899	73.9 (6.5), ≥65	62	**Social network**: number of contacts, frequency of contact **Social activity**: cultural and leisure activities, paid/ volunteer work	**Global cognition**: composite measure of episodic memory (immediate and delayed recall), perceptual speed (symbol digit modalities test), and the MMSE	40
Barnes et al. (2007)	USA, *Study of Osteoporotic Fractures*	Maximum: 15	9704	71.7 (5.3), 65-99	100	**Social network**: Lubben Social Network Scale (LSNS)	**Global cognition**: Modified MMSE	37
Bosma et al. (2002)	Netherlands, *Longitudinal Maastricht Aging Study*	3	818	NR, 49-81	NR	**Social activity**: organisational membership	**Global cognition**: MMSE	40
Bourassa (2017)	Europe**, *Survey of Health, Ageing, and Retirement in Europe*	6	19832	64.4 (10.0), ≥50	54	**Social activity**: volunteer work, leisure activity, group membership	**Memory**: immediate and delayed word recall **Executive function**: category fluency task	40
Brown et al. (2012)[1]	Sweden, *Origins of Variance in the Oldest-Old (OCTO)*	Maximum: 8	524	83.2 (2.9), ≥80	66	**Social activity**: number of social contacts	**Memory**: immediate recall	38
	USA, *Long Beach Longitudinal Study*	Maximum: 9	565	73.8 (9.1), ≥55	49	**Social activity**: frequency of social contact, volunteer work, leisure activity, visiting friends and family	**Memory**: immediate recall **Executive function**: word fluency test	
	USA, *Seattle Longitudinal Study*	Maximum 21	1657	67.1 (8.2), ≥55	52			
Gallucci et al. (2013)	Italy, *Treviso Longeva*	7	309	79.1 (9.7), 70-105	60	**Social activity**: visiting friends, volunteer work, social groups	**Global cognition**: MMSE	37
Ghisletta et al. (2006)	Switzerland, *Swiss Interdisciplinary Longitudinal Study on the Oldest Old*	5	529	83.4 (2.6), 80-85	52	**Social activity**: cultural and leisure activities	**Global cognition**: composite measure of executive function (category fluency test) and perceptual speed (cross-out test)	37

Ho et al. (2001)	China, *Sample of Chinese elderly*	3	Men: 519 Women: 469	77.4 (5.99), ≥70	47	**Social network and activity combined**: contact with friends, relatives, neighbours, religious attendance, community groups	**Global cognition**: composite measure of the Clifton Assessment Procedure for the Elderly, MMSE, and the Mental Status Questionnaire	40
Holtzman et al. (2004)	USA, *Epidemiologic Catchment Area survey, Baltimore*	Mean: 12.4 Maximum: 15	341	61.3 (6.9), 50-81	69	**Social network**: living arrangement, frequency of contact	**Global cognition**: MMSE	41
Hughes et al. (2008)	USA, *Charlotte County Healthy Aging Study*	Mean: 4.9 Range 4.6-5.3	217	72.4 (6.2), ≥65	52	**Social network**: frequency of social contact, number of contacts	**Global cognition**: Modified MMSE Memory	40
Iwasa et al. (2012)	Japan, *Otasha-Kenshin*	5	567	75.8 (3.5), 70-84	50	**Social activity**: volunteer work, group social activities	**Global cognition**: MMSE	41
Jedrziewski et al. (2014)	USA, *National Long Term Care Survey*	10	927	NR, ≥65	65	**Social activity**: frequency of social contact, organisation membership, religious attendance	**Global cognition**: SPMSQ	40
Kåreholt et al. (2011)	Sweden, *Random samples of the Swedish population*	Mean: 22.8 Range: 21-24	1643	57.4 (NR), 46-85	59	**Social activity**: visiting/being visited by friends and relatives	**Global cognition**: MMSE	40
Katja et al. (2014)	Finland, *Evergreen Project*	21	1181	NR, 65-84	66	**Social activity**: cultural and leisure activities, organisation membership, volunteer work	**Global cognition**: Mini-D	38
Lee et al. (2009)	South Korea, *Suwon Longitudinal Aging Study*	2	977	73.0 (5.7), ≥65	61	**Social activity**: frequency of social contact, leisure and cultural activity	**Global cognition**: MMSE	40
Lee & Kim (2016)	Korea, *Korean Longitudinal Study of Aging*	4	1568	71.06 (.12) ≥65	46	**Social activity**: organisation membership, religious attendance **Social network**: frequency of social contact	**Global cognition**: MMSE	40
Leung et al. (2011)*	China, *Population based community survey of Hong Kong Chinese*	22 months	505	74.5 (7.1), 61-100	55	**Social activity**: volunteer work, cultural and leisure activity	**Global cognition**: MMSE	35
Li & Hsu (2015)[2]	Taiwan, *Taiwan Longitudinal Study of Aging*	4	3226	62.7 (9.6), ≥65	54	**Social activity**: volunteer/paid work, organisation/group membership	**Global cognition**: SPMSQ	38
McGue & Christensen (2007)	Denmark, *Longitudinal Study of Aging Danish Twins*	Maximum: 8	70	75.7 (5.2), ≥75	63	**Social activity**: leisure activity, visiting or being visited by friends and family	**Global cognition**: MMSE **Global cognition**: composite measure of executive function (verbal fluency), working memory (forward and backward digit span) and memory (immediate and delayed recall)	39
McHugh Power et al. (2017)	Ireland, *Community dwelling Irish*	2	624	72 (6.8), 60-89	68	**Social network**: Lubben Social Network Scale (LSNS)	**Global cognition**: MMSE	39
Monastero et al. (2007)	Sweden, *Kungsholmen Project*	Mean: 3.4	718	80.4, 75-95	74	**Social activity**: leisure activity **Social network**: number of contacts	**Global cognition**: MMSE	39
Mousavi-Nasab et al. (2014)	Sweden, *Betula Project*	5	794	74.1 (7.1), 65-85	55	**Social activity**: visiting family and friends, cultural and leisure activity	**Episodic memory**: free and cued recall and recognition	38

							Semantic memory: vocabulary and verbal fluency	
Obisesan & Gillum (2009)	USA, *The Third National Health and Nutrition Examination Survey*	Mean: 8.5 Range: 6-12	5908	NR, ≥60	NR	**Social network and activity combined**: marital status, frequency of social contact, religious attendance, volunteer wok	**Global cognition**: Short Index of Cognitive Function	38
Plehn et al. (2004)*	USA, *Community dwelling Virigina*	Mean: 3.6 Range: 3.2-4.3	96	75.6 (7.9), ≥55	78	**Social activity**: social subscale from the SELF-scale	**Global cognition**: composite measure of Mattis Dementia Rating Scale, Fuld object memory evaluation, and MMSE	37
Seeman et al. (2001)	USA, *McArthur Studies of Successful Aging*	Mean 7.4	706	74.2, 70-79	55	**Social activity**: marital status, number of social contacts **Social network**: social group membership	**Global cognition**: composite measure of language (Boston naming test), abstraction (similarities subtest of the WAIS-R), spatial ability (copying), delayed spatial recognition, immediate and delayed story recall	38
Shatenstein et al. (2012)	Canada, *Nutrition and Cognition Study*	3	1208	74.2, 67-84	53	**Social activity**: cultural and leisure activity, community groups	**Global cognition**: 3MS	40
Tomioka et al. (2016)	Japan, *Community dwelling Japanese*	3	6093	72.8, 65-96	55	**Social activity**: leisure activity, volunteer work, social groups, organisation membership	**Global cognition**: Cognitive Performance Scale	41
Van Ness & Kasl (2003)	USA, *Yale Health and Aging Project*	6	1245	74.6 (6.9), ≥65	58	**Social network and activity combined**: marital status, frequency of contact with family and friends, social groups	**Global cognition**: SPMSQ	36
Wang et al. (2006)	China, *Sample of Chinese elderly people*	Mean: 4.7 Maximum: 5	5437	63.4 (NR), ≥55	51	**Social activity**: visiting friends and family	**Global cognition**: MMSE	39
Wang et al. (2013)	China, *Longitudinal population-based study of Chinese*	Mean: 2.4 Range: 2.3-2.6	1463	71.0 (5.0), ≥65	49	**Social activity**: visiting or being visited by friends and family, giving advice	**Global cognition**: CSID **Episodic memory**: word list learning and recall, and story recall **Executive function**: token test	40

Note: NR = not reported, MMSE = Mini-Mental State Examination, WAIS-R = Wechsler Adult Intelligence Scale-Revised, SPMSQ = Short Portable Mental Status Questionnaire, PCL = Leganés' Cognitive Test (Prueba Cognitiva de Leganés), TICS-M = Modified Telephone Interview for Cognitive Status – Memory, TICS-Mental status = Modified Telephone Interview for Cognitive Status – Mental status, CSID = Community Screening Instrument for Dementia, AD = Alzheimer's disease.

[1] This study reports data for four different cohorts: Origins of Variance in the Oldest-Old, Long Beach Longitudinal Study Participants, Seattle Longitudinal Study, and Victoria Longitudinal Study.

[2] Data for the total sample is reported in all meta-analyses except for the sub-analysis on gender where data for men and women are reported separately.

* Data not reported in the meta-analysis

** Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Italy, Netherlands, Poland, Sweden, Spain, and Switzerland

Excluded articles

Fourteen articles were excluded from the meta-analysis for the following reasons: two articles contained no useable data (Leung et al. 2011; Plehn, Marcopulos & McLain, 2004) and twelve articles were based on the same study populations and used the same social and cognitive measures included elsewhere in the review (Albert et al. 1995; Béland et al. 2005; Boyle, Buchman, Barnes & Bennett, 2010; Brown et al. 2016; Ertel et al. 2008; Hsu, 2007; James, Boyle, Buchman, Barnes & Bennett, 2011; Marioni et al. 2014; Marioni et al. 2015; Small, Dixon, McArdle & Grimm, 2012; Thomas, 2011b; Zhang, 2006).

Included articles

Of the 51 articles included in the meta-analysis, seventeen were combined to create eight cohorts of participants as they included the same participants but reported different social and/ or cognitive measures as follows: Longitudinal Aging Study Amsterdam (Aartsen et al. 2002; Ellwardt et al. 2015; Klaming, Annese, Veltman & Comijs, 2017), Rush Memory and Aging Project (Bennett et al. 2006; James, Wilson et al. 2011), Australian Longitudinal Study of Ageing (Bielak, Gerstorf, Anstey & Luszcz, 2014; Giles, Anstey, Walker & Luszcz, 2012), Study of Health and Living Status of the Elderly in Taiwan (Glei et al. 2005; Yen et al. 2010), English Longitudinal Study of Ageing (Haslam et al. 2014; Shankar et al. 2013), Hispanic Established Populations for Epidemiologic Study of the Elderly (Hill et al. 2006; Howrey, Raji, Masel & Peek, 2015), Irish Longitudinal Study of Ageing (McHugh Power, Tang, Lawlor, Kenny & Kee, 2018; Santini et al. 2017), and Singapore Longitudinal Aging Studies (Niti et al. 2008; Schwingel, Niti, Tang & Ng, 2009). One article reported findings from four cohorts separately (Brown et al. 2012) and each cohort was included separately in the meta-analysis. One article (Bourassa, Memel, Woolverton & Sbarra, 2017) split and analysed the sample into two distinct groups so each group was included as an individual study for the purposes of the meta-analysis. Five articles (Ho et al. 2001; Katja, Timo, Taina & Tiina-Mari, 2014; Thomas, 2011a; Tomioka, Kurumatani & Hosoi, 2016; Zunzunegui et al. 2003) reported results for men and women separately. Two articles reported data for men and women together and separately (Giles et al. 2012; Li, & Hsu, 2015); therefore, combined data were reported in the main analyses while separate data for men and women was included in the gender sub-analysis. One article reported findings for women only (Barnes et al. 2007) and so was included in main analyses and sub-analyses for gender.

Fifty-one cohorts were included in the meta-analysis with a combined sample of 102,035 unique participants. Thirty-four articles assessed social isolation based on social activity or engagement, 15 assessed isolation based on social networks, and 9 articles assessed isolation based on a

combination of both social activity and social networks. The duration of follow-up ranged from 2 to 24 years and the sample size of cohorts ranged from 70 to 19,832 participants (Table 4.1).

Association between social isolation and cognitive function

There was a statistically significant association between social isolation (i.e. social activity and social networks) and cognitive function, although the effect size was small and there was a moderate degree of heterogeneity (r = .054, p <.001, I^2 = 58.86; Table 4.2, Figure 4.2). When considering specific measures of cognition, social measures were most strongly associated with measures of global cognition (r = .061, p <.001, I^2 = 78.80), followed by measures of memory (r = .050, p <.001, I^2 = 64.51), and then executive function (r = .031, p <.001, I^2 = 34.95). Effect sizes were small and statistically significant but there was considerable heterogeneity for global measures and tests of memory.

Engagement in social activity and cognitive function

Thirty-nine cohorts assessed the relationship between social activity and cognitive function (Table 4.2, Figure 4.2). Results suggest that engaging in social activity is significantly associated with better cognitive outcomes on all cognitive measures (r = .070, p <.001, I^2 = 84.48). When considering each type of cognitive measure separately, social activity was most strongly associated with better cognitive outcomes on global measures of cognition (r = .072, p <.001, I^2 = 84.59), followed by memory (r = .049, p <.001, I^2 = 71.39) and executive function (r = .032, p = .002, I^2 = 45.47). Effect sizes were small and statistically significant but there was considerable heterogeneity except for tests of executive function.

Social networks and cognitive function

The association between social networks and cognitive function was assessed in 17 cohorts of participants (Table 4.2, Figure 4.2). The meta-analysis found that larger social networks were significantly associated with better cognitive function when all cognitive measures were combined (r = .072, p <.001, I^2 = 89.77). This relationship was similar when considering global measures of cognition (r = .067, p <.001, I^2 = 90.13). Effect sizes were small and statistically significant but with considerable heterogeneity. When measures of memory were considered separately there was no significant association with social networks (r = .107, p = .156, I^2 = 66.51). While the effect size for the association between social networks and memory was marginally larger than for global measures there were only two cohorts included so this should be treated with some caution, particularly as there was a moderate degree of heterogeneity.

Combination of social activity and social networks and cognitive function

Ten cohorts included measures that assessed both social activity and social networks and the relationship with cognitive function (Table 4.2, Figure 4.2). The associations between these combined social measures and all measures of cognitive function were statistically significant (r = .036, p <.001, I^2 = .00). The association with global measures (r = .036, p <.001, I^2 = 6.05) was the same as the overall association, and similar for memory (r = .046, p <.001, I^2 = .00). Effect sizes were small and statistically significant, and there was little heterogeneity, suggesting that the effect sizes may be reliable. However, there were only two cohorts included in the memory comparison.

Effect of gender

We next investigated the relationship between social isolation and cognitive function in cohorts that report data for men and women separately. The effect of larger social relationships was similar for men (r = .048, p <.001, I^2 = 7.48) and women (r = .059, p <.001, I^2 = 61.83). Effect sizes were small and statistically significant with a slight advantage for women (Table 4.2, Figure 4.2), though there was considerably more heterogeneity for women than men.

Effect of follow-up time

Finally, we investigated the association between social isolation and cognitive outcomes over different follow-up times (Table 4.2, Figure 4.2). Effect sizes for each time point were small, statistically significant, but with moderate heterogeneity. Effect sizes were slightly larger for cohorts with a 4-9 (r = .058, p <.001, I^2 = 69.63) and 10-24 (r = .059, p <.001, I^2 = 60.09) year follow-up compared to cohorts with a shorter follow-up of 2-3 years (r = .046, p <.001, I^2 = 49.00).

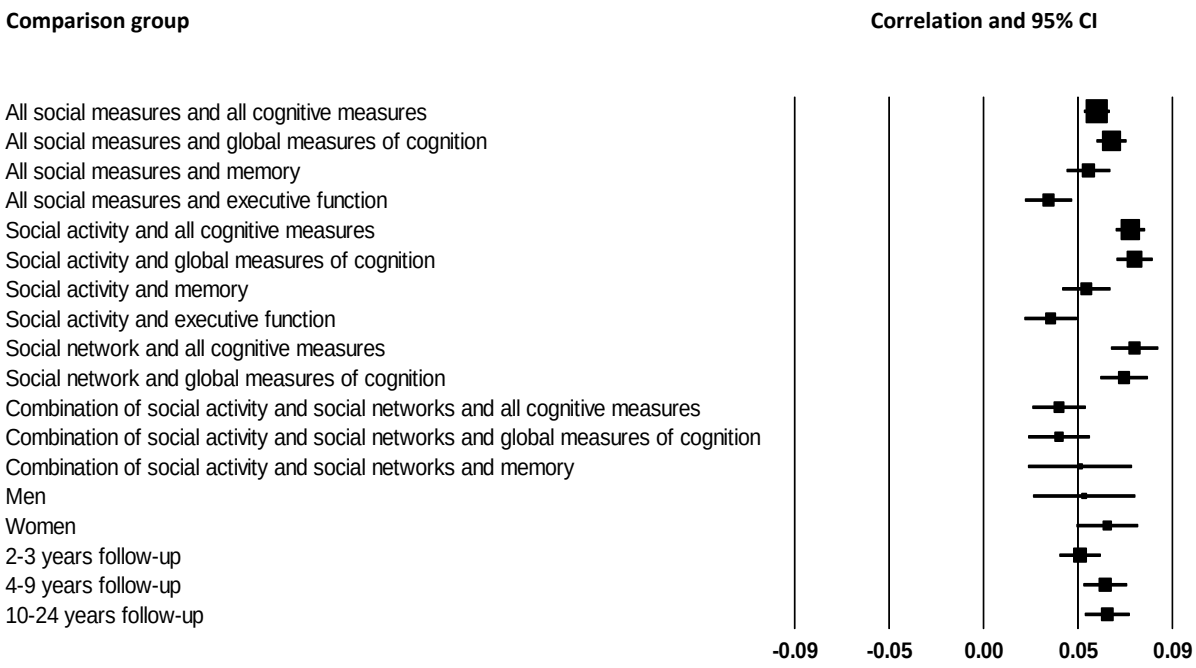


Figure 4.2. Forest plot of the positive association between social measures and cognitive measures, and differences between men and women, and number of years follow-up.

Note: forest plots for each sub-analysis can be found in Appendix L.

Table 4.2. *Random effects meta-analysis and sub-analyses for aspects of social isolation and cognitive function.*

Variables	n	k	*r*	95% CI	*p*	Heterogeneity		
						Q	Q *p*	I^2
All social measures								
All cognitive measures [a b c]	102,035	51	.054	.043, .065	<.001	121.46	<.001	58.86
Global measures [a b]	74,933	43	.061	.044, .079	<.001	198.12	<.001	78.80
Memory [c]	35,230	13	.050	.028, .072	<.001	33.81	<.001	64.51
Executive function	30,528	7	.031	.015, .047	<.001	9.22	.161	34.95
Social activity								
All cognitive measures [a b c]	77,954	39	.070	.050, .089	<.001	244.89	<.001	84.48
Global measures [a b]	51,804	31	.072	.048, .095	<.001	194.68	<.001	84.59
Memory [c]	29,099	10	.049	.023, .075	<.001	31.46	<.001	71.39
Executive function	24,494	6	.032	.011, .052	.002	9.17	.103	45.47
Social network								
All cognitive measures [a]	30,037	17	.072	.032, .112	<.001	156.41	<.001	89.77
Global measures [a]	29,684	16	.067	.026, .108	<.001	151.95	<.001	90.13
Memory	570	2	.107	-.041, .250	.156	2.99	.084	66.51
Executive function								
Combination of social activity and social networks								
All cognitive measures	23,783	10	.036	.024, .049	<.001	7.32	.604	.00
Global measures	17,749	9	.036	.020, .052	<.001	8.52	.385	6.05
Memory	6,237	2	.046	.021, .070	<.001	.16	.693	.00
Executive function								
All social measures and all cognitive measures								
Gender								
Men	6,448	7	.048	.021, .074	<.001	6.49	.371	7.48
Women	17,649	8	.059	.028, .090	<.001	18.34	.011	61.83
Follow-up time								
2-3 years [b]	39,328	16	.046	.030, .062	<.001	29.41	.014	49.00
4-9 years [a c]	35,374	21	.058	.036, .080	<.001	65.86	<.001	69.63
10-24 years	33,393	17	.059	.039, .078	<.001	40.09	<.001	60.09

Note: Removing [a] Haslam et al. (2014), [b] McHugh Power et al. (2018), and [c] Brown et al. OCTO (2012) reduced I^2 and the effect size *r* (see Appendix M for details).

Methods of assessing social isolation

The different approaches to assessing social isolation in all articles identified by the systematic review (N = 65) are summarised below. Some indicators of social activity and social networks overlap and were used to assess both concepts.

Social activity

Fifty-two articles identified by the systematic review assessed social activity. Each of the articles assessed social activity using different indicators of social activity and many articles used more than one indicator within the measure (Table 4.3). Twenty-seven articles assessed social and community activities, 21 assessed frequency of visits from or to family, friends, and neighbours, 23 articles assessed participation in voluntary or paid work, and 36 articles assessed participation in cultural and leisure activities. Ten articles asked about engagement in groups or clubs generally and did not specify the type of groups.

Social networks

Twenty-seven articles in the systematic review assessed social networks. Various indicators were used to assess social networks and were included in different combinations within measures across articles (Table 4.4). Eighteen articles assessed the number of people within the social network, 19 assessed the frequency of interaction with social contacts, 12 assessed marital status, three assessed living arrangements, and three assessed additional indicators such as satisfaction with social relationships, perception of feeling understood by others, and how many people the participant felt close to.

Table 4.3. *Summary of the different indicators of social activity measured across articles.*

Social activity indicator	Articles that used indicator
Social and community activities *E.g. attending social or senior citizen clubs, engagement in neighbourhood associations, political organizations, and other community groups.*	Aartsen et al. (2002); Béland et al. (2005); Bielak et al. (2014); Bosma et al. (2002); Bourassa (2015); Gallucci et al. (2013); Glei et al. (2005); Haslam et al. (2014); Ho et al. (2001); Hsu. (2007); Iwasa et al. (2012); James, Wilson et al. (2011); Katja et al. (2014); Klaming et al. (2017); Lee & Kim (2016); Leung et al. (2011); Li & Hsu (2015); Marioni et al. (2010); Niti et al. (2008); Shankar et al. (2013); Shatenstein et al. (2012); Stoykova et al. (2011); Thomas (2011a); Tomioka et al. (2016); Van Ness & Kasl (2003); Yen et al. (2010); Zunzunegui et al. (2003)
Frequency of visits from or to family, friends, and neighbours	Bielak et al. (2014); Brown et al. (2012); Brown et al. (2016); Gallucci et al. (2013); Glei et al. (2005); Haslam et al. (2014); Ho et al. (2001); James, Wilson et al. (2011); Jedrziewski et al. (2014); Kåreholt et al. (2011); Lee & Kim (2016); Lee et al. (2009); Leung et al. (2011); Marioni et al. (2010); McGue & Christensen (2007); Mousavi-Nasab et al. (2014); Small et al. (2012); Thomas (2011a); Wang et al. (2003); Wang et al. (2006); Zunzunegui et al. (2003)
Participation in voluntary or paid work	Aartsen et al. (2002); Barnes et al. (2004); Bassuk et al. (1999); Bourassa (2015); Brown et al. (2012); Brown et al. (2016); Ertel et al. (2008); Gallucci et al. (2013); Glei et al. (2005); Hsu. (2007); Iwasa et al. (2012); James, Wilson et al. (2011); Katja et al. (2014); Leung et al. (2011); Li & Hsu (2015); Nelson et al. (2013); Obisesan & Gillum (2009); Santini et al. (2017); Schwingel et al. (2009); Thomas (2011a); Tomioka et al. (2016); Wang et al. (2003); Yen et al. (2010)
Cultural and leisure activities *E.g. attendance to religious organizations, participating in sport, attending the theatre, cinema, or a concert, attending museums or exhibitions, eating at restaurants, travelling and overnight trips, attendance to parties, playing games, engaging in hobbies, and reading.*	Aartsen et al. (2002); Barnes et al. (2004); Béland et al. (2005); Bourassa (2015); Brown et al. (2012); Brown et al. (2016); Ghisletta et al. (2006); Glei et al. (2005); Haslam et al. (2014); Hill et al. (2006); Ho et al. (2001); Howrey et al. (2015); Hsu. (2007); James, Wilson et al. (2011); Jedrziewski et al. (2014); Katja et al. (2014); Klaming et al. (2017); Lee & Kim (2016); Lee et al. (2009); Leung et al. (2011); Li & Hsu (2015); Li & Zhang (2015); McGue & Christensen (2007); McHugh Power et al. (2018); Mousavi-Nasab et al. (2014); Niti et al. (2008); Obisesan & Gillum (2009); Santini et al. (2017); Seeman et al. (2001); Shankar et al. (2013); Shatenstein et al. (2012); Small et al. (2012); Thomas (2011a); Tomioka et al. (2016); Wang et al. (2006); Zunzunegui et al. (2003)
Engagement in groups or clubs *Type of groups/ clubs not specified*	Barnes et al. (2004); Bassuk et al. (1999); Brown et al. (2012); Brown et al. (2016); Hsu. (2007); Jedrziewski et al. (2014); Li & Zhang (2015); Monastero et al. (2007); Santini et al. (2017); Seeman et al. (2001)

Table 4.4. *Summary of the different indicators of social networks measured across articles.*

Social network indicator	Articles that used indicator
Social network size *E.g. count of the number of social contacts*	Albert et al. (1995); Barnes et al. (2004); Barnes et al. (2007); Béland et al. (2005); Bennett et al. (2006); Boyle et al. (2010); Ellwardt et al. (2015); Giles et al. (2012); Glei et al. (2005); Hughes et al. (2008); James, Boyle et al. (2011); Li & Zhang (2015); Marioni et al. (2014); McHugh Power et al. (2017); Monastero et al. (2007); Seeman et al. (2001); Stoykova et al. (2011); Zunzunegui et al. (2003)
Frequency of interaction with social contacts	Barnes et al. (2007); Bassuk et al. (1999); Béland et al. (2005); Bennett et al. (2006); Boyle et al. (2010); Ertel et al. (2008); Giles et al. (2012); Glei et al. (2005); Hill et al. (2006); Hughes et al. (2008); James, Boyle et al. (2011); McHugh Power et al. (2017); Nelson et al. (2013); Obisesan & Gillum (2009); Santini et al. (2017); Shankar et al. (2013); Van Ness & Kasl (2003); Zhang (2006); Zunzunegui et al. (2003)
Marital status	Bassuk et al. (1999); Ertel et al. (2008); Glei et al. (2005); Hill et al. (2006); Li & Zhang (2015); Nelson et al. (2013); Obisesan & Gillum (2009); Santini et al. (2017); Seeman et al. (2001); Shankar et al. (2013); Van Ness & Kasl (2003); Zhang (2006)
Living arrangements and proximity to other family	Béland et al. (2005); Giles et al. (2012); Hill et al. (2006)
Other indicators *E.g. Satisfaction with social relationships, perception of feeling understood, and how many people feel close to*	Giles et al. (2012); Zhang (2006); Stoykova et al. (2011)

Association between specific indicators of social activity or social networks and cognitive function

Further sub-analyses were conducted to determine whether the different indicators of social activity and social networks could explain heterogeneity or were more associated with measures of cognitive function. There was not enough data to investigate the effects of different social indicators on global cognitive function, memory, and executive function separately, hence we considered the association between specific social indicators and all measures of cognitive function combined. Few articles reported findings for specific indicators separately but where possible sub-analyses were conducted. Social and community activities were described in nine articles (Aartsen et al. 2002; Bielak et al. 204; Bosma et al. 2002; Klaming et al. 2017; Lee & Kim, 2016; Shatenstein et al. 2012; Tomioka et al. 2016; Yen et al. 2010; Zunzunegui et al. 2003), frequency of visits from or to, family,

friends, and neighbours were described in seven articles (Bielak et al. 2014; Brown et al. 2012; Haslam et al. 2014; Kåreholt, Lennartsson, Gatz & Parker, 2011; Lee & Kim, 2016; Wang et al. 2013; Zunzunegui et al. 2003), voluntary or paid work was described in six articles (Aartsen et al. 2002; Katja et al. 2014; Li & Hsu, 2015; Schwingel et al. 2009; Tomioka et al. 2016; Yen et al. 2010), cultural and leisure activities were described in 12 articles (Aartsen et al. 2002; Ghisletta, Bickel & Lövdén, 2006; Haslam et al. 204; Howrey et al. 2015; Katja et al. 2014; Klaming et al. 2017; Lee & Kim, 2016; McHugh Power et al. 2018; Niti et al. 2008; Seeman et al. 2001; Tomioka et al. 2016; Zunzunegui et al. 2003), social network size was described in six articles (Barnes et al. 2004; Ellwardt et al. 2015; Holtzman et al. 2004; Monastero, Palmer, Qiu, Winblad & Fratiglioni, 2007; Seeman et al. 2001; Zunzunegui et al. 2003), and marital status was described in two articles (Glei et al. 2005; Seeman et al. 2001). Heterogeneity was considerably reduced for social and community activities, voluntary or paid work, social network size, and marital status, but remained high for frequency of visits from or to, family, friends, and neighbours, and cultural and leisure activities (Table 4.5).

Table 4.5. *Random effects sub-analyses for specific indicators of social activity and social network and all measures of cognitive function.*

	n	**k**	***r***	**95% CI**	***p***	**Heterogeneity**		
						Q	Q *p*	I^2
Social activity								
Social and community activities	13,903	10	.037	.020, .054	<.001	7.79	.555	.00
Frequency of visits from or to family, friends, and neighbours	10,489	8	.074	.029, .120	<.001	33.42	<.001	79.06
Voluntary or paid work	14,522	8	.043	.024, .062	<.001	8.72	.273	19.72
Cultural and leisure activities	27,120	14	.090	.028, .151	.005	317.48	<.001	95.91
Social network								
Social network size	7,716	6	.048	.022, .074	<.001	5.75	.332	13.00
Frequency of interaction with social contacts								
Marital status	3,093	2	.015	-.021, .050	.413	.08	.774	.00
Living arrangements and proximity to other family								

Methods of assessing cognitive function

Cognitive function was mostly assessed using measures of global cognitive function. The MMSE was most consistently used across studies (Aartsen et al. 2002; Barnes et al. 2007; Bosma et al. 2002; Ellwardt et al. 2015; Gallucci et al. 2013; Hill et al. 2006; Holtzman et al. 2004; Howrey et al. 2015; Hughes et al. 2008; Iwasa et al. 2012; Kåreholt et al. 2011; Lee et al. 2009; Lee & Kim, 2016; Li & Zhang, 2015; McGue & Christensen, 2007; Monastero et al. 2007; Niti et al. 2008; Santini et al. 2017; Schwingel et al. 2009; Stoykova et al. 2011; Wang et al. 2006) and was the only measure with sufficient data to investigate the association with: all social measures, measures of social activity, measures of social networks, and measures that combined social activity and networks. Heterogeneity was considerably reduced for each group of social measures when the MMSE was the only cognitive measure included in the sub-analyses (Table 4.6).

Table 4.6. *Random effects sub-analyses for aspects of social isolation and the Mini-Mental State Examination (MMSE).*

	n	**k**	***r***	**95% CI**	***p***	**Heterogeneity**		
						Q	Q *p*	I^2
MMSE								
All social measures	36,587	18	.038	.025, .050	<.001	20.91	.230	18.71
Social activity	17,695	12	.042	.023, .062	<.001	15.63	.156	29.60
Social network	16,801	7	.031	.015, .048	<.001	6.35	.385	5.57
Combination of social activity and social networks	8,695	3	.036	.012, .061	.003	2.54	.282	21.11

Methodological quality and publication bias

The results of the methodological quality assessment are reported in Table 4.1. Scores on the quality checklist ranged from 28 to 41 with a mean score of 38.11. Most articles did not use a standardised measure of social isolation and did not consider or compare the characteristics of participants lost to follow-up. There were no articles judged to be of poor methodological quality.

Funnel plots suggest that the results may be slightly overestimated due to publication bias: Egger's test: b = 1.52, 95% CI: .746, 2.285, p <.001 (See Appendix N for details).

4.5 Discussion

The findings from this systematic review and meta-analysis of longitudinal cohort studies suggest that aspects of social isolation, including low levels of social activity and poor social networks, are significantly associated with poor cognitive function in later life. There was little difference in the effect sizes of reported associations when measures of social isolation were divided into social activity, social networks, and a combination of these two concepts, despite heterogeneous tests of global cognition, memory, and executive function being used. Effect sizes were also similar for men and women, and for number of years follow-up. The effect sizes indicate that having a large social network and engaging in social activity makes a small but statistically significant contribution to preventing poor cognitive function in later life. The size of effect is consistent with a previous review assessing the relationship between poor structural aspects of social relationships and cognitive decline (Kuiper et al. 2016). The small effect size is unsurprising given the range of factors that contribute to maintaining healthy cognitive function (Baumgart et al. 2015; Clare et al. 2017).

The moderate to high heterogeneity observed in the meta-analysis can be explained by several factors. First, three articles (Brown et al. 2012; Haslam et al. 2014; McHugh Power et al. 2018) reported effect sizes that were considerably higher than those reported by other included articles. Removing these studies from the meta-analysis reduced heterogeneity considerably and slightly reduced effect sizes. Second, sub-analyses were conducted on articles that assessed cognitive function using the MMSE, and hence reduced the variance in assessments of cognitive function. This also considerably reduced heterogeneity and while effect sizes were reduced they remained statistically significant suggesting that global cognition as measured by the MMSE contributes to social activity and social networks.

A wide range of indicators to assess social networks (e.g. number of contacts, frequency of interaction, marital status, living arrangement) and social activity (e.g. attending social groups, visiting family, friends, and neighbours, engaging in voluntary or paid work, participation in cultural or leisure activities) was employed across articles, which may account for the remaining observed heterogeneity (Kelly et al. 2017; Kuiper et al. 2016). Indeed, further sub-analyses suggested that the heterogeneity may partly be explained by including a range of indicators within measures of social activity and social networks. Heterogeneity was considerably lower for indicators that were specific in nature, such as voluntary or paid work, a count of the number of people within the social network, or social and community activities, which specifically considers social groups and community meetings where the primary outcome is social.

Conversely, heterogeneity was high for cultural and leisure activities, which reflects the diversity of activities that may be included within this indicator and highlights an important methodological issue. Many measures of social activity include questions regarding leisure and cultural activities (Haslam et al. 2014; James, Wilson et al. 2011; Klaming et al. 2017). These activities are not necessarily social in nature; for example, watching a film or engaging in hobbies may have less social input than visiting friends and family or attending a party. Many cultural and leisure activities present additional demands, for example, playing a game may be both cognitively and socially demanding, and engaging in group sport may be physically, cognitively, and socially demanding (Aartsen et al. 2002). Individual differences may also influence the extent to which an activity is socially demanding (Toepoel, 2013). For example, one person may join a bowling club to engage in physical activity, whereas another may enjoy the social aspect of group sports, and a third may gain more cognitive stimulation from thinking strategically about the game. This variation is reflected in the high heterogeneity reported for the specific indicator of leisure and cultural activities and highlights the complexity of assessing social concepts independently from other lifestyle factors and determining the extent of social demand across activities (Aartsen et al. 2002; Toepoel, 2013). Heterogeneity was also high for frequency of visits from or to, family, friends, and neighbours. This may be accounted for to some extent by differences in response scales employed across studies, for example, some studies ask about the number of visits received or made within a month (Brown et al. 2012; Zunzunegui et al. 2003) while others consider frequency of visits ranging from daily, to yearly/ less than yearly (Haslam et al. 2014; Lee & Kim, 2016) and others are more specific and require participants to give the number of hours spent visiting others or being visited (Bielak et al. 2014). Other studies categorise participants as receiving a high or low number of visits (Wang et al. 2013) and some are less specific with response categories ranging from never, sometimes, often (Kåreholt et al. 2011). The variation in methodological approaches to categorising 'frequency' of visits may account for this heterogeneity.

Few studies reported findings for indicators of social activity or social networks separately and many indicators were included as a range of combinations in measures across studies, which again may account for the heterogeneity observed. Future research should aim to achieve consistency in measures of social concepts and report findings for specific indicators separately. This would enable conclusions regarding the nature of the association between specific aspects of social isolation and cognitive function to be established and inform future cohort or intervention studies (Kelly et al. 2017; Kuiper et al. 2016).

Few randomized controlled trials have investigated the effect of interventions to enhance social connections and cognitive function in later life (Wang et al. 2012; Yaffe & Hoang, 2013). In a

community-dwelling sample of 250 participants, an intervention to enhance social interaction improved cognitive function and resulted in significant increases in brain volume compared to a control group after 40 weeks (Mortimer et al. 2012). Likewise, increased social activity in 235 lonely people enhanced cognitive function compared to a control group after 12 months (Pitkala et al. 2011). While the effect size for this intervention was moderate the intervention was administered to people who were lonely and so may not be as effective for people who are socially isolated. A six-week intervention to increase social engagement facilitated by internet video communication was found to improve language based executive functions and psychomotor speed in cognitively healthy older people (Dodge et al. 2015). This suggests that communication facilitated by the internet may be a cost-effective home-based intervention to enhance social contact and improve cognitive function. Another study reported no beneficial effect of a pilot intervention to enhance social connections on cognitive function (Park et al. 2014). Nonetheless, only five participants were assigned to the social intervention in this study, therefore findings were likely underpowered and should be treated with caution. Although these studies provide some evidence that interventions to enhance social connections may support the maintenance of cognitive function, both Mortimer et al. (2012) and Park et al. (2014) report that interventions of physical activity and cognitive activity were more beneficial for cognitive function than interventions to enhance social connections. This evidence, together with the small effect size reported in the meta-analysis may suggest that interventions targeting social isolation alone may be insufficient to reduce poor cognitive function in later life (Ngandu et al. 2015).

It is not surprising that the reported association between social isolation and cognitive function is small. There are multiple factors that could impact on trajectories of cognitive decline, including other modifiable lifestyle factors, such as physical exercise, educational level, occupational complexity, and cognitive activity (Baumgart et al. 2015; Clare et al. 2017). It is likely that a range of lifestyle factors, such as cognitive, social, and physical activity, contribute to the maintenance of healthy cognitive function (Fratiglioni et al. 2004; Rizzuto & Fratiglioni, 2014). Cognitive reserve theory suggests that a combination of lifestyle factors across the lifespan contributes to enhancing cognitive reserve and hence maintaining cognitive function (Stern, 2002). Therefore, diverse environments and activities that increase cognitive stimulation through supporting a range of protective lifestyle factors may be most suitable to build cognitive reserve (Wang et al. 2012). The lifestyle factors underpinning cognitive reserve are potentially amenable to change and hence may provide a basis for preventative intervention (Kulmala et al. 2018; Tucker & Stern, 2011). This is supported by findings from a recent randomised controlled trial that suggests multi-domain interventions may be most appropriate for the maintenance of cognitive function (Ngandu et al.

2015). Given the small effect sizes reported in the meta-analysis, an intervention to reduce social isolation may be most effective when implemented within a wider intervention that combines a range of lifestyle factors to enhance cognitive reserve (Middleton & Yaffe, 2010; Ngandu et al. 2015; Wang et al. 2012).

Among the key strengths of this review, the comprehensive search included several concepts that are associated with social isolation. This enabled us to compare associations between different aspects of social isolation and cognitive function, including social activity and social networks both overall and separately. We consider the effects that different aspects of social isolation may have on global cognitive function and the specific cognitive domains of memory and executive function (Golden et al. 2009). Although fewer studies assessed memory and executive function we found evidence that social isolation is associated with these specific cognitive domains. We excluded articles reporting findings from cross-sectional data to reduce the risk of reverse causality and enhance the reliability of findings in terms of causality (Aartsen et al. 2004; Kuiper et al. 2016). Only one previous review has used meta-analytic techniques to consider how aspects of social relationships may be associated with cognitive function (Kuiper et al. 2016). We extend this review by considering aspects of social isolation and the association with cognitive function, as well as investigating gender differences in longitudinal studies. Considering gender differences is particularly important given that women may be more likely to engage in frequent social activity and are more likely to maintain close relationships and wider social networks than men (Antonucci, 1994; Kavanagh, Bentley, Turrell, Broom & Subramanian, 2006; Takagi, Kondo & Kawachi, 2013; Tomioka et al. 2016; Wang et al. 2013). Although we report a small association, this still reflects the benefits of social integration on cognitive function in later life for both men and women and is consistent with the findings of Kuiper et al. (2016).

Some limitations of the review need to be addressed. First, there was considerable between-article heterogeneity. Additional analysis suggests that this may partly be accounted for by the differences in methodological approaches and a range of indicators used to assess social concepts and cognitive function (Kuiper et al. 2016) and that other lifestyle factors may contribute to the maintenance of cognitive function (Baumgart et al. 2015; Clare et al. 2017); however this limits our ability to draw definite conclusions regarding the nature of the association. There was evidence of a possible publication bias therefore the observed effect size may be slightly inflated. Studies with a larger sample size and that report a significant association between social relationships and cognitive function are more likely to be reported (Altman, 2014; Heneghan et al. 2017; Williams, Tse, Harlan & Zarin, 2010) which may account for the publication bias found in the meta-analysis. Including grey literature may have reduced this bias, however grey literature tends to include studies with small

samples and non-significant findings, and a number of large studies were included in the review that reported statistically non-significant findings. There are large differences in the number of years follow-up across articles which makes it difficult to compare findings. However, findings suggest that there were similar effect sizes irrespective of follow-up duration. An additional limitation applicable to most later life social isolation research is that although socially isolated older people are not uncommon, this group is particularly difficult to engage in research (Kelly et al. 2017). People who are more extremely isolated may be underrepresented in studies that assess the association between social isolation and cognitive function and hence the effect size may be larger than that which we report. Finally, methodological quality was assessed by one reviewer, which may have influenced the methodological quality ratings. However, the ratings were based on standardised criteria and none of the studies were judged to be of poor quality.

We have demonstrated that in later life larger social networks and engagement in social activity are associated with better cognitive function. The reported association was small, which may be attributed to the methodological issues associated with assessing social concepts and the fact that social connections is only one of many factors that influence cognitive function over time. Future studies would benefit from using standardised measures to assess specific social concepts independently. More randomized controlled trials that assess the effectiveness of interventions to enhance social connections in later life should be conducted to determine whether this may improve cognitive function. This may further help to clarify the nature of the association between social connections and cognitive function in later life.

Given that existing published literature implicates an association between social isolation and cognitive function, this association is explored further in empirical work in Chapters 5–8. None of the studies identified by the systematic review considered the role of underlying mechanisms that may be implicated in the association. Chapters 5–7 extend our current understanding of the association between social isolation and cognitive function by considering the moderating role of cognitive reserve in this relationship. These associations are first considered in a group of community dwelling older people without depression, dementia, or cognitive impairment (Chapter 5). These associations are then considered in people who may be more vulnerable to experiencing social isolation and hence may be at greater risk of poor cognitive function, including people with depression or anxiety (Chapter 6) and people who live alone (Chapter 7). Finally, few studies included in the systematic review considered satisfaction with social contact in measures of social networks and social activity. Therefore, associations between a measure of satisfaction with social contact and a structural measure of social isolation with cognitive function were considered (Chapter 8).

Chapter 5: Social isolation, cognitive reserve, and cognition in later life

5.1 Summary

The systematic review and meta-analysis (Chapter 4) suggested that a low level of social isolation may have a small but significant association with better cognitive function in later life. This chapter is an empirical study that uses cross-sectional and longitudinal data from CFAS-Wales to consider the association between social isolation and cognitive function in a group of community-dwelling older people without dementia, cognitive impairment, or depression. This chapter extends previous work by considering the moderating role of cognitive reserve in this relationship, a mechanism suggested to enhance cognitive function.

Background: There is evidence to suggest that social isolation is associated with poor cognitive function, although findings are contradictory. One reason for inconsistency in reported findings may be a lack of consideration of underlying mechanisms that could influence this relationship. Cognitive reserve is a theoretical concept that may account for the role of social isolation and its association with cognitive outcomes in later life.

Objective: To examine the relationship between social isolation and cognitive function in later life, and to consider the role of cognitive reserve in this relationship.

Method: Baseline and two year follow-up data from CFAS-Wales were analysed. Linear regression modelling was used to assess the relationship between social isolation and cognitive function. To assess the role of cognitive reserve in this relationship, moderation analysis was used to test for interaction effects.

Results: After controlling for age, gender, educational level, and physically limiting health conditions, social isolation was associated with cognitive function at baseline and two year follow-up. Cognitive reserve moderated this association longitudinally.

Conclusions: Findings suggest that maintaining a socially active lifestyle in later life may enhance cognitive reserve and benefit cognitive function. This has important implications for interventions that may target social isolation to improve cognitive function.

5.2 Introduction

Cognitive function is an important aspect of healthy ageing. As people get older, they may experience subtle changes in their cognitive ability, a process referred to as 'cognitive ageing' (Liverman et al. 2015). It is widely thought that while cognitive ageing is a normal part of healthy ageing, more significant changes in cognitive function are not (Christensen, 2001; Deary et al. 2007). Variation is observed in the trajectories of cognitive ageing across older people (Wilson, Beckett et al. 2002). While some individuals retain a high level of cognitive ability from mid- to late- life, others may experience decline (Gow et al. 2007). A decline in cognitive function can be detrimental to the independence, wellbeing, and quality of life of older people (Hendrie et al. 2006; Nishiguchi et al. 2013). Understanding the mechanisms underlying differences in cognitive ageing is important to reduce the impact of poor cognitive function in later life.

Cognitive reserve is a theoretical concept that can account for the differences observed in late-life cognitive trajectories. The theory suggests that individuals differ in their degree of resilience against age-related brain pathology and hence may show differences in cognitive function in relation to an equivalent level of pathology (Stern, 2002, 2012). These differences are linked to the ability of an individual to recruit protective mechanisms associated with cognitive abilities built up over the lifespan, and actively compensate for damage caused by pathology (Stern, 2009). Observational and some experimental evidence suggests that reserve can be built up through a combination of experiences across the lifespan, such as physical exercise, educational level, occupational complexity, and participation in social and cognitively stimulating activities. These experiences may create a buffer against cognitive decline by enhancing brain processes such as neural connectivity and hence cognitive ability. This might then protect the individual against the effects of disease pathology in the first instance, and also compensate for damage and recruit alternative neural pathways when required. This may reduce or delay the extent of impairment experienced and protect against the expression of pathological processes (Siedlecki et al. 2009).

Compared to other lifestyle factors that may build cognitive reserve, the association between social connections and cognitive function is less well understood. Having a range of good social connections has been identified as an important aspect of successful ageing (Rowe & Kahn, 1997) and is associated with lower mortality rates (Holt-Lunstad & Smith, 2012; Steptoe et al. 2013), better health outcomes (Cornwell & Waite, 2009; Umberson & Montez, 2010), higher reported wellbeing (Olesen & Berry, 2011; Tomaszewski, 2013), and enhanced quality of life (Bowling, 2005; Scharf et al. 2004). There is also evidence to suggest that social isolation may be associated with poor cognitive function (Kuiper et al. 2016). Social isolation can be defined as a state in which an individual has a minimal number of social contacts and lacks engagement with others and the wider community

(Nicholson Jr, 2009). Based on the cognitive reserve theory, social integration would provide mental stimulation through complex communication and interaction with others (Bennett et al. 2006; Fratiglioni et al. 2000). In contrast, being isolated would not provide this stimulation and hence may not build reserve.

There is some evidence that social isolation is associated with poorer cognitive outcomes (DiNapoli et al. 2014; Holwerda et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007). However, findings are inconsistent and some studies report conflicting relationships (Holwerda et al. 2012; Simning et al. 2014; Wilson, Krueger et al. 2007). Inconsistency in results assessing the relationship between social isolation and cognitive function may be attributed to conceptual and methodological challenges associated with defining and measuring social isolation. There is no consistent definition used within the literature and this inconsistency is reflected in the measures selected to assess social isolation. Some authors include other indicators in definitions and measures of isolation, such as being unmarried and living alone (Holwerda et al. 2012; Shankar et al. 2013) or social support (Holwerda et al. 2012). Including these indicators in measures of isolation reduces the validity of findings, as they do not necessarily reflect isolation. Some studies use standardised measures of social isolation, such as the Lubben Social Network Scale–6 (LSNS-6: DiNapoli et al. 2014; Simning et al. 2014), whereas others compose measures that capture features of social isolation, such as social networks or social engagement (Shankar et al. 2013; Wilson, Krueger et al. 2007). Likewise, the assessment of cognitive outcomes varies across studies, with some using domain-specific measures of cognitive ability such as attention, or executive function (DiNapoli et al. 2014; Shankar et al. 2013), and others using more comprehensive global measures of cognitive function (Simning et al. 2014), or dementia diagnosis (Holwerda et al. 2012; Wilson, Krueger et al. 2007). Variation in approaches to assessing and defining social isolation and cognitive outcomes may contribute to inconsistency and complicate the interpretation of empirical findings.

Given that current findings are conflicting, this study aims to assess the relationship between social isolation and cognitive function. This relationship will be examined using baseline and two year follow-up data from CFAS-Wales. Although previous work suggests that cognitive reserve may be important in this association, to our knowledge, this has not been explored. One previous study has assessed the moderating effect of educational level on the association between social isolation and cognitive function (Shankar et al. 2013). The authors reported a moderating effect for delayed recall, but not for immediate recall or verbal fluency (Shankar et al. 2013). Educational level alone is not a comprehensive indication of cognitive reserve and it is suggested that multiple proxy indicators representing reserve at different stages of life are preferable (Opdebeeck et al. 2016; Tucker & Stern, 2011). Therefore, we aim to consider whether cognitive reserve moderates the association

between social isolation and cognitive function, using a comprehensive measure of cognitive reserve.

5.3 Method

Design

The relationship between social isolation, cognitive reserve, and cognitive function was examined using data from CFAS-Wales. CFAS-Wales is a longitudinal study of people aged 65 and over, conducted across two locations in Wales, one rural (Gwynedd and Ynys Môn) and one urban (Neath Port Talbot). Participants were assessed at baseline and again two years later. CFAS-Wales aims to investigate physical and cognitive health in later life and to examine environmental factors that may contribute to activity and participation in community and civic life.

Study population

People aged 65 and over were randomly sampled from general practice lists between 2011 and 2013. Participants were stratified by age to ensure a representative sample across two age groups (65–74 and ≥75). People who consented to take part completed an interview in their home. Interviews were conducted by research assistants who had completed training provided by staff at the co-ordinating centre in Cambridge and participants could choose to complete their interview in English or Welsh. Baseline interviews took place between 2011 and 2013 and follow-up interviews were completed two years later, between 2013 and 2015.

The present study uses baseline data which were collected for 3,593 people and follow-up data which were collected for 2,236 people. We excluded people at baseline with cognitive impairment (MMSE score ≤25; N = 908) or with an Automated Geriatric Assisted Taxonomy (AGECAT) classification of dementia (N = 185) to reduce the risk of reverse causation. The AGECAT is a diagnostic algorithm embedded in the CFAS-Wales interview that assesses symptoms to determine whether a person has a healthy diagnosis, or a diagnosis of dementia, depression, or anxiety (Copeland et al. 1986). Given that depression is also associated with cognitive impairment, people with an AGECAT classification of depression (N = 333) were excluded, as were people living in an institution (N = 95) as it is considered that the experience of social isolation will differ between community and residential settings. Participants with missing data on the measures used at baseline (N = 146) and follow-up (N = 700) were also excluded. This gave a final sample of 2,224 for cross-sectional analyses and 1,524 for longitudinal analyses. A comparison of participants that were included for cross-sectional analyses, but excluded for longitudinal analyses because of missing data at follow-up, can be found in Table 5.1. Those who were excluded were older, had a poorer

CAMCOG score at baseline, had fewer years of education, engaged in less cognitive activity, had a lower occupational complexity and cognitive reserve score, were more socially isolated, had poorer eyesight, and required significantly more help with daily tasks, but were no more likely to be women or have problems with hearing.

Table 5.1. *Comparison of included and excluded participants at two year follow-up.*

Variable	**Included participants (N = 1,524)**	**Excluded participants (N = 700)**	***t*(df) or X^2(df) *p***
Age (years), *M* (SD)	73.23 (6.14)	73.99 (6.54)	*t*(1, 2222) = 2.67 *p* = .007
Gender, *N* (%)			
Men	758 (49.74)	339 (48.43)	$X^2(1) = .33$
Women	766 (50.26)	361 (51.57)	*p* = .566
Baseline CAMCOG score, *M* (SD)	94.17 (4.95)	92.01 (5.88)	*t*(1, 2222) = -8.93 *p* <.001
Educational level (years), *M* (SD)	12.18 (2.83)	11.77 (2.66)	*t*(1, 2222) = -3.25 *p* <.001
Cognitive activity, *M* (SD)	21.57 (5.15)	20.81 (5.23)	*t*(1, 2222) = -3.22 *p* <.001
Occupational complexity, *M* (SD)	8.34 (3.30)	7.59 (3.32)	*t*(1, 2222) = -4.98 *p* <.001
Cognitive reserve score, *M* (SD)	61.34 (11.46)	58.86 (11.04)	*t*(1, 2222) = -5.36 *p* <.001
LSNS-6, *M* (SD)	16.43 (5.79)	15.49 (5.64)	*t*(1, 2222) = -3.58 *p* <.001
Health conditions, *N* (%)[a]			
Hearing	429 (28.15)	200 (28.57)	$X^2(1) = .04$ *p* = .837
Eyesight	192 (12.60)	119 (17.00)	$X^2(1) = 7.73$ *p* = .005
Require help with daily tasks, *N* (%)	400 (26.25)	237 (33.86)	$X^2(1) = 13.59$ *p* <.001

Note: [a] Number and percentage of people who have these health conditions and rate these conditions as physically limiting.

Measures

Cognitive function

Cognitive function was assessed using the Cambridge Cognitive Examination (CAMCOG: Roth et al. 1986). The CAMCOG is a standardised measure that consists of 67 items, assessing cognitive function along eight subscales, including orientation, comprehension, expression, memory (remote, recent, and learning), attention and calculation, praxis, abstract thinking, and perception. Total scores range from 0–107 and a lower score indicates poor cognitive function. Both baseline and follow-up CAMCOG scores are used in the analyses.

Social isolation

Social isolation was measured in CFAS-Wales using the Lubben Social Network Scale–6 (LSNS-6: Lubben et al. 2006). The LSNS-6 is a standardised measure of social isolation, constructed of three sets of questions that assess family ties, and a set of three comparable questions assessing non-kinship ties. The three items assess the number of relatives/ friends the participant sees or hears from at least once a month, could call on for help, and can speak with about private matters. Responses are collected using a six category response, in which the participant indicates the number of relatives/ friends available. Response scores range from 0 (no relatives/ friends) to 5 (nine or more relatives/ friends). The overall scores for each six questions are summed and range from 0-30, with higher scores indicating lower social isolation. A score of ≤12 may be taken to indicate the presence of social isolation (Lubben et al. 2006). Baseline LSNS-6 scores were used for all analyses.

Cognitive reserve

Cognitive reserve was measured by combining three proxy indicators: educational level, occupational complexity, and cognitive activity at baseline. Educational level was recorded as the number of years in full time education. Occupational complexity was assessed using social class and the social economic group and complexity of the participant's main employment. These were combined to create an occupational complexity score ranging from 1 (lower class and less complex occupations, e.g. cleaner) to 14 (high class and complex occupations, e.g. doctor or lawyer). Cognitive activity was assessed by seven questions asking about engagement in a range of cognitive activities (including listening to the radio, reading a newspaper, magazine, or book, playing games such as cards or chess, and completing crosswords or puzzles). Responses were recorded on a 5-point Likert scale (once a year or less, several times a year, several times a month, several times a week, or everyday/ almost every day) and higher scores indicate greater cognitive activity.

Scores for each proxy indicator were weighted based on the interquartile range to ensure that each component contributed equally to determining the cognitive reserve score. This gave the following formula: cognitive reserve score = (2.33 x educational level) + (1.40 x occupational complexity) + (1 x cognitive activity). A higher score indicates higher levels of cognitive reserve.

Covariates

Several covariates were controlled for in the analyses, including age (years), gender, and educational level (years) at baseline, which are established covariates of late-life cognitive function (Barnes et al. 2003; Tervo et al. 2004; Tilvis et al. 2004). Educational level was not controlled for in analyses that assessed cognitive reserve. Sensory problems (hearing and eyesight) at baseline were also controlled for as these problems may reduce an individual's ability to be socially engaged and hence contribute to an increased level of social isolation (Cook, Brown-Wilson & Forte, 2006; Horowitz, 2004). Participants were asked whether hearing or sight problems limit day-to-day activities (yes/ no). If hearing or eyesight problems are not problematic because the participant wears a hearing aid or glasses then this is rated as no. Finally, the participants' ability to complete daily tasks alone (such as housework, getting dressed, getting up and down stairs, carrying things, etc.) at baseline was controlled for. Participants were asked if they receive any help with day-to-day activities and respond yes/ no. Being unable to complete such tasks may indicate limitations in physical ability and mobility, which may influence ability to be socially engaged, and hence increase level of social isolation (Mendes de Leon, Glass & Berkman, 2003).

Statistical analysis

All analyses were conducted in Stata version 15.0. Descriptive information is reported for the overall sample at baseline, and separately for those who are socially isolated (score of ≤12 on the LSNS-6) and those who are not isolated. CAMCOG scores were normally distributed at baseline (skewness of -.84 and kurtosis of 4.48) and follow-up (skewness of -1.16 and kurtosis of 5.44). The LSNS-6 was also normally distributed at baseline (skewness of -.13 and kurtosis of 2.61). For baseline data, linear regression modelling was used to assess the association between social isolation, as determined by scores on the LSNS-6, and cognitive function, adjusting for covariates. This approach was also used to assess the relationship between social isolation at baseline and cognitive change over two year follow-up. For longitudinal analyses, a cognitive change score was calculated by subtracting the CAMCOG score at baseline from the CAMCOG score at two year follow-up. Each participant's cognitive change score was then standardised by the standard deviation value of the baseline CAMCOG score. In step one of the model unadjusted effects for the association between social isolation and cognition are reported. Step two adjusts for age, gender, and educational level. Step

three adjusts for age, gender, educational level, physically limiting health conditions (eyesight and hearing), and help with daily activities. Adjusted R^2 values were reported for regression models to indicate the proportion of variance explained by variables in the model. Regression coefficients were also reported, along with 95% confidence intervals. All measures were standardised to provide comparable coefficients. Moderation analyses were conducted to determine whether cognitive reserve moderates the association between social isolation and cognitive function or cognitive change. These analyses tested for an interaction between social isolation and the cognitive reserve score and were adjusted for all covariates (including baseline age, gender, eyesight and hearing, and help with daily activities) except for educational level, as this is a component of the cognitive reserve score.

5.4 Results

The mean age of participants was 73.47 years and 51% of participants were women. At baseline, 601 (27%) of participants were classed as isolated by the LSNS-6. People who were isolated were older, more likely to be men, had a poorer CAMCOG score, fewer years of education, participated in fewer cognitive activities, and had lower cognitive reserve scores (Table 5.2). There was little change in the mean CAMCOG scores at baseline (*M* = 93.48, SD = 5.35) and two year follow-up (*M* = 93.73, SD = 6.08) across the total sample.

Table 5.2. *Summary of baseline characteristics of participants in CFAS-Wales.*

Variable	Total sample (N = 2,224)		Not socially isolated (N = 1,623)	Socially isolated (N = 601)	
	***M* (SD) or *N* (%)**	**Range**	***M* (SD) or *N* (%)**	***M* (SD) or *N* (%)**	***t*(df) or X^2(df) *p***
Age (years), *M* (SD)	73.47 (6.28)	65–100	73.09 (6.00)	74.50 (6.91)	t(1, 2222) = -4.72 *p* <.001
Gender, *N* (%)					
Men	1,097 (49.33)		766 (47.20)	331 (55.07)	X^2(1) = 10.89
Women	1,127 (50.67)		857 (52.80)	270 (44.93)	*p* <.001
Baseline CAMCOG score, *M* (SD)	93.48 (5.35)	63–105	93.84 (5.21)	92.51 (5.62)	t(1, 2222) = 5.24 *p* <.001
Educational level (years), *M* (SD)	12.05 (2.79)	1–30	12.17 (2.85)	11.73 (2.59)	t(1, 2222) = 3.31 *p* <.001
Cognitive activity, *M* (SD)	21.33 (5.19)	7–34	21.90 (5.05)	19.78 (5.24)	t(1, 2222) = 8.72 *p* <.001
Occupational complexity, *M* (SD)	8.11 (3.32)	1–14	8.18 (3.33)	7.90 (3.31)	t(1, 2222) = 1.82 *p* = .070
Cognitive reserve score, *M* (SD)	60.77 (11.40)	33.53–109.30	61.72 (11.48)	58.17 (10.77)	t(1, 2222) = 6.58 *p* <.001
LSNS-6, *M* (SD)	16.14 (5.76)	0–30	18.83 (3.97)	8.85 (2.74)	t(1, 2222) = 56.82 *p* <.001
Health conditions, *N* (%)[a]					
Hearing	629 (28.28)		449 (27.66)	180 (29.95)	X^2(1) = 1.13 *p* = .288
Eyesight	311 (13.98)		213 (13.12)	98 (16.31)	X^2(1) = 3.69 *p* = .055
Require help with daily tasks, *N* (%)	637 (28.64)		452 (27.85)	185 (30.78)	X^2(1) = 1.85 *p* = .174

Note: [a] Number and percentage of people who have these health conditions and rate these conditions as physically limiting.

Association between social isolation and cognitive function

Baseline

A linear regression was conducted to assess the cross-sectional association between social isolation and cognitive function (Table 5.3). Social isolation was significantly associated with cognition, adjusted R^2 = .02, $F(1, 2222) = 35.99$, p <.001. After adjusting for all covariates, the association remained significant, adjusted R^2 = .17, $F(7, 2216) = 64.67$, p <.001. This model suggested that people

who are less socially isolated had better CAMCOG scores and the model explained about 17% of the variance in CAMCOG scores.

Table 5.3. *Cross-sectional association between social isolation and cognition (N = 2,224).*

	Model 1 *B* (95% CI) *p*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *p*
Social isolation	.07 (.05, .10) <.001	.05 (.02, .07) <.001	.04 (.02, .07) <.001
Age		-.03 (-.03, -.02) <.001	-.02 (-.03, -.02) <.001
Gender		-.08 (-.12, -.04) <.001	-.08 (-.12, -.03) <.001
Educational level		.04 (.03, .05) <.001	.04 (.03, .05) <.001
Eyesight (impaired)			-.11 (-.17, -.05) <.001
Hearing (impaired)			-.06 (-.11, -.01) .016
Require help with daily activity (yes)			-.07 (-.12, -.02) .007

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3: adjusted for age, gender, years of education, physically limiting health conditions (eyesight and hearing), and help with daily activities.

We ran a linear regression for men and women separately to consider gender differences, controlling for all covariates, except for gender. The association between social isolation and cognitive function was significant for women, adjusted R^2 = .17, $F(6, 1120) = 38.41$, p <.001, but not men, adjusted R^2 = .09, $F(6, 1090) = 35.85$, p = .099. There was a significant interaction between social isolation and gender, adjusted R^2 = .17, $F(8, 2215) = 57.23$, p = .036.

We conducted further regression analyses to determine whether social isolation was more associated with any specific cognitive domains assessed by the CAMCOG (Table 5.4). Social isolation was significantly associated with orientation (adjusted R^2 = .02, $F(7, 2216) = 6.23$, p <.001), expression (adjusted R^2 = .13, $F(7, 2216) = 48.30$, p <.001), praxis (adjusted R^2 = .06, $F(7, 2216) = 21.60$, p <.001), and perception (adjusted R^2 = .11, $F(7, 2216) = 42.04$, p <.001), but not with comprehension (adjusted R^2 = .02, $F(7, 2216) = 7.11$, p <.001), memory (adjusted R^2 = .04, $F(7, 2216) = 14.60$, p <.001), attention and calculation (adjusted R^2 = .03, $F(7, 2216) = 9.36$, p <.001), or abstract thinking (adjusted R^2 = .05, $F(7, 2216) = 16.80$, p <.001).

Table 5.4. *Cross-sectional association between social isolation and sub-domains of cognition assessed by the CAMCOG (N = 2,224).*

	Orientation	**Comprehension**	**Expression**	**Memory**	**Attention and calculation**	**Praxis**	**Abstract thinking**	**Perception**
	B (95% CI) *p*	*B* (95% CI) *P*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*
Social isolation	.01 (0, .02) .003	0 (-.02, .01) .514	.02 (.01, .03) .002	.02 (0, .03) .072	.01 (0, .03) .109	.03 (.01, .05) <.001	0 (-.02, .03) .809	.05 (.02, .09) .002
Age	0 (0, 0) .413	0 (-.01, 0) <.001	-.01, (-.02, -.01) <.001	-.01 (-.01, 0) <.001	0 (-.01, 0) .043	-.01 (-.01, -.01) <.001	-.01 (-.01, -.01) <.001	-.04 (-.04, -.03) <.001
Gender	0 (-.01, .02) .807	.03 (0, .05) .059	.02 (-.01, .04) .199	-.07 (-.10, -.03) <.001	-.09 (-.12, -.06) <.001	-.07 (-.11, -.03) <.001	.05 (0, .09) .045	-.07 (-.14, -.01) .025
Educational level	0 (0, .01) <.001	.01 (0, .01) .003	.02 (.02, .02) <.001	.01 (.01, .02) <.001	.01 (.01, .02) <.001	.02 (.01, .02) <.001	.03 (.02, .04) <.001	.02 (.01, .03) <.001
Eyesight (impaired)	.02 (0, .04) .041	.01 (-.03, .05) .643	-.01 (-.04, .03) .742	-.05 (-.10, -.01) .026	-.02 (-.07, .02) .301	-.07 (-.12, -.02) .009	-.13 (-.20, -.07) <.001	-.09 (-.19, 0) .055
Hearing (impaired)	0 (-.02, .02) .996	-.01 (-.04, .02) .376	-.01 (-.04, .02) .491	-.04 (-.08, -.01) .023	.01 (-.03, .05) .588	-.06 (-.10, -.02) .003	-.01 (-.05, .04) .826	-.05 (-.13, .02) .146
Require help with daily activity (yes)	-.03 (-.04, -.01) <.001	-.04 (-.07, -.01) .013	-.03 (-.06, 0) .021	-.02 (-.05, .02) .372	-.01 (-.05, .02) .476	-.04 (-.08, .0) .065	-.01 (-.06, .04) .777	-.06 (-.14, .01) .092

Note: adjusted for age, gender, years of education, physically limiting health conditions (eyesight and hearing), and help with daily activities.

Longitudinal

A linear regression was conducted to assess the association between social isolation and cognitive change over two year follow-up (Table 5.5). Social isolation was significantly associated with cognitive change, adjusted R^2 = .01, $F(1, 1522) = 8.92$, p = .003. After adjusting for covariates, the association between social isolation and cognitive change remained significant, adjusted R^2 = .05, $F(7, 1516) = 11.95$, p <.001. This suggests that people who are less socially isolated show less decline in CAMCOG scores over two year follow-up.

Table 5.5. *Longitudinal association between social isolation and cognitive change score (N = 1,524)*.

	Model 1 *B* (95% CI) *p*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *p*
Social isolation	.07 (.02, .12) .003	.05 (0, .10) .030	.05 (.01, .10) .028
Age		-.03 (-.04, -.02) <.001	-.03 (-.04, -.02) <.001
Gender		-.07 (-.16, .02) .109	-.06 (-.15, .03) .190
Educational level		.01 (0, .03) .173	.01 (0, .03) .176
Eyesight (impaired)			-.02 (-.15, .12) .775
Hearing (impaired)			.09 (-.01, .19) .093
Require help with daily activity (yes)			-.03 (-.14, .07) .555

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3: adjusted for age, gender, years of education, physically limiting health conditions (eyesight and hearing), and help with daily activities.

To consider differences in gender, we ran a linear regression for men and women separately, controlling for all covariates, except for gender. The association between social isolation and cognitive function was significant for women, adjusted R^2 = .08, $F(6, 759) = 11.57$, p = .021, but not men, adjusted R^2 = .03, $F(6, 751) = 4.65$, p = .388. The interaction term between social isolation and gender was not significant, adjusted R^2 = .05, $F(8, 1515) = 10.75$, p = .132.

As there was little cognitive change observed in the sample, a logistic regression was conducted as a sensitivity analysis to determine the reliability of the regression analysis. A binary variable was created to distinguish cognitive decliners from non-decliners. Decliners were defined as a decline in

two year follow-up CAMCOG score of one standard deviation unit from the baseline CAMCOG score. In total, 203 (13%) participants were classified as cognitive decliners and 1,321 (87%) participants maintained good cognitive function. The logistic regression was significant suggesting that social isolation was associated with a decline in CAMCOG score over two years, $X^2(1) = 8.20$, $p = .004$. This remained significant after controlling for covariates, $X^2(7) = 88.80$, $p < .001$. This suggests that people who are less socially isolated have a small reduction in risk of cognitive decline over a two year follow-up, whereas people who are isolated have a greater risk of cognitive decline (Table 5.6).

Table 5.6. *Longitudinal association between social isolation and cognitive change (N = 1,524).*

	Model 1 OR (95% CI) *p*	**Model 2** OR (95% CI) *p*	**Model 3** OR (95% CI) *P*
Social isolation	.80 (.69, .93) .004	.85 (.73, 1.00) .052	.85 (.73, 1.00) .050
Age		1.10 (1.07, 1.12) <.001	1.10 (1.08, 1.13) <.001
Gender		1.30 (.95, 1.77) .096	1.33 (.97, 1.82) .079
Educational level		.93 (.88, .99) .020	.93 (.87, .99) .015
Eyesight (impaired)			1.06 (.69, 1.65) .781
Hearing (impaired)			.76 (.53, 1.08) .129
Require help with daily activity (yes)			.74 (.51, 1.06) .098

Note: OR = odds ratio, CI = confidence interval. Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3: adjusted for age, gender, years of education, physically limiting health conditions (eyesight and hearing), and help with daily activities.

We conducted further regression analyses to determine whether social isolation was associated with any specific cognitive domains assessed by the CAMCOG using longitudinal data (Table 5.7). Social isolation was significantly associated with comprehension (adjusted $R^2 = .01$, $F(7, 1516) = 2.14$, $p = .037$), but not with orientation (adjusted $R^2 = .01$, $F(7, 1516) = 2.74$, $p = .008$), expression (adjusted $R^2 = 0$, $F(7, 1516) = 1.72$, $p = .099$), memory (adjusted $R^2 = .04$, $F(7, 1516) = 9.06$, $p < .001$), attention and calculation (adjusted $R^2 = .01$, $F(7, 1516) = 2.95$, $p = .005$), praxis (adjusted $R^2 = 0$, $F(7, 1516) = 1.95$, $p = .059$), abstract thinking (adjusted $R^2 = .01$, $F(7, 1516) = 2.77$, $p = .007$), and perception (adjusted $R^2 = .01$, $F(7, 1516) = 1.44$, $p = .184$).

Table 5.7. *Longitudinal association between social isolation and sub-domains of cognition assessed by the CAMCOG (N = 1,524).*

	Orientation	**Comprehension**	**Expression**	**Memory**	**Attention and calculation**	**Praxis**	**Abstract thinking**	**Perception**
	B (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*
Social isolation	.04 (-.13, .20) .675	.08 (.01, .16) .023	.05 (-.01, .11) .099	.04 (-.01, .08) .146	.03 (-.04, .10) .377	-.02 (-.08, .04) .484	.04 (-.02, .11) .182	-.01 (-.07, .04) .622
Age	-.05 (-.07, -.02) <.001	-.01 (-.02, 0) .030	-.01 (-.02, 0) .268	-.03 (-.04, -.02) <.001	-.02 (-.03, -.01) <.001	-.01 (-.02, 0) .015	-.02 (-.03, 0) .005	-.01 (-.02, 0) .030
Gender	.07 (-.26, .40) .668	-.08 (-.22, .06) .290	.05 (-.07, .17) .392	-.02 (-.12, .07) .631	-.10 (-.24, .04) .152	-.02 (-.13, .09) .749	-.04 (-.17, .09) .535	-.02 (-.13, .08) .662
Educational level	.02 (-.04, .08) .478	.01 (-.02, .03) .561	0 (-.02, .02) .774	0 (-.01, .02) .827	.02 (-.01, .04) .187	.02 (0, .04) .084	.01 (-.01, .03) .395	0 (-.02, .01) .723
Eyesight (impaired)	-.04 (-.53, .45) .865	-.02 (-.23, .19) .823	.03 (-.15, .21) .726	-.12 (-.26, .02) .102	.09 (-.11, .29) .386	.11 (-.05, .27) .187	.20 (.01, .39) .037	-.05 (-.20, .11) .542
Hearing (impaired)	.30 (-.07, .66) .108	.13 (-.03, .29) .100	-.12 (-.25, .01) .078	.14 (.03, .25) .009	-.07 (-.22, .08) .370	.10 (-.02, .22) .102	-.02 (-.16, .12) .746	.10 (-.01, .22) .081
Require help with daily activity (yes)	-.33 (-.71, .05) .092	0 (-.16, .17) .974	.12 (-.02, .25) .098	.01 (-.10, .12) .831	0 (-.16, .16) .994	-.04 (-.16, .09) .571	-.10 (-.24, .05) .195	-.07 (-.19, .06) .290

Note: adjusted for age, gender, years of education, physically limiting health conditions (eyesight and hearing), and help with daily activities.

Association between social isolation, cognitive reserve, and cognitive function

Baseline

A moderation analysis was conducted to assess whether cognitive reserve score moderated the cross-sectional relationship between social isolation and cognitive function, controlling for all covariates. The interaction term between social isolation and the cognitive reserve score did not explain a significant increase in cognitive function (*B* = .01; 95% CI: -.01, .04). None of the individual components of the cognitive reserve score (educational level, occupational complexity, and cognitive activity) significantly moderated the relationship between social isolation and cognitive function.

Longitudinal

A moderation analysis was conducted to assess whether cognitive reserve moderated the longitudinal association between social isolation and cognitive change over two year follow-up, controlling for all covariates. The interaction term between social isolation and cognitive reserve score significantly moderated the cognitive change score (*B* = .05; 95% CI: .10, 0).

Post-hoc analyses were conducted to examine the contribution of each component of the cognitive reserve score to determine whether any of the individual components were contributing to the relationship more. The interaction terms between social isolation and educational level (*B* = -.04; 95% CI: -.08, .01) and social isolation and cognitive activity (*B* = -.01; 95% CI: -.06, .03) did not explain a significant increase in cognitive function after adjusting for covariates. The interaction terms between social isolation and occupational complexity were significant (*B* = -.05; 95% CI: -.10, -.01,).

To investigate the relationship between social isolation, occupational complexity, and cognitive change further, participants were separated into two groups: high and low occupational complexity. The occupational complexity score ranges from 1-14 and so people with a score of ≤7 (N = 578) were considered to have low occupational complexity and a score of ≥8 (N = 946) were considered to have high occupational complexity. People with higher occupational complexity had a slightly higher CAMCOG score at baseline (*M* = 94.68, SD = 4.79) compared to people with lower occupational complexity (*M* = 93.29, SD = 5.09: $t(1, 1522) = 5.3817$, $p < .001$). Regression analyses to assess the association between social isolation and cognitive function were conducted for each group separately, controlling for all covariates. The association between social isolation and cognitive change was non-significant for those with high occupational complexity (*B* = .03; 95% CI: -.02, .09), but was significant for those with low occupational complexity (*B* = .08; 95% CI: 0, .15; Figure 5.1).

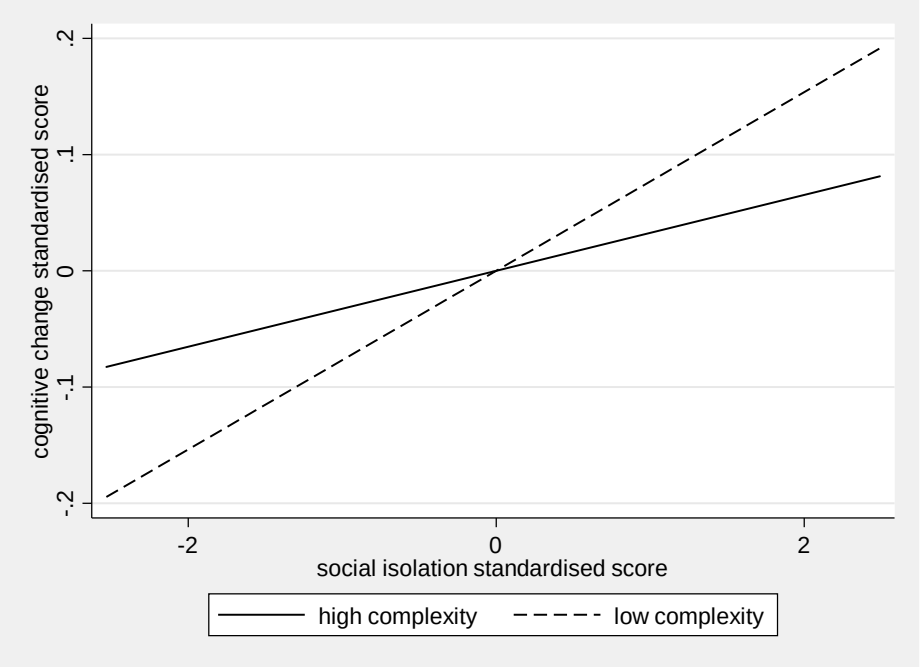


Figure 5.1. The association between social isolation and cognitive change by high and low occupational complexity groups.

5.5 Discussion

This study aimed to assess the relationship between social isolation and cognitive function, and to consider the role of cognitive reserve in this relationship. Findings suggest that being isolated in later life is detrimental to cognitive function. We also find that cognitive reserve moderates this association at two year follow-up.

The finding that social isolation is associated with cognitive function at baseline and two year follow-up is consistent with previous studies that assess these relationships using baseline (DiNapoli et al. 2014) and longitudinal data (Holwerda et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007). This suggests that being socially integrated in later life is beneficial to cognitive function. Social isolation may be detrimental to cognitive function as isolated individuals experience less social contact with others. Such individuals are likely to receive less cognitive stimulation through social contact, resulting in lower cognitive reserve and hence poorer cognitive function (Stern, 2002, 2012).

We also found that the relationship between social isolation and cognitive function is moderated by cognitive reserve longitudinally, but not cross-sectionally. This suggests that having higher cognitive reserve further benefits late-life cognitive function. Cognitive reserve may explain the differences in cognitive trajectories observed in later life (Stern, 2002). When each aspect of the cognitive reserve measure was separated in moderation analyses, we found that educational level and cognitive

activity did not moderate the association, but occupational complexity did. Further analyses shows that the association of social isolation with cognitive change was significant in individuals with low occupational complexity, but not high occupational complexity. This suggests that good social interactions may be more beneficial to cognitive function in individuals with low mid-life reserve, as measured by occupational complexity (Fratiglioni et al. 2007; Shankar et al. 2013). Similar findings have been reported for other health outcomes. For instance, participation in social activities has been associated with better health among participants from low socioeconomic groups (Heritage, Wilkinson, Grimaud & Pickett, 2008). Likewise, it has been found that good social resources benefit health outcomes for those in low-income groups (Schöllgen, Huxhold, Schüz & Tesch-Römer, 2011). This provides further support for the beneficial effect of social connections on individuals with low mid-life reserve (Schöllgen et al. 2011; Shankar et al. 2013). This finding could also be explained by the observation that people with higher occupational complexity had higher CAMCOG scores at baseline.

Educational level alone did not moderate the association between social isolation and cognitive function. This is inconsistent with a previous study by Shankar and colleagues (2013) which reported that educational level did moderate this association. However, the authors of this study assessed three sub-domains of cognitive function, and found that educational level moderated the association between social isolation and cognition for delayed recall, but not for verbal fluency or immediate recall. The measure of education in the present study is a relatively crude index and only considers the number of years of education. Shankar and colleagues measure educational level based on the highest qualification obtained, and classify participant's educational level as either low (no formal qualifications) or high. This measure of educational level is much more sensitive and reflects how methodological differences across studies may be accountable for differences in findings.

Cognitive ability can be improved across the lifespan based on lifestyle and engagement (Richards & Deary, 2005). This has important implications for preventative interventions. Although some aspects of early- and mid- life reserve cannot be modified in later life, such as educational level or occupational complexity, there are other aspects of reserve that can be modified, such as social activity, to contribute to building reserve and reducing poor cognitive function in later life. This may be particularly useful for individuals that have poor early- and mid- life reserve. The results of the present study reflect that social isolation in later life is detrimental to cognitive function. Interventions to reduce social isolation in older people may benefit cognitive function both directly and indirectly through building cognitive reserve.

This study has many strengths, including the use of a large scale, population-based cohort study. Participants in CFAS-Wales were sampled from general practice registers and approached to participate, giving a representative sample of older people, including those who are extremely isolated. Studies that acquire samples through participants responding to advertised studies may be more at risk of bias to a 'self-selected' sample that are more engaged in social and community activities, and hence are not isolated. A second advantage is that the cognitive reserve measure combined several proxy indicators from early- (educational level), mid- (occupational complexity), and late- (cognitive activity) life. This approach is preferable as it accounts for the variance in reserve built at different stages of life (Opdebeeck et al. 2016; Tucker & Stern, 2011). Each of these components was weighted equally to generate a cognitive reserve score. However, the contribution of each of these components of the cognitive reserve score may vary considerably across participants. For example, an individual with a poor educational level and a low occupational complexity may compensate for this through good social relationships (Shankar et al. 2013). These individual differences may not be adequately reflected in the measure.

This study has some limitations. It is possible that social isolation may be prodromal to poor cognitive function (Barnes et al. 2004). However, we excluded participants with poor cognitive function or dementia at baseline which reduces the risk of reverse causation. Limited cognitive change was observed across the sample between baseline and follow-up. Some participants had improved on their CAMCOG scores at follow-up. This limits the validity of the longitudinal analyses as they may replicate the cross-sectional findings, rather than reliably representing the longitudinal relationship between social isolation and cognitive change. The follow-up period of two years may not be sufficient to observe cognitive change.

The findings of this study suggest that being socially isolated in later life is associated with poor cognitive function. This has important implications for interventions, suggesting that targeting isolation may be beneficial for cognitive function. The finding that cognitive reserve moderates this association reflects the importance of being engaged throughout the lifespan in order to build reserve to protect against poor cognitive function in later life.

The next chapter uses the same theoretical and statistical approach used in this chapter but considers the associations between social isolation, cognitive reserve, and cognitive function in people with depression or anxiety who may be at greater risk of social isolation. This is important as the findings from the present chapter and previous work suggest that social isolation is associated with poorer cognitive function. Therefore, people who are more vulnerable to social isolation may be at greater risk of experiencing poor cognitive function.

Chapter 6: Social isolation, cognitive reserve, and cognitive function in older people with depression or anxiety

6.1 Summary

The findings from Chapter 5 suggest that being isolated is associated with poor cognitive function in older people without cognitive impairment, dementia, or depression. This chapter aims to assess this relationship in older people with symptoms of depression or anxiety using cross-sectional and longitudinal data from CFAS-Wales. The association may be different for people with depression or anxiety as symptoms may alter the way in which social relationships are experienced.

Background: There is some evidence to suggest that poor social connections are associated with poor cognitive function in older people who are not experiencing symptoms of depression or anxiety, and this association is moderated by cognitive reserve. However, it is not clear whether this relationship is the same for older people with symptoms of depression or anxiety. People with depression or anxiety may be more vulnerable to experiencing social isolation and hence may be at greater risk of poor cognitive function.

Objective: To determine whether people with depression or anxiety are more at risk of social isolation and feelings of loneliness, and to explore the association between social isolation, cognitive reserve, and cognitive function in older people with depression or anxiety.

Method: Baseline and two year follow-up data were analysed from CFAS-Wales. We compared levels of social isolation, loneliness, social contact, cognitive function, and cognitive reserve at baseline amongst older people with and without depression or anxiety. Linear regression was used to assess the relationship between isolation and cognitive function at baseline and two year follow-up in a sub-group of older people meeting pre-defined criteria for depression or anxiety. A moderation analysis tested for the moderating effect of cognitive reserve.

Results: Older people with depression or anxiety perceived themselves as more isolated and lonely than those without depression or anxiety, despite having an equivalent level of social contact with friends and family. In people with depression or anxiety, social isolation was associated with poor cognitive function at baseline, but not with cognitive change at two year follow-up. Cognitive reserve did not moderate this association.

Conclusions: Social isolation was associated with poor cognitive function at baseline, but not two year follow-up. This may be attributed to a reduction in mood-related symptoms at follow-up which may have led to improved cognitive function.

6.2 Introduction

Cognitive ageing refers to a normal process in healthy ageing in which some subtle changes in cognitive function are observed (Harada et al. 2013; Liverman et al. 2015). Trajectories of cognitive change can vary from healthy cognitive ageing to more advanced unhealthy cognitive decline or progression to dementia (Gow et al. 2007; Wilson, Beckett et al. 2002).

Cognitive reserve theory can account for differences in late-life cognitive trajectories and suggests that individuals differ in their resilience against damage caused by age-related brain pathology (Stern, 2002, 2012). Hence, individuals with an equivalent level of pathology may present with differing levels of cognitive ability (Stern, 2009). These differences may be accounted for by factors across the lifespan that build cognitive reserve, including experiences and opportunities such as educational level or complex occupations, or lifestyle factors such as physical exercise and participation in social and cognitively stimulating activities (Stern, 2002, 2012). This reserve can act as a protective mechanism that compensates for damage and recruits alternative neural networks if required (Siedlecki et al. 2009). Individuals differ in the level of reserve built across the lifespan, which results in differences in the level of resilience against pathology and hence differences in trajectories of late-life cognitive function (Siedlecki et al. 2009).

Compared to other factors that are thought to build cognitive reserve, the relationship between social isolation and cognitive function is less well studied. Social isolation is defined as having few social contacts and little engagement with others and the wider community (Nicholson Jr, 2009). Social isolation may not be a choice, particularly for people with poor physical and mental health who may desire social contact but are unable to engage due to the impact of illness or stigma (Corrigan & Rao, 2012). Additional barriers such as poor transport, living in rural areas, having no children or family nearby, and a lack of opportunity for social engagement in the community are also highly influential in determining social isolation (Bordone & Weber, 2012; Bowling & Stafford, 2007; Rosso et al. 2013; Wen et al. 2006).

From a cognitive reserve perspective, having a wide range of social contacts and frequent engagement in social activities may provide mental stimulation through challenging and complex interactions with others and hence build reserve (Bennett et al. 2006; Fratiglioni et al. 2000). Evidence suggests that being isolated may be associated with poor cognitive function in healthy older people (DiNapoli et al. 2014; Shankar et al. 2013; Wilson, Krueger et al. 2007); however, some studies do not find this association (Holwerda et al. 2012; Simning et al. 2014; Wilson, Krueger et al. 2007).

The association between social isolation and cognitive function may be different in people with depression or anxiety, who may have fewer social interactions due to symptoms of, or underlying reasons for, illness (García-Peña et al. 2013; Litwin, 2012; Segrin, 2000). In turn, having less frequent social contact may increase feelings of loneliness and isolation (Domènech-Abella et al. 2017; Luanaigh & Lawlor, 2008; Yaacob et al. 2017), hypervigilance to social threats, or expectations of negative social interactions, which may intensify and reinforce social isolation and feelings of loneliness (Cacioppo & Hawkley, 2009; Granerud & Severinsson, 2006). In addition to possibly benefitting cognitive function, social connections are fundamental for good mental health and may reduce symptoms of depression or anxiety (Diener & Seligman, 2004; Kuchibhatla et al. 2012; Santini et al. 2015; Sonnenberg et al. 2013).

The association between depression or anxiety, social relationships, and cognitive function is complex, as although good social relationships may enhance wellbeing, individuals who have greater wellbeing may experience better social relationships (Diener & Seligman, 2004). Depression and anxiety are also associated with poor cognitive function (Aggarwal et al. 2017; Pietrzak et al. 2012; Potvin et al. 2011; Yochim et al. 2013) and an increased risk of dementia (Burton et al. 2012; Diniz et al. 2013; Gulpers et al. 2016). However, findings are inconsistent and some studies report that although depression or anxiety may accompany poor cognitive function, symptoms of depression and anxiety do not necessarily precede poor cognitive function (Andreescu et al. 2014; Okereke & Grodstein, 2013; Potvin et al. 2013; Richard et al. 2013).

The evidence reviewed suggests that older people with depression or anxiety may have more negative experiences of social relationships than those without depression or anxiety, which may intensify social isolation and feelings of loneliness. Previous studies report that people with mood disorders have poorer cognitive function. Previous work in older people without depression or anxiety suggests that good social relationships may be associated with better cognitive function and higher levels of cognitive reserve. It is possible that the negative experiences of social relationships in those with depression or anxiety may influence how social relationships contribute to cognitive reserve, and hence cognition. Therefore, the present study aimed to investigate the following:

1. Do older people with depression or anxiety experience greater feelings of loneliness, more social isolation, and less social contact than people without depression or anxiety?
2. Do people with depression or anxiety have poorer cognitive function and lower cognitive reserve than people without depression or anxiety?
3. Is social isolation associated with poor cognitive function in older people with depression or anxiety?

4. Does cognitive reserve moderate the association between social isolation and cognitive function in older people with depression or anxiety?

6.3 Method

Design

Data from CFAS-Wales, a longitudinal population-based study, were used to address the study aims.

Study population

People age ≥65 years were randomly selected from general practice databases across two study sites (Gwynedd/ Ynys Môn and Neath Port Talbot). To ensure that participants were age representative of the general population, participants were stratified into two age groups (65-74 years and ≥75 years). People who agreed to participate completed an extensive questionnaire administered by a trained research assistant at the participant's home. Baseline data were collected between 2011 and 2013 and follow-up interviews were conducted two years later, between 2013 and 2015.

Baseline data were collected for 3,593 participants and follow-up data were collected for 2,236 participants. To reduce the risk of reverse causation we excluded participants with an Automated Geriatric Assisted Taxonomy (AGECAT) classification of dementia (N = 185) or cognitive impairment (MMSE score ≤25; N = 908) at baseline. The AGECAT is a diagnostic algorithm embedded in the CFAS-Wales interview that assesses symptoms to determine whether a person has a diagnosis of dementia, depression, anxiety, or no diagnosis (Copeland et al. 1986). We excluded participants living in an institution at baseline (N = 95) as social relationships are experienced differently in institutional care compared to in the community. Participants with missing data at baseline (N = 796) and follow-up (N = 686) were also excluded. This gave a final baseline sample of 2,135 participants, of which 154 (7%) participants had an AGECAT classification of depression, 32 (1.5%) participants had an AGECAT classification of anxiety, and 1,949 (91%) participants had no AGECAT diagnosis. The sample size at two year follow-up was 1,449 participants, of whom 101 (7%) participants had a classification of depression, 22 (2%) had a classification of anxiety, and 1,326 (92%) had no AGECAT diagnosis. A comparison of the participants included in baseline analyses but excluded from longitudinal analyses because of missing data is presented in Table 6.1. Those excluded at follow-up had poorer cognitive scores, but there were no differences in any other baseline variables.

Table 6.1. *Comparison of included and excluded participants at two year follow-up.*

Variable	**Included participants (N = 123)**	**Excluded participants (N = 63)**	***t*(df) or X^2(df) *p***
Age (years), *M* (SD)	72.76 (5.97)	73.14 (6.05)	*t*(1, 184) = .42 *p* = .678
Gender, *N* (%)			
Men	47 (38.21)	19 (30.16)	X^2(1) = 1.18
Women	76 (61.79)	44 (69.84)	*p* = .277
CAMCOG score, *M* (SD)	93.42 (5.14)	91.11 (5.31)	*t*(1, 184) = -2.87 *p* = .004
Educational level (years), *M* (SD)	11.82 (3.12)	11.63 (2.11)	*t*(1, 184) = -.43 *p* = .670
Cognitive activity, *M* (SD)	21.09 (4.86)	20.37 (4.58)	*t*(1, 184) = -.98 *p* = .328
Occupational complexity, *M* (SD)	7.90 (3.15)	7.29 (3.26)	*t*(1, 184) = -1.25 *p* = .213
Cognitive reserve score, *M* (SD)	59.70 (11.40)	57.67 (8.90)	*t*(1, 184) = -1.23 *p* = .221
LSNS-6, *M* (SD)			
Overall	16.21 (5.75)	15.41 (5.06)	*t*(1, 184) = -.93 *p* = .352
Family	8.48 (3.61)	7.71 (3.13)	*t*(1, 184) = -1.43 *p* = .155
Friends	7.73 (3.55)	7.70 (3.49)	*t*(1, 184) = -.06 *p* = .952
Social contact, *M* (SD)	6.93 (2.04)	7.00 (2.13)	*t*(1, 184) = .23 *p* = .820
Loneliness, *M* (SD)			
Overall	1.80 (1.41)	1.68 (1.31)	*t*(1, 184) = -.58 *p* = .566
Social loneliness	.60 (.92)	.71 (.91)	*t*(1, 184) = .79 *p* = .428
Emotional loneliness	1.20 (.96)	.97 (.88)	*t*(1, 184) = -1.63 *p* = .105
Health conditions, *N* (%)			
Stroke	7 (5.69)	3 (4.76)	X^2(1) = .07 *p* = .790
Heart attack	13 (10.57)	9 (14.29)	X^2(1) = .55 *p* = .458
Hypertension	61 (49.59)	35 (55.56)	X^2(1) = .59 *p* = .441

Measures

Depression and anxiety

Depression and anxiety were assessed at baseline using the AGECAT (Copeland et al. 1986), a semi-structured interview designed to assess whether older people have symptoms of depression,

anxiety, dementia, or no illness. An algorithm is used to assign scores ranging from 0–5 and diagnoses are given based on the severity of symptoms, reflecting either no or few symptoms (0-1), some symptoms and a probable sub-threshold illness (2), or clinically relevant symptoms and a probable clinically significant case (3-5). The algorithm uses a hierarchical system to determine one main diagnosis for which the individual exhibits the most symptoms. Symptoms of depression and anxiety are assessed in the same cluster and may overlap therefore this algorithm may give precedence to a classification of depression over anxiety. The AGECAT has high concordance with diagnoses given by trained psychiatrists (Cohen's k = .84: Copeland et al. 1986; Copeland et al. 2002).

Cognitive function

Cognitive function was assessed at baseline and follow-up using the CAMCOG (Roth et al. 1986). The CAMCOG assesses cognition under the following dimensions: orientation, language (comprehension and expression), memory (remote, recent, and learning), praxis, attention, abstract thinking, perception, and calculation. Scores range from 0–107 and a lower score indicates poorer cognitive function. The CAMCOG has good inter-rater reliability (r = .97) and high sensitivity (92%) and specificity (96%) in detecting cognitive impairment (Roth et al. 1986).

Cognitive reserve

A composite measure of cognitive reserve was calculated using three proxy measures: educational level, occupational complexity, and cognitive activity, based on previous cognitive reserve scores created in MRC-CFAS (Valenzuela et al. 2011) and CFAS-II (Opdebeeck et al. 2018). Educational level was measured as the number of years in full time education. Occupational complexity was determined by the complexity and socioeconomic group of the participant's main occupation and social class (Valenzuela et al. 2011). Complexity scores ranged from 1 (low occupational complexity, e.g. unskilled and low socioeconomic group, such as a cleaner) to 14 (high occupational complexity, e.g. skilled and high socioeconomic group, such as a lawyer or doctor). Cognitive activity was assessed by seven questions asking about engagement in cognitive activities (e.g. reading, playing games). Responses were recorded on a five-point scale ranging from once a year or less to everyday and higher scores indicated greater cognitive activity.

Scores for each of the proxy measures were weighted based on the interquartile range to ensure that each item contributed equally to determine the cognitive reserve score. This gave the following formula: Cognitive reserve score = (2.33 × educational level) + (1.40 × occupational complexity) + (1 × cognitive activity). Higher scores indicate higher levels of reserve.

Social isolation

Social isolation was assessed at baseline using the Lubben Social Network Scale–6 (LSNS-6: Lubben et al. 2006), a standardised measure consisting of three questions assessing isolation from family and three comparable questions assessing isolation from friends. The questions ask participants to report the number of relatives/friends they have seen or heard from at least once in the past month, can call on for help, and can speak with about private matters. Participants respond on a six-item category response scale ranging from 0 (no relatives/ friends) to 5 (nine or more relatives/ friends). Total scores range from 0-30 and lower scores indicate more social isolation. The LSNS-6 can be scored for family and friends separately to indicate level of isolation from kin and non-kinship relationships. Questions specific to family and friends are summed separately, scores for each subscale range from 0-15, and social isolation is indicated by a lower score.

Social contact

Social contact was assessed at baseline based on the frequency of contact with friends and family. For each question, participants could respond as daily (5), 2-3 times a week (4), weekly (3), monthly (2), less often (1), or never/ no relatives (0). Scores for each question were combined ranging from 0-10, with zero indicating less social contact and ten indicating greater social contact.

Loneliness

Loneliness was assessed at baseline using the six-item de Jong Gierveld scale (de Jong Gierveld & van Tilburg, 2006) which assesses social and emotional loneliness using three questions for each type of loneliness. Participants respond either yes, more or less, or no. Scores range from 0–6 and higher scores indicate greater feelings of loneliness. For the social and emotional loneliness subscales, scores range from 0–3 and higher scores indicate greater feelings of social or emotional loneliness.

Covariates

Covariates included were age (years), gender, and educational level (years) at baseline as these are established covariates of late-life cognition (Barnes et al. 2003; Tervo et al. 2004; Tilvis et al. 2004) and cardiovascular risk factors including stroke, heart attack, and hypertension (Grodstein, 2007). Cardiovascular risk factors may indicate poorer health and this may limit an individual's ability to be socially engaged and hence may increase level of social isolation or feelings of loneliness (Grodstein, 2007; Mendes de Leon et al. 2003).

Statistical analysis

Analyses were conducted in Stata version 15.0. T-tests were conducted to examine the differences in social isolation, social contact, loneliness, cognitive function, and cognitive reserve across older people with and without depression or anxiety. Means and standard deviations of scores were reported, along with the *t* value, degrees of freedom, and the *p* value. The relationship between social isolation and cognitive reserve was examined in a sub-group of people with depression or anxiety (N = 186 for baseline analyses, N = 123 for longitudinal analyses). A linear regression was conducted to determine whether there was a relationship between social isolation and cognitive function at baseline. To assess this relationship using longitudinal data, a cognitive change score was calculated by subtracting the CAMCOG score at baseline from the CAMCOG score at follow-up. Each participant's cognitive change score was then standardised by the standard deviation value of the baseline CAMCOG score. A linear regression was conducted to determine whether social isolation at baseline was associated with cognitive change over two year follow-up. These analyses were adjusted for all covariates. Adjusted R^2 values were reported for regression models to indicate the proportion of variance explained by variables in the model. Regression coefficients were also reported, along with 95% confidence intervals. All measures were standardised to provide comparable coefficients. Moderation analyses were conducted to determine whether cognitive reserve moderates the association between social isolation and cognitive function or cognitive change in the sub-group of people with depression or anxiety. These analyses tested for an interaction between social isolation and the cognitive reserve score and were adjusted for all covariates except for educational level as this was a component of the cognitive reserve score.

6.4 Results

At baseline, the mean age of participants was 73 years and 51% were women. The mean cognitive reserve score was 60.76 and ranged from 33.53–109.30. Scores on the CAMCOG ranged from 63–105 with a mean of 93.49 at baseline and 76–103 with a mean of 92.99 at follow-up. People with depression or anxiety were significantly more likely to be women, and to have poorer cognitive scores and lower cognitive reserve scores than people without depression or anxiety, but there were no differences in age, educational level, cognitive activity, occupational complexity, stroke, heart attack, or hypertension (Table 6.2).

Social relationships in older people with and without depression or anxiety

Older people with depression or anxiety were classified as significantly more isolated on the total LSNS-6 scale, and on the family and friends subscales, than people without depression or anxiety. Older people with depression or anxiety indicated significantly higher feelings of overall loneliness,

social, and emotional loneliness than people without depression or anxiety. There was no significant difference in social contact scores (Table 6.2).

Cognitive function and cognitive reserve in older people with and without depression or anxiety

Older people without depression or anxiety scored significantly higher on the CAMCOG than people with depression or anxiety. Likewise, people without depression or anxiety scored significantly higher on the cognitive reserve measure than people with anxiety or depression. There was no significant difference in the scores for each individual component of the cognitive reserve score (educational level, occupational complexity, and cognitive activity: Table 6.2).

Table 6.2. *Summary of baseline characteristics of participants in CFAS-Wales.*

Variable	**Total sample (N = 2,135)**	**People without depression or anxiety (N = 1,949)**	**People with depression or anxiety (N = 186)**	***t* (df) or X^2 (df) *p***
Age (years), *M* (SD)	73.26 (6.18)	73.29 (6.20)	72.89 (5.98)	*t*(2133) = -.86 *p* = .393
Gender, *N* (%)				
Men	1,047 (49.04)	981 (50.33)	66 (35.48)	X^2 (1) = 14.98
Women	1,088 (50.96)	968 (49.67)	120 (64.52)	*p* <.001
CAMCOG score, *M* (SD)	93.49 (5.31)	93.57 (5.30)	92.64 (5.30)	*t*(2133) = -2.29 *p* = .022
Educational level (years), *M* (SD)	12.05 (2.82)	12.08 (2.82)	11.76 (2.81)	*t*(2133) = -1.50 *p* = .133
Cognitive activity, *M* (SD)	21.37 (5.13)	21.42 (5.16)	20.84 (4.73)	*t*(2133) = -1.48 *p* = .140
Occupational complexity, *M* (SD)	8.07 (3.32)	8.10 (3.33)	7.69 (3.19)	*t*(2133) = -1.61 *p* = .107
Cognitive reserve score, *M* (SD)	60.76 (11.44)	60.92 (11.50)	59.01 (10.64)	*t*(2133) = -2.18 *p* = .029
Social isolation, *M* (SD)				
Overall	16.94 (5.29)	17.03 (5.25)	15.94 (5.62)	*t*(2133) = -2.70 *p* = .007
Family	8.73 (3.28)	8.77 (3.25)	8.22 (3.47)	*t*(2133) = -2.20 *p* = .027
Friends	8.21 (3.39)	8.26 (3.37)	7.72 (3.52)	*t*(2133) = -2.08 *p* = .037
Social contact, *M* (SD)	7.05 (1.89)	7.05 (1.88)	6.95 (2.06)	*t*(2133) = -.71 *p* = .479
Loneliness, *M* (SD)				
Overall	.86 (1.07)	.77 (.99)	1.76 (1.37)	*t*(2133) = 12.58 *p* <.001
Social loneliness	.42 (.74)	.40 (.71)	.64 (.91)	*t*(2133) = 4.24 *p* <.001
Emotional loneliness	.43 (.68)	.37 (.61)	1.12 (.94)	*t*(2133) = 15.27 *p* <.001
Health conditions, *N* (%)				
Stroke	108 (5.06)	98 (5.03)	10 (5.38)	X^2 (1) = .04 *p* = .836
Heart attack	184 (8.62)	162 (8.31)	22 (11.83)	X^2 (1) = 2.67 *P* = .103
Hypertension	1,002 (46.93)	906 (46.49)	96 (51.61)	X^2 (1) = 1.79 *P* = .181

Social isolation and cognitive function in older people with depression or anxiety

Baseline

The association between social isolation and cognitive function at baseline was assessed in the sub-group of people with depression or anxiety. Social isolation was significantly associated with CAMCOG scores in the fully adjusted model (adjusted R^2 = .17, $F(7, 178) = 6.41$, $p < .001$). The model suggested that people with depression or anxiety who were less socially isolated had better CAMCOG scores and the model explained 17% of the variance in CAMCOG scores (Table 6.3, Figure 6.1).

Table 6.3. *Cross-sectional association between social isolation and cognition in older people with depression or anxiety (N = 186).*

CAMCOG score	**Model 1** *B* (95% CI) *P*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *p*
Social isolation	.12 (.03, .20) .008	.11 (.03, .19) .009	.11 (.03, .19) .007
Age		-.02 (-.04, -.01) <.001	-.02 (-.04, -.01) <.001
Gender		-.17 (-.33, -.01) .039	-.17 (-.33, -.01) .043
Educational level		.06 (.04, .09) <.001	.06 (.04, .09) <.001
Stroke (yes)			-.22 (-.55, .11) .186
Heart attack (yes)			.09 (-.15, .33) .452
Hypertension (yes)			.03 (-.11, .18) .651

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3 adjusted for age, gender, years of education, stroke, heart attack, and hypertension.

Longitudinal

The association between social isolation and cognitive change over two year follow-up was assessed in the sub-group of people with depression or anxiety at baseline. Social isolation was not significantly associated with cognitive change in the fully adjusted model (adjusted R^2 = 0, $F(7, 115) = 1.06$, $p = .396$: Table 6.4, Figure 6.2).

Table 6.4. *Longitudinal association between social isolation and cognitive change score over two years in older people with depression or anxiety (N= 123).*

CAMCOG score	**Model 1** *B* (95% CI) *P*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *p*
Social isolation	-.17 (-.35, .01) .067	-.16 (-.35, .03) .092	-.16 (-.35, .03) .101
Age		-.01 (-.04, .02) .533	-.01 (-.04, .02) .435
Gender		-.09 (-.47, .29) .635	-.03 (-.42, .36) .883
Educational level		0 (-.06, .06) .956	.01 (-.05, .06) .820
Stroke (yes)			.68 (-.09, 1.45) .082
Heart attack (yes)			.13 (-.47, .73) .663
Hypertension (yes)			.02 (-.33, .37) .911

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3 adjusted for age, gender, years of education, stroke, heart attack, and hypertension.

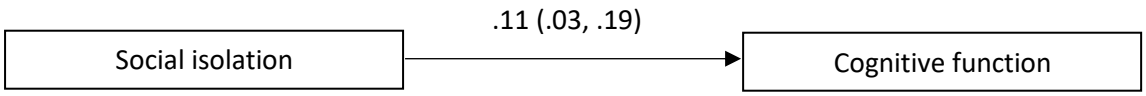


Figure 6.1. The significant association between social isolation and cognitive function at baseline in people with depression or anxiety (N = 186), adjusted for age, gender, years of education, stroke, heart attack, and hypertension.

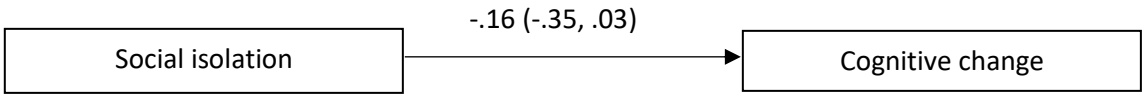


Figure 6.2. The non-significant association between social isolation and cognitive function at two year follow-up in people with depression or anxiety (N = 123), adjusted for age, gender, years of education, stroke, heart attack, and hypertension.

People with persistent depression or anxiety

Of the 123 participants with an AGECAT classification of either depression or anxiety at baseline, 70 (57%) of these participants had a healthy AGECAT classification at follow-up. Fifty-two (42%) participants had an AGECAT diagnosis of depression or anxiety at baseline and two year follow up. Information for the AGECAT diagnosis at two year follow-up was missing for one (1%) participant.

T-tests were conducted to determine whether people with persistent depression or anxiety had poorer scores on the CAMCOG at baseline and two year follow-up. People with an AGECAT diagnosis of depression or anxiety at baseline and two year follow-up had slightly lower scores on the CAMCOG at baseline (*M* = 92.37) and two year follow-up (*M* = 90.98) than people with a healthy AGECAT diagnosis at two year follow-up (baseline *M* = 94.14, two year follow-up *M* = 94.49). The difference in CAMCOG scores was significant at two year follow-up: $t(120) = 3.69$, $p < .001$, and was marginally significant at baseline: $t(120) = 1.91$, $p = .059$.

A linear regression analysis was conducted to determine the association between social isolation and cognitive function over two year follow-up in people with persistent depression or anxiety (N = 52). Social isolation was significantly associated with poorer cognitive function for people with persistent depression or anxiety (adjusted R2 = .10, F(7, 44) = 1.84, p = .103: Table 6.5).

Table 6.5. *Longitudinal association between social isolation and cognitive change score over two years in older people with persistent depression or anxiety (N= 52).*

CAMCOG score	**Model 1** *B* (95% CI) *P*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *P*
Social isolation	-.30 (-.62, .01) .059	-.37 (-.73, -.01) .045	-.44 (-.79, -.08) .017
Age		-.03 (-.09, .03) .283	-.04 (-.10, .02) .178
Gender		.25 (-.52, 1.02) .519	.46 (-.32, 1.25) .243
Educational level		-.03 (-.15, .08) .584	-.01 (-.12, .11) .926
Stroke (yes)			1.47 (.23, 2.70) .021
Heart attack (yes)			.09 (-.92, 1.09) .863
Hypertension (yes)			.22 (-.44, .88) .511

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3 adjusted for age, gender, years of education, stroke, heart attack, and hypertension.

Social isolation, cognitive reserve, and cognitive function in older people with depression or anxiety

Baseline

The moderating effect of cognitive reserve on the association between social isolation and cognitive function was assessed in the sub-group of people with depression or anxiety. The interaction term between social isolation and the cognitive reserve score did not explain a significant increase in cognitive function in the unadjusted model (*B* = -.02; 95% CI: -.11, .07, *p* = .628), or after adjusting for age, gender, stroke, heart attack, and hypertension (*B* = -.01; 95% CI: -.10, .07, *p* = .781; Figure 6.3).

Longitudinal

The moderating effect of cognitive reserve on the association between social isolation and cognitive change was assessed in the sub-group of people with depression or anxiety at baseline. The interaction term between social isolation and cognitive reserve score did not significantly moderate the cognitive change score in the unadjusted model (*B* = .02; 95% CI: -.17, .23, *p* = .789), or after adjusting for age, gender, stroke, heart attack, and hypertension (*B* = .02; 95% CI: -.18, .23, *p* = .831; Figure 6.4).

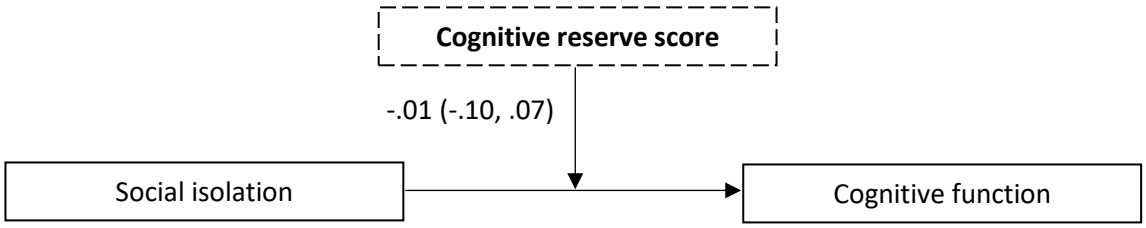


Figure 6.3. The non-significant moderating effect of cognitive reserve on the association between social isolation and cognitive function at baseline in people with depression or anxiety (N = 186), adjusted for age, gender, stroke, heart attack, and hypertension.

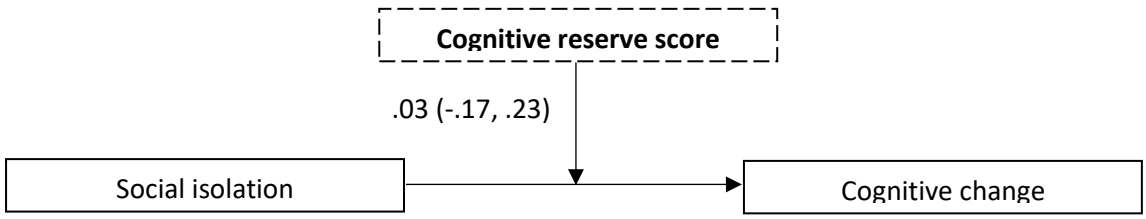


Figure 6.4. The non-significant moderating effect of cognitive reserve on the association between social isolation and cognitive function at two year follow-up in people with depression or anxiety (N = 123), adjusted for age, gender, stroke, heart attack, and hypertension.

6.5 Discussion

This study aimed to assess differences in experiences of social relationships across those with and without symptoms of depression or anxiety, as determined by the AGECAT classification. We also aimed to examine differences in cognitive function and cognitive reserve. In a sub-group of people with symptoms of depression or anxiety at baseline, we aimed to assess the relationship between social isolation and cognitive function, and to consider the moderating role of cognitive reserve in this relationship. Findings suggest that people with depression or anxiety experience poorer social relationships and poorer cognitive function, and have lower levels of cognitive reserve. Social isolation was associated with poor cognitive function in older people with depression or anxiety at baseline, but not with cognitive change at two year follow-up. Cognitive reserve did not moderate this association.

Our results suggest that people with depression or anxiety experience higher levels of social isolation and loneliness compared to those without depression or anxiety. This is in line with previous research that suggests loneliness and social isolation often co-occur with depression (Cacioppo & Hawkley, 2009; Luanaigh & Lawlor, 2008). Interestingly, however, there was no significant difference in the frequency of social contact with friends and family across participants. This suggests that although people with and without depression or anxiety have the same frequency of contact, people with depression or anxiety report significantly higher feelings of loneliness and are more isolated. This may be explained by the tendency for people with depression to recall more negative than positive information about social relationships and interactions than people without depression (Beck, 2008; Lewis et al. 2017). People with depression may hold more negative social expectations, which may increase feelings of loneliness and isolation, despite having opportunities to engage in social contact (Cacioppo & Hawkley, 2009; Granerud & Severinsson, 2006).

People with depression or anxiety scored lower on a test of cognitive function than people without depression or anxiety. We also found that people with persistent depression or anxiety scored lower on a test of cognitive function at two year follow-up than at baseline. People who had a healthy AGECAT diagnosis at two year follow-up had slightly improved cognitive scores at follow-up compared to baseline. This finding is in line with previous research that suggests depression or anxiety are associated with poor cognitive function (Aggarwal et al. 2017; Pietrzak et al. 2012; Yates, Clare, & Woods, 2017; Yochim et al. 2013) and a greater risk of Alzheimer's disease (Diniz et al. 2013; Gulpers et al. 2016). We also found that scores for cognitive reserve were lower for people with depression or anxiety.

Social isolation was associated with poor cognitive function in people with depression or anxiety at baseline, but not with cognitive change at two year follow-up. One explanation for the difference in finding at follow-up may be the variance in mood-related symptoms experienced by participants. Over half of people who were experiencing clinically relevant symptoms of depression or anxiety at baseline were experiencing no, or few, symptoms two years later. Previous work suggests that people with depression may experience significant cognitive impairment during episodes of illness, which may persist after symptom reduction (Airaksinen, Wahlin, Larsson & Forsell, 2006) or remission (Gruber, Rathgeber, Bräunig & Gauggel, 2007; Nakano et al. 2008). Further work suggests that, over time, cognitive ability may improve following the reduction of mood-related symptoms (Biringer et al. 2005; Rock et al. 2014). The reduction of such symptoms at follow-up in the present sample may therefore account for the non-significant relationship between social isolation and cognitive change at follow-up. Indeed, participants who were not experiencing clinically relevant symptoms of depression or anxiety at two year follow-up had slight improvements in their cognitive test scores. Whereas participants who had persistent symptoms of depression or anxiety at baseline and two year follow-up had poorer cognitive scores at follow-up compared to their baseline cognitive scores. There was limited cognitive change observed across the sample as a whole between baseline and two year follow-up. This may also account for why there was an association at baseline but not with cognitive change at follow-up. Alternatively, as the number of people with depression or anxiety at follow-up was small, this may have limited the power to detect interaction effects in the longitudinal analysis.

Cognitive reserve did not moderate the association between social isolation and cognitive function or cognitive change at two year follow-up. It may be that there are other mechanisms that are more important in explaining the relationship between social isolation and cognitive function. For example, it has been proposed that social networks may be used in the transmission of health information (Berkman & Glass, 2000; Kim, Kreps & Shin, 2015; Masic, Sivic, Toromanovic, Borojevic & Pandza, 2012). It is also suggested that good social relationships may directly influence positive psychological states, such as a sense of belonging, purpose, or security, and acknowledgement of self-worth (Cohen et al. 2000; Thoits, 2011). In turn, these positive psychological states may benefit mental health, due to an increased motivation for self-care (e.g. regular exercise, not smoking, moderate alcohol consumption) which may indirectly benefit cognitive function (Thoits, 2011).

These findings have several implications. First, people within the social networks of those with depression or anxiety may be encouraged to engage more actively with such individuals in attempt to alter their perceptions of isolation and loneliness. It is likely that people within the networks of older people are also aged and may face several barriers to engaging in social contact themselves,

such as limited mobility and transport, poor health, geographical distance, living in rural areas, poverty, and limited opportunities within the community to engage (Bowling & Stafford, 2007; Rosso et al. 2013; Wen et al. 2006). Therefore, this approach may be too simplistic; instead, it may be necessary to engage the wider community and address the physical and psychosocial barriers (Weden, Carpiano & Robert, 2008). The findings also implicate that interventions to alleviate symptoms of depression or anxiety may be beneficial to reduce poor cognitive function (Bhalla et al. 2006). There are a range of psychological and psychosocial interventions available including cognitive behavioural therapy (Laidlaw et al. 2008), interpersonal therapy (Reynolds et al. 2006), problem solving therapy (Areán et al. 2010), reminiscence and life review (Pinquart & Forstmeier, 2012), and social groups (Cruwys et al. 2014). This is particularly relevant given that cognitive function may improve following the reduction of mood-related symptoms (Biringer et al. 2005; Rock et al. 2014) and the suggestion that a reduction in the prevalence of depression by 10% could result in approximately 326,000 fewer cases of Alzheimer's disease worldwide (Barnes & Yaffe, 2011).

Second, the study confirms that people with depression or anxiety may have poorer cognitive function compared to older people without depression or anxiety. The observation that over half of the individuals with clinically relevant symptoms of depression or anxiety at baseline were experiencing no mood-related symptoms two years later is positive. The small number of participants with such problems in the present sample at baseline suggests that mood problems are relatively uncommon and the reduction in symptoms at follow-up indicates that mood problems are not necessarily stable over time. This is consistent with prevalence rates in similar study samples, which have reported prevalence rates of 8.7% for depression (McDougall et al. 2007). However, the prevalence of anxiety was particularly low in the present sample and previous studies of similar cohorts usually find prevalence rates of 3.1% (Kvaal, McDougall, Brayne, Matthews & Dewey, 2008). This may be accounted for by the use of the AGECAT for diagnoses in the present study. The AGECAT uses a hierarchical system to determine a main diagnosis of either depression, anxiety, dementia, or no diagnosis, and may give precedence to a diagnosis of depression over anxiety when overlapping symptoms are reported. The observed change in mood-related symptoms can account for the finding that social isolation was associated with poor cognitive function at baseline, but not with change over time. It suggests that during episodes of depression or anxiety, being isolated may be detrimental to cognitive function. It may be that isolated individuals who also have depression or anxiety do not receive the benefits of cognitive stimulation through frequent and complex social contact with others (Bennett et al. 2006; Fratiglioni et al. 2000). However, when individuals are not experiencing symptoms of depression or anxiety, social isolation does not play such an important role.

This study has many strengths. CFAS-Wales is a large scale, representative, population-based cohort of older people. Participants were recruited through general practice registers. This ensures that individuals who are extremely isolated and who have depression or anxiety are more adequately represented than is the case with studies that recruit participants on a voluntary basis. This study also has limitations. We used the AGECAT algorithm to provide a diagnosis of depression or anxiety. This algorithm provides a diagnosis of either dementia, anxiety, depression, or no illness based on the presence of symptoms associated with these illnesses. Only one diagnosis is made, which is problematic as participants may have symptoms of more than one illness, but the algorithm can only identify the illness for which the participant presents the most symptoms. Given this, many diagnoses may have been missed. This is particularly problematic as many symptoms of depression and anxiety overlap and the disorders are often co-morbid (Beaudreau & O'hara, 2008). An additional limitation is the small number of people with anxiety compared those with depression, and the significantly larger group of people without depression or anxiety in CFAS-Wales. This may limit the power of the study and reduce comparability across the three groups. Future work may consider more comprehensive assessments of depression or anxiety that may capture co-morbidity of mood-related symptoms and ensure that each group of participants is adequately represented. Finally, it was not possible to determine the quality of social relationships or whether social interactions were negative in CFAS-Wales. Understanding this component of social relationships and how this relates to the quality of social interactions may provide a more comprehensive understanding of how social relationships may contribute to health outcomes, such as cognitive function and mood disorders. This is a relatively under-researched area and would serve well for further exploration (Santini et al. 2015).

We have demonstrated that older people with depression or anxiety are more isolated and feel lonelier than people without depression or anxiety, despite reporting a comparable level of social contact. Social isolation is associated with poor cognitive function in people with depression or anxiety at baseline. This relationship may not be observed longitudinally due to the transient nature of mood disorders and a reduction in related symptoms, leading to improvements in cognitive function. Cognitive reserve does not seem to play a role in the association between isolation and cognitive function in people experiencing symptoms of depression or anxiety. It may be that symptoms of depression or anxiety are more associated with cognitive outcomes than social relationships.

This chapter has demonstrated that the associations between social isolation, cognitive reserve, and cognitive function are different for people with depression or anxiety who are more vulnerable to social isolation. This has not been considered in previous work and so this chapter expands current

knowledge and highlights that the needs of people with depression or anxiety, in relation to social connections and cognitive function, are different to people without depression or anxiety. The next chapter considers people who live alone in later life; a group of people who may also be more vulnerable to social isolation and hence may be at greater risk of poor cognitive function.

Chapter 7: Living alone and cognitive function in later life

7.1 Summary

The previous two chapters have focused on social isolation and its association with cognitive function in 'healthy' older people and people with depression or anxiety. The scoping review (Chapter 3) identified some empirical evidence that suggested living alone in later life may be associated with poor cognitive function, although findings were inconsistent. People who live alone may be more vulnerable to social isolation which may exacerbate risk of poor cognitive function. This chapter uses cross-sectional and longitudinal data from CFAS-Wales to further investigate the association between living alone and cognitive function in later life. Previous studies have not considered underlying mechanisms in this association, therefore the moderating role of cognitive reserve is considered in this analysis.

Background: Living alone may be associated with greater risk for social isolation and loneliness. Living alone, social isolation, and loneliness have all been associated with poorer cognitive function in later life. Hence, if individuals who live alone are also at greater risk of isolation and loneliness, this may exacerbate poor cognitive function.

Objective: To determine whether people living alone are more at risk of social isolation and feelings of loneliness, and to examine the associations between living alone, cognitive reserve, and cognitive function in later life.

Method: Baseline (N = 2,197) and two year follow-up (N = 1,498) data from community-dwelling participants, age ≥65 years, who did not have cognitive impairment or depression at baseline from CFAS-Wales were used. Linear regression analyses were conducted to assess the association between living situation and cognitive function at baseline and two year follow-up. Moderation analysis assessed the role of cognitive reserve in this relationship.

Results: People living alone were more isolated from family and experienced more emotional loneliness than those living with others, but were not more isolated from friends and did not experience more social loneliness. Living alone was not associated with poorer cognitive function at baseline or two year follow-up.

Discussion: These findings have positive implications and suggest that people who live alone in later life are not at greater risk of poor cognitive function at baseline or two year follow-up.

7.2 Introduction

The proportion of people living alone in later life continues to rise as a result of population ageing, decreased family sizes, and government policies that promote ageing at home as an alternative to institutional care (Genet et al. 2011; Hays, 2002; Murphy & Grundy, 2003). People who live alone in later life may be more vulnerable in terms of social, behavioural, functional, and socioeconomic factors (Bergland & Engedal, 2011; Haslbeck, McCorkle & Schaeffer, 2012; Hughes & Waite, 2002; Shaw, Fors, Fritzell, Lennartsoon & Agahi, 2017). Good social relationships are identified as an important aspect of successful ageing (Rowe & Khan, 1997) and having poor social relationships has been associated with a range of negative health outcomes (Holt-Lunstad & Smith, 2012; Scharf et al. 2004; Steptoe et al. 2013; Tomaszewski, 2013; Umberson & Montez, 2010).

Older people face changes in their social environments and as a result may be at greater risk of social isolation and feelings of loneliness (Finlay & Kobayashi, 2018; Klinenberg, 2016; Victor et al. 2000). Social isolation is objective and relates to the absence of social relationships and disengagement from the wider community (Nicholson Jr, 2009). Loneliness refers to subjective feelings of dissatisfaction with aspects of social relationships, due to a perceived lack of close social contacts or emotional ties (Victor et al. 2000). Loneliness can be further divided into social and emotional loneliness. Social loneliness relates to the negative feelings that arise as a result of the absence of meaningful relationships and social integration, whereas emotional loneliness refers to the perceived lack of an attachment figure or confidant (Dahlberg & McKee, 2014; Holmén et al. 2000; Weiss, 1973). In later life, social networks are likely to reduce in size due to the increasing independence of adult children, the death of close social contacts, and the increased selectivity of social interactions with age (Baltes & Baltes, 1990; Bordone & Weber, 2012; Carstensen, 1992; de Jong Gierveld & Havens, 2004; Fredrickson & Carstensen, 1990; Freund & Baltes, 1998; Victor et al. 2000). Deterioration of mental and physical health and limited mobility may also reduce capacity for social engagement. This may limit opportunities for social contact and hence people who live alone may be at risk of social isolation (Carstensen, 1992; de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Kobayashi et al. 2009) and feelings of loneliness (Newall et al. 2014; Victor et al. 2005).

Living alone, social isolation, and loneliness are distinct concepts and living alone does not necessarily mean that an individual will be isolated or feel lonely (Klinenberg, 2016; Victor et al. 2000). Although the prevalence of living alone increases with age, feelings of loneliness may decrease (Stepler, 2016). People may anticipate smaller social networks and increased isolation with age and may prepare for this (Achenbaum & Bengstom, 1994; Cornwell & Waite, 2009). Furthermore, an individual can be isolated but not feel lonely, or feel lonely but not be isolated.

Although these concepts are related, they have only a weak-to-moderate correlation (Cornwell & Waite, 2009; Steptoe et al. 2013; Victor et al. 2000).

Social isolation, feelings of loneliness, and living alone simultaneously confer risk for impaired health and poorer wellbeing (Kharicha et al. 2007; Klinenberg, 2016; Pimouguet et al. 2015; Udell et al. 2012). Living alone in later life may increase the risk of poor cognitive function (Gow et al. 2007; Gow et al. 2013; van Gelder et al. 2006; Yaffe et al. 2009) and dementia (Fratiglioni et al. 2000; Holwerda et al. 2012). Social isolation (DiNapoli et al. 2014; Shankar et al. 2013) and feelings of loneliness (Conroy et al. 2010; Ellwardt et al. 2013; Fung et al. 2011; Gerst-Emerson et al. 2014; Gow et al. 2013; O'Luanaigh et al. 2012; Shankar et al. 2013; Tilvis et al. 2004) have both been associated with poor cognitive outcomes, although findings are mixed and not all studies report this association (DiNapoli et al. 2014; Holwerda et al. 2012; Simning et al. 2014). If older people living alone are at more risk of isolation and loneliness this may exacerbate poor cognitive outcomes. However, findings from studies that assess the association between living alone and cognitive function are conflicting. Some studies have reported an association between living alone and poorer scores on tests of global cognitive function (van Gelder et al. 2006; Yaffe et al. 2009), immediate and delayed recall, orientation (Mazzuco et al. 2016), processing speed (Gow et al. 2013), and IQ (Gow et al. 2007). Other studies have found no association between living alone and poorer scores on measures of global cognitive function (Conroy et al. 2010; Gow et al. 2013; Mahoney et al. 2000; Wang et al. 2015; Yeh & Liu, 2003), memory, IQ (Gow et al. 2013), verbal fluency, and numeracy (Mazzuco et al. 2016). Most of these studies have been cross-sectional (Conroy et al. 2010; Gow et al. 2007; Gow et al. 2013; Wang et al. 2015; Yeh & Liu, 2003). Some are longitudinal and report the association between living alone and cognitive function over two (Mazzuco et al. 2016), eight (Yaffe et al. 2009), and ten (van Gelder et al. 2006) years, and one study had a follow-up of one month (Mahoney et al. 2000).

Cognitive reserve may account for some discrepancies in findings relating to living situation and cognitive function. Cognitive reserve theory suggests that individuals differ in their level of resilience against brain pathology and hence may exhibit differences in cognitive function despite equivalent levels of pathology (Stern, 2002, 2012). Reserve can be built through a range of experiences across the lifespan, such as educational level, occupational complexity, and social and cognitive activity (Stern, 2009). This reserve may protect against a decline in cognitive function by compensating for damage and recruiting alternative neural networks to maintain good cognitive function (Siedlecki et al. 2009).

From a cognitive reserve perspective, living with others may enhance cognitive function directly through the stimulation arising from regular social interaction with others (van Gelder et al. 2006). Social interactions are effortful and require the mobilisation of complex cognitive processes, and therefore may help to build reserve and maintain cognitive function (Barnes et al. 2004; Fratiglioni et al. 2004). Individuals who live alone may have less frequent opportunity for social contact, may be more isolated (Carstensen, 1992; de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Kobayashi et al. 2009), and may feel more lonely (Newall et al. 2014; Victor et al. 2005) than those who live with others, which may result in reduced cognitive stimulation and lower cognitive reserve (Gow et al. 2007).

We aimed to determine whether people who live alone in later life are at greater risk of social isolation or loneliness. Given that people who live alone may be at greater risk of social isolation and loneliness, which have been associated with poor cognitive function, we examined the association between living alone and cognitive function using baseline and two year follow-up data from CFAS-Wales. We also considered whether cognitive reserve moderated the association between living alone and cognitive function.

7.3 Method

Design

The study aims were addressed using data from CFAS-Wales, a longitudinal study of people age ≥65 years. The study was conducted in Wales across two locations, one rural (Gwynedd/ Ynys Môn) and one urban (Neath Port Talbot). The aim of CFAS-Wales was to investigate the physical and cognitive health of older people and to consider environmental factors that may influence activity and participation in community life.

Study population

Participant recruitment was completed between 2011 and 2013. People aged ≥65 years were randomly selected from general practice registers and stratified into two age groups (65-74 and ≥75) to ensure a representative sample. Selected participants were sent information regarding the study and informed consent was obtained if they wished to take part. In-depth interviews were conducted by trained research assistants at the participants' homes. Baseline data were collected between 2011 and 2013 and participants were followed up two years later between 2013 and 2015.

The present study uses baseline (N = 3,593) and follow-up (N = 2,236) data. To reduce the risk of reverse causation in analyses, participants with cognitive impairment (MMSE score ≤25; N = 908) or an Automated Geriatric Assisted Taxonomy (AGECAT) classification of dementia (N = 185) at baseline

were excluded. The AGECAT is a diagnostic algorithm that assesses symptoms to determine whether a person has dementia, depression, anxiety, or no diagnosis (Copeland et al. 1986). Participants with an AGECAT classification of depression (N = 333) at baseline were excluded as depression is known to be associated with poor cognitive function. We excluded people living in an institution (N = 95) as living with others in institutional care is different to living with others in the community. Finally, we excluded people with missing data for variables assessed in the present study at baseline (N = 463) and follow-up (N = 699). This gave a final sample of 2,197 participants for cross-sectional analyses and 1,498 participants for analyses at two year follow-up. A comparison of participants that were included at both time points with those that were included in cross-sectional analyses but excluded from follow-up analyses due to missing data at follow-up is reported in Table 7.1. Those who were excluded at follow-up were older, more likely to have impairments in activities of daily living (ADLs), had fewer years of education, lower cognitive and cognitive reserve scores, lower occupational complexity, engaged in less cognitive activity and were more socially isolated, but were no more likely to be women, live alone, or experience greater feelings of loneliness, and there was no difference in marital status.

Table 7.1. *Comparison of participants assessed at baseline who were included at two year follow-up with those who were included at baseline but excluded at two year follow-up.*

Variable	**Included participants (N = 1,498)**	**Excluded participants (N = 699)**	***t*(df) or X^2(df) *p***
Age (years)[1]	73.22 (6.15)	73.97 (6.52)	*t*(1, 2195) = 2.63 *p* = .009
Gender[2]			
Men	747 (49.87)	338 (48.35)	X^2(1) = .44 *p* = .509
Women	751 (50.13)	361 (51.65)	
Living alone[2]	430 (28.70)	194 (27.75)	X^2(1) = .21 *p* = .645
Marital status[2]			
Married	1,033 (68.96)	455 (65.09)	X^2(4) = 5.13 *p* = .274
Cohabiting	20 (1.34)	15 (2.15)	
Single	55 (3.67)	27 (3.86)	
Widowed	300 (20.03)	161 (23.03)	
Divorced/ separated	90 (6.01)	41 (5.87)	
ADL Impairment[2]	371 (24.77)	241 (34.48)	X^2(1) = 22.38 *p* <.001
CAMCOG score[1]	94.16 (4.94)	92.03 (5.91)	*t*(1, 2195) = -8.85 *p* <.001
Educational level (years)[1]	12.20 (2.85)	11.77 (2.67)	*t*(1, 2195) = -3.38 *p* <.001
Cognitive activity[1]	21.54 (5.14)	20.83 (5.23)	*t*(1, 2195) = -3.00 *p* = .003
Occupational complexity[1]	8.35 (3.31)	7.60 (3.32)	*t*(1, 2195) = -4.91 *p* <.001
Cognitive reserve score[1]	61.66 (11.51)	58.90 (11.07)	*t*(1, 2195) = -5.30 *p* <.001
Social isolation[1]			
Overall	16.48 (5.77)	15.50 (5.58)	*t*(1, 2195) = -3.76 *p* <.001
Family	8.79 (3.31)	8.47 (3.30)	*t*(1, 2195) = -2.11 *p* = .035
Friends	8.69 (4.07)	7.03 (3.89)	*t*(1, 2195) = -3.61 *p* <.001
Loneliness[1]			
Overall	.82 (1.04)	.81 (1.05)	*t*(1, 2195) = -.08 *p* = .938
Social loneliness	.45 (.76)	.43 (.77)	*t*(1, 2195) = -.50 *p* = .616
Emotional loneliness	.37 (.61)	.39 (.64)	*t*(1, 2195) = .48 *p* = .628

Note: [1] *M* (SD); [2] *N* (%); ADL = Activities of Daily Living; CAMCOG = Cambridge Cognitive Examination

Measures

Living alone

Living alone was assessed by asking participants 'does anyone else live here?' (yes/ no).

Social isolation

Social isolation was assessed with the Lubben Social Network Scale–6 (LSNS-6; Lubben et al. 2006). The LSNS-6 is a standardised measure of social isolation and consists of three questions assessing isolation from family and three comparable questions assessing isolation from friends. The questions ask participants to report the number of relatives/ friends seen or heard from in the past month, that they feel at ease to talk with about private matters, and that they feel they could call on for help. Responses are coded along a six-item category response scale ranging from 0 (no relatives/ friends) to 5 (nine or more relatives/ friends). An overall score for isolation is calculated by summing responses to all questions. Scores range from 0-30 and lower scores indicate social isolation. Questions for family and friends can be scored separately, providing two subscale scores which range from 0-15 and lower scores indicate greater isolation.

Loneliness

Loneliness was assessed using the De Jong Gierveld scale (De Jong Gierveld & van Tilburg, 2006), which consists of three questions to assess social loneliness and a further three questions to assess emotional loneliness. Participants respond either yes, more or less, or no. Scores are summed to provide an overall loneliness score, which ranges from 0–6. Scores for the social and emotional subscale range from 0–3. Higher scores indicate greater feelings of loneliness.

Cognitive function

Cognitive function was assessed using the Cambridge Cognitive Examination (CAMCOG: Roth et al. 1986), a standardised measure of cognitive function. The measure consists of 67 items that assess cognitive function along eight subscales, including orientation, memory, praxis, attention, abstract thinking, perception, and calculation. Scores range from 0–107 and a lower score indicates poor cognitive function. The CAMCOG has good inter-rater reliability (r = .97), high sensitivity (92%) and specificity (96%: Roth et al. 1986; Wouters, van Gool, Schmand, Zwinderman & Lindeboom, 2010).

Cognitive reserve

Cognitive reserve was assessed by combining three proxy measures to represent experiences that may build reserve across the lifespan: educational level, occupational complexity, and cognitive activity (Opdebeeck et al. 2018; Tucker & Stern, 2011; Valenzuela et al. 2011). Educational level was

determined by the number of years in full time education. Occupational complexity was measured by the participant's social class and the complexity and social economic grouping of the participant's main employment. This gave a complexity score ranging from 1 (less complex occupations) to 14 (more complex occupations). Cognitive activity was assessed by asking the participant about engagement in seven cognitive activities (listening to the radio, reading a newspaper, magazine, or book, playing cards or chess, and completing crosswords or puzzles). Participants respond either once a year or less, several times a year, several times a month, several times a week, or everyday/ almost every day. Higher scores indicate greater cognitive activity.

Scores for each indicator were weighted based on the interquartile range to ensure that each proxy item contributed equally to determining the cognitive reserve score. This gave the following formula: cognitive reserve score = (2.33 × educational level) + (1.40 × occupational complexity) + (1 × cognitive activity). Higher scores indicate higher levels of cognitive reserve.

Marital status

Participants indicated their marital status at baseline as either married, cohabiting, single, widowed, or divorced/ separated.

Activities of daily living

Activities of daily living (ADLs) were measured as a dichotomous variable (impaired/ not impaired) based on five questions considered to capture ADL ability (Bond & Carstairs, 1982). At baseline, participants were asked about their ability to wash, prepare a hot meal, put on their own shoes, do the housework, and go shopping independently. If the participant indicated a need for help to complete any of these tasks, or was rated by the research assistant as being either housebound, chairfast, or bedfast, they were considered to be impaired in ADLs.

Covariates

Baseline age (years), gender, and educational level (years) were controlled for in all analyses, except for those that assessed cognitive reserve, as educational level was a component of the cognitive reserve score. These factors are all well-established covariates of late-life cognitive function (Barnes et al. 2003; Tervo et al. 2004; Tilvis et al. 2004). Social isolation and loneliness were also controlled for as these factors have been associated with living alone (Victor et al. 2000; Victor et al. 2005) and with cognitive function (DiNapoli et al. 2014; Ellwardt et al. 2013; Gerst-Emerson et al. 2014; Gow et al. 2013; Shankar et al. 2013). We also controlled for marital status as people who are unmarried in later life may be more likely to live alone (Victor et al. 2000) and for impairment in ADLs as people

with ADL limitations may have reduced mobility which may limit ability to be socially engaged, and hence increase level of social isolation or feelings of loneliness (Mendes de Leon et al. 2003).

Statistical analysis

Analyses were conducted in Stata version 15.0. Descriptive information is reported for the overall sample at baseline and separately for those who were living alone or with others. T-tests or chi squared tests were conducted to determine whether there were differences in social isolation, loneliness, and other demographic variables across these groups. A linear regression was conducted to assess the relationship between living situation and cognitive function at baseline. A second linear regression was conducted to determine the association between living situation and cognitive change over the two year follow-up. A cognitive change score was calculated by subtracting the baseline CAMCOG score from the CAMCOG score at two year follow-up. Each participant's cognitive change score was then standardised by the standard deviation value of the baseline CAMCOG score. Adjusted R^2 values were reported for regression models to indicate the proportion of variance explained by variables in the model. Standardised regression coefficients were also reported, along with 95% confidence intervals. Moderation analyses were conducted to determine whether cognitive reserve moderated the association between living situation and cognitive function at baseline or two year follow-up. The analyses tested for an interaction between living situation and cognitive reserve score.

7.4 Results

The mean age of participants was 73 years and 51% were women. Scores on the CAMCOG at baseline ranged from 63–105 with a mean of 93.48, and at two year follow-up ranged from 53–106 with a mean of 93.74. At baseline 624 people were living alone. Those living alone were significantly older, more likely to be women, less likely to be married or cohabiting, more likely to be single, widowed, or divorced, were more likely to have impairments in ADLs, and had poorer CAMCOG scores. There was no difference in educational level, occupational complexity, cognitive activity, or cognitive reserve score (Table 7.2).

Social relationships in older people living alone or with others

T-tests were conducted to compare social isolation and loneliness among people living alone and those living with others (Table 7.2). People living alone were more likely to be socially isolated overall and to be isolated from family than those living with others, but there was no difference in isolation from friends. People living alone reported significantly greater feelings of overall loneliness and emotional loneliness, but there was no difference in feelings of social loneliness.

Table 7.2. *Summary of baseline characteristics of participants in CFAS-Wales.*

Variable	Total sample (N = 2,197)	Living alone (N = 624)	Living with others (N =1,573)	*t*(df) or X^2(df) *p*
Age (years)[1]	73.46 (6.28)	75.96 (6.91)	72.46 (5.71)	*t*(1, 2195) = 12.19 *p* <.001
Gender[2]				
Men	1,085 (49.39)	186 (29.81)	899 (57.15)	X^2(1) = 133.64 *p* <.001
Women	1,112 (50.61)	438 (70.19)	674 (42.85)	
Marital status[2]				
Married	1,488 (67.73)	62 (9.94)	1,426 (90.65)	
Cohabiting	35 (1.59)	2 (.32)	33 (2.10)	
Single	82 (3.73)	71 (11.38)	11 (.70)	X^2(4) = 6.81 *p* <.001
Widowed	461 (20.98)	393 (62.98)	68 (4.32)	
Divorced/ separated	131 (5.96)	96 (15.38)	35 (2.23)	
ADL Impairment[2]	612 (27.86)	215 (34.46)	397 (25.24)	X^2(1) = 18.89 *p* <.001
CAMCOG score[1]	93.48 (5.36)	92.49 (5.74)	93.88 (5.15)	*t*(1, 2195) = -5.51 *p* <.001
Educational level (years)[1]	12.07 (2.80)	12.09 (2.79)	12.05 (2.81)	*t*(1, 2195) = .31 *p* = .760
Cognitive activity[1]	21.31 (5.18)	21.12 (5.43)	21.39 (5.07)	*t*(1, 2195) = -1.08 *p* = .279
Occupational complexity[1]	8.11 (3.33)	8.17 (3.30)	8.09 (3.34)	*t*(1, 2195) = .52 *p* = .601
Cognitive reserve score[1]	60.78 (11.45)	60.74 (11.57)	60.79 (11.40)	*t*(1, 2195) = -.10 *p* = .919
Social isolation[1]				
Overall	16.17 (5.73)	15.75 (5.69)	16.33 (5.74)	*t*(1, 2195) = -2.14 *p* = .032
Family	8.69 (3.31)	8.31 (3.42)	8.83 (3.25)	*t*(1, 2195) = -3.34 *p* = <.001
Friends	7.48 (4.02)	7.44 (3.95)	7.50 (4.05)	*t*(1, 2195) = -.30 *p* = .762
Loneliness[1]				
Overall	.82 (1.04)	.99 (1.15)	.75 (.99)	*t*(1, 2195) = 4.86 *p* <.001
Social loneliness	.44 (.76)	.44 (.79)	.44 (.75)	*t*(1, 2195) = -.02 *p* = .982
Emotional loneliness	.38 (.62)	.55 (.74)	.31 (.55)	*t*(1, 2195) = 8.28 *p* <.001

Note: [1] *M* (SD); [2] *N* (%); ADL = activities of daily living; CAMCOG = Cambridge Cognitive Examination

Association between living situation and cognitive function

Baseline

A linear regression was conducted to assess the relationship between living situation and cognitive function at baseline. Living alone was not significantly associated with poorer CAMCOG scores in the fully adjusted model adjusted (R^2 = .17, *F*(8, 2188) = 56.50, *p* <.001: Table 7.3).

Table 7.3. *Cross-sectional association between living alone and cognitive function (N = 2,197).*

CAMCOG score	**Model 1** *B* (95% CI) *p*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *p*
Living alone (no)	.15 (.09, .20) <.001	.04 (-.01, .09) .162	-.02 (-.10, .05) .527
Age		-.03 (-.03, -.02) <.001	-.02 (-.03, -.02) <.001
Gender		-.07 (-.11, -.02) .002	-.05 (-.10, -.01) .022
Educational level		.04 (.04, .05) <.001	.04 (.03, .05) <.001
Social isolation			.05 (.03, .07) <.001
Loneliness			.03 (0, .05) .041
Marital status (not married)			-.08 (-.16, -.01) .029
ADL impairment (yes)			-.11 (-.16, -.06) <.001

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3 adjusted for age, gender, years of education, social isolation, loneliness, marital status, and ADL impairment.

Further regression analyses were conducted to determine whether living alone was more associated with any specific cognitive domain assessed by the CAMCOG (Table 7.4). Living alone was significantly associated with praxis (adjusted R^2 = .07, *F*(8, 2188) = 21.11, *p* <.001), but not orientation (adjusted R^2 = .02, *F*(8, 2188) = 5.24, *p* <.001), comprehension (adjusted R^2 = .02, *F*(8, 2188) = 6.34, *p* <.001), expression (adjusted R^2 = .14, *F*(8, 2188) = 46.34, *p* <.001), memory (adjusted R^2 = .04, *F*(8, 2188) = 11.59, *p* <.001), attention and calculation (adjusted R^2 = .03, *F*(8, 2188) = 8.10, *p* <.001), abstract thinking (adjusted R^2 = .04, *F*(8, 2188) = 12.73, *p* <.001), or perception (adjusted R^2 = .12, *F*(8, 2188) = 38.04, *p* <.001).

Table 7.4. *Cross-sectional association between living alone and sub-domains of cognition assessed by the CAMCOG (N = 2,197).*

	Orientation	**Comprehension**	**Expression**	**Memory**	**Attention and calculation**	**Praxis**	**Abstract thinking**	**Perception**
	B (95% CI) *p*	*B* (95% CI) *P*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*
Living alone (no)	-.02 (-.05, 0) .076	-.04 (-.09, 0) .065	.03 (-.01, .07) .198	-.05 (-.10, .01) .104	-.01 (-.06, .05) .828	.08 (.01, .14) .019	-.02 (-.10, .05) .554	-.05 (-.17, .06) .379
Age	0 (0, 0) .099	0 (-.01, 0) <.001	-.01 (-.01, -.01) <.001	-.01 (-.01, 0) <.001	0 (-.01, 0) .042	-.01 (-.01, 0) <.001	-.01 (-.01, -.01) <.001	-.04 (-.04, -.03) <.001
Gender	0 (-.02, .01) .815	.03 (0, .05) .050	.03 (0, .05) .023	-.06 (-.10, -.03) <.001	-.09 (-.13, -.06) <.001	-.04 (-.08, 0) .055	.05 (0, .10) .034	-.05 (-.12, .01) .115
Educational level	0 (0, .01) <.001	.01 (0, .01) .002	.02 (.01, .02) <.001	.02 (.01, .02) <.001	.01 (.01, .02) <.001	.02 (.01, .02) <.001	.03 (.02, .04) <.001	-02 (.01, .03) .002
Social isolation	.01 (0, .02) .011	0 (-.02, .01) .682	.02 (.01, .04) <.001	.02 (0, .04) .026	.02 (0, .04) .044	.03 (.01, .05) .002	.01 (-.02, .03) .666	.05 (.02, .09) .003
Loneliness	0 (-.01, .01) .802	0 (-.02, .01) .821	.02 (0, .03) .016	.01 (-.01, .03) .192	.02 (0, .04) .060	.01 (-.02, .03) .616	.02 (-.01, .04) .212	0 (-.03, .04) .804
Marital status (not married)	0 (-.03, .02) .702	-.06 (-.11, -.02) .007	-.01 (-.05, .03) .621	-.05 (-.10, .01) .090	-.02 (-.07, .04) .524	0 (-.06, .06) .979	-.04 (-.12, .03) .274	-.10 (-.22, .01) .068
ADL impairment (yes)	-.02 (-.04, 0) .017	-.02 (-.06, .01) .108	-.06 (-.09, -.03) <.001	-.01 (-.05, .02) .485	0 (-.03, .04) .809	-.12 (-.16, -.07) <.001	-.04 (-.09, .01) .126	-.14 (-.21, -.06) <.001

Note: adjusted for age, gender, years of education, social isolation, loneliness, marital status, and ADL impairment.

Longitudinal

A linear regression was conducted to assess the association between living situation and change in cognitive function over the two year follow-up. Living situation was not significantly associated with change in cognitive function in the fully adjusted model (adjusted R^2 = .05, $F(8, 1489) = 11.88$, p <.001: Table 7.5).

Table 7.5. *Longitudinal association between living alone and cognitive change score over two years (N = 1,498).*

CAMCOG change score	**Model 1** *B* (95% CI) *p*	**Model 2** *B* (95% CI) *p*	**Model 3** *B* (95% CI) *p*
Living alone (no)	.16 (.05, .27) .004	.02 (-.09, .14) .704	.04 (-.14, .22) .697
Age		-.03 (-.04, -.03) <.001	-.03 (-.04, -.02) <.001
Gender		-.08 (-.18, .02) .127	-.07 (-.17, .03) .176
Educational level		.01 (0, .03) .131	.01 (-.01, .03) .286
Social isolation			.07 (.01, .12) .013
Loneliness			.03 (-.02, .09) .238
Marital status (not married)			.02 (-.16, .20) .816
ADL impairment (yes)			-.14 (-.26, -.02) <.001

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3 adjusted for age, gender, years of education, social isolation, loneliness, marital status, and ADL impairment.

Limited cognitive change was observed in the CFAS-Wales sample and many people maintained their cognitive score or had an improved cognitive score. A logistic regression was conducted as a sensitivity analysis to determine the reliability of the regression analysis. To distinguish cognitive decliners from non-decliners, a binary variable was created and decliners were defined as a decline in two year follow-up CAMCOG score of one standard deviation unit from the baseline CAMCOG score. In total, 262 (17%) participants were cognitive decliners and 1,236 (83%) participants maintained good cognitive function. Although the overall model was significant ($X^2(8) = 93.80$, p

<.001) living alone was not associated with a decline in CAMCOG scores over two years in the fully adjusted model (Table 7.6).

Table 7.6. *Longitudinal association between living alone and cognitive change (N = 1,498).*

	Model 1 OR (95% CI) *p*	**Model 2** OR (95% CI) *p*	**Model 3** OR (95% CI) *p*
Living alone (no)	.73 (.55, .96) .027	1.05 (.76, 1.44) .767	.95 (.56, 1.61) .861
Age		1.10 (1.07, 1.12) <.001	1.09 (1.07, 1.12) <.001
Gender		1.15 (.86, 1.53) .344	1.19 (.89, 1.60) .247
Educational level		.94 (.89, .99) .014	.94 (.89, .99) .031
Social isolation			.79 (.68, .92) .002
Loneliness			.88 (.75, 1.05) .150
Marital status (not married)			.90 (.53, 1.52) .693
ADL impairment (yes)			1.03 (.75, 1.42) .844

Note: Model 1: unadjusted; Model 2: adjusted for age, gender, and years of education; Model 3 adjusted for age, gender, years of education, social isolation, loneliness, marital status, and ADL impairment.

Further regression analyses were conducted to determine whether living alone was more associated with cognitive change in any specific cognitive domain assessed by the CAMCOG (Table 7.7). Living alone was significantly associated with two year change in scores on the praxis subscale (adjusted R^2 = 0, $F(8, 1489) = 1.87$, $p = .061$), but not with orientation (adjusted R^2 = .02, $F(8, 1489) = 4.40$, p <.001), comprehension (adjusted R^2 = .01, $F(8, 1489) = 3.15$, $p = .002$), expression (adjusted R^2 = 0, $F(8, 1489) = 1.41$, $p = .189$), memory (adjusted R^2 = .04, $F(8, 1489) = 7.85$, p <.001), attention and calculation (adjusted R^2 = .01, $F(8, 1489) = 2.93$, $p = .003$), abstract thinking (adjusted R^2 = .01, $F(8, 1489) = 3.16$, $p = .002$), or perception (adjusted R^2 = 0, $F(8, 1489) = 1.37$, $p = .205$).

Table 7.7. *Longitudinal association between living alone and sub-domains of cognition assessed by the CAMCOG (N = 1,498).*

	Orientation	**Comprehension**	**Expression**	**Memory**	**Attention and calculation**	**Praxis**	**Abstract thinking**	**Perception**
	B (95% CI) *p*	*B* (95% CI) *P*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*	*B* (95% CI) *p*
Living alone (no)	.02 (-.30, .34) .891	.24 (-.03, .50) .077	-.03 (-.22, .16) .751	.05 (-.13, .22) .584	.02 (-.23, .27) .883	-.21 (-.41, 0) .045	.04 (-.17, .25) .705	.09 (-.10, .28) .346
Age	-.03 (-.05, -.02) <.001	-.01 (-.02, 0) .150	-.01 (-.02, 0) .047	-.02 (-.03, -.02) <.001	-.02 (-.03, -.01) <.001	-.01 (-.02, 0) .004	-.01 (-.02, 0) .005	-.01 (-.02, 0) .058
Gender	-.08 (-.27, .10) .358	-.05 (-.09, .10) .530	-.02 (-.12, .08) .708	-.01 (-.10, .09) .892	-.09 (-.23, .05) .202	-.07 (-.18, .04) .217	-.02 (-.13, .10) .765	-.02 (-.13, .08) .655
Educational level	.02 (-.01, .05) .224	0 (-.02, .03) .855	0 (-.02, .02) .838	0 (-.02, .02) .980	.02 (-.01, .04) .167	.01 (-.01, .03) .186	.01 (-.01, .03) .415	0 (-.02, .01) .708
Social isolation	.04 (-.05, .14) .370	.10 (.02, .17) .013	.06 (0, .11) .034	.04 (-.01, .09) .137	.02 (-.05, .10) .552	-.03 (-.09, .03) .374	.07 (.01, .13) .031	0 (-.06, .05) .907
Loneliness	-.03 (-.13, .08) .624	.07 (-.01, .16) .081	.03 (-.03, .09) .337	.01 (-.05, .06) .821	.01 (-.07, .09) .837	-.02 (-.08, .05) .602	.02 (-.04, .09) .522	.04 (-.02, .10) .235
Marital status (not married)	-.01 (-.32, .31) .958	.23 (-.03, .49) .080	.07 (-.11, .26) .422	-.03 (-.21, .14) .690	-.03 (-.27, .22) .834	-.11 (-.31, .09) .274	0 (-.20, .20) .983	.06 (-.12, .26) .480
ADL impairment (yes)	-.18 (-.39, .03) .089	-.23 (-.40, -.07) .006	.04 (-.08, .16) .512	-.10 (-.21, .01) .080	-.08 (-.24, .08) .351	.08 (-.05, .21) .238	-.12 (-.26, .01) .066	-.09 (-.22, .03) .146

Note: adjusted for age, gender, years of education, social isolation, loneliness, marital status, and ADL impairment.

Association between living situation, cognitive reserve, and cognitive function

Baseline

A moderation analysis was conducted to determine whether cognitive reserve score moderated the relationship between living situation and cognitive function at baseline. The interaction term between living situation and the cognitive reserve score did not explain differences in cognitive function in the unadjusted model (*B* = -.02; 95% CI: -.07, .03; *p* = .502) or after adjusting for age, gender, social isolation, loneliness, marital status, and ADL impairment (*B* = -.01; 95% CI: -.06, .03; *p* = .573).

Longitudinal

A moderation analysis was conducted to determine whether cognitive reserve moderated the longitudinal association between living situation and change in cognitive function over the two year follow-up. The interaction term between living situation and cognitive reserve score did not explain differences in two year cognitive change score in the unadjusted model (*B* = -.01; 95% CI; -.12, .10; *p* = .815) or after adjusting for age, gender, social isolation, loneliness, marital status, and ADL impairment (*B* = -.01; 95% CI; -.11, .10; *p* = .913).

7.5 Discussion

Living alone is a common experience for many people in later life (Evandrou et al. 2001; Kharicha et al. 2007; Mazzuco et al. 2016; Victor et al. 2000). This study aimed to determine whether people living alone are at greater risk of social isolation and feelings of loneliness. Consistent with previous work, we found that people living alone are more isolated (de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Kobayashi et al. 2009; Iliffe et al. 2007; Kharicha et al. 2007) and feel lonelier (de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Gow et al. 2013; Newall et al. 2014; Victor et al. 2005) than those living with others. More specifically, people living alone reported greater isolation from family and greater feelings of emotional loneliness than those living with others, but there was no difference in isolation from friends or feelings of social loneliness. Although people who live alone were significantly more isolated and lonelier than those who live with others, there was little difference in the mean scores on these measures. Therefore, the significant differences reported in scores on these measures may not be meaningful and ought to be interpreted with caution.

The finding that living alone is not significantly associated with cognitive function at baseline is consistent with most previous studies (Conroy et al. 2010; Gow et al. 2013; Mahoney et al. 2000; Wang et al. 2015; Yeh & Liu, 2003). The present findings are inconsistent with one study that reports

an association between living alone and cognitive function determined by a measure of IQ at baseline (Gow et al. 2007). This difference may be accounted for by the differences in measures used to assess cognitive function. The measure of IQ used in Gow et al. (2007) assesses reasoning, arithmetic, following directions, and analogies. Previous studies that do not find an association assess cognitive function using measures of global cognitive function, such as the MMSE (Mahoney et al. 2000; Wang et al. 2015), the Abbreviated Mental Test (Conroy et al. 2010), the Short Portable Mental State Questionnaire (Yeh & Liu, 2003), and the CAMCOG in the present study. The measure of IQ used in Gow et al. (2007) assesses different cognitive abilities to those assessed by the CAMCOG and other global measures of cognitive function which may be more affected by ageing than a measure of IQ and hence may account for differences in findings. However, a study that also assessed the association between living alone and the same measure of IQ as in Gow et al. (2007) found no association (Gow et al. 2013). It is not clear why there were differences in the reported associations between living alone and IQ score in two relatively similar cohorts. One explanation could be that there were twice as many people living alone in Gow et al. (2007) compared to Gow et al. (2013) and so there may have been more statistical power in Gow et al. (2007) to detect an association. It has been suggested that crystallised cognitive abilities, such as those assessed in the measure of IQ may be less associated with cognitive ageing, whereas fluid cognitive domains such as executive functions and memory may be more affected by ageing (Christensen, 2001; Deary et al. 2009; Hedden & Gabrieli, 2004; Mazzuco et al. 2016; Park & Reuter-Lorenz, 2009). Therefore, the findings from Gow et al. (2007) seem inconsistent with most previous literature and the present study which report nonsignificant findings in both crystallised and fluid cognitive abilities.

There was no association between living alone and global cognitive function at two year follow-up. This is inconsistent with previous findings (van Gelder et al. 2006; Yaffe et al. 2009). These studies had a follow-up period of eight (Yaffe et al. 2009) and ten (van Gelder et al. 2006) years which is longer than the two year follow-up in CFAS-Wales. It may be that the associations between living situation and cognitive function would manifest in longer term follow-up assessments. In addition, there was little cognitive change observed over two years in the present sample and many people had improvements in their cognitive scores, which may account for the non-significant finding at follow-up. The present findings are consistent with a study that reported findings from eight European countries and found that living alone was not associated with poorer scores in several cognitive domains, including orientation (no association in five countries), immediate recall (no association in six countries), delayed recall (no association in six countries), verbal fluency (no association in seven countries), or numeracy (no association in eight countries) over two year follow-up (Mazzuco et al. 2016). The authors concluded that living with others may be protective in some

countries and for some specific abilities, but there was mostly no protective effect of living with others on cognitive function. We did find that living alone was significantly associated with poorer scores in praxis at baseline and follow-up in the present study. However, given that the present study and other previous studies find no significant association between living alone and cognitive function in specific domains, this significant finding in the present study is unlikely to be meaningful (Mazzuco et al. 2016).

We considered whether cognitive reserve moderated the association between living alone and cognitive function. In line with cognitive reserve theory, we predicted that people living alone may have less opportunity for social contact and the resulting cognitive stimulation and hence may have lower levels of cognitive reserve and poorer cognitive function (de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Kobayashi et al. 2009; Stern, 2012). We found no difference in cognitive reserve scores at baseline between those living alone and with others, and cognitive reserve did not moderate the association between living alone and cognitive function at baseline, or cognitive change two years later.

The present findings have several implications. There is an assumption that living alone may be less cognitively stimulating, yet it is possible that living alone has many benefits. People who live alone are often solely responsible for completing household tasks, such as paying the bills, shopping, cleaning, maintenance, and answering the telephone or door, which all require cognitive input (Jekel et al. 2015; Njegovan, Man-Son-Hing, Mitchell & Molnar, 2001). People living with others may have less responsibility for completing these tasks, and in some households and partnerships, one individual may take charge, leaving the other partner to take a more passive role. People who live alone and are unable to complete household tasks due to poor cognitive function or health are unlikely to manage independently at home and may be more likely to move into a care home (Cornelis, Gorus, Beyer, Bautmans & De Vriendt, 2017; Wang et al. 2015). Those able to manage may gain cognitive stimulation from these tasks, along with stimulation from social interactions with others outside the home. Living situation is a basic structural assessment of social connections and does not consider the wider social context. Social interaction with the individual(s) with whom an older person resides are likely to be insufficient to build or maintain cognitive reserve alone (Berkman & Glass, 2000; Mazzuco et al. 2016). It is possibly the more complex web of social contacts and interactions the individual engages with that builds reserve and enhances cognitive function (Berkman, 2000). This may explain why no differences in cognitive function or cognitive change over two years are found between those living alone and with others in the present study. There has been little focus on these possible benefits and how they may enhance health outcomes for older people. Living alone is not necessarily a risk factor in itself for people who are in good health and

have sufficient social connections; it may be a positive state for many people and reflect the maintenance of functional independence (Kharicha et al. 2007; Mazzuco et al. 2016).

The present findings seem to implicate that age, social isolation, and impairments in ADLs may be more associated with cognitive function than living alone at baseline and two year follow-up. Indeed, previous work suggests that people who are older (Hendrie et al. 2006; Lipnicki et al. 2013), or are more isolated (DiNapoli et al. 2014; Evans et al. 2018; Holwerda et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007), or have impairments in ADLs or poorer mobility (Demnitz et al. 2017; Tolea & Galvin, 2016; Zhao, Tranovich & Wright, 2014) may be at greater risk of poor cognitive function in later life. This further reinforces the importance of social isolation in later life and the benefits of having a wide social network and engagement in frequent social activity on cognitive function.

This study has a number of strengths. CFAS-Wales is a large population-based cohort that is representative of the general population. Participants were sampled from general practice registers and invited to participate. This ensures that individuals who were living alone and particularly isolated were more adequately represented in CFAS-Wales than in self-selected samples.

This study has several limitations. Limited cognitive decline was observed across the sample over the two year follow-up, and some participants had significant improvements in their CAMCOG scores at follow-up. It is possible that a two year follow-up period is insufficient to observe cognitive decline and hence an association with living alone could not be detected. People who dropped out between baseline and follow-up were more likely to be socially isolated and to experience feelings of loneliness, and had poorer scores on measures of cognitive function and cognitive reserve. Hence, the follow-up sample was to some degree a selective sample of higher-functioning individuals in terms of social and cognitive variables. This may account for the limited cognitive change observed over the two years and for the non-significant association between living alone and cognitive function at follow-up. It was not possible to determine for how long people had been living alone in the present sample. Social situations are fluid and frequently change (van Gelder et al. 2006). People who are currently living alone may have previously lived with others, or may have started living alone only recently. It is possible that people who are used to living alone and have done so for many years are able to compensate and adapt for subtle impairments in cognitive function, and hence impairments may not be detected by cognitive measures. Those who have been living alone for a shorter period of time may be less able to make such compromises and so impairment may be more apparent and the risk of experiencing negative health outcomes as a result may increase (Cacioppo & Hawkley, 2003). It is also possible that different circumstances for living alone may

influence cognitive function. For example, people living alone who are recently bereaved may be at greater risk of poor cognitive function (Aartsen et al. 2005; Karlamangla et al. 2009; Mousavi-Nasab, Kormi-Nouri, Sundström & Nilsson, 2012; Shin, Kim & Park, 2018; van Gelder et al. 2006). Although findings relating to widowhood and cognitive function are mixed and may be attributed to experiences that precede widowhood (Vable, Subramanian, Rist & Glymour, 2015; Vidarsdottir et al. 2014; Woodruff et al. 2014).

Finally, most previous research, including the present study, focuses on global, person-level variables when assessing living situation. There is little research which considers the immediate experience of living alone and what that may be like for an older person (Larson, Zuzanek & Mannell, 1985; Pauly, Lay, Nater, Scott & Hoppmann, 2017). It would be interesting to gain a qualitative perspective and determine whether any specific aspects of living alone are more or less favourable. Likewise, the positive aspects of living alone in later life are frequently overlooked in research. These perspectives could be considered in future work to provide further insight into how living alone may benefit or hinder cognitive function and other health outcomes.

In summary, we report that people who live alone may be more isolated in terms of family networks but that their friendship networks are as strong as those of people living with others, which may mitigate the degree of isolation from family and feelings of loneliness and hence benefit cognitive function. We also find that people living alone are no more vulnerable to poor cognitive function at baseline, or to cognitive decline over a two year period, than those living with others. This finding provides a positive message for people living alone in later life, a time when transition to living alone may be more likely than at any other period in the lifespan.

This chapter has demonstrated that although people who live alone may be more vulnerable to social isolation, they are at no greater risk of poor cognitive function. It also supports the findings from Chapter 5 and suggests that social isolation may be a more important factor implicated in cognitive function in later life. The next chapter aims to address a limitation of structural measures of social isolation identified by the scoping review; specifically the lack of consideration of satisfaction with social contact within structural measures of isolation.

Chapter 8: Social isolation, satisfaction with social contact, and cognitive function

8.1 Summary

Findings from the scoping review (Chapter 3) and the systematic review (Chapter 4) have suggested that a range of indicators are used to measure social isolation. These indicators focus on structural aspects but do not account for satisfaction with social contact. Previous work implicates satisfaction is an important factor associated with a range of health outcomes and therefore it may be useful to consider this in measures of isolation. This chapter uses data from PROTECT to consider the degree of consistency in scores on a structural measure of social isolation and a measure of satisfaction with social contact, and how efficient these measures are in predicting cognitive function.

Background: Variation in findings relating to the association between social isolation and cognitive function in later life may partly be explained by measures of isolation focusing on structural features of social connections. This approach cannot account for satisfaction with social contact, which may be important in characterising social contexts and predicting cognitive outcomes.

Objective: To determine the degree of consistency in scores on a structural measure of social isolation and a measure of satisfaction with social contact, and to determine how efficient these measures are in predicting cognitive function.

Method: Cross-sectional analyses were conducted on data from a sub-sample of the PROTECT cohort (N = 4,616) age ≥60 years. ANOVAs compared the characteristics of people with congruent and incongruent scores on a structural measure of isolation and a measure of satisfaction with social contact. Linear regressions assessed the associations between each of these measures and cognitive function in four domains. Moderation analyses assessed whether satisfaction with social contact moderated the association between a structural measure of isolation and cognitive function.

Results: Most participants had congruent scores (N = 3,627, 79%) on the structural measure of isolation and the measure of satisfaction with social contact. After controlling for depression, age, gender, and educational level, the structural measure did not predict poor cognitive function, but dissatisfaction with social contact was associated with poorer function in verbal and spatial working memory. Satisfaction with social contact did not moderate the association between the structural measure of social isolation and cognitive function.

Conclusions: A small minority of people are classified as isolated by structural measures yet are satisfied with this contact. Satisfaction with social contact may be a better predictor of poor cognitive function than structural indicators after controlling for depression. This reflects that satisfaction with social contact is important and should be assessed alongside structural aspects.

8.2 Introduction

Social isolation defines a state in which an individual has a minimal number of social contacts and lacks engagement with others and the wider community (Nicholson Jr, 2009). Although social isolation can be experienced by anyone throughout the lifespan, it is widely assumed to be more prevalent in later life (Victor et al. 2000). Estimates of social isolation in community dwelling older people range from 2-29% (Hawthorne, 2008; Smith & Hirdes, 2009; Victor et al. 2000). Beyond being a difficult experience, being socially isolated has a range of negative health implications in later life, including poor cognitive function (DiNapoli et al. 2014; Holwerda et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007). However, findings are inconsistent and some studies report no association with cognitive function (Holwerda et al. 2012; Simning et al. 2014; Wilson, Krueger et al. 2007).

Variation in findings relating to social isolation and cognitive function may be accounted for by differences in the approaches used to assess social isolation. Social isolation is typically measured by structural aspects of social connections. For example, many measures are created using a combination of questions that assess social network size, frequency of social contact, and engagement in social activity (DiNapoli et al. 2014; Holwerda et al. 2012; O'Luanaigh et al. 2012; Shankar et al. 2013; Simning et al. 2014; Wilson, Krueger et al. 2007). There are also some validated measures such as the Lubben Social Network Scale (LSNS) that also assess structural aspects (Lubben, 1988; Lubben et al. 2006). Scores on these measures are usually summed and a threshold determines whether an individual is classified as isolated or not. Such approaches to measuring social isolation are restrictive as they focus on the quantity of social relationships rather than the quality. Therefore, measures cannot capture person-level factors that may influence social connections in later life, such as satisfaction with social contact or individual differences in preferences for degree of contact. Operationalised cut-points categorise people as isolated based on a number of contacts that is thought to be sufficient (Lubben et al. 2006). This is problematic as a measure may categorise an individual with few social contacts as socially isolated, yet the individual may not feel isolated and may be satisfied with this level of social contact (Hughes et al. 2008).

Individuals' perceptions of their social context are important and may be associated with health outcomes (Hughes et al. 2008). One previous study that assessed the relationship between social isolation and cognitive function reported that a measure of satisfaction with social contact accounted for nearly twice as much of the variance in cognitive function as did a structural measure of social isolation (DiNapoli et al. 2014). Furthermore, it has been found that infrequent social contact does not increase the risk of Alzheimer's disease or poor cognitive function if this level of contact is experienced as satisfying by the individual (Fratiglioni et al. 2000; Gow et al. 2013). Several

further studies report that greater satisfaction with social contact is associated better cognitive function (Hughes et al. 2008; Yeh & Liu, 2003). However, one study did not find an association between satisfaction with social contact and cognitive function (Crooks et al. 2008). Overall, however, these findings suggest that satisfaction is an important aspect that may be associated with cognitive function in later life.

In summary, measures of satisfaction with social contact may capture perceptions of social isolation and preferences for, and subjective experiences of, social contact with others. Conversely, measures of social isolation based on structural aspects are more objective and seem more related to the quantity and frequency of social interaction and activity (Hawkley et al. 2008). Not accounting for satisfaction with social contact in structural measures of social isolation may account for some of the discrepancy observed in findings relating to the association with cognitive function. Therefore, we aimed to address the following research questions by surveying a large online cohort of people over the age of 60:

1. How do scores on a structural measure of social isolation compare to scores on a measure of satisfaction with social contact?
2. To what extent does a structural measure of social isolation and a measure of satisfaction with social contact predict cognitive function?
3. Does satisfaction with social contact moderate the association between a structural measure of social isolation and cognitive function?

8.3 Method

Design and participants

PROTECT is an ongoing ten year study of people ≥50 years that aims to explore the role of genetic, lifestyle, and medical factors on cognitive function and how these factors may contribute to cognitive decline and dementia in later life. Participants were eligible for inclusion if they were aged ≥50 years, living in the UK, were able to use a computer, had access to the internet, and could speak English. The study was publicised in the national media and people who were interested in participating were directed to the study website where they could read the information sheet and sign a consent form if they wished to take part. People were excluded if they had a diagnosis of dementia. Baseline assessment (wave one) was completed between November 2015 and August 2016 and participants are invited to complete follow-up assessments annually.

For the present study, a sub-sample of participants were recruited through the PROTECT platform. Email invitations were sent to people aged ≥60 years who had completed cognitive and mental

health assessments at the wave three annual assessment (between November 2017 and February 2018). The email contained a link to an online information sheet and participants could sign a consent form if they wished to participate; following this they were given a link to access the survey. The survey included a structural measure of social isolation and a measure of satisfaction with social contact and data were collected in February 2018. Data for cognitive and mental health measures completed at the wave three annual assessment were accessed from the PROTECT platform for the people who opted to take part in the social connections study. Ethical approval for the study was granted by the University of Exeter ethics committee (reference number: eCLESPsy000045).

A total of 5,001 participants enrolled in the social connections study. We excluded people with missing data for the measures required in the present study, including mental health and cognitive assessments, and incomplete social measures (N = 385) which gave a final sample size of 4,616 participants.

Measures

Structural measure of social isolation

Social isolation was assessed using the Lubben Social Network Scale–6 (LSNS-6: Lubben et al. 2006). The LSNS-6 is a structural measure of social isolation, constructed of three sets of questions that assess ties with family, and a set of three comparable questions assessing non-kinship ties. The three items assess the number of relatives/ friends the participant sees or hears from at least once a month, could call on for help, and can speak with about private matters. The participant indicates the number of relatives/ friends available on a response scale ranging from 0 (no relatives/ friends) to 5 (nine or more relatives/ friends). The overall scores for each of the six questions are summed and range from 0-30, with zero indicating social isolation and 30 no social isolation. A score of ≤12 indicates social isolation (Lubben et al. 2006).

Satisfaction with social contact

Satisfaction with social contact was assessed using a measure from the Canadian Study of Health and Aging (Andrew & Rockwood, 2010). The measure consists of eight questions that assess whether participants feel they need more people to talk with, need to spend more time with family and friends, need more advice about important matters, need more help and support, feel they get out as much as they would like to, are satisfied with the amount of contact they have with family and friends (each scored as yes/ no), and how satisfied the participants feel with their life in terms of family relationships and friendships (seven point scale ranging from terrible to delighted). Responses to dichotomous questions (yes/ no) are scored as zero if the social deficit is absent and one if

present. Intermediate values are scored in equal increments from 0-1 (i.e. terrible = 1, unhappy = 0.83, mostly dissatisfied = 0.67, mixed = 0.5, mostly satisfied = 0.33, pleased = 0.17, and delighted = 0). Scores are summed and range from 0-8. Higher scores indicate dissatisfaction with social contact. We considered a score of one standard deviation above the mean score for all participants (a score of ≥3.52) to indicate dissatisfaction with social contact.

Cognitive function

Cognitive function was assessed using a validated online cognitive measure (Corbett et al. 2015) consisting of four tasks, including the digit span task to assess verbal working memory (Huntley et al. 2016), the paired associate learning task to assess visual episodic memory (Owen et al. 1993), the self-ordered search task to assess spatial working memory (Owen et al. 1990), and the grammatical reasoning task to assess verbal reasoning (Baddeley, 1968). Participants completed each of the cognitive tests up to three times over seven days as part of their annual assessment at wave three. The mean score of the participant's performance over the three trials in each cognitive domain was taken as the score for cognitive function in that domain. Lower scores indicate poorer cognitive function across each cognitive domain.

Covariates

Age (years), gender, and educational level are well-established covariates of late-life cognitive function (Barnes et al. 2003; Tervo et al. 2004; Tilvis et al. 2004) and were controlled for in all analyses. Educational level was assessed by asking participants to report their highest level of education as follows: GCSEs (or equivalent), A-level or vocational qualification (or equivalent), or university degree.

We controlled for depression, which is associated with poor cognitive function in general (Alexopoulos, Meyers et al. 1993; Alexopoulos, Young et al. 1993; Bhalla et al. 2006) and in specific domains including working memory and episodic memory (Butters et al. 2000; Butters et al. 2004; Huntley et al. 2018; Nebes et al. 2001; Nebes et al. 2002). Depression may also be associated with social isolation and dissatisfaction with social contact (Domènech-Abella et al. 2017; García-Peña, 2013; Litwin, 2012; Kupferberg, Bicks & Hasler, 2016; Luanaigh & Lawlor, 2008; Segrin, 2000; Weightman, Air & Baune, 2014; Yaacob et al. 2017). Depression was assessed using the Patient Health Questionnaire–9 (PHQ-9: Kroenke et al. 2001). This measure assesses how often the participant has experienced nine symptoms of depression in the past two weeks. Responses are recorded from not at all (0) to nearly every day (3). Scores range from 0-27 and scores of 0-4 indicate

minimal depression, scores of 5-14 indicate mild to moderate depression, and scores of ≥15 indicate moderately severe to severe depression (Kroenke et al. 2001).

Statistical analysis

Analyses were conducted in Stata version 15.0. Participants were classified into four groups based on their scores on the two measures of social contact; participants who were not isolated but were satisfied with social contact, participants who were isolated but were dissatisfied with social contact, participants who were not isolated but dissatisfied with social contact, and participants who were isolated but satisfied with social contact. These four groups could be collapsed into two categories; participants with congruent scores on the two measures and participants with incongruent scores on the two measures. Descriptive information was reported for variables in the study for all participants and separately for each of the four groups. ANOVAs compared these groups on all variables and were adjusted for multiple comparisons using Bonferroni. A logistic regression was conducted to determine which factors were associated with congruent or incongruent scores on the structural measure of social isolation (LSNS-6) and the measure of satisfaction with social contact. Two sets of linear regression analyses were conducted. The first aimed to determine the association between scores on the standardised measure of social isolation (LSNS-6) and each cognitive domain, and the second to determine the association between scores on the measure of satisfaction with social contact and each cognitive domain. Finally, a moderation analysis was conducted to determine whether the association between the standardised measure of social isolation (LSNS-6) and cognitive function in each domain was moderated by satisfaction with social contact.

8.4 Results

The mean age of participants was 68 and ranged from 60–102 years. In total, 75% of participants were women, 56% had received a university level education, and 94% were white British. The structural measure of social isolation (LNS-6) classified 671 (15%) participants as isolated and the measure of satisfaction with social contact classified 862 (19%) participants as dissatisfied with their level of social contact (Table 8.1).

Table 8.1. *Descriptive information about the participants.*

			Congruent scores on social measures		Incongruent scores on social measures		
	Total sample N = 4,616	**Range**	**Not isolated, satisfied[0] N = 3,355**	**Isolated, dissatisfied[1] N = 272**	**Not isolated, dissatisfied[2] N = 590**	**Isolated, satisfied[3] N = 399**	**ANOVA *p***
Age, *M* (SD)	68.18 (5.65)	60 – 102	68.20 (5.65)	68.40 (6.25)	67.89 (5.48)	68.36 (5.41)	*F*(3, 4615) = .81 *p* = .490
Women, *N* (%)	3,439 (74.50)		2,563 (76.39)	183 (67.28)	455 (77.12)	238 (59.65)	*F*(3, 4615) = 21.02 ***p* <.001[A]**
Educational level, *N* (%)							
Secondary education (GCSEs)	666 (14.43)		450 (13.41)	49 (18.01)	87 (14.75)	80 (20.05)	*F*(3, 4615) = 4.09
A-levels or vocational qualification	1,429 (30.96)		1,046 (31.18)	75 (27.57)	185 (31.36)	123 (30.83)	*p* = .007
University level education	2,521 (54.61)		1,859 (55.41)	148 (54.41)	196 (49.12)	196 (49.12)	
Ethnicity							
White British, *N* (%)	4,351 (94.26)		3,175 (94.63)	251 (92.28)	552 (93.56)	373 (93.48)	*F*(3, 4615) = 1.66 *p* = .174
Cognitive function, *M* (SD)							
Verbal working memory	7.47 (1.68)	0 – 20	7.51 (1.70)	7.40 (1.56)	7.33 (1.57)	7.48 (1.76)	*F*(3, 4615) = 2.08 *p* = .100
Visual episodic memory	4.56 (.99)	0 – 16	4.58 (1.00)	4.45 (.97)	4.52 (.95)	4.55 (1.00)	*F*(3, 4615) = .66 *p* = .579
Verbal reasoning	35.08 (10.53)	0 – 79	35.10 (10.61)	34.50 (9.92)	35.01 (10.41)	35.44 (10.50)	*F*(3, 4615) = .44 *p* = .723
Spatial working memory	7.30 (2.73)	0 – 20	7.33 (2.69)	7.04 (2.90)	7.10 (2.81)	7.51 (2.81)	*F*(3, 4615) = 2.75 *p* = .042
Depression, *M* (SD)	2.50 (3.14)	0 – 24	1.98 (2.53)	5.82 (5.19)	3.94 (3.56)	2.53 (3.26)	*F*(3, 4615) = 195.16 ***p* <.001[B]**
Social isolation (LSNS-6), *M* (SD)	18.19 (5.25)	0 – 30	20.05 (3.91)	8.83 (2.84)	17.70 (3.42)	9.65 (2.50)	*F*(3, 4615) = 1,582.44 ***p* <.001[C]**
Satisfaction with social contact, *M* (SD)	1.73 (1.79)	0 – 8	.96 (.92)	5.27 (1.20)	4.73 (.90)	1.38 (.96)	*F*(3, 4615) = 4,061.07 ***p* <.001[D]**

Note: **bold** = remained significant at the 5% level after Bonferroni correction. Between group comparisons that were significant after adjusting for Bonferroni (number corresponds to group name in title row): [A]0>1, 0>3, 1<2, 2>3; [B]0<1, 0<3, 0<2, 1>3, 1>2, 3<2; [C]0>1, 0>3, 0>2, 1<3, 1<2, 3<2; [D]0<1, 0<3, 0<2, 1>3, 1>2, 3<2.

How do scores on a structural measure of social isolation compare to a measure of satisfaction with social contact?

In total, 3,627 (79%) participants had congruent scores on the structural measure of social isolation (LSNS-6) and the measure of satisfaction with social contact. Most participants were not isolated and were satisfied (N = 3,355, 73%) and a small number of people were isolated and dissatisfied (N = 272, 6%). 989 (21%) participants had incongruent scores on social measures. Some participants were isolated but satisfied (N = 399, 8%) and others were not isolated and were dissatisfied (N = 590, 13%).

There was no difference in age, educational level, ethnicity, or function in any of the cognitive domains after adjusting for Bonferroni across people with congruent and incongruent scores. There were significant differences for gender; fewer women were isolated and satisfied. People who were isolated and dissatisfied had more symptoms of depression that people who were not isolated and satisfied, isolated and satisfied, or not isolated and dissatisfied (Table 8.1).

The PHQ-9 classified 392 (12%) people who scored as not isolated and satisfied, 139 (51%) people who were isolated and dissatisfied, 67 (17%) people who were isolated and satisfied, and 209 (35%) people who were not isolated but dissatisfied, as having clinically relevant symptoms of depression.

A logistic regression was conducted to determine which factors were associated with congruent and incongruent scores on the structural measure of social isolation and the measure of satisfaction with social contact. This suggested that gender, having a university level education, and depression predicted congruent or incongruent group status. People in congruent groups were more likely to be women (N = 2,746, 76%) than those in incongruent groups (N = 693, 70%), were more likely to have a university level education (N = 2,007, 55%) than those in incongruent groups (N = 392, 40%), and had lower scores on the measure of depression (*M* = 2.27, *SD* = 2.99) than people in incongruent groups (*M* = 3.37, *SD* = 3.51). Age, A-level/ vocational education, and function in specific cognitive domains did not predict congruent or incongruent group status (Table 8.2).

Table 8.2. *Factors that predict congruent or incongruent group status (N = 4,616).*

	OR (SE)	*P*	95% CI
Age	1.00 (.01)	.858	.99, 1.01
Gender	.67 (.06)	<.001	.57, .78
Educational level (up to GCSEs as reference)			
A-levels/ vocational training	.83 (.09)	.096	.66, 1.03
University education	.80 (.09)	.035	.66, .98
Depression	1.12 (.02)	<.001	1.09, 1.16
Cognitive function			
Verbal working memory	.98 (.02)	.459	.94, 1.03
Visual episodic memory	.98 (.04)	.601	.91, 1.06
Verbal reasoning	1.00 (0)	.856	.99, 1.01
Spatial working memory	.99 (.01)	.450	.96, 1.01

To what extent does a structural measure of social isolation and a measure of satisfaction with social contact predict cognitive function?

Linear regression analyses were conducted to assess the association between scores on the structural measure of social isolation (LSNS-6) and each cognitive domain. There was a marginally significant association between LSNS-6 and verbal working memory and visual episodic memory in the unadjusted model. After controlling for depression, these associations became non-significant. There was no association between the LSNS-6 and verbal reasoning or spatial working memory (Table 8.3).

Linear regression analyses were conducted to assess the association between scores on the measure of satisfaction with social contact and each cognitive domain. Satisfaction with social contact was significantly associated with verbal working memory and spatial working memory in the unadjusted model and remained significant after controlling for all covariates. There was no association between satisfaction with social contact and visual episodic memory or verbal reasoning (Table 8.4).

Table 8.3. *The association between a structural measure of social isolation (LSNS-6) and domains of cognitive function (N = 4,616).*

	Verbal working memory			Visual episodic memory			Verbal reasoning			Spatial working memory		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Social isolation (LSNS-6)	.01 (0)[1] .052[2] 0, .02[3]	.01 (0) .225 0, .02	.01 (0) .166 0, .02	.01 (0) .051 0, .01	0 (0) .112 0, .01	0 (0) .129 0, .01	.04 (.03) .192 -.02, .10	.05 (.03) .122 -.01, .11	.02 (.03) .589 -.04, .07	.01 (.01) .101 0, .03	.01 (.01) .297 -.01, .02	.01 (.01) .262 -.01, .02
Depression		-.02 (.01) .002 -.04, -.01	-.02 .003 -.04, -.01		-.01 (0) .151 -.02, 0	-.01 (0) .055 -.02, 0		.06 (.05) .215 -.04, .16	.05 (.05) .341 -.05, .14		-.03 (.01) .011 -.06, -.01	-.03 (.01) .010 -.06, -.01
Age			-.04 (0) <.001 -.05, -.03			-.03 (0) <.001 -.04, -.03			-.46 (.03) <.001 -.51, -.41			-.07 (.01) <.001 -.08, -.06
Gender			-.22 (.06) <.001 -.33, -.11			-.03 (.03) .443 -.09, .04			.35 (.34) .314 -.33, 1.02			-.26 (.09) .005 -.45, -.08
Educational level (up to GCSEs as reference)												
A-levels or vocational qualification			.14 (.08) .074 -.01, .29			-.07 (.05) .138 -.16, .02			2.74 (.47) <.001 1.82, 3.65			.13 (.13) .294 -.12, .38
University education			.34 (.07) <.001 .20, .48			0 (.04) .997 -.08, .08			5.71 (.44) <.001 4.85, 6.56			.41 (.12) <.001 .18, .64

Note: [1] *B*; [2] *p*; [3] 95% CI; Model 1: unadjusted; Model 2: adjusted for depression; Model 3: adjusted for depression, age, gender, and educational level.

Table 8.4. *The association between a measure of satisfaction with social contact and domains of cognitive function (N = 4,616).*

	Verbal working memory			**Visual episodic memory**			**Verbal reasoning**			**Spatial working memory**		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Satisfaction with social contact	-.05 (.01)[1] <.001[2] -.08, -.02[3]	-.04 (.01) .016 -.07, -.01	-.04 (.01) .015 -.06, -.01	-.01 (.01) .083 -.03, 0	-.01 (.01) .265 -.03, .01	-.01 (.01) .379 -.02, .01	-.10 (.09) .227 -.27, .07	-.06 (.09) .090 -.34, .02	-.12 (.09) .178 -.29, .05	-.07 (.02) <.001 -.12, -.03	-.06 (.02) .015 -.11, -.01	-.06 (.02) .018 -.10, -.01
Depression		-.02 (.01) .024 -.04, 0	-.02 (.01) .029 -.04, 0		-.01 (.01) .209 -.02, 0	-.01 (0) .072 -.02, 0		.08 (.05) .132 -.02, .19	.07 (.05) .191 -.03, .17		-.02 (.01) .092 -.05, 0	-.02 (.01) .076 -.05, 0
Age			-.04 (0) <.001 -.05, -.03			-.03 (0) <.001 -.04, -.03			-.46 (.03) <.001 -.51, -.41			-.07 (.01) <.001 -.08, -.06
Gender			-.21 (.06) <.001 -.33, -.10			-.02 (.03) .551 -.09, .05			.35 (.34) .301 -.32, 1.02			-.26 (.09) .005 -.44, -.08
Educational level (up to GCSEs as reference)												
A-levels or vocational qualification			.14 (.08) .067 -.01, .30			-.07 (.05) .151 -.16, .02			2.74 (.47) <.001 1.83, 3.66			.14 (.13) .277 -.11, .39
University education			.35 (.07) <.001 -.21, .49			0 (.04) .932 -.08, .09			5.72 (.44) <.001 4.87, 6.58			.42 (.12) <.001 .19, .65

Note: [1] *B*; [2] *p*; [3] 95% CI; Model 1: unadjusted; Model 2: adjusted for depression; Model 3: adjusted for depression, age, gender, and educational level.

Does satisfaction with social contact moderate the association between a structural measure of social isolation and cognitive function?

Moderation analyses were conducted to determine whether satisfaction with social contact moderated the association between scores on the structural measure of social isolation (LSNS-6) and functioning across the four cognitive domains. The interaction term between the LSNS-6 score and satisfaction with social contact did not explain a significant increase in any of the cognitive domains in unadjusted models (verbal working memory: *B* = 0, 95% CI; -.01, 0, *p* = .412, visual episodic memory: *B* = 0, 95% CI; 0, 0, *p* = .337, verbal reasoning: *B* = 0; 95% CI; -.03, .03, *p* = .966, spatial working memory: *B* = 0, 95% CI; -.01, .01, *p* = .951) or adjusted models controlling for age, gender, educational level, and depression (verbal working memory: *B* = 0, 95% CI; -.01, 0, *p* = .275, visual episodic memory: *B* = 0, 95% CI; 0, 0, *p* = .322, verbal reasoning: *B* = .01; 95% CI; -.02, .03, *p* = .709, spatial working memory: *B* = 0, 95% CI; -.01, .01, *p* = .925).

8.5 Discussion

This is one of few studies to consider the association between social isolation, satisfaction with social contact, and cognitive function in later life. We found that few people were classified as isolated by the structural measure of social isolation and few people were dissatisfied with their social contact. Scores on the structural measure of social isolation and the measure of satisfaction with social contact were similar. Most people who were classified as isolated by the structural measure indicated that they were dissatisfied with their level of social contact and most people who were not classified as isolated indicated that they were satisfied with this level of contact. There were differences in the associations of the two social measures with cognitive function. The structural measure of social isolation was not associated with poor cognitive function across any of the cognitive domains, whereas the measure of satisfaction with social contact was associated with poorer scores on the verbal and spatial working memory tasks after adjusting for depression, age, gender, and educational level. Satisfaction with social contact did not moderate the association between social isolation, as determined by a structural measure, and cognitive function.

The finding that most people have congruent scores on a structural measure of social isolation and a measure of satisfaction with social contact is positive. It suggests that people's perceptions of their social connections tend to reflect the scoring of structural measures of isolation. Only a small number of people had incongruent scores across the two measures. People with congruent scores were more likely to be women, have a university level education, and have lower scores on the measure of depression than people with incongruent scores. It is not surprising that depression predicted congruency group. Over half of the people who were isolated and dissatisfied with their

social contact, and approximately one third of people who were not isolated but were dissatisfied, were classified as depressed. People with depression may be more likely to interpret their social networks and interactions more negatively and hence be less satisfied with their social contact (Bourke, Douglas & Porter, 2010; Ehnvall et al. 2014; Platt, Kadosh & Lau, 2013; Tse & Bond, 2004). People who were not isolated and were satisfied with their social contact were least likely to be classified as depressed. People who were classified as isolated but were satisfied with their social contact had similar levels of depression to people who were not isolated and were satisfied. It is likely that these people are content with little social contact and hence do not have negative perceptions of their social context. This reflects the importance of considering satisfaction with social relationships, as this can influence health outcomes. It also suggests that individual differences in social contact are important, as although individuals may be classified as isolated by structural measures, this level of social contact may feel acceptable and enable optimal functioning.

The standardised measure of social isolation and the measure of satisfaction with social contact differed in their prediction of cognitive function. In fully adjusted models, the association between satisfaction with social contact and verbal and spatial working memory was significant which is consistent with previous findings (Boss et al. 2015; Wilson, Krueger et al. 2007). The association between the structural measure of social isolation and verbal working memory and visual episodic memory was not significant after adjusting for depression. This is also consistent with previous studies that report no association between structural measures of social isolation and cognitive functioning in cross-sectional data (DiNapoli et al. 2014; Elwood et al. 1999; Glei et al. 2005; Golden et al. 2009; O'Luanaigh et al. 2012; Paúl et al. 2010; Simning et al, 2014). This suggests that these effects may have been driven by symptoms of depression.

The association between social isolation, satisfaction with social contact, and cognitive function is complex and may be influenced by depression. People with depression may interpret their social networks and interactions more negatively and hence be less satisfied with their social contact (Bourke et al. 2010; Ehnvall et al. 2014; Platt et al. 2013; Tse & Bond, 2004) even if the structure of their social networks and level of contact is comparable to that of people without symptoms of depression (Cacioppo & Hawkley, 2009; Luanaigh & Lawlor, 2008; Chapter 6). Measures of depression typically capture how individuals feel about their life in terms of a range of problems (Kroenke et al. 2001). Therefore measures of satisfaction with social contact and depression capture individuals' perceptions of their social contexts and other aspects of their lives in a way that structural measures of isolation do not. Indeed, satisfaction with social contact and depression have both been associated with poorer function in working memory (Boss et al. 2015; Christopher &

MacDonald, 2005; Dumas & Newhouse, 2015; Huntley et al. 2018; LeMoult, Carver, Johnson & Joormann, 2015; Rose & Ebmeier, 2006; Wilson, Schneider et al. 2007).

Satisfaction with social contact did not moderate the association between a structural measure of social isolation and cognitive function across any of the cognitive domains. This is inconsistent with previous work that suggests that poor social contact does not increase the risk of poor cognitive function if the individual experiences this as satisfactory (Fratiglioni et al. 2000; Gow et al. 2013). There are several possible reasons for this difference. Both of these studies were longitudinal and hence findings may not be replicated in the present cross-sectional analysis. Cognitive outcomes differed from the present study and used a measure of IQ (Gow et al. 2013) or dementia diagnosis (Fratiglioni et al. 2000). The measure of IQ in Gow et al. (2013) was a composite of several crystallised cognitive abilities and aggregating scores may be less sensitive than tests specifically developed to assess abilities that are known to be affected in cognitive ageing, such as the domain-specific measures in PROTECT (Christensen, 2001; Deary et al. 2009; Hedden & Gabrieli, 2004; Park & Reuter-Lorenz, 2009). IQ was also assessed on one occasion in Gow et al. (2013) whereas cognitive function in PROTECT was assessed on three occasions. Likewise, dementia diagnosis (Fratiglioni et al. 2000) requires more severe cognitive deficits to be detected across more than one domain. Hence the specificity of the cognitive measures in the present study may have limited the ability to detect a relationship between social isolation, satisfaction, and cognitive function. In addition, a single item question (Fratiglioni et al. 2000) and a six-item scale assessing satisfaction with social support (Gow et al. 2013) were used as measures of satisfaction in previous studies. The present study uses a more comprehensive measure that may provide more insight into satisfaction with several aspects of an individual's social connections rather than focusing on social support, which may account for a difference in findings.

The present findings have positive implications for the assessment of social isolation in later life. Most people had congruent scores on the structural measure of social isolation and the measure of satisfaction with social contact. This suggests that people who are isolated are generally dissatisfied, and people who are not isolated are generally satisfied, with social contact. However, while most people have congruent scores, some do not, and hence it may be useful to assess satisfaction with social contact in structural measures of isolation. This is particularly relevant given that people who indicated they were dissatisfied with their social contact were more likely to be classified as depressed than people who were satisfied. Structural measures cannot capture these personal factors, such as depression, which may influence social relationships, whereas measures of satisfaction are more able to account for such factors. This is further reinforced by the finding that dissatisfaction with social contact predicted poorer scores in domains of verbal and spatial working

memory after controlling for depression, whereas a structural measure of social isolation was not associated with poorer cognitive scores after controlling for depression. This suggests that it is not just depression that accounts for the association between dissatisfaction with social contact and verbal and spatial working memory and that satisfaction has an important predictive role for cognitive outcomes.

The group of people who are classified as isolated structurally, but are satisfied with this level of contact, are an interesting group. These people have less contact than is assumed by structural measures to be appropriate and hence are classified as isolated yet this level of contact is perceived to be acceptable to them. A small number of people in this group were classified as depressed which reflects their positive appraisal of their structurally low level of social contact. Their responses suggest there are individual differences in preference for social contact that cannot be captured by structural measures that use cut-points to determine is an individual is isolated or not. Preference for contact may be influenced by a range of factors including personality (Bolger & Eckenrode, 1991; Finch & Graziano, 2001; Hughes, Rowe, Batey & Lee, 2012; Suurmeijer et al. 2005; Tov et al. 2016), mental health (Cacioppo & Hawkley, 2009; Kashdan & Roberts, 2007; Oliveira et al. 2015), or physical health (Fung, Carstensen & Lutz, 1999; Uchino, 2004; Wilkinson & Marmot, 2003). Future work may explore this group of people further to understand why a smaller social network and less frequent social contact is considered satisfying and how this may influence health outcomes.

This study has a number of strengths. First, the cognitive measures in PROTECT assess verbal working memory, visual episodic memory, spatial working memory, and verbal reasoning separately. This allowed us to determine whether any specific domains of cognitive function are most affected by structural measures of social isolation or satisfaction with social contact. There are, however, several aspects of cognitive function that are not assessed, such as executive function. Cognitive measures were completed by each participant up to three times within seven days and an average score was calculated to represent the participant's cognitive score. This approach enables participants to familiarise themselves with the measures and ensure they receive a cognitive score that adequately represents their cognitive ability rather than their ability to complete cognitive measures (Goldberg, Harvey, Wesnes, Synder & Schneider, 2015; Wesnes & Pincock, 2002).

However, this study has some limitations. Firstly, the study was cross-sectional in design and so it is not possible to determine causation, as social isolation and dissatisfaction with social contact may be the result of poor cognitive function, rather than being causally associated with poor cognitive function (Zunzunegui et al. 2003). Many participants completed their mental health and cognitive assessments up to four months prior to completing the social measures. It is possible that there may

have been some changes in cognitive function or symptoms of mental health during this time. The PROTECT sample is self-selected rather than population representative, and the over-representation of white, highly educated women was evident in the sample for the present study. Participants are required to complete all assessments online which further limits the sample to computer-literate older people. Although this may limit the generalisability of results to a wider population, the results provide information on how a structural measure of social isolation and a measure of satisfaction with social contact may influence cognitive function. Two of the questions taken from the Canadian Study of Health and Aging ask participants to respond on a six-point scale which uses emotive responses such as 'terrible' and 'delighted'. These words are culturally more acceptable in North America and may not be the typical words used to describe situations by people in the UK, and therefore this may have influenced the responses to these questions from participants in PROTECT. However, given that all participants were presented with these response choices, it is likely most participants will have interpreted the response choices in the same way and so the validity of results may not be greatly affected. Finally, the number of people who were grouped as not isolated and satisfied was much larger than the number of people in other groups. This may limit the power of analyses and reduce comparability across groups.

We have demonstrated that satisfaction with social contact is an important aspect to consider in the assessment of social isolation. Scores on structural measures of social isolation and satisfaction with social contact are congruent for most people which is positive and suggests that structural approaches to assessing social isolation are able in most cases to capture satisfaction with social contact. Where people have poor satisfaction with their social contact, depression may be an important factor due to a bias for negative evaluations, and poor recall, of social interaction. Some people, albeit a small minority, are classified as isolated by structural measures of social isolation but are satisfied with this level of social contact. Satisfaction with social contact was a better predictor of poor cognitive function than the structural measure of social isolation, even after controlling for depression. This suggests that depression is not the only factor that can account for the associations with cognitive function and that satisfaction is important and ought to be assessed alongside structural aspects.

Chapter 9: Discussion

9.1 Introduction

With the current trend of an ageing population (Mathers et al. 2015; Wasay et al. 2016) and the increase in projections of poor cognitive function in later life (Jagger et al. 2009; Prince et al. 2015), identifying modifiable lifestyle factors that may prevent or delay the onset of poor cognitive function is paramount. This thesis has considered the association between social connections and cognitive function in later life. Unlike previous work, this thesis considers the role of cognitive reserve, a mechanism that may underpin the association between social connections and cognitive function.

To summarise, this thesis has identified that a wide range of terms are associated with social connections and are often used interchangeably within the literature. Chapter 3 examined the literature relating to social connections and cognitive function in later life to clarify the definitions and approaches to measuring each of these concepts. Social isolation was the most poorly defined and inconsistently assessed concept identified and hence this thesis has focused on social isolation to further our understanding of the concept and its association with cognitive function. Chapter 4 explored the association between social isolation and cognitive function in existing empirical work. None of the studies identified in the systematic review considered the role of underlying mechanisms in this association. Chapter 5 assessed the association between social isolation and cognitive function in people without cognitive impairment, dementia, or depression at baseline. This work is novel as it considers the role of cognitive reserve in this association to develop our understanding of how this mechanism may function. Chapters 6 and 7 are novel as they consider these associations in groups of people who may be more vulnerable to social isolation, including people with depression or anxiety and people who live alone. This is especially relevant given that social isolation is associated with poor cognitive function and hence poor cognitive function may be exacerbated in people who are more vulnerable to isolation. To our knowledge, the association between social isolation, cognitive reserve, and cognitive function has not been assessed previously in people with depression or anxiety. Previous findings regarding the association between living situation and cognitive function are conflicting and have not considered the role of cognitive reserve. Chapter 8 considers the role of satisfaction with social contact which is not typically included in structural measures of isolation but may be important in predicting cognitive outcomes.

Overall, the findings from this thesis extend our understanding of the way that social connections may be associated with cognitive function in later life. In the following sections of this chapter each of the research questions will be discussed in turn. Findings from the examination of existing literature in Chapters 3 and 4, and the empirical studies in Chapters 5–8, will be summarised and discussed in relation to wider literature. Methodological limitations will then be considered,

followed by suggestions for future research, and finally the theoretical and practical implications of this work will be discussed.

9.2 Research question one

How are concepts associated with social connections conceptualised and measured in the literature relating to cognitive function in later life?

In Chapter 3 a scoping review was conducted to examine which social concepts are assessed in studies that consider the association between social connections and cognitive function. The review identified a range of concepts, including concepts related to structural aspects of social connections, such as marital status, living situation, social networks, social isolation, and social engagement, concepts related to functional aspects, including social support, and concepts related to an individual's appraisal of their social context, including loneliness. Approaches to defining and measuring these concepts were disparate across studies. Few standardised measures were used and many studies created their own measures using various social indicators.

These findings have implications for the assessment of social connections in later life. The lack of consistency in measures that assess social concepts means it is difficult to reliably depict the association of these constructs with cognitive function. In addition, various indicators of social connections may be differentially associated with cognitive function. Measures that are comprehensive and include a wide range of indicators are likely to be less specific in that they assess multiple social concepts rather than one specific concept. For example, Holwerda et al. (2008) assess social isolation based on marital status, living situation, and social support. This measure may not be a valid means to assess social isolation, as living alone, being unmarried, and receiving a low level of social support does not necessarily mean an individual is isolated. This reflects how measures may use multiple indicators that assess related concepts but do not assess the social concept specified and hence may lack validity. Conversely, measures with only one, or few, indicators may be specific and assess one particular concept. This level of specificity is preferable and can determine the extent to which specific social concepts and indicators are associated with cognitive function. However, it is likely that each of the social concepts identified by the scoping review interact to contribute to an individual's social context and so considering concepts separately may over-simplify these complex interactions (Victor et al. 2000). It may be useful for future studies to report findings for specific indicators both separately and in combination to help determine the nature of the association between specific indicators of social connections and cognitive function. Future work would also benefit from consensus in approaches to defining and measuring these concepts. This would enable a better understanding of these associations, further inform the prevention literature and the

development of interventions, and more reliably estimate the association between social connections and cognitive function.

The findings of the scoping review provided a basis for clear delineation of the different concepts relating to social connections. The review has also highlighted valid and reliable approaches to assess each concept in line with definitions and the standardised measures that are available. Social isolation was the least well defined and most inconsistently measured concept identified, and findings relating to associations with cognitive function were mixed. Therefore social isolation was explored further in Chapters 4–8 to expand the literature relating to this concept and determine its association with cognitive function. The scoping review highlighted several limitations of existing literature which are addressed in the following research questions. First, few studies consider the role of underlying mechanisms in the association between social isolation and cognitive function (examined in Chapters 5–7). In addition, this association is typically assessed in 'healthy' community dwelling people. This is problematic as the associations may be different for people at greater risk of social isolation, such as people with depression or anxiety (examined in Chapter 6) and people who live alone (examined in Chapter 7). Few studies consider satisfaction with social contact which may be an important factor related to health outcomes, and so the possible associations with cognitive function were explored further in this thesis (Chapter 8).

9.3 Research question two

What is the association between social isolation, cognitive reserve, and cognitive function in healthy older people?

The association between social isolation and cognitive function is addressed in Chapters 4 and 5. In Chapter 4 the existing literature which examines the association between social isolation and cognitive function was systematically searched and data from 51 articles were included in a series of meta-analyses. A small but significant positive association was found between social isolation and poor cognitive function in later life. This is consistent with a previous review which reported that small social networks and infrequent social contact with others was associated with cognitive decline (Kuiper et al. 2016). Chapter 5 builds on the findings of Chapter 4 and empirically assesses the association between social isolation and cognitive function in older people without cognitive impairment, dementia, or depression in CFAS-Wales. Being isolated was associated with poorer cognitive function at baseline and a decline in cognitive function over two years, consistent with previous studies (DiNapoli et al. 2014; Holwerda et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007). Chapter 5 is novel and extends previous work by considering the role of cognitive reserve. Cognitive reserve moderated the association at two year follow-up, which suggests that higher levels

of reserve may further benefit cognitive function. These findings are in line with the cognitive reserve theory which suggests that the maintenance of large social networks and frequently engaging in social activity may stimulate cognitive function and hence build reserve and enhance cognitive function (Bennett et al. 2006; Fratiglioni et al. 2000; Fratiglioni et al. 2004; Stern 2002, 2009; Watson & Andrews, 2002). It is also possible that people who have better cognitive reserve are more able to maintain good social contact and hence be more protected against poor cognitive function.

Given that social isolation is a lifestyle factor that may be amenable to change, investigation of interventions to reduce isolation would be beneficial, allowing us to explore how this may prevent or delay poor cognitive function. A small number of randomized controlled trials have investigated how interventions to enhance social connections could improve cognitive function in later life for community-dwelling people. These trials have reported beneficial effects on cognitive function and increases in overall brain volume for people in social intervention groups compared to control groups (Dodge et al. 2015; Mortimer et al. 2012; Pitkala et al, 2011). One of these interventions to enhance social contact was successfully facilitated by video internet communication (Dodge et al. 2015). This is positive and suggests that the internet could be a cost-effective vehicle for intervention, although this approach may not be suitable for older people who are not computer-literate. These trials use small numbers of people and so may be underpowered, and one intervention was administered to a group of lonely older people (Pitkala et al. 2011). This intervention may not be as effective for people who are isolated but not lonely. A further randomized controlled trial reported no beneficial effect of a social intervention on cognitive function (Park et al. 2014). Two of these trials have reported that interventions focused on cognitive and physical activity were more beneficial to cognitive function than social interventions (Mortimer et al. 2012; Park et al. 2014). This is unsurprising given that cognitive function is influenced by a range of potentially modifiable lifestyle factors (Ngandu et al. 2015).

Findings from this thesis suggest that being socially isolated is associated with poorer cognitive function in later life. Reported effect sizes in the systematic review (Chapter 4) were small and there was a considerable amount of variance in cognitive scores that was not accounted for by social isolation alone (Chapter 5). It is not surprising that social isolation contributes a small amount in explaining cognitive function. There are a range of modifiable lifestyle factors that contribute to the maintenance of cognitive function, including physical exercise, educational level, occupational complexity, cognitive activity, diabetes, obesity, hypertension, and diet (Barnes & Yaffe, 2011; Baumgart et al. 2015; Bennett et al. 2014; Beydoun et al. 2014; Clare et al. 2017; Di Marco et al. 2014; Kim et al. 2012; Plassman et al. 2010). Cognitive reserve theory suggests that the maintenance

of cognitive function is likely supported by the synergistic effect of multiple lifestyle factors and experiences across the lifespan (Fratiglioni et al. 2004; Lee, Kim & Back, 2009; Rizzuto & Fratiglioni, 2014; Stern, 2002, 2003, 2009, 2012). Therefore, interventions that target a range of factors across diverse environments may be most effective in maintaining cognitive function. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER: Kivipelto et al. 2013; Ngandu et al. 2015) is a multi-domain intervention in which participants engage in exercise training, cognitive training, nutritional guidance, social stimulation, and monitoring of metabolic and cardiovascular risk factors, in group and one-to-one sessions. Findings suggest that the intervention could help to improve or maintain cognitive function (Ngandu et al. 2015). Other multi-domain trials have reported similar successes (Andrieu et al. 2017; Beishuizen et al. 2017; Coley et al. 2017; de Souto Barreto, Andrieu, Rolland & Vellas, 2018). FINGER targets people considered at risk of cognitive decline and therefore the success of such interventions may differ for those who have a lower risk. Despite this, current theoretical and empirical evidence implies that targeting multiple, rather than individual, lifestyle factors may be the most effective approach for preventing poor cognitive function.

Although the findings from Chapters 4 and 5 implicate that social isolation is associated with poor cognitive function, the findings generate further questions. Some of the unexplained variance in Chapters 4 and 5 can be explained by other modifiable lifestyle factors that contribute to cognitive function as discussed. However there are other factors that may account for this variance, such as mental health, or circumstances such as living situation (Baumgart et al. 2015; Bowling & Stafford, 2007; Rosso et al. 2013; Wen et al. 2006). The next research question aimed to consider these factors, specifically in relation to groups of older people that may be more at risk of social isolation.

9.4 Research question three

Does the association between social isolation, cognitive reserve, and cognitive function differ for older people who are more at risk of social isolation?

Chapters 6 and 7 use the same model as Chapter 5 to consider how the association between social isolation, cognitive reserve, and cognitive function may differ for people with depression or anxiety and people who live alone, compared to 'healthy' community dwelling older people (Chapter 5). These associations have not previously been considered in people with depression or anxiety, and previous findings for people who live alone are conflicting and do not consider cognitive reserve (Conroy et al. 2010; Gow et al. 2007; Gow et al. 2013; Mahoney et al. 2000; van Gelder et al. 2006; Wang et al. 2015; Yaffe et al. 2009; Yeh & Liu, 2003); hence these chapters extend existing knowledge.

Consistent with previous literature, Chapter 6 found that people with depression or anxiety were more at risk of social isolation and feelings of loneliness compared to people without depression or anxiety (Cacioppo & Hawkley, 2009; Luanaigh & Lawlor, 2008) but had the same frequency of contact with family and friends. This may be explained by the tendency for people with depression to recall negative information and to hold more negative expectations for social interactions, which may increase social isolation and feelings of loneliness, despite having opportunities to engage in social contact (Cacioppo & Hawkley, 2009; Granerud & Severinsson, 2006; Luanaigh & Lawlor, 2008). Social isolation was associated with poor cognitive function at baseline but not two year follow-up in people with symptoms of depression or anxiety. The difference in findings at baseline and follow-up may be explained by the variance in mood-related symptoms. Over half of the people who were experiencing symptoms of depression or anxiety at baseline were no longer experiencing symptoms at two year follow-up. This is not surprising and reflects the transient nature of mood-related symptoms and the robust finding that cognitive function can improve following the reduction of such symptoms (Aggarwal et al. 2017; Airaksinen et al. 2006; Biringer et al. 2005; Gruber et al. 2007; Nakano et al. 2008; Pietrzak et al. 2012; Potvin et al. 2011; Rock et al. 2014; Yochim et al. 2013). Previous work has estimated that a reduction in the prevalence of depression by up to 10% could result in 68,000 fewer cases of Alzheimer's disease in the USA, and up to 326,000 fewer cases worldwide (Barnes & Yaffe, 2011). These findings suggest that interventions to reduce symptoms of depression or anxiety may be most beneficial to improve cognitive function in the first instance (Bhalla et al. 2006). Interventions to enhance social connections or multi-domain interventions which target other modifiable lifestyle factors may be more effective once mood-related symptoms have been alleviated.

There are several psychological approaches that can be used to reduce mood-related symptoms in later life, such as cognitive behavioural therapy (Coon & Thompson, 2003; Gould, Coulson & Howard, 2012; Laidlaw et al. 2008; Pinquart, Duberstein & Lyness, 2007; Wilson, Mottram & Vassilas, 2008), interpersonal therapy (Reynolds et al. 1999; Reynolds et al. 2006; van Schaik et al. 2006), problem solving therapy (Areán et al. 2010; Areán, Hegel, Vannoy, Fan & Unuzter, 2008; Gellis et al. 2008; Malouff, Thorsteinsson & Schutte, 2007), and reminiscence and life review (Bohlmeijer, Smit & Cuijpers, 2003; Korte, Bohlmeijer, Cappeliez, Smit & Westerhof, 2012; Pinquart & Forstmeier, 2012). There are also some psychosocial approaches to reducing symptoms of depression. Evidence suggests that social isolation precipitates and contributes to the maintenance of symptoms of depression (Cacioppo et al. 2010; Trivedi et al. 2005). Interventions to facilitate group social interaction have been found to reduce symptoms of depression (Cruwys et al. 2013; Cruwys et al. 2014; Gleibs et al. 2011; Houston, Cooper & Ford, 2002; Vanderhorst & McLaren, 2005). However,

interventions that promote the development of friendships or aim to enhance one-to-one contact have not been effective (Cattan, White, Bond & Learmouth, 2005; Perese & Wolf, 2005). Successful group interventions have emphasised the importance of being able to identify collectively with others in a social context. Indeed, it has been reported that social identification in a group situation is a better predictor of reduced symptoms of depression than social contact alone, and hence group interventions may be most effective (Cruwys, Haslam, Dingle, Haslam & Jetten, 2014; Sani, Herrera, Wakefield, Boroch & Gulyas, 2012), and may benefit cognitive function. The findings from Chapter 6 extend existing literature by suggesting that the association between social isolation and cognitive function is different for people with depression or anxiety compared to 'healthy' older people and that reducing mood-related symptoms may benefit cognitive function.

In line with previous empirical work, Chapter 7 found that people living alone in later life were at greater risk of social isolation and feelings of loneliness than those living with others (de Jong Gierveld, 2003; de Jong Gierveld & Havens, 2004; Kobayashi et al. 2009; Iliffe et al. 2007; Kharicha et al. 2007; Newall et al. 2014; Victor et al. 2005). Living alone was not associated with cognitive function at baseline or two year follow-up. The finding that living alone is associated with poor cognitive function at baseline is consistent with previous findings (Conroy et al. 2010; Gow et al. 2013; Mahoney et al. 2000; Wang et al. 2015; Yeh & Liu, 2003) but the finding at follow-up is not (van Gelder et al. 2006; Yaffe et al. 2009). These studies have a follow-up period of eight (Yaffe et al. 2009) to ten (van Gelder et al. 2006) years which is much longer than the two year follow-up in CFAS-Wales. The negative effects of living alone on cognitive function may manifest over longer follow-up durations. However, findings from Chapter 7 suggest that living alone may not be detrimental to cognitive function, at least over a relatively short period. These findings have positive implications and challenge the assumption that living alone may be less cognitively stimulating (Kharicha et al. 2007). The findings also suggest that social interaction and ties with the individual(s) with whom an older person resides are likely insufficient to influence cognitive function. It is plausible that larger and more complex social networks, frequent social interaction and engagement with others, and participation in activities in the wider community are more beneficial to cognitive function than living situation alone (Berkman, 2000; Berkman & Glass, 2000).

It has been suggested that being alone or feeling alone, rather than living alone, enhances risk of poor cognitive function (Berkman, 2000; Feng et al. 2014; Gow et al. 2007; Mousavi-Nasab et al. 2012). Being unmarried has been found to be a stronger predictor of poor cognitive function than living alone (van Gelder et al. 2006). Findings from Chapter 7 suggest that marital status and feelings of loneliness were associated with poorer cognitive function at baseline, but these factors did not predict change in cognitive score at two year follow-up. Age, social isolation, and impairment in ADLs

were the only factors associated with poor cognitive function at baseline and cognitive change at two year follow-up. This further supports the importance of social isolation in later life and its association with poor cognitive function, and emphasises the benefits of frequent interaction with a wide range of social contacts and engagement in social activity (DiNapoli et al. 2014; Holwerda et al. 2012; Shankar et al. 2013; Wilson, Krueger et al. 2007).

Chapters 6 and 7 found that cognitive reserve did not moderate the association between social isolation and cognitive function in people with depression or anxiety, or the association between living alone and cognitive function. This reflects that other mechanisms may be important in explaining the relationships between social isolation and cognitive function. It has been proposed that social networks can facilitate the transmission of information and behaviours that promote good health (Berkman & Glass, 2000; Kim et al. 2015; Masic et al. 2012). Observing others engaging in healthy lifestyles may encourage positive lifestyle choices and behaviours that maintain good health through informal social control (Berkman, 1985; Berkman & Glass, 2000; Cassel, 1976). Having good social connections may evoke positive psychological states of increased self-worth, sense of belonging, security, and purpose which may increase motivation for self-care (e.g. regular exercise, not smoking, and moderate alcohol consumption). Subsequently, this may alleviate negative psychological states, increase wellbeing and perceived quality of life, and hence indirectly benefit cognitive function (Cohen et al. 2000). Alternatively, good social connections may enhance an individual's perception of the availability of adequate social support. This may reduce the emotional, behavioural, and physiological response to adverse life events and reduce stress, which has also been associated with poor cognitive function (Cacioppo & Hawkley, 2009; Li et al. 1999; Wilson et al. 2003). Finally, it is possible that good social connections indicate a healthy lifestyle in general, which may be linked to better cognitive function (Fratiglioni et al. 2004). These mechanisms offer an alternative explanation for how good social connections may benefit cognitive function.

The findings from Chapters 6 and 7 have demonstrated that other factors, such as depression or anxiety, may influence the association between social isolation and cognitive function. Satisfaction with social contact is another factor that may influence these associations. The scoping review (Chapter 3) reported that measures of social isolation are typically based on structural indicators and categorise people as isolated or not using cut-scores. This does not allow for consideration of individual differences in preference for level of social contact. This may be particularly important for people with depression who may be more likely to interpret social interactions negatively and may perceive a lower level of social contact to be optimal (Angermeyer & Matschinger, 2003; Cacioppo & Hawkley, 2009; Granerud & Severinsson, 2006; Kashdan & Roberts, 2007; Oliveira et al. 2015; Wai & Bond, 2004). The next research question aimed to address these issues.

9.5 Research question four

Are structural measures of social isolation consistent with measures of satisfaction with social contact and what is their association with cognitive function in later life?

Chapter 8 is novel in that it assesses differences in how people respond to two types of measure of social connection and considers the associations of these measures with cognitive function. Findings suggest that scores on a structural measure of social isolation and a measure of satisfaction with social contact were mostly congruent. This is positive and suggests that measures that classify people as isolated or not seem to reflect how people feel in terms of their satisfaction with social contact. However, there was a small number of people with incongruent scores. Some people were classified as not isolated by a structural measure of social isolation, but were dissatisfied with their level of social contact. Over half of these people had clinically relevant symptoms of depression. People with depression are more likely to interpret and perceive their social interactions negatively (Bourke, Douglas & Porter, 2010; Ehnvall et al. 2014; Platt, Kadosh & Lau, 2013; Tse & Bond, 2004). Therefore, these findings can be accounted for by current symptoms of depression experienced by people in this group. A second group of people were classified as isolated by a structural measure of social isolation, but indicated they were satisfied with this level of social contact. These people have little social contact but do not perceive this negatively. Few of these people had clinically relevant symptoms of depression.

There were differences observed in the prediction of cognitive function between the structural measure of social isolation and the measure of satisfaction with social contact. There was no association between the structural measure of social isolation and poor cognitive function after controlling for depression, age, gender, and educational level. This is consistent with some previous work (DiNapoli et al. 2014; Elwood et al. 1999; Glei et al. 2005; Golden et al. 2009; O'Luanaigh et al. 2012; Paúl et al. 2010; Simning et al, 2014) but inconsistent with other work (DiNapoli et al. 2014), including findings presented in Chapter 5. Dissatisfaction with social contact was associated with poorer scores on measures of verbal and spatial working memory after controlling for depression, age, gender, and educational level. This is consistent with previous work (Boss et al. 2015; Wilson, Krueger et al. 2007) and suggests that the way individuals' feel about their social contact is important and may be associated with cognitive function and is not accounted for solely by depression.

These findings have implications for the assessment of social isolation in later life. After controlling for depression, satisfaction with social contact was a better predictor of poor cognitive function than the structural measure of social isolation. This suggests that depression is not the only factor that

can account for the associations with poor cognitive function and that satisfaction with social contact should be considered alongside structural measures of isolation. Considering satisfaction with social contact may increase the reliability and validity of measures of social isolation. This argument is further supported by the finding that a small group of people indicated they were satisfied with less social contact than is assumed appropriate in structural measures of isolation. This also reflects that it is important to consider individual differences in satisfaction with social contact. The needs of this group may also differ in terms of interventions. Attempting to increase the level of social contact may be detrimental to this group of people who are content with little social contact. This supports the recent emphasis on the need to tailor interventions to suit the needs and circumstances of individuals (Andrieu, Coley, Lovestone, Aisen & Vellas, 2015; Livingston et al. 2017; Winblad et al. 2016).

9.6 Methodological considerations

Researching the association between social connections, cognitive reserve, and cognitive function is associated with a number of methodological challenges. These issues should be considered when interpreting the findings presented in this thesis.

Little cognitive change was observed over two years across participants in CFAS-Wales and some participants' CAMCOG scores improved at follow-up. This may limit the validity of follow-up analyses that aim to assess how cognitive function may change in relation to social isolation as follow-up analyses may replicate the cross-sectional findings. There are several possible explanations for the limited cognitive change observed. The follow-up period of two years may be insufficient to observe cognitive change and examine these associations. Studies with a longer follow-up duration may identify a larger number of people who begin to decline in cognitive function and hence produce more reliable results.

Practice effects may account for the limited cognitive change observed in CFAS-Wales. It is possible that participants have undergone cognitive testing for medical reasons or as part of other research assessments. Repeated testing may lead individuals to improve or maintain their performance in cognitive measures, despite cognitive decline (Abner et al. 2012; Ferrer, Salthouse, Stewart & Schwartz, 2004; Salthouse, 2010b). This criticism is also relevant to participants in the PROTECT study who complete each cognitive measure three times within seven days at each annual assessment. The average score of the three trials represents the participant's cognitive score. The advantage of this approach is that participants can familiarise themselves with the measure and receive a cognitive score that reflects their cognitive ability rather than their ability to complete a cognitive measure. The measure is computerised meaning that the stimuli for measures are changed

slightly on each test; for example, cues are in different positions or different visual stimuli are presented, but each are of equal difficulty (Goldberg et al. 2015; Wesnes & Pincock, 2002). It could be argued that this repeated testing in PROTECT increases practice effects and familiarity with the measure and reflects ability to complete a cognitive measure rather than actual level of cognitive function.

People who were included in baseline analyses but excluded at two year follow-up due to missing data in CFAS-Wales tended to be less healthy (i.e. older, poorer CAMCOG scores, fewer years of education, less cognitive activity, lower occupational complexity, lower cognitive reserve score, more socially isolated, poorer eyesight, and impairments in ADLs) than those included at follow-up. Those in poorest health are no longer accounted for in follow-up analyses and so these analyses may fail to represent the original study group which was representative of the wider population, including those in poor health (van Beijsterveldt et al. 2002). This may account for the limited cognitive change that was observed in CFAS-Wales. This reflects how those in poorer health are less likely to complete study measures and so are excluded from analyses which gives a selected sample of high functioning individuals.

One limitation of most studies of ageing and cognitive function that is also relevant to CFAS-Wales and PROTECT is that many people decline to take part as they are either too healthy and do not have the time to participate, or are too ill and so are not able to participate (Minder, Müller, Gillmann, Beck & Stuck, 2002). People with limited financial or social support, or with functional limitations, are less likely to participate due to practical difficulties (Ford et al. 2008). People who are most extremely isolated are also underrepresented in research due to having few social ties and a lack of integration with the wider community (Kelly et al. 2017). CFAS-Wales attempts to overcome this selection bias by sampling participants from GP registers to capture a range of people who are in good and poor health. Furthermore, assessments were conducted at the participant's home which may overcome obstacles relating to financial, social, and functional difficulties. This also ensures that people who are most extremely isolated are included and may increase the generalizability and validity of findings. Conversely, participants in PROTECT are a self-selected sample of volunteers and hence are more likely to be engaged in social and community activities. The cohort overall is skewed and over-represents white, highly educated, women, meaning findings may be less generalizable.

It is possible that associations between social isolation and cognitive function reported in this thesis are due to reverse causation (Berger et al. 1998; Cloutier et al. 2015; Masliah & Salmon, 2016; Small et al. 2000). People with cognitive impairment or dementia in CFAS-Wales were excluded from analyses in Chapters 5–7 to reduce the risk of reverse causation. This approach can be criticised as

early symptoms of cognitive impairment and dementia can be missed by neuropsychological tests and therefore people in studies of healthy ageing may be misclassified as cognitively healthy during study enrolment (Phillipson et al. 2015; Ross et al. 1997). The follow-up duration in CFAS-Wales was two years. This may be insufficient to eliminate the possibility of reverse causation as underlying symptoms of cognitive impairment may present between five (Gauthier et al. 2006) and nine (Amieva et al. 2005; Mahncke et al. 2006) years prior to symptoms being detected by cognitive measures.

Furthermore, a cut-score of ≤25 was used on the MMSE to exclude people with baseline cognitive impairment in CFAS-Wales analyses. MMSE scores are highly influenced by age, educational level, and cultural factors (Black et al. 1999; Ng et al. 2007). Cut-scores are often validated within samples of a specific age (Kahle-Wrobleski, Corrada, Li & Kawas, 2007), educational level (Lezak, 2004; Lezak, Howieson, Bigler & Tranel, 2012; O'Bryant et al., 2008), or ethnic group (Cullen et al., 2005; Fillenbaum, Heyman, Williams, Prosnitz & Burchett, 1990; Rait et al., 2000), and therefore may not adequately reflect cognitive function across different groups. For example, people with older age, fewer years of education, or non-white ethnicity may achieve lower MMSE scores (Lorentz, Scanlan & Borson, 2002) but these scores may represent good cognitive function for this group of people. Using a cut-score of ≤25 may exclude some people at baseline with good cognitive function relative to their age, educational level, and ethnicity. This may reduce the generalizability of findings to these groups of people.

Reverse causation is also problematic in the PROTECT analyses. People with cognitive impairment were not excluded from analyses as the cognitive measures used do not have validated cut-scores to indicate impairment. The study was cross-sectional in design and many participants completed measures of cognitive function and depression up to four months prior to completing social measures. This was due to the way in which the PROTECT study and the social connections study were set up. Participants were enrolled to PROTECT and completed baseline (wave one) assessments between November 2015 to August 2016. Wave three annual assessments began in November 2017 and are ongoing until August 2018. Participants are invited to complete follow-up assessments annually on the date they completed their baseline assessment. Data collection for the social connections study began and was completed in February 2018 and hence could have been completed up to four months after wave three assessment. It is possible that people may have experienced a change in cognitive or mental health during this time which may have influenced responses to the social connections questionnaires. However it is not possible to determine this from the data available.

The approach to assessing cognitive reserve is a strength of this thesis. There is a growing argument to support the view that cognitive reserve is a fluid concept that is not fixed by one experience or time period (Nucci et al., 2012; Richards & Deary, 2005; Richards & Sacker, 2003; Rodríguez et al. 2011; Stern, 2009; Tucker & Stern, 2011; Whalley, Dick & McNeill, 2006). Cognitive reserve may be more accurately assessed by measures that combine multiple proxy measures of reserve rather than considering proxy measures individually. The cognitive reserve measure in this thesis was comprehensive and included indicators of early-, mid-, and late- life reserve meaning lifestyle experiences that build reserve are captured at different points in the lifespan. Scores were weighted to ensure that each proxy contributed equally to the overall score (Opdebeeck et al. 2018; Tucker & Stern, 2011; Valenzuela et al. 2011). The indicators included are not exhaustive and there are additional indicators that may contribute to reserve, such as physical or social activity (Stern, 2009). Social activity was not included in the cognitive reserve measure as social isolation and related social concepts were a key focus of the thesis and so including this in the cognitive reserve score would have confounded analyses.

An additional methodological consideration is that depression and anxiety were assessed in CFAS-Wales using the AGECAT (Copeland et al. 1986). This measure was selected as MRC-CFAS and CFAS-II also use this measure to assess dementia, depression, and anxiety. Using this approach in CFAS-Wales enables direct comparison across the CFAS studies to consider changes in the prevalence of these conditions since MRC-CFAS began in 1991. The algorithm assigns one diagnosis of either dementia, depression, anxiety, or no diagnosis based on the symptoms the participant presents most for. Symptoms of depression and anxiety are measured within the same cluster of symptoms and the algorithm may give preference for a classification of depression than anxiety. Many symptoms of depression and anxiety overlap and are comorbid meaning the number of people with anxiety may be underestimated in CFAS-Wales (Beaudreau & O'hara, 2008). The AGECAT was designed over 30 years ago and it is possible that the worries or concerns of older people have changed. Updated measures may be more appropriate to gain a valid and reliable representation of depression and anxiety in later life.

The assessment of social connections within the literature and in this thesis presents another limitation. Measures of social connections often do not consider individuals' satisfaction with their level of social contact, networks, and activity. This thesis has attempted to address this in Chapter 8. However, the quality of social relationships and interactions is another important aspect that may influence cognitive function. It was not possible to address this in the thesis as there were no questions in CFAS-Wales or PROTECT that considered the quality of relationships and interactions. The quality of social interactions may vary greatly across individuals. For example, when attending

social groups, or talking to family, friends, or neighbours, it is possible to take either an active or passive role. People who are actively engaged in conversations or activities with others may be more likely to gain cognitive stimulation that may benefit cognitive function. In contrast, people who take a passive role in social interaction may not gain this level of stimulation and hence social interaction may not benefit cognitive function to the same degree. This may be influenced by other factors such as personality or preference for social contact. Introverts, for example, may prefer to be passive in social interactions, whereas extraverts may prefer to take an active role (Bolger & Eckenride, 1991; McHugh Power et al. 2017; Tov et al. 2016). These factors may account for the variance in findings across studies that do not consider the quality of interaction, personality, or preference for social contact.

An additional limitation relating to the quality of social interactions is that the measures in this thesis (as well as most other measures of social connections across the literature) assume that social interactions are positive. It is possible that some interactions may be negative and characterised by a high level of criticism, frequent disagreements, distress (e.g. resentment, sadness, or shame), interference or an invasion of privacy, failing to provide promised help, or discouraging the expression of emotion (Hughes et al., 2008; Lincoln, 2000; Seeman et al., 2001; Wilson et al. 2015; Xu et al., 2015). Negative interactions may have a different impact on cognitive function than positive interactions (Lincoln, 2000). The few studies that have considered negative interactions report conflicting findings. One study reported that more frequent negative social interactions were associated with a higher incidence of MCI and more rapid cognitive decline. The authors suggest that chronic negative social interactions may enhance stress in everyday life and contribute to cognitive decline (Wilson et al. 2015). Conversely, several studies have reported that frequent negative social interactions may benefit cognitive function as they require greater cognitive capacity to process and respond to, and hence may enhance cognitive reserve and benefit cognitive function (Hughes et al., 2008; Seeman et al., 2001; Xu et al., 2015).

9.7 Future research directions

The work presented in this thesis has contributed to our understanding of the associations between social isolation, cognitive reserve, and cognitive function. Social connections seem to be an important factor associated with cognitive function in later life. The findings and consideration of existing literature also raise some further questions and point to directions for future research.

Future work may consider additional groups of people who may be at greater risk of social isolation. For example, people who live in remote rural locations, with poor transportation links, and limited opportunities for social engagement in the community may be at greater risk of isolation and hence

poor cognitive function (Levasseur et al. 2015). It may be interesting to consider people in poor health, for example those who are frail or who have a chronic health condition, as symptoms may result in social isolation and also poor cognitive function. In addition, nursing home placement is associated with a change in living environment and in particular with reduced social interaction with family and friends, and a lack of engagement with the wider community (Drageset, Kirkevold & Espehaug, 2011). These changes in social relationships may influence cognitive function for people who transition from living in the community to institutional care.

It would be interesting to assess the associations between structural measures of social isolation, satisfaction with social contact, and cognitive function in longitudinal data. It may be useful to consider the associations in additional domains of cognitive function, such as executive function which may be more age related (Deary et al. 2009; Ferreira et al. 2015; Gunstad et al. 2006; Huntley et al. 2018) or global measures of cognitive function. Further work may examine people who are classified as isolated by structural measures of isolation but are satisfied with this level of social contact. Understanding the characteristics of this group and why this level of contact is sufficient may enhance our understanding of how the needs of these people differ to those who require more social contact. It may also be useful to consider people who feel dissatisfied with their social contact and explore further reasons for this and how this may have a negative impact on cognitive function. It may be that people who are dissatisfied with social contact are in poorer health, less mobile, older, or living in rural areas, or areas with poor transportation, or limited opportunities for contact, and hence are unable to be as socially engaged as they would like. These factors may be related to poor cognitive function and hence these associations may be complex (Davis et al. 2015; Frisoni et al. 2000; Mattos et al. 2017; Roberts et al. 2015; Tinetti et al. 2011). Further insight into individual differences in preference for social contact can inform intervention studies and suggest approaches to tailor interventions to the needs of individuals (Andrieu et al. 2015; Livingston et al. 2017; Winblad et al. 2016).

As discussed in the methodological considerations section, there has been little research that assesses the impact of negative social interactions or the quality of social interactions on cognitive function in later life. These may be important factors associated with cognitive function and warrant further investigation (Santini et al. 2015). Accounting for quality may also address some of the variation in findings relating to cognitive function across studies. People who are more actively engaged in social interactions may benefit more than those who take a passive role (Cruwys et al. 2014). Likewise, frequent negative social interactions may be beneficial to cognitive function based on the cognitive stimulation required to process and respond to these interactions, or may be harmful due to the negative emotions and stress associated with such interactions, which has also

been associated with poor cognitive function (Cacioppo & Hawkley, 2009; Li et al. 1999; Lincoln, 2000; Wilson et al. 2003).

This thesis has considered the role of cognitive reserve in the associations between social connections and cognitive function. Future work may consider the role of brain reserve and the complex interactions between cognitive reserve and brain reserve capacity. The variation in cognitive function across individuals assumed by differences in level of cognitive reserve must have a physiologic or neural basis (Stern, 2009). The active model of cognitive reserve theory assumes that experiences across the lifespan can build reserve and influence the variability in an individual's resilience against brain pathology (Stern, 2009, 2012). The passive model of brain reserve suggests that there are differences in an individual's brain size and quantity of neural substrate and networks (Satz, 1993; Stern, 2002). Presumably, the ability of an individual to utilise or build their cognitive reserve depends on their level of brain reserve at the anatomical level (Stern, 2009). For example, an individual with high cognitive reserve, but low brain reserve, may have less capacity to actively compensate for brain pathology using their cognitive reserve, than an individual with higher brain reserve. This is further supported by research which suggests that individuals with a higher IQ (Kesler, Adams, Blasey & Bigler, 2003; Pietschnig, Penke, Wicherts, Zeiler & Voracek, 2015; Willerman, Schultz, Rutledge & Bigler, 1991), who participate in cognitively stimulating activities (Köbe et al. 2016; Schultz et al. 2015), and who engage in frequent social activity and have wider social networks (Bickart et al. 2011; Bickart et al. 2012; Hampton et al. 2016; Kanai et al. 2011; Lewis et al. 2011; Powell et al. 2012; Von Der Heide et al. 2014; Zou et al. 2016) have a larger brain volume. Evidence also suggests that exercise and stimulating environments can promote neurogenesis, increase neuronal plasticity, and enhance resistance to cell death (Brown et al. 2003; Van Praag, Shubert, Zhao & Gage, 2005). It is also suggested that an enriched environment may directly slow or prevent the accumulation of Alzheimer's disease pathology (Lazarov et al. 2005). Together, this evidence suggests that the interactions between brain reserve capacity and cognitive reserve are complex. It was beyond the scope of this thesis to investigate how brain reserve and cognitive reserve may interact to enable individuals to maintain good cognitive function, but this ought to be investigated in future work.

9.8 Implications of the research findings

The findings from this thesis have suggested that social isolation is associated with poor cognitive function in later life. This suggests that being socially active and engaged in later life is positive and may build cognitive reserve and contribute to maintained cognitive function.

The finding that there was limited cognitive change in a sample of community dwelling older people in CFAS-Wales is positive and suggests that many older people are maintaining cognitive function, at least over a relatively short period. Previous analyses comparing the prevalence of dementia in MRC-CFAS and CFAS-II suggest a reduction in dementia prevalence by 24% from 1991 to 2011. This may have been unexpected given the rise in population ageing (Matthews et al. 2013). Subsequent comparative analyses confirm that several aspects of lifestyle have improved, including better overall physical health and more years of education (Jagger et al. 2016). These improvements in health and lifestyle may have enhanced cognitive reserve and benefitted cognitive function (Stern 2002, 2009). Hence, targeting modifiable lifestyle factors known to be associated with increased risk of poor cognitive function may help to prevent or delay onset (Baumgart et al 2015; Matthews et al. 2013; Wu, Fratiglioni et al. 2016; Wu, Teale et al. 2016).

This prevalence reduction is limited to Western countries and the proportion of older people with poor cognitive function and dementia continues to rise in low and middle income countries (Prince et al. 2015). It is probable that the reduction in prevalence observed in Western countries is due to policies that promote awareness of the benefits of a healthy lifestyle. Several policymakers in the UK and globally emphasise the importance of regular social contact and frequent engagement in social activities to promote healthy ageing and the maintenance of cognitive function. These policies also emphasise the importance of a healthy lifestyle in general, including regular exercise, moderate alcohol consumption, not smoking, engaging in cognitively stimulating activity, and maintaining a healthy diet and weight (Age UK, 2011; Global Council on Brain Health, 2017; National Institute for Health and Care Excellence, 2015; NHS England, 2015; World Health Organization, 2015).

In line with policy recommendations and the findings of the thesis, older people should maintain socially active to promote healthy ageing and maintain cognitive function (Fratiglioni et al. 2004). This could be achieved by encouraging older people to make a more conscious effort to increase the frequency of social contact with friends and family, either through face-to-face meetings or over the phone. Being integrated with the wider community and engaging in a range of social activities, such as joining a social or sports club, volunteering, or taking group trips may also promote a socially active lifestyle. This may be difficult for some people to achieve, including those in poor physical, mental, or cognitive health, those with limited mobility, and those living in rural locations or areas with poor transportation links (Bordone & Weber, 2012; Bowling & Stafford, 2007; Davis et al. 2015; Frisoni et al. 2000; Mattos et al. 2017; Roberts et al. 2015; Rosso et al. 2013; Tinetti et al. 2011; Wen et al. 2006). Future policies or interventions should consider how best to engage people who may face challenges with being socially connected. Findings from this thesis and previous empirical work emphasise the importance of being satisfied with the level of social contact achieved, as this may be

associated with cognitive outcomes (DiNapoli et al. 2014; Fratiglioni et al. 2000; Gow et al. 2013; Hughes et al. 2008; Yeh & Liu, 2003). Hence, individuals should be free to engage in a level of social contact that is desirable and optimal for their own preferences and personal circumstances.

Interventions to increase social contact in older people have shown some benefit to cognitive function (Dodge et al. 2015; Mortimer et al. 2012; Pitkala et al, 2011). However, cognitive function is most likely to be benefitted by implementing a healthy lifestyle that encompasses a range of protective factors. For example, an individual who engages in regular social, physical, and cognitive activity, has a healthy diet, consumes a moderate amount of alcohol, does not smoke, and is in good physical health is more likely to build cognitive reserve and maintain cognitive function. Conversely, an individual who has a lifestyle that encompasses few protective factors is likely to build less reserve and may be at greater risk for poor cognitive function. Older people need to maintain a healthy lifestyle in general if they are to be protected against poor cognitive function. Indeed, many multi-domain interventions and national policies with recommendations to prevent poor cognitive function emphasise the need to enhance a range of protective lifestyle factors (National Institute for Health and Care Excellence, 2015; Ngandu et al. 2015). Many of these prevention interventions and policies focus on factors associated with cardiovascular health (e.g. physical activity, obesity, and smoking) and fail to incorporate other lifestyle factors such as cognitive or social activity (Collins, Silarova & Clare, in press; Department of Health, 2009). Neglecting these additional lifestyle factors that may protect against poor cognitive function is problematic and limits our understanding of how these factors may further promote success in multi-domain interventions. Likewise, policies ought to identify the full range of lifestyle factors and provide specific recommendations to help people implement a healthy lifestyle to reduce their risk of poor cognitive function (Collins et al. in press). This is particularly relevant give that findings presented in this thesis along with previous empirical work suggest that social isolation is associated with an increased risk of poor cognitive function in later life (DiNapoli et al. 2014; Holwerda et al. 2012; Kuiper et al. 2016; Shankar et al. 2013; Wilson, Krueger et al. 2007).

9.9 Conclusion

Older people form an increasing proportion of the population and identifying modifiable lifestyle factors that contribute to the maintenance of cognitive function is of great significance to policymakers and older people alike. The results of this thesis contribute to the growing body of evidence showing that good social connections are an important factor associated with the maintenance of cognitive function in later life. Findings suggest that social isolation is associated with poor cognitive function and that cognitive reserve moderates this association in older people without cognitive impairment, dementia, or depression. This thesis has considered people who may

be more vulnerable to social isolation. For people with depression or anxiety, findings suggest that mood-related symptoms may have stronger associations than social connections with cognitive function. The findings regarding living situation are positive and suggest that people who live alone are at no greater risk of poor cognitive function than those who live with others, at least over a two year period. Findings also have implications for the assessment of social connections and suggest that greater consistency across studies would be helpful in order to delineate the nature of the association between social connections and cognitive function. Individuals' perceptions of their social contexts are important and should be considered alongside structural indicators. Overall, findings suggest that encouraging older people to engage in frequent social contact and social activities is beneficial to cognitive function. It is important to acknowledge individual differences in preference for social contact in later life and this may help to clarify the nature of the associations between social connections and cognitive function in future work.

References

Aartsen, M. J., Smits, C. H., van Tilburg, T., Knipscheer, K. C., & Deeg, D. J. (2002). Activity in older adults: cause or consequence of cognitive functioning? A longitudinal study on everyday activities and cognitive performance in older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 57,* 153-162.

Aartsen, M. J., van Tilburg, T., Smits, C. H., & Knipscheer, K. C. (2004). A longitudinal study of the impact of physical and cognitive decline on the personal network in old age. *Journal of Social and Personal Relationships, 21,* 249-266.

Aartsen, M. J., van Tilburg, T., Smits, C. H., Comijs, H. C., & Knipscheer, K. C. (2005). Does widowhood affect memory performance of older persons? *Psychological Medicine, 35*, 217-226.

Abner, E. L., Dennis, B. C., Mathews, M. J., Mendiondo, M. S., Caban-Holt, A., Kryscio, R. J., Scmitt, F. A., & Crowley, J. J. (2012). Practice effects in a longitudinal, multi-center Alzheimer's disease prevention clinical trial. *Trials, 13*, 217.

Achenbaum, W. A., & Bengtson, V. L. (1994). Re-engaging the disengagement theory of aging: On the history and assessment of theory development in gerontology. *The Gerontologist, 34*, 756-763.

Adams, K. B., Leibbrandt, S., & Moon, H. (2011). A critical review of the literature on social and leisure activity and wellbeing in later life. *Ageing and Society, 31*, 683-712.

Aerts, L., Heffernan, M., Kochan, N. A., Crawford, J. D., Draper, B., Trollor, J. N., Sachdev, P. S., & Brodaty, H. (2017). Effects of MCI subtype and reversion on progression to dementia in a community sample. *Neurology, 88*, 2225-2232.

Age UK. (2011). Healthy ageing evidence review. Accessed 01/09/2018: https://www.ageuk.org.uk/globalassets/age-uk/documents/reports-and-publications/reports-and-briefings/health--wellbeing/rb_april11_evidence_review_healthy_ageing.pdf

Aggarwal, R., Kunik, M., & Asghar-Ali, A. (2017). Anxiety in later life. *Focus, 15,* 157-161.

Airaksinen, E., Wahlin, Å., Larsson, M., & Forsell, Y. (2006). Cognitive and social functioning in recovery from depression: results from a population-based three-year follow-up. *Journal of Affective Disorders, 96,* 107-110.

Albert, M. S., Jones, K., Savage, C. R., Berkman, L., Seeman, T., Blazer, D., & Rowe, J. W. (1995). Predictors of cognitive change in older persons: MacArthur studies of successful aging. *Psychology and Aging, 10*, 578-589.

Alexopoulos, G. S. (2005). Depression in the elderly. *The Lancet, 365,* 1961-1970.

Alexopoulos, G. S., Meyers, B. S., Young, R. C., Mattis, S., & Kakuma, T. (1993). The course of geriatric depression with "reversible dementia": a controlled study. *American Journal of Psychiatry, 150,* 1693-1693.

Alexopoulos, G. S., Young, R. C., & Meyers, B. S. (1993). Geriatric depression: age of onset and dementia. *Biological Psychiatry, 34*, 141-145.

Almeida, O. P., Alfonso, H., Hankey, G. J., & Flicker, L. (2010). Depression, antidepressant use and mortality in later life: the Health in Men Study. *PLoS One, 5*, e11266.

Altman, D. G. (2014). The time has come to register diagnostic and prognostic research. *Clinical Chemistry, 60,* 580-582.

Altman, D. G., & Bland, M. B. (2011). How to obtain the p value from a confidence interval. *British Medical Journal, 343*, d2304.

American Psychiatric Association (1987). *Diagnostic and statistical manual of mental disorders* (3rd edition – revised: DSM-III-R). Washington, DC, USA: American Psychiatric Association Publications.

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders* (4th edition: DSM-IV). Washington, DC, USA: American Psychiatric Association Publications.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th edition: DSM-5). Washington, DC, USA: American Psychiatric Association Publications.

Amieva, H., Jacqmin-Gadda, H., Orgogozo, J. M., Le Carret, N., Helmer, C., Letenneur, L., Barberger-Gateau, P., Fabrigoule, C., & Dartigues, J. F. (2005). The 9 year cognitive decline before dementia of the Alzheimer type: a prospective population-based study. *Brain, 128*, 1093-1101.

Andreescu, C., Teverovsky, E., Fu, B., Hughes, T. F., Chang, C. C. H., & Ganguli, M. (2014). Old worries and new anxieties: behavioral symptoms and mild cognitive impairment in a population study. *The American Journal of Geriatric Psychiatry, 22,* 274-284.

Andrew, M. K., & Rockwood, K. (2010). Social vulnerability predicts cognitive decline in a prospective cohort of older Canadians. *Alzheimer's & Dementia, 6*, 319-325.

Andrieu, S., Coley, N., Lovestone, S., Aisen, P. S., & Vellas, B. (2015). Prevention of sporadic Alzheimer's disease: lessons learned from clinical trials and future directions. *The Lancet Neurology, 14*, 926-944.

Andrieu, S., Guyonnet, S., Coley, N., Cantet, C., Bonnefoy, M., Bordes, S., Bories, L., Cufi, M. N., Thierry, D., Dartigues, J. F., Desclaux, F., Gabelle, A., Gasnier, Y., Pesce, A., Sudres, K., Touchon, J., Robert, P., Rouaud, O., Legrang, P., Payoux, P., Caubere, J. P., Weiner, M., Carrie, I., Ousset, . J., & Vellas, B. (2017). Effect of long-term omega 3 polyunsaturated fatty acid supplementation with or without multi-domain intervention on cognitive function in elderly adults with memory complaints (MAPT): a randomised, placebo-controlled trial. *The Lancet Neurology, 16*, 377-389.

Angermeyer, M. C., & Matschinger, H. (2003). The stigma of mental illness: effects of labelling on public attitudes towards people with mental disorder. *Acta Psychiatrica Scandinavica, 108*, 304-309.

Anstey, K. J., Cherbuin, N., & Herath, P. M. (2013). Development of a new method for assessing global risk of Alzheimer's disease for use in population health approaches to prevention. *Prevention Science, 14*, 411-421.

Anstey, K. J., von Sanden, C., Salim, A., & O'kearney, R. (2007). Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. *American Journal of Epidemiology, 166,* 367-378.

Antonucci, T. C. (1990). Social supports and social relationships. *Handbook of Aging and the Social Sciences, 3*, 205-226.

Antonucci, T. C., Lansford, J. E., & Akiyama, H. (2001). Impact of positive and negative aspects of marital relationships and friendships on well-being of older adults. *Applied Developmental Science, 5,* 68-75.

Areán, P. A., Raue, P., Mackin, R. S., Kanellopoulos, D., McCulloch, C., & Alexopoulos, G. S. (2010). Problem-solving therapy and supportive therapy in older adults with major depression and executive dysfunction. *American Journal of Psychiatry, 167*, 1391-1398.

Areán, P., Hegel, M., Vannoy, S., Fan, M. Y., & Unuzter, J. (2008). Effectiveness of problem-solving therapy for older, primary care patients with depression: results from the IMPACT project. *The Gerontologist, 48,* 311-323.

Armstrong, J. J., Mitnitski, A., Andrew, M. K., Launer, L. J., White, L. R., & Rockwood, K. (2015). Cumulative impact of health deficits, social vulnerabilities, and protective factors on cognitive dynamics in late life: a multistate modeling approach. *Alzheimer's Research and Therapy, 7,* 38.

Atti, A. R., Forlani, C., De Ronchi, D., Palmer, K., Casadio, P., Dalmonte, E., & Fratiglioni, L. (2010). Cognitive impairment after age 60: clinical and social correlates in the "Faenza Project". *Journal of Alzheimer's Disease, 21,* 1325-1334.

Austin, M. P., Ross, M., Murray, C., O'Cańroll, R. E., Ebmeier, K. P., & Goodwin, G. M. (1992). Cognitive function in major depression. *Journal of Affective Disorders, 25*, 21-29.

Baddeley, A. D. (1968). A three minute reasoning test based on grammatical transformation. *Psychonomic Science, 10,* 341-342.

Baltes, P. B., & Baltes, M. M. (1990). Psychological perspectives on successful aging: The model of selective optimization with compensation. *Successful Aging: Perspectives from the Behavioral Sciences, 1,* 1-34.

Barnes, D. E., & Yaffe, K. (2011). The projected effect of risk factor reduction on Alzheimer's disease prevalence. *The Lancet Neurology, 10,* 819-828.

Barnes, D. E., Cauley, J. A., Lui, L. Y., Fink, H. A., McCulloch, C., Stone, K. L., & Yaffe, K. (2007). Women who maintain optimal cognitive function into old age. *Journal of the American Geriatrics Society, 55*, 259-264.

Barnes, L. L., De Leon, C. M., Wilson, R. S., Bienias, J. L., & Evans, D. A. (2004). Social resources and cognitive decline in a population of older African Americans and whites. *Neurology, 63*, 2322-2326.

Barnes, L. L., Wilson, R. S., Schneider, J. A., Bienias, J. L., Evans, D. A., & Bennett, D. A. (2003). Gender, cognitive decline, and risk of AD in older persons. *Neurology, 60*, 1777-1781.

Bassuk, S. S., Glass, T. A., & Berkman, L. F. (1999). Social disengagement and incident cognitive decline in community-dwelling elderly persons. *Annals of Internal Medicine, 131,* 165-173.

Baumeister, R. F., & Leary, M. R. (1995). The need to belong: desire for interpersonal attachments as a fundamental human motivation. *Psychological Bulletin, 117,* 497-529.

Baumgart, M., Snyder, H. M., Carrillo, M. C., Fazio, S., Kim, H., & Johns, H. (2015). Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimer's & Dementia, 11*, 718-726.

Beaudreau, S. A., & O'hara, R. (2008). Late-life anxiety and cognitive impairment: a review. *The American Journal of Geriatric Psychiatry, 16,* 790-803.

Beaudreau, S. A., & O'hara, R. (2009). The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults. *Psychology and Aging, 24*, 507-512.

Beck, A. T. (2008). The evolution of the cognitive model of depression and its neurobiological correlates. *American Journal of Psychiatry, 165*, 969-977.

Beishuizen, C. R., Coley, N., Moll van Charante, E. P., van Gool, W. A., Richard, E., & Andrieu, S. (2017). Determinants of Dropout and Nonadherence in a Dementia Prevention Randomized Controlled Trial: The Prevention of Dementia by Intensive Vascular Care Trial. *Journal of the American Geriatrics Society, 65*, 1505-1513.

Béland, F., Zunzunegui, M. V., Alvarado, B., Otero, A., & del Ser, T. (2005). Trajectories of cognitive decline and social relations. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 60,* P320-P330.

Bennett, D. A., Arnold, S. E., Valenzuela, M. J., Brayne, C., & Schneider, J. A. (2014). Cognitive and social lifestyle: links with neuropathology and cognition in late life. *Acta Neuropathologica, 127*, 137-150.

Bennett, D. A., Schneider, J. A., Tang, Y., Arnold, S. E., & Wilson, R. S. (2006). The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study. *The Lancet Neurology, 5,* 406-412.

Berger, A. K., Small, B. J., Forsell, Y., Winblad, B., & Bäckman, L. (1998). Preclinical symptoms of major depression in very old age: a prospective longitudinal study. *American Journal of Psychiatry, 155*, 1039-1043.

Bergland, A., & Engedal, K. (2011). Living arrangements, social networks, health, mobility, and balance of older women. *Physical & Occupational Therapy in Geriatrics, 29*, 90-101.

Berkman, L. F. (1985). *The relationship of social networks and social support to morbidity and mortality.* San Diego, CA, US: Academic Press, 241–262.

Berkman, L. F. (2000). Which influences cognitive function: living alone or being alone? *The Lancet, 355,* 1291-1292.

Berkman, L. F., & Glass, T. (2000). Social integration, social networks, social support, and health. *Social Epidemiology, 1*, 137-173.

Berkman, L. F., Glass, T., Brissette, I., & Seeman, T. E. (2000). From social integration to health: Durkheim in the new millennium. *Social Science & Medicine, 51*, 843-857.

Beydoun, M. A., Beydoun, H. A., Gamaldo, A. A., Teel, A., Zonderman, A. B., & Wang, Y. (2014). Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis. *BioMed Central: Public Health, 14*, 643.

Bhalla, R. K., Butters, M. A., Mulsant, B. H., Begley, A. E., Zmuda, M. D., Schoderbek, B., Pollock, B. G., Reynolds, C. F., & Becker, J. T. (2006). Persistence of neuropsychologic deficits in the remitted state of late-life depression. *The American Journal of Geriatric Psychiatry, 14,* 419-427.

Bickart, K. C., Hollenbeck, M. C., Barrett, L. F., & Dickerson, B. C. (2012). Intrinsic amygdala–cortical functional connectivity predicts social network size in humans. *Journal of Neuroscience, 32*, 14729-14741.

Bickart, K. C., Wright, C. I., Dautoff, R. J., Dickerson, B. C., & Barrett, L. F. (2011). Amygdala volume and social network size in humans. *Nature Neuroscience, 14*, 163-164.

Bielak, A. A., Gerstorf, D., Anstey, K. J., & Luszcz, M. A. (2014). Longitudinal associations between activity and cognition vary by age, activity type, and cognitive domain. *Psychology and Aging, 29*, 863-872.

Biringer, E., Lundervold, A., Stordal, K., Mykletun, A., Egeland, J., Bottlender, R., & Lund, A. (2005). Executive function improvement upon remission of recurrent unipolar depression. *European Archives of Psychiatry and Clinical Neuroscience, 255,* 373-380.

Black, S. A., Espino, D. V., Mahurin, R., Lichtenstein, M. J., Hazuda, H. P., Fabrizio, D., Ray, L. A., & Markides, K. S. (1999). The influence of noncognitive factors on the Mini-Mental State Examination in older Mexican-Americans: Findings from the Hispanic EPESE. *Journal of Clinical Epidemiology, 52*, 1095-1102.

Boden-Albala, B., Litwak, E., Elkind, M. S. V., Rundek, T., & Sacco, R. L. (2005). Social isolation and outcomes post stroke. *Neurology, 64*, 1888-1892.

Bohlmeijer, E., Smit, F., & Cuijpers, P. (2003). Effects of reminiscence and life review on late-life depression: a meta-analysis. *International Journal of Geriatric Psychiatry, 18*, 1088-1094.

Bolger, N., & Eckenrode, J. (1991). Social relationships, personality, and anxiety during a major stressful event. *Journal of Personality and Social Psychology, 61,* 440-449.

Bond, A., & Lader, M. (1974). The use of analogue scales in rating subjective feelings. *British Journal of Medical Psychology, 47*, 211-218.

Bond, J., & Carstairs, V. (1982). *Services for the elderly: a survey of the characteristics and needs of a population of 5000 old people.* Scottish Health Service Studies No. 42. Edinburgh: Scottish Home and Health Department.

Bordone, V. & Weber, D. (2012). Number of children and cognitive abilities in later life. *Vienna Yearbook of Population Research, 10,* 95-126.

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2005). *Comprehensive meta-analysis, version 2*. Engelwood, CO, USA: Biostat.

Bosma, H., van Boxtel, M. P., Ponds, R. W. H. M., Jelicic, M., Houx, P., Metsemakers, J., & Jolles, J. (2002). Engaged lifestyle and cognitive function in middle and old-aged, non-demented persons: a reciprocal association? *Zeitschrift für Gerontologie und Geriatrie, 35*, 575-581.

Boss, L., Kang, D. H., & Branson, S. (2015). Loneliness and cognitive function in the older adult: a systematic review. *International Psychogeriatrics, 27,* 541-553.

Bourassa, K. J., Memel, M., Woolverton, C., & Sbarra, D. A. (2017). Social participation predicts cognitive functioning in aging adults over time: comparisons with physical health, depression, and physical activity. *Aging & Mental Health, 21*, 133-146.

Bourke, C., Douglas, K., & Porter, R. (2010). Processing of facial emotion expression in major depression: a review. *Australian and New Zealand Journal of Psychiatry, 44*, 681-696.

Bowling, A. (2005). *Ageing well: Quality of life in old age*. Maidenhead, UK: McGraw-Hill Education.

Bowling, A., & Stafford, M. (2007). How do objective and subjective assessments of neighbourhood influence social and physical functioning in older age? Findings from a British survey of ageing. *Social Science & Medicine, 64,* 2533-2549.

Boyle, P. A., Buchman, A. S., Barnes, L. L., & Bennett, D. A. (2010). Effect of a purpose in life on risk of incident Alzheimer disease and mild cognitive impairment in community-dwelling older persons. *Archives of General Psychiatry, 67*, 304-310.

Bravo, G., & Hébert, R. (1997). Age-and education-specific reference values for the Mini-Mental and Modified Mini-Mental State Examinations derived from a non-demented elderly population. *International Journal of Geriatric Psychiatry, 12,* 1008-1018.

Brayne, C. (2007). The elephant in the room—healthy brains in later life, epidemiology and public health. *Nature Reviews Neuroscience, 8*, 233-239.

Broadhead, W. E., Gehlbach, S. H., & Kaplan, B. H. (1989). Functional versus structural social support and health care utilization in a family medicine outpatient practice. *Medical Care, 27*, 221-233.

Brown, J., Cooper-Kuhn, C. M., Kempermann, G., Van Praag, H., Winkler, J., Gage, F. H., & Kuhn, H. G. (2003). Enriched environment and physical activity stimulate hippocampal but not olfactory bulb neurogenesis. *European Journal of Neuroscience, 17*, 2042-2046.

Brown, C. L., Gibbons, L. E., Kennison, R. F., Robitaille, A., Lindwall, M., Mitchell, M. B., Shirk, S. D., Atri, A., Cimino, C. R., Benitez, A., MacDonald, S. W. S., Zelinski, E. M., Willis, S. L., Warner-Schaie, K., Johansson, B., Dixon, R. A., Mungas, D. M., Hofer, S. M., Piccin, A. M. (2012). Social activity and

cognitive functioning over time: a coordinated analysis of four longitudinal studies. *Journal of Aging Research*, *2012*, 287438.

Brown, C. L., Robitaille, A., Zelinski, E. M., Dixon, R. A., Hofer, S. M., & Piccinin, A. M. (2016). Cognitive activity mediates the association between social activity and cognitive performance: A longitudinal study. *Psychology and Aging, 31*, 831-846.

Brown, S. L., Nesse, R. M., Vinokur, A. D., & Smith, D. M. (2003). Providing social support may be more beneficial than receiving it results from a prospective study of mortality. *Psychological Science, 14,* 320-327.

Buber, I. & Engelhardt, H. (2008). Children's impact on the mental health of their older mothers and fathers: findings from the Survey of Health, Ageing and Retirement in Europe. *European Journal of Ageing, 5*, 31-45.

Bunce, D., Batterham, P. J., Mackinnon, A. J., & Christensen, H. (2012). Depression, anxiety and cognition in community-dwelling adults aged 70 years and over. *Journal of Psychiatric Research, 46*, 1662-1666.

Burger, J. M. (1995). Individual differences in preference for solitude. *Journal of Research in Personality, 29*, 85-108.

Burholt, V., & Scharf, T. (2013). Poor health and loneliness in later life: the role of depressive symptoms, social resources, and rural environments. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 69,* 311-324.

Burton, C., Campbell, P., Jordan, K., Strauss, V., & Mallen, C. (2012). The association of anxiety and depression with future dementia diagnosis: a case-control study in primary care. *Family Practice, 30,* 25-30.

Butters, M. A., Becker, J. T., Nebes, R. D., Zmuda, M. D., Mulsant, B. H., Pollock, B. G., & Reynolds III, C. F. (2000). Changes in cognitive functioning following treatment of late-life depression. *American Journal of Psychiatry, 157,* 1949-1954.

Butters, M. A., Whyte, E. M., Nebes, R. D., Begley, A. E., Dew, M. A., Mulsant, B. H., Zmuda, M. D., Bhalla, R., Cidis Meltzer, C., Pollock, B. G., Reynolds, C. F., & Becker, J. T. (2004). The nature and determinants of neuropsychological functioning in late-life depression. *Archives of General Psychiatry, 61,* 587-595.

Byrne, R., & Whiten, A. (1989). *Machiavellian intelligence: social expertise and the evolution of intellect in monkeys, apes, and humans*. Oxford, UK: Oxford Science Publications.

Cacioppo, J. T., & Hawkley, L. C. (2003). Social isolation and health, with an emphasis on underlying mechanisms. *Perspectives in Biology and Medicine, 46*, S39-S52.

Cacioppo, J. T., & Hawkley, L. C. (2009). Perceived social isolation and cognition. *Trends in Cognitive Sciences, 13,* 447-454.

Cacioppo, J. T., Hawkley, L. C., & Thisted, R. A. (2010). Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychology and Aging, 25,* 453-463.

Carstensen, L. L. (1992). Social and emotional patterns in adulthood: support for socioemotional selectivity theory. *Psychology and Aging, 7,* 331-338.

Carstensen, L. L., Fung, H. H., & Charles, S. T. (2003). Socioemotional selectivity theory and the regulation of emotion in the second half of life. *Motivation and Emotion, 27*, 103-123.

CASP: Critical Appraisal Skills Programme. (2013). 12 questions to help you make sense of a cohort study. Accessed 12/12/2016: http://media.wix.com/ugd/dded87_e37a4ab637fe46a0869f9f977dacf134.pdf

Cassel, J. (1976). The contribution of the social environment to host resistance – the fourth wade Hampton frost lecture. *American Journal of Epidemiology, 104*, 107-123.

Cattan, M., White, M., Bond, J., & Learmouth, A. (2005). Preventing social isolation and loneliness among older people: a systematic review of health promotion interventions. *Ageing & Society, 25*, 41-67.

Cattell, V. (2001). Poor people, poor places, and poor health: the mediating role of social networks and social capital. *Social Science & Medicine, 52*, 1501-1516.

Charles, S. T., & Piazza, J. R. (2007). Memories of social interactions: Age differences in emotional intensity. *Psychology and Aging, 22*, 300-309.

Chen, Y. F., Dewey, M. E., & Avery, A. J. (2001). Self-reported medication use for older people in England and Wales. *Journal of Clinical Pharmacy and Therapeutics, 26*, 129-140.

Cheng, G., Huang, C., Deng, H., Wang, H. (2012). Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. *Internal Medical Journal, 42,* 484–91.

Christakis, N. A., & Fowler, J. H. (2007). The spread of obesity in a large social network over 32 years. *New England Journal of Medicine*, 370-379.

Christensen, H. (2001). What cognitive changes can be expected with normal ageing? *Australian and New Zealand Journal of Psychiatry, 35*, 768-775.

Christopher, G., & MacDonald, J. (2005). The impact of clinical depression on working memory. *Cognitive Neuropsychiatry, 10,* 379-399.

Clare, L., Wu, Y. T., Teale, J. C., MacLeod, C., Matthews, F., Brayne, C., Woods, B., & CFAS-Wales study team. (2017). Potentially modifiable lifestyle factors, cognitive reserve, and cognitive function in later life: A cross-sectional study. *PLoS Medicine, 14*, e1002259.

Cloutier, S., Chertkow, H., Kergoat, M. J., Gauthier, S., & Belleville, S. (2015). Patterns of cognitive decline prior to dementia in persons with mild cognitive impairment. *Journal of Alzheimer's Disease, 47*, 901-913.

Cohen, S., Underwood, L. G., & Gottlieb, B. H. (2000). *Social support measurement and intervention: A guide for health and social scientists*. Oxford, UK: Oxford University Press.

Coley, N., Ngandu, T., Cantet, C., Lehtisalo, J., Vellas, B., Kivipelto, M., & Andrieu, S. (2017). Adherence to Multidomain Interventions for the Prevention of Alzheimer's Disease: Data from the MAPT and FINGER Trials. Alzheimer's & Dementia: *The Journal of the Alzheimer's Association, 13*, P895-P896.

Collins, R. Silarova, B., & Clare, L. (in press). Dementia primary prevention policies and strategies and their local implementation: a scoping review using England as a case study. *Journal of Alzheimer's Disease.*

Conroy, R. M., Golden, J., Jeffares, I., O'Neill, D., & McGee, H. (2010). Boredom-proneness, loneliness, social engagement and depression and their association with cognitive function in older people: a population study. *Psychology, Health & Medicine, 15*, 463-473.

Cook, G., Brown-Wilson, C., & Forte, D. (2006). The impact of sensory impairment on social interaction between residents in care homes. *International Journal of Older People Nursing, 1*, 216-224.

Coon, D. W., & Thompson, L. W. (2003). The relationship between homework compliance and treatment outcomes among older adult outpatients with mild-to-moderate depression. *The American Journal of Geriatric Psychiatry, 11,* 53-61.

Cooper, C., Sommerlad, A., Lyketsos, C. G., & Livingston, G. (2015). Modifiable predictors of dementia in mild cognitive impairment: a systematic review and meta-analysis. *American Journal of Psychiatry, 172*, 323-334.

Copeland, J. R. M., Dewey, M. E., & Griffiths-Jones, H. M. (1986). A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. *Psychological Medicine, 16*, 89-99.

Copeland, J. R. M., Prince, M., Wilson, K. C. M., Dewey, M. E., Payne, J., & Gurland, B. (2002). The Geriatric Mental State Examination in the 21st century. *International Journal of Geriatric Psychiatry, 17*, 729-732.

Corbett, A., Owen, A., Hampshire, A., Grahn, J., Stenton, R., Dajani, S., Burns, A., Howard, R., Williams, N., Williams, G., & Ballard, C. (2015). The effect of an online cognitive training package in healthy older adults: an online randomized controlled trial. *Journal of the American Medical Directors Association, 16,* 990-997.

Cornelis, E., Gorus, E., Beyer, I., Bautmans, I., & De Vriendt, P. (2017). Early diagnosis of mild cognitive impairment and mild dementia through basic and instrumental activities of daily living: Development of a new evaluation tool. *PLoS medicine, 14,* e1002250.

Cornwell, B. (2009). Good health and the bridging of structural holes. *Social Networks, 31*, 92-103.

Cornwell, B., & Laumann, E. O. (2015). The health benefits of network growth: New evidence from a national survey of older adults. *Social Science & Medicine, 125*, 94-106.

Cornwell, E. Y., & Waite, L. J. (2009). Social disconnections, perceived isolation, and health among older adults. *Journal of Health and Social Behavior, 50*, 31-48.

Corrigan, P. W., & Rao, D. (2012). On the self-stigma of mental illness: Stages, disclosure, and strategies for change. *The Canadian Journal of Psychiatry, 57,* 464-469.

Courtin, E., & Knapp, M. (2017). Social isolation, loneliness and health in old age: a scoping review. *Health & Social Care in the Community, 25*, 799-812.

Coyle, C. E., & Dugan, E. (2012). Social isolation, loneliness and health among older adults. *Journal of Aging and Health, 24,* 1346-1363.

Crooks, V. C., Lubben, J., Petitti, D. B., Little, D., & Chiu, V. (2008). Social network, cognitive function, and dementia incidence among elderly women. *American Journal of Public Health, 98*, 1221-1227.

Cruwys, T., Dingle, G. A., Haslam, C., Haslam, S. A., Jetten, J., & Morton, T. A. (2013). Social group memberships protect against future depression, alleviate depression symptoms and prevent depression relapse. *Social Science & Medicine, 98,* 179-186.

Cruwys, T., Haslam, S. A., Dingle, G. A., Haslam, C., & Jetten, J. (2014). Depression and social identity: An integrative review. *Personality and Social Psychology Review, 18*, 215-238.

Cruwys, T., Haslam, S. A., Dingle, G. A., Jetten, J., Hornsey, M. J., Chong, E. D., & Oei, T. P. (2014). Feeling connected again: Interventions that increase social identification reduce depression symptoms in community and clinical settings. *Journal of Affective Disorders, 159*, 139-146.

Cullen, B., Fahy, S., Cunningham, C. J., Coen, R. F., Bruce, I., Greene, E., Coakley, D, J., Walsh, B., & Lawlor, B. A. (2005). Screening for dementia in an Irish community sample using MMSE: a comparison of norm-adjusted versus fixed cut-points. *International Journal of Geriatric Psychiatry, 20*, 371-376.

Dahlberg, L., & McKee, K. J. (2014). Correlates of social and emotional loneliness in older people: evidence from an English community study. *Aging & Mental Health, 18*, 504-514.

Davis, J. C., Best, J., Hsu, C. L., Nagamatsu, L. S., Dao, E., & Liu-Ambrose, T. (2015). Examining the Effect of the Relationship Between Falls and Mild Cognitive Impairment on Mobility and Executive Functions in Community-Dwelling Older Adults. *Journal of the American Geriatrics Society, 63*, 590-593.

de Jong Gierveld, J. (2003). Social networks and social well-being of older men and women living alone. *Gender and Ageing*, 95-111.

de Jong Gierveld, J., & Havens, B. (2004). Cross-national comparisons of social isolation and loneliness: introduction and overview. *Canadian Journal on Aging, 23,* 109-113.

de Jong Gierveld, J., & Kamphuls, F. (1985). The development of a Rasch-type loneliness scale. *Applied Psychological Measurement, 9*, 289-299.

de Jong Gierveld, J., & van Tilburg, T. (2006). A 6-item scale for overall, emotional, and social loneliness: Confirmatory tests on survey data. *Research on Aging, 28*, 582-598.

de Souto Barreto, P., Andrieu, S., Rolland, Y., Vellas, B., & DSA MAPT Study Group. (2018). Physical activity domains and cognitive function over three years in older adults with subjective memory complaints: Secondary analysis from the MAPT trial. *Journal of Science and Medicine in Sport, 21*, 52-57.

Deary, I. J., Corley, J., Gow, A. J., Harris, S. E., Houlihan, L. M., Marioni, R. E., Penke, L., Rafnsson, S. B., & Starr, J. M. (2009). Age-associated cognitive decline. *British Medical Bulletin, 92*, 135-152.

Deary, I. J., Gow, A. J., Taylor, M. D., Corley, J., Brett, C., Wilson, V., Campbell, H., Whalley, L. J., Visscher, P. M., Porteous, D. J., & Starr, J. M. (2007). The Lothian Birth Cohort 1936: a study to examine influences on cognitive ageing from age 11 to age 70 and beyond. *BioMed Central: Geriatrics, 7,* 28.

Deary, I. J., Whalley, L. J., Lemmon, H., Crawford, J. R., & Starr, J. M. (2000). The stability of individual differences in mental ability from childhood to old age: follow-up of the 1932 Scottish Mental Survey. *Intelligence, 28*, 49-55.

Deary, I. J., Whiteman, M. C., Starr, J. M., Whalley, L. J., & Fox, H. C. (2004). The impact of childhood intelligence on later life: following up the Scottish mental surveys of 1932 and 1947. *Journal of Personality and Social Psychology, 86,* 130-147.

Demnitz, N., Zsoldos, E., Mahmood, A., Mackay, C. E., Kivimäki, M., Singh-Manoux, A., Dawes, H., Johansen-Berg, H., Ebmeier, K. P., & Sexton, C. E. (2017). Associations between mobility, cognition, and brain structure in healthy older adults. *Frontiers in Aging Neuroscience, 9,* 155.

Department of Health. (2009). Living well with dementia: a national dementia strategy. Accessed 03/09/2018: https://www.gov.uk/government/publications/living-well-with-dementia-a-national-dementia-strategy

DerSimonian, R., & Kacker, R. (2007). Random-effects model for meta-analysis of clinical trials: an update. *Contemporary Clinical Trials, 28*, 105-114.

Di Marco, L. Y., Marzo, A., Muñoz-Ruiz, M., Ikram, M. A., Kivipelto, M., Ruefenacht, D., Venneri, A., Soininen, H., Wanke, I., Ventikos, Y. A., & Frangi, A. F. (2014). Modifiable lifestyle factors in dementia: a systematic review of longitudinal observational cohort studies. *Journal of Alzheimer's Disease, 42*, 119-135.

Dickens, A. P., Richards, S. H., Greaves, C. J., & Campbell, J. L. (2011). Interventions targeting social isolation in older people: a systematic review. *BioMed Central: Public Health, 11*, 1.

Diener, E. D., Emmons, R. A., Larsen, R. J., & Griffin, S. (1985). The satisfaction with life scale. *Journal of Personality Assessment, 49*, 71-75.

Diener, E., & Seligman, M. E. (2004). Beyond money: Toward an economy of well-being. *Psychological Science in the Public Interest, 5,* 1-31.

DiNapoli, E. A., Wu, B., & Scogin, F. (2014). Social isolation and cognitive function in Appalachian older adults. *Research on Aging, 36*, 161-179.

Diniz, B. S., Butters, M. A., Albert, S. M., Dew, M. A., & Reynolds, C. F. (2013). Late-life depression and risk of vascular dementia and Alzheimer's disease: systematic review and meta-analysis of community-based cohort studies. *The British Journal of Psychiatry, 202*, 329-335.

Dodge, H. H., Kadowaki, T., Hayakawa, T., Yamakawa, M., Sekikawa, A., & Ueshima, H. (2005). Cognitive impairment as a strong predictor of incident disability in specific ADL–IADL tasks among community-dwelling elders: the Azuchi Study. *The Gerontologist, 45*, 222-230.

Domènech-Abella, J., Lara, E., Rubio-Valera, M., Olaya, B., Moneta, M. V., Rico-Uribe, L. A., Ayuso-Mateos, J. L., Mundo, J., & Haro, J. M. (2017). Loneliness and depression in the elderly: the role of social network. *Social Psychiatry and Psychiatric Epidemiology, 52*, 381-390.

Donnelly, E. A., & Hinterlong, J. E. (2009). Changes in social participation and volunteer activity among recently widowed older adults. *The Gerontologist, 50,* 158-169.

Dowd, J. J. (1975). Aging as exchange: A preface to theory. *Journal of Gerontology, 30*, 584-594.

Downs, S. H., & Black, N. (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology and Community Health, 52*, 377-384.

Drageset, J., Kirkevold, M., & Espehaug, B. (2011). Loneliness and social support among nursing home residents without cognitive impairment: a questionnaire survey. *International Journal of Nursing Studies, 48*, 611-619.

Dumas, J. A., & Newhouse, P. A. (2015). Impaired working memory in geriatric depression: an fMRI study. *The American Journal of Geriatric Psychiatry, 23*, 433-436.

Dunbar, R. I. (1998). The social brain hypothesis. *Brain, 9*, 178-190.

Dunstan, F., Weaver, N., Araya, R., Bell, T., Lannon, S., Lewis, G., Patterson, J., Thomas, H., Jones, P., & Palmer, S. (2005). An observation tool to assist with the assessment of urban residential environments. *Journal of Environmental Psychology, 25*, 293-305.

Edland, S. D., Rocca, W. A., Petersen, R. C., Cha, R. H., & Kokmen, E. (2002). Dementia and Alzheimer disease incidence rates do not vary by sex in Rochester, Minn. *Archives of Neurology, 59*, 1589-1593.

Ehnvall, A., Mitchell, P. B., Hadzi-Pavlovic, D., Parker, G., Frankland, A., Loo, C., Breakspear, M., Wright, A., Roberts, G., Lau, P., & Perich, T. (2014). Rejection sensitivity and pain in bipolar versus unipolar depression. *Bipolar Disorders, 16*, 190-198.

Ellwardt, L., Aartsen, M., Deeg, D., & Steverink, N. (2013). Does loneliness mediate the relation between social support and cognitive functioning in later life? *Social Science & Medicine, 98*, 116-124.

Ellwardt, L., van Tilburg, T. G., & Aartsen, M. J. (2015). The mix matters: Complex personal networks relate to higher cognitive functioning in old age. *Social Science & Medicine, 125*, 107-115.

Elwood, P. C., Gallacher, J. E., Hopkinson, C. A., Pickering, J., Rabbitt, P., Stollery, B., Brayne, C., Huppert, F. A., & Bayer, A. (1999). Smoking, drinking, and other life style factors and cognitive function in men in the Caerphilly cohort. *Journal of Epidemiology and Community Health, 53*, 9-14.

Ertel, K. A., Glymour, M. M., & Berkman, L. F. (2008). Effects of social integration on preserving memory function in a nationally representative US elderly population. *American Journal of Public Health, 98*, 1215-1220.

Ertel, K. A., Glymour, M. M., & Berkman, L. F. (2009). Social networks and health: A life course perspective integrating observational and experimental evidence. *Journal of Social and Personal Relationships, 26,* 73-92.

Evandrou, M., Falkingham, J., Rake, K., & Scott, A. (2001). The dynamics of living arrangements in later life: evidence from the British Household Panel Survey. *Population Trends London*, 37-44.

Evans, I. E., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne, C., Clare, L., & CFAS-Wales research team. (2018). Social isolation, cognitive reserve, and cognition in healthy older people. *PloS One, 13*, e0201008.

Feng, L., Ng, X. T., Yap, P., Li, J., Lee, T. S., Håkansson, K., Kua, E. H., & Ng, T. P. (2014). Marital status and cognitive impairment among community-dwelling Chinese older adults: the role of gender and social engagement. *Dementia and Geriatric Cognitive Disorders Extra, 4*, 375-384.

Ferreira, N., Owen, A., Mohan, A., Corbett, A., & Ballard, C. (2015). Associations between cognitively stimulating leisure activities, cognitive function and age-related cognitive decline. *International Journal of Geriatric Psychiatry, 30*, 422-430.

Ferrer, E., Salthouse, T. A., Stewart, W. F., & Schwartz, B. S. (2004). Modeling age and retest processes in longitudinal studies of cognitive abilities. *Psychology and Aging, 19*, 243-259.

Field, D., & Minkler, M. (1988). Continuity and change in social support between young-old and old-old or very-old age. *Journal of Gerontology, 43,* P100-P106.

Fillenbaum, G., Heyman, A., Williams, K., Prosnitz, B., & Burchett, B. (1990). Sensitivity and specificity of standardized screens of cognitive impairment and dementia among elderly black and white community residents. *Journal of Clinical Epidemiology, 43*, 651-660.

Fillit, H. M., Butler, R. N., O'connell, A. W., Albert, M. S., Birren, J. E., Cotman, C. W., Greenough, W. T., Gold, P. E., & Perls, T. T. (2002). Achieving and maintaining cognitive vitality with aging. *Mayo Clinic Proceedings, 77,* 681-696.

Finch, J. F., & Graziano, W. G. (2001). Predicting depression from temperament, personality, and patterns of social relations. *Journal of Personality, 69*, 27-55.

Findlay, R. A. (2003). Interventions to reduce social isolation amongst older people: where is the evidence? *Ageing & Society, 23*, 647-658.

Fingerman, K. L., Hay, E. L., & Birditt, K. S. (2004). The best of ties, the worst of ties: Close, problematic, and ambivalent social relationships. *Journal of Marriage and Family, 66*, 792-808.

Finlay, J. M., & Kobayashi, L. C. (2018). Social isolation and loneliness in later life: A parallel convergent mixed-methods case study of older adults and their residential contexts in the Minneapolis metropolitan area, USA. *Social Science & Medicine, 208*, 25-33.

Flicker, C., Ferris, S. H., & Reisberg, B. (1991). Mild cognitive impairment in the elderly predictors of dementia. *Neurology, 41*, 1006-1006.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Folstein, M. F., Folstein, S. E., McHugh, P. R., & Fanjiang, G. (2001). *Mini-Mental State Examination user’s guide.* Odessa, FL, USA: Psychological Assessment Resources.

Ford, J. G., Howerton, M. W., Lai, G. Y., Gary, T. L., Bolen, S., Gibbons, M. C., Tilburt, J., Baffi, C., Tanpitukpongse, T. P., Wilson, R. F., Powe, N. R., & Bass, E. B. (2008). Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. *Cancer: Interdisciplinary International Journal of the American Cancer Society, 112*, 228-242.

Fratiglioni, L., & Wang, H. X. (2007). Brain reserve hypothesis in dementia. *Journal of Alzheimer's Disease, 12*, 11-22.

Fratiglioni, L., Paillard-Borg, S., & Winblad, B. (2004). An active and socially integrated lifestyle in late life might protect against dementia. *The Lancet Neurology, 3*, 343-353.

Fratiglioni, L., Wang, H. X., Ericsson, K., Maytan, M., & Winblad, B. (2000). Influence of social network on occurrence of dementia: a community-based longitudinal study. *The Lancet, 355*, 1315-1319.

Fredrickson, B. L., & Carstensen, L. L. (1990). Choosing social partners: how old age and anticipated endings make people more selective. *Psychology and Aging, 5*, 335-347.

Freund, A. M., & Baltes, P. B. (1998). Selection, optimization, and compensation as strategies of life management: correlations with subjective indicators of successful aging. *Psychology and Aging, 13*, 531-543.

Frisoni, G. B., Fratiglioni, L., Fastbom, J., Guo, Z., Viitanen, M., & Winblad, B. (2000). Mild cognitive impairment in the population and physical health: data on 1,435 individuals aged 75 to 95. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 55,* M322-M328.

Fung, A. W. T., Leung, G. T. Y., & Lam, L. C. W. (2011). Modulating factors that preserve cognitive function in healthy ageing. *East Asian Archives of Psychiatry, 21*, 152-156.

Fung, H. H., Carstensen, L. L., & Lutz, A. M. (1999). Influence of time on social preferences: Implications for life-span development. *Psychology and Aging, 14,* 595-604.

Gallacher, J., Bayer, A., Fish, M., Pickering, J., Pedro, S., Dunstan, F., Ebrahim, S., & Ben-Shlomo, Y. (2009). Does anxiety affect risk of dementia? Findings from the Caerphilly Prospective Study. *Psychosomatic Medicine, 71,* 659-666.

Gallucci, M., Mazzuco, S., Ongaro, F., Di Giorgi, E., Mecocci, P., Cesari, M., Albani, D, Forloni, G. L., Durante, E., Gajo, G. B., Zanardo, A., Siculi, M., Caberlotto, L., & Regini, C. (2013). Body mass index, lifestyles, physical performance and cognitive decline: the "Treviso Longeva (TRELONG)" study. *The Journal of Nutrition, Health & Aging, 17*, 378-384.

García-Peña, C., Wagner, F. A., Sánchez-García, S., Espinel-Bermúdez, C., Juárez-Cedillo, T., Pérez-Zepeda, M., Arango-Lopera, V., Franco-Marina, F., Ramirez-Aldana, R., & Gallo, J. J. (2013). Late-life depressive symptoms: prediction models of change. *Journal of Affective Disorders, 150*, 886-894.

Gauthier, S., Reisberg, B., Zaudig, M., Petersen, R. C., Ritchie, K., Broich, K., Belleville, S., Brodaty, H., Bennett, D., Chertkow, H., Cummings, J. L., de Leon, M., Feldman, H., Ganguli, M., Hampel, H., Scheltens, P., Tierney, M. C., Whitehouse, P., & Cummings, J. L. (2006). Mild cognitive impairment. *The Lancet, 367,* 1262-1270.

Gellis, Z. D., McGinty, J., Tierney, L., Jordan, C., Burton, J., & Misener, E. (2008). Randomized controlled trial of problem-solving therapy for minor depression in home care. *Research on Social Work Practice, 18*, 596-606.

Genet, N., Boerma, W. G., Kringos, D. S., Bouman, A., Francke, A. L., Fagerström, C., Melchiorre, MG., Greco, C., & Devillé, W. (2011). Home care in Europe: a systematic literature review. *BioMed Central: Health Services Research, 11*, 207.

George, L. K. (1996). *Social factors and illness: Handbook of aging and the social sciences*. London, UK: Academic Press

Gerst-Emerson, K., Shovali, T. E., & Markides, K. S. (2014). Loneliness among very old Mexican Americans: Findings from the Hispanic established populations epidemiologic studies of the elderly. *Archives of Gerontology and Geriatrics, 59*, 145-149.

Ghisletta, P., Bickel, J. F., & Lövdén, M. (2006). Does activity engagement protect against cognitive decline in old age? Methodological and analytical considerations. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 61*, P253-P261.

Giebel, C. M., Sutcliffe, C., Stolt, M., Karlsson, S., Renom-Guiteras, A., Soto, M., Verbeek, H., Zabalegui, A., & Challis, D. (2014). Deterioration of basic activities of daily living and their impact on quality of life across different cognitive stages of dementia: a European study. *International Psychogeriatrics, 26*, 1283-1293.

Giles, L. C., Anstey, K. J., Walker, R. B., & Luszcz, M. A. (2012). Social networks and memory over 15 years of followup in a cohort of older Australians: results from the Australian Longitudinal Study of Ageing. *Journal of Aging Research*, *2012,* 856048.

Glass, T. A., De Leon, C. F. M., Seeman, T. E., & Berkman, L. F. (1997). Beyond single indicators of social networks: a LISREL analysis of social ties among the elderly. *Social Science & Medicine, 44*, 1503-1517.

Glei, D. A., Landau, D. A., Goldman, N., Chuang, Y. L., Rodriguez, G., & Weinstein, M. (2005). Participating in social activities helps preserve cognitive function: an analysis of a longitudinal, population-based study of the elderly. *International Journal of Epidemiology, 34*, 864-871.

Gleibs, I. H., Haslam, C., Jones, J. M., Alexander Haslam, S., McNeill, J., & Connolly, H. (2011). No country for old men? The role of a 'Gentlemen's Club' in promoting social engagement and psychological well-being in residential care. *Aging & Mental Health, 15,* 456-466.

Global Council on Brain Health. (2017). The Brain and Social Connectedness: GCBH recommendations on social engagement and brain health. Accessed 03/07/2018: https://www.aarp.org/content/dam/aarp/health/brain_health/2017/02/gcbh-social-engagement-report.pdf

Goldberg, T. E., Harvey, P. D., Wesnes, K. A., Snyder, P. J., & Schneider, L. S. (2015). Practice effects due to serial cognitive assessment: implications for preclinical Alzheimer's disease randomized controlled trials. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 1*, 103-111.

Golden, J., Conroy, R. M., & Lawlor, B. A. (2009). Social support network structure in older people: underlying dimensions and association with psychological and physical health. *Psychology, Health & Medicine, 14*, 280-290.

Gould, R. L., Coulson, M. C., & Howard, R. J. (2012). Cognitive behavioral therapy for depression in older people: a meta-analysis and meta-regression of randomized controlled trials. *Journal of the American Geriatrics Society, 60,* 1817-1830.

Goveas, J. S., Espeland, M. A., Woods, N. F., Wassertheil-Smoller, S., & Kotchen, J. M. (2011). Depressive symptoms and incidence of mild cognitive impairment and probable dementia in elderly women: the Women's Health Initiative Memory Study. *Journal of the American Geriatrics Society, 59*, 57-66.

Gow, A. J., & Mortensen, E. L. (2016). Social resources and cognitive ageing across 30 years: the Glostrup 1914 Cohort. *Age and Ageing, 45,* 480–486.

Gow, A. J., Corley, J., Starr, J. M., & Deary, I. J. (2013). Which social network or support factors are associated with cognitive abilities in old age? *Gerontology, 59,* 454-463.

Gow, A. J., Pattie, A., Whiteman, M. C., Whalley, L. J., & Deary, I. J. (2007). Social support and successful aging: Investigating the relationships between lifetime cognitive change and life satisfaction. *Journal of Individual Differences, 28*, 103-115.

Granerud, A., & Severinsson, E. (2006). The struggle for social integration in the community–the experiences of people with mental health problems. *Journal of Psychiatric and Mental Health Nursing, 13,* 288-293.

Graves, A. B., Rajaram, L., Bowen, J. D., McCormick, W. C., McCurry, S. M., & Larson, E. B. (1999). Cognitive decline and Japanese culture in a cohort of older Japanese Americans in King County, WA: the Kame Project. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 54,* S154-S161.

Green, A. F., Rebok, G., & Lyketsos, C. G. (2008). Influence of social network characteristics on cognition and functional status with aging. *International Journal of Geriatric Psychiatry, 23,* 972-978.

Grenade, L., & Boldy, D. (2008). Social isolation and loneliness among older people: issues and future challenges in community and residential settings. *Australian Health Review, 32*, 468-478.

Grodstein, F. (2007). Cardiovascular risk factors and cognitive function. *Alzheimer's & Dementia, 3*, S16-S22.

Gruber, S., Rathgeber, K., Bräunig, P., & Gauggel, S. (2007). Stability and course of neuropsychological deficits in manic and depressed bipolar patients compared to patients with major depression. *Journal of Affective Disorders, 104,* 61-71.

Gulpers, B., Ramakers, I., Hamel, R., Köhler, S., Voshaar, R. O., & Verhey, F. (2016). Anxiety as a predictor for cognitive decline and dementia: a systematic review and meta-analysis. *The American Journal of Geriatric Psychiatry, 24*, 823-842.

Gunstad, J., Paul, R. H., Brickman, A. M., Cohen, R. A., Arns, M., Roe, D., Lawrence, J. J., & Gordon, E. (2006). Patterns of cognitive performance in middle-aged and older adults: A cluster analytic examination. *Journal of Geriatric Psychiatry and Neurology, 19*, 59-64.

Håkansson, K., Rovio, S., Helkala, E. L., Vilska, A. R., Winblad, B., Soininen, H., Nissinen, A., Mohammed, A. H., & Kivipelto, M. (2009). Association between mid-life marital status and cognitive function in later life: population based cohort study. *British Medical Journal, 339*, b2462.

Hampton, W. H., Unger, A., Von Der Heide, R. J., & Olson, I. R. (2016). Neural connections foster social connections: a diffusion-weighted imaging study of social networks. *Social Cognitive and Affective Neuroscience, 11*, 721-727.

Harada, C. N., Love, M. C. N., & Triebel, K. L. (2013). Normal cognitive aging. *Clinics in Geriatric Medicine, 29*, 737-752.

Hardy, J., & Selkoe, D. J. (2002). The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. *Science, 297*, 353-356.

Haslam, C., Cruwys, T., & Haslam, S. A. (2014). "The we's have it": Evidence for the distinctive benefits of group engagement in enhancing cognitive health in aging. *Social Science & Medicine, 120,* 57-66.

Haslbeck, J. W., McCorkle, R., & Schaeffer, D. (2012). Chronic illness self-management while living alone in later life: a systematic integrative review. *Research on Aging, 34*, 507-547.

Havens, B., Hall, M., Sylvestre, G., & Jivan, T. (2004). Social isolation and loneliness: Differences between older rural and urban Manitobans. *Canadian Journal on Aging, 23*, 129-140.

Hawkley, L. C., Hughes, M. E., Waite, L. J., Masi, C. M., Thisted, R. A., & Cacioppo, J. T. (2008). From social structural factors to perceptions of relationship quality and loneliness: the Chicago health, aging, and social relations study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 63*, S375-S384.

Hawthorne, G. (2008). Perceived social isolation in a community sample: its prevalence and correlates with aspects of peoples' lives. *Social Psychiatry and Psychiatric Epidemiology, 43*, 140-150.

Hays, J. C. (2002). Living arrangements and health status in later life: a review of recent literature. *Public Health Nursing, 19*, 136-151.

Hedden, T., & Gabrieli, J. D. (2004). Insights into the ageing mind: a view from cognitive neuroscience. *Nature Reviews Neuroscience, 5*, 87-96.

Hendrie, H. C., Albert, M. S., Butters, M. A., Gao, S., Knopman, D. S., Launer, L. J., Yaffe, K., Cuthbert, B. N., Edwards, E., & Wagster, M. V. (2006). The NIH cognitive and emotional health project: report of the critical evaluation study committee. *Alzheimer's & Dementia, 2*, 12-32.

Heneghan, C., Mahtani, K. R., Goldacre, B., Godlee, F., Macdonald, H., & Jarvies, D. (2017). Evidence based medicine manifesto for better healthcare: A response to systematic bias, wastage, error and fraud in research underpinning patient care. *British Medical Journal: Evidence-Based Medicine.* Accessed 28/08/2018: https://ebm.bmj.com/content/early/2017/07/18/ebmed-2017-j2973rep.citation-tools

Heritage, Z., Wilkinson, R. G., Grimaud, O., & Pickett, K. E. (2008). Impact of social ties on self-reported health in France: Is everyone affected equally? *BioMed Central: Public Health, 8*, 243.

Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *British Medical Journal, 327,* 557-560.

Hill, R. A., & Dunbar, R. I. (2003). Social network size in humans. *Human Nature, 14*, 53-72.

Hill, T. D., Burdette, A. M., Angel, J. L., & Angel, R. J. (2006). Religious attendance and cognitive functioning among older Mexican Americans. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 61,* P3-P9.

Ho, S. C., Woo, J., Sham, A., Chan, S. G., & Ashley, L. M. (2001). A 3-year follow-up study of social, lifestyle and health predictors of cognitive impairment in a Chinese older cohort. *International Journal of Epidemiology, 30,* 1389-1396.

Holmén, K., Ericsson, K., & Winblad, B. (2000). Social and emotional loneliness among non-demented and demented elderly people. *Archives of Gerontology and Geriatrics, 31*, 177-192.

Holt-Lunstad, J., & Smith, T. B. (2012). Social relationships and mortality. *Social and Personality Psychology Compass, 6,* 41-53.

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: a meta-analytic review. *PLoS Med, 7*, e1000316.

Holtzman, R. E., Rebok, G. W., Saczynski, J. S., Kouzis, A. C., Doyle, K. W., & Eaton, W. W. (2004). Social network characteristics and cognition in middle-aged and older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 59,* P278-P284.

Holwerda, T. J., Deeg, D. J., Beekman, A. T., van Tilburg, T. G., Stek, M. L., Jonker, C., & Schoevers, R. A. (2012). Feelings of loneliness, but not social isolation, predict dementia onset: results from the Amsterdam Study of the Elderly (AMSTEL). *Journal of Neurology, Neurosurgery & Psychiatry, 85,* 135-142.

Hong, T. B., Zarit, S. H., & Johansson, B. (2003). Mild cognitive impairment in the oldest old: a comparison of two approaches. *Aging & Mental Health, 7,* 271-276.

Horowitz, A. (2004). The prevalence and consequences of vision impairment in later life. *Topics in Geriatric Rehabilitation, 20*, 185-195.

Houston, T. K., Cooper, L. A., & Ford, D. E. (2002). Internet support groups for depression: a 1-year prospective cohort study. *American Journal of Psychiatry, 159*, 2062-2068.

Howrey, T. B., Raji, A. M., Masel, M. M., & Peek, K. M. (2015). Stability in cognitive function over 18 years: prevalence and predictors among older Mexican Americans. *Current Alzheimer Research, 12*, 614-621.

Hsu, H. C. (2007). Does social participation by the elderly reduce mortality and cognitive impairment? *Aging & Mental Health, 11*, 699-707.

Hughes, D. J., Rowe, M., Batey, M., & Lee, A. (2012). A tale of two sites: Twitter vs. Facebook and the personality predictors of social media usage. *Computers in Human Behavior, 28*, 561-569.

Hughes, M. E. & Waite, L. J. (2002). Health in household context: living arrangements and health in late middle-age. *Journal of Health and Social Behaviour, 43*, 1-21.

Hughes, M. E., Waite, L. J., Hawkley, L. C., & Cacioppo, J. T. (2004). A short scale for measuring loneliness in large surveys results from two population-based studies. *Research on Aging, 26,* 655-672.

Hughes, T. F., Andel, R., Small, B. J., Borenstein, A. R., & Mortimer, J. A. (2008). The association between social resources and cognitive change in older adults: Evidence from the Charlotte County Healthy Aging Study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 63,* P241-P244.

Hughes, T. F., Flatt, J. D., Fu, B., Chang, C. C. H., & Ganguli, M. (2013). Engagement in social activities and progression from mild to severe cognitive impairment: the MYHAT study. *International Psychogeriatrics, 25,* 587-595.

Hultsch, D. F., Hammer, M., & Small, B. J. (1993). Age differences in cognitive performance in later life: Relationships to self-reported health and activity life style. *Journal of Gerontology, 48,* P1-P11.

Hultsch, D. F., Hertzog, C., Small, B. J., & Dixon, R. A. (1999). Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? *Psychology and Aging, 14*, 245.

Huntley, J. D., Hampshire, A., Bor, D., Owen, A., & Howard, R. J. (2016). Adaptive working memory strategy training in early Alzheimer's disease: randomised controlled trial. *The British Journal of Psychiatry: the Journal of Mental Science, 210*, 61-66.

Huntley, J., Corbett, A., Wesnes, K., Brooker, H., Stenton, R., Hampshire, A., & Ballard, C. (2018). Online assessment of risk factors for dementia and cognitive function in healthy adults. *International Journal of Geriatric Psychiatry, 33*, 1-8.

Huppert, F. A., Brayne, C., Gill, C., Paykel, E. S., & Beardsall, L. (1995). CAMCOG – A concise neuropsychological test to assist dementia diagnosis: Socio-demographic determinants in an elderly population sample. *British Journal of Clinical Psychology, 34*, 529-541.

Iliffe, S., Kharicha, K., Harari, D., Swift, C., Gillmann, G., & Stuck, A. E. (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, 57*, 277-282.

Iwasa, H., Yoshida, Y., Kai, I., Suzuki, T., Kim, H., & Yoshida, H. (2012). Leisure activities and cognitive function in elderly community-dwelling individuals in Japan: a 5-year prospective cohort study. *Journal of Psychosomatic Research, 72,* 159-164.

Jagger, C., Matthews, F. E., Wohland, P., Fouweather, T., Stephan, B. C., Robinson, L., Arthur, A., & Brayne, C. (2016). A comparison of health expectancies over two decades in England: results of the Cognitive Function and Ageing Study I and II. *The Lancet, 387,* 779-786.

Jagger, C., Matthews, R., Lindesay, J., Robinson, T., Croft, P., & Brayne, C. (2009). The effect of dementia trends and treatments on longevity and disability: a simulation model based on the MRC Cognitive Function and Ageing Study (MRC CFAS). *Age and Ageing, 38*, 319-325.

James, B. D., Boyle, P. A., Buchman, A. S., Barnes, L. L., & Bennett, D. A. (2011). Life space and risk of Alzheimer disease, mild cognitive impairment, and cognitive decline in old age. *The American Journal of Geriatric Psychiatry, 19*, 961-969.

James, B. D., Wilson, R. S., Barnes, L. L., & Bennett, D. A. (2011). Late-life social activity and cognitive decline in old age. *Journal of the International Neuropsychological Society, 17*, 998-1005.

Jedrziewski, M. K., Ewbank, D. C., Wang, H., & Trojanowski, J. Q. (2014). The impact of exercise, cognitive activities, and socialization on cognitive function: results from the national long-term care survey. *American Journal of Alzheimer's Disease & Other Dementias, 29,* 372-378.

Jekel, K., Damian, M., Wattmo, C., Hausner, L., Bullock, R., Connelly, P. J., Dubois, B., Eriksdotter, M., Ewers, M., Graessel, E., Kramberger, M. G., Law, E., Mecocci, P., Molinuevo, J. L., Nygård, L., Olde-Rikkert, M. G. M., Orgogozo, J., Pasquier, F., Peres, K., Salmon, E., Sikkes, S. A. M., Sobow, T., Spiegel, R., Tsolaki, M., Winblad, B., & Kramberger, M. G. (2015). Mild cognitive impairment and deficits in instrumental activities of daily living: a systematic review. *Alzheimer's Research & Therapy, 7,* 1.

Jolly, A. (1966). Lemur social behavior and primate intelligence. *Science, 153*, 501-506.

Jylhä, M. (2004). Old age and loneliness: cross-sectional and longitudinal analyses in the Tampere Longitudinal Study on Aging. *Canadian Journal on Aging, 23*, 157-168.

Jylhä, M., & Jokela, J. (1990). Individual experiences as cultural–a cross-cultural study on loneliness among the elderly. *Ageing & Society, 10*, 295-315.

Kahle-Wrobleski, K., Corrada, M. M., Li, B., & Kawas, C. H. (2007). Sensitivity and Specificity of the Mini-Mental State Examination for Identifying Dementia in the Oldest-Old: The 90+ Study. *Journal of the American Geriatrics Society, 55,* 284-289.

Kanai, R., Bahrami, B., Roylance, R., & Rees, G. (2011). Online social network size is reflected in human brain structure. *Proceedings of the Royal Society B*, rspb20111959.

Kåreholt, I., Lennartsson, C., Gatz, M., & Parker, M. G. (2011). Baseline leisure time activity and cognition more than two decades later. *International Journal of Geriatric Psychiatry, 26*, 65-74.

Karlamangla, A. S., Miller-Martinez, D., Aneshensel, C. S., Seeman, T. E., Wight, R. G., & Chodosh, J. (2009). Trajectories of cognitive function in late life in the United States: demographic and socioeconomic predictors. *American Journal of Epidemiology, 170*, 331-342.

Karp, A., Paillard-Borg, S., Wang, H. X., Silverstein, M., Winblad, B., & Fratiglioni, L. (2005). Mental, physical and social components in leisure activities equally contribute to decrease dementia risk. *Dementia and Geriatric Cognitive Disorders, 21*, 65-73.

Kashdan, T. B., & Roberts, J. E. (2007). Social anxiety, depressive symptoms, and post-event rumination: Affective consequences and social contextual influences. *Journal of Anxiety Disorders, 21,* 284-301.

Katja, P., Timo, T., Taina, R., & Tiina-Mari, L. (2014). Do mobility, cognitive functioning, and depressive symptoms mediate the association between social activity and mortality risk among older men and women? *European Journal of Ageing, 11*, 121-130.

Katzman, R. (1993). Education and the prevalence of dementia and Alzheimer's disease. *Neurology, 43*, 13-20.

Katzman, R., Terry, R., DeTeresa, R., Brown, T., Davies, P., Fuld, P., Renbing, X., & Peck, A. (1988). Clinical, pathological, and neurochemical changes in dementia: a subgroup with preserved mental status and numerous neocortical plaques. *Annals of Neurology, 23*, 138-144.

Kavanagh, A. M., Bentley, R., Turrell, G., Broom, D. H., & Subramanian, S. V. (2006). Does gender modify associations between self-rated health and the social and economic characteristics of local environments? *Journal of Epidemiology & Community Health, 60*, 490-495.

Kawachi, I., & Berkman, L. F. (2001). Social ties and mental health. *Journal of Urban health, 78*, 458-467.

Kelly, M. E., Duff, H., Kelly, S., Power, J. E. M., Brennan, S., Lawlor, B. A., & Loughrey, D. G. (2017). The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review. *BioMed Central: Systematic Reviews, 6*, 259.

Kesler, S. R., Adams, H. F., Blasey, C. M., & Bigler, E. D. (2003). Premorbid intellectual functioning, education, and brain size in traumatic brain injury: an investigation of the cognitive reserve hypothesis. *Applied Neuropsychology, 10*, 153-162.

Kharicha, K., Iliffe, S., Harari, D., Swift, C., Gillmann, G. & Stuck, A. (2007). Health risk appraisal in older people: are older people living alone an 'at-risk' group? *British Journal of General Practice, 57*, 271-276.

Kim, J. W., Lee, D. Y., Lee, B. C., Jung, M. H., Kim, H., Choi, Y. S., & Choi, I. G. (2012). Alcohol and cognition in the elderly: a review. *Psychiatry Investigation, 9*, 8-16.

Kim, W., Kreps, G. L., & Shin, C. N. (2015). The role of social support and social networks in health information–seeking behavior among Korean Americans: a qualitative study. *BioMed Central: International Journal for Equity in Health, 14*, 40.

Kivipelto, M., Solomon, A., Ahtiluoto, S., Ngandu, T., Lehtisalo, J., Antikainen, R., Backman, L., Hanninen, T., Jula, A., Laatikainen, T., Lindstrom, J., Mangialasche, F., Nissinen, A., Paajanen, T., Pajala, S., Peltonen, M., Rauramaa, R., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto. J., &Soininen, H. (2013). The Finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER): study design and progress. *Alzheimer's & Dementia, 9*, 657-665.

Klaming, R., Annese, J., Veltman, D. J., & Comijs, H. C. (2017). Episodic memory function is affected by lifestyle factors: a 14-year follow-up study in an elderly population. *Aging, Neuropsychology, and Cognition, 24*, 528-542.

Klinenberg, E. (2016). Social isolation, loneliness, and living alone: Identifying the risks for public health. *American Journal of Public Health, 106*, 786-787.

Kobayashi, K. M., 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, 21*, 374-397.

Köbe, T., Witte, A. V., Schnelle, A., Lesemann, A., Fabian, S., Tesky, V. A., Pantel, J., & Flöel, A. (2016). Combined omega-3 fatty acids, aerobic exercise and cognitive stimulation prevents decline in gray matter volume of the frontal, parietal and cingulate cortex in patients with mild cognitive impairment. *Neuroimage, 131*, 226-238.

Korte, J., Bohlmeijer, E. T., Cappeliez, P., Smit, F., & Westerhof, G. J. (2012). Life review therapy for older adults with moderate depressive symptomatology: a pragmatic randomized controlled trial. *Psychological Medicine, 42,* 1163-1173.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9. *Journal of General Internal Medicine, 16*, 606-613.

Kuchibhatla, M. N., Fillenbaum, G. G., Hybels, C. F., & Blazer, D. G. (2012). Trajectory classes of depressive symptoms in a community sample of older adults. *Acta Psychiatrica Scandinavica, 125*, 492-501.

Kuiper, J. S., Zuidersma, M., Zuidema, S. U., Burgerhof, J. G., Stolk, R. P., Voshaar, R. C. O., & Smidt, N. (2016). Social relationships and cognitive decline: a systematic review and meta-analysis of longitudinal cohort studies. *International Journal of Epidemiology*, *45*, 1169-1206.

Kulmala, J., Ngandu, T., & Kivipelto, M. (2018). Prevention Matters: Time for Global Action and Effective Implementation. *Journal of Alzheimer's Disease, 64*, S191-S198.

Kupferberg, A., Bicks, L., & Hasler, G. (2016). Social functioning in major depressive disorder. *Neuroscience & Biobehavioral Reviews, 69,* 313-332.

Kvaal, K., McDougall, F. A., Brayne, C., Matthews, F. E., & Dewey, M. E. (2008). Co-occurrence of anxiety and depressive disorders in a community sample of older people: results from the MRC CFAS (Medical Research Council Cognitive Function and Ageing Study). *International Journal of Geriatric Psychiatry, 23,* 229-237.

Kwak, S., Joo, W. T., Youm, Y., & Chey, J. (2018). Social brain volume is associated with in-degree social network size among older adults. *Proceedings of the Royal Society B, 285*, 20172708.

Laidlaw, K., Davidson, K., Toner, H., Jackson, G., Clark, S., Law, J., Howley, M., Bowie, G., Connery, H., & Cross, S. (2008). A randomised controlled trial of cognitive behaviour therapy vs treatment as usual in the treatment of mild to moderate late life depression. *International Journal of Geriatric Psychiatry, 23*, 843-850.

Lansford, J. E., Sherman, A. M., & Antonucci, T. C. (1998). Satisfaction with social networks: An examination of socioemotional selectivity theory across cohorts. *Psychology and Aging, 13*, 544-552.

Larson, R., Zuzanek, J., & Mannell, R. (1985). Being alone versus being with people: Disengagement in the daily experience of older adults. *Journal of Gerontology, 40,* 375-381.

Lazarov, O., Robinson, J., Tang, Y. P., Hairston, I. S., Korade-Mirnics, Z., Lee, V. M. Y., Hersh, L. B., Sapolsky, R. M., Mirnics, K., & Sisodia, S. S. (2005). Environmental enrichment reduces Aβ levels and amyloid deposition in transgenic mice. *Cell, 120*, 701-713.

Lee, S. H., & Kim, Y. B. (2016). Which type of social activities may reduce cognitive decline in the elderly? A longitudinal population-based study. *BioMed Central: Geriatrics, 16*, 165.

Lee, Y., Kim, J., & Back, J. H. (2009). The influence of multiple lifestyle behaviors on cognitive function in older persons living in the community. *Preventive Medicine, 48*, 86-90.

LeMoult, J., Carver, C. S., Johnson, S. L., & Joormann, J. (2015). Predicting change in symptoms of depression during the transition to university: The roles of BDNF and working memory capacity. *Cognitive, Affective, & Behavioral Neuroscience, 15*, 95-103.

Leung, G. T. Y., Fung, A. W. T., Tam, C. W. C., Lui, V. W. C., Chiu, H. F. K., Chan, W. M., & Lam, L. C. W. (2011). Examining the association between late-life leisure activity participation and global cognitive decline in community-dwelling elderly Chinese in Hong Kong. *International Journal of Geriatric Psychiatry, 26*, 39-47.

Levasseur, M., Cohen, A. A., Dubois, M. F., Généreux, M., Richard, L., Therrien, F. H., & Payette, H. (2015). Environmental factors associated with social participation of older adults living in metropolitan, urban, and rural areas: The NuAge study. *American Journal of Public Health, 105,* 1718-1725.

Lewis, G., Kounali, D. Z., Button, K. S., Duffy, L., Wiles, N. J., Munafo, M. R., Harmer, C. J., & Lewis, G. (2017). Variation in the recall of socially rewarding information and depressive symptom severity: a prospective cohort study. *Acta Psychiatrica Scandinavica, 135*, 489-498.

Lewis, P. A., Rezaie, R., Brown, R., Roberts, N., & Dunbar, R. I. (2011). Ventromedial prefrontal volume predicts understanding of others and social network size. *Neuroimage, 57*, 1624-1629.

Lezak, M. D. (2004). *Neuropsychological assessment*. Oxford, UK: Oxford University Press.

Lezak, M. D., Howieson, D. B., Bigler, E. D., & Tranel. D. (2012). *Neuropsychological assessment*. Oxford, UK: Oxford University Press.

Li, C. L., & Hsu, H. C. (2015). Cognitive function and associated factors among older people in Taiwan: Age and sex differences. *Archives of Gerontology and Geriatrics, 60*, 196-200.

Li, T., & Zhang, Y. (2015). Social network types and the health of older adults: Exploring reciprocal associations. *Social Science & Medicine, 130*, 59-68.

Lin, J. S., O'Connor, E., Rossom, R. C., Perdue, L. A., & Eckstrom, E. (2013). Screening for cognitive impairment in older adults: a systematic review for the US Preventive Services Task Force. *Annals of Internal Medicine, 159*, 601-612.

Lin, N., Ye, X., & Ensel, W. M. (1999). Social support and depressed mood: a structural analysis. *Journal of Health and Social Behavior, 40,* 344-359.

Lincoln, K. D. (2000). Social support, negative social interactions, and psychological well-being. *Social Service Review, 74*, 231-252.

Lindeboom, J., & Weinstein, H. (2004). Neuropsychology of cognitive ageing, minimal cognitive impairment, Alzheimer's disease, and vascular cognitive impairment. *European Journal of Pharmacology, 490*, 83-86.

Lindstrom, H. A., Fritsch, T., Petot, G., Smyth, K. A., Chen, C. H., Debanne, S. M., Lerner, A. J., & Friedland, R. P. (2005). The relationships between television viewing in midlife and the development of Alzheimer's disease in a case-control study. *Brain and Cognition, 58*, 157-165.

Lipnicki, D. M., Sachdev, P. S., Crawford, J., Reppermund, S., Kochan, N. A., Trollor, J. N., Draper, B., Slavin, M. J., Kang, K., Lux, O., Mather, K. A., & Brodaty, H. (2013). Risk factors for late-life cognitive decline and variation with age and sex in the Sydney Memory and Ageing Study. *PloS One, 8,* e65841.

Litwin, H. (2012). Physical activity, social network type, and depressive symptoms in late life: An analysis of data from the National Social Life, Health and Aging Project. *Aging & Mental Health, 16*, 608-616.

Litwin, H., & Stoeckel, K. J. (2013). *The social networks of older Europeans.* Boston, MA, USA: Springer.

Liverman, C. T., Yaffe, K., & Blazer, D. G. (2015). *Cognitive aging: Progress in understanding and opportunities for action*. Washington, DC, USA: National Academies Press.

Livingston, G., Sommerlad, A., Orgeta, V., Costafreda, S. G., Huntley, J., Ames, D., Ballard, C., Banerjee, S., Burns, A., Cohen-Mansfield, J., Cooper, C., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Larson, E., Ritchie, K., Rockwood, K., Sampson, E. L., Samus, Q., Schneider, L. S., Selbæk, G., Teri, L., & Mukadam, N. (2017). Dementia prevention, intervention, and care. *The Lancet, 390*, 2673-2734.

Lopez, O. L., Kuller, L. H., Becker, J. T., Dulberg, C., Sweet, R. A., Gach, H. M., & DeKosky, S. T. (2007). Incidence of dementia in mild cognitive impairment in the cardiovascular health study cognition study. *Archives of Neurology, 64*, 416-420.

Lorentz, W. J., Scanlan, J. M., & Borson, S. (2002). Brief screening tests for dementia. *Canadian Journal of Psychiatry, 47,* 723-733.

Luanaigh, C. Ó., & Lawlor, B. A. (2008). Loneliness and the health of older people. *International Journal of Geriatric Psychiatry, 23,* 1213-1221.

Lubben, J. E. (1988). Assessing social networks among elderly populations. *Family & Community Health, 11*, 42-52.

Lubben, J., Blozik, E., Gillmann, G., Iliffe, S., von Renteln Kruse, W., Beck, J. C., & Stuck, A. E. (2006). Performance of an abbreviated version of the Lubben Social Network Scale among three European community-dwelling older adult populations. *The Gerontologist, 46*, 503-513.

Mahncke, H. W., Bronstone, A., & Merzenich, M. M. (2006). Brain plasticity and functional losses in the aged: scientific bases for a novel intervention. *Progress in Brain Research, 157*, 81-109.

Mahoney, J. E., Eisner, J., Havighurst, T., Gray, S., & Palta, M. (2000). Problems of older adults living alone after hospitalization. *Journal of General Internal Medicine, 15,* 611-619.

Malouff, J. M., Thorsteinsson, E. B., & Schutte, N. S. (2007). The efficacy of problem solving therapy in reducing mental and physical health problems: a meta-analysis. *Clinical Psychology Review, 27*, 46-57.

Marioni, R. E., Proust-Lima, C., Amieva, H., Brayne, C., Matthews, F. E., Dartigues, J. F., & Jacqmin-Gadda, H. (2014). Cognitive lifestyle jointly predicts longitudinal cognitive decline and mortality risk. *European Journal of Epidemiology, 29,* 211-219.

Marioni, R. E., Proust-Lima, C., Amieva, H., Brayne, C., Matthews, F. E., Dartigues, J. F., & Jacqmin-Gadda, H. (2015). Social activity, cognitive decline and dementia risk: a 20-year prospective cohort study. *BioMed Central: Public Health, 15*, 1089.

Marsden, P. V., & Friedkin, N. E. (1994). Network studies of social influence. *Sociological Methods & Research, 22*, 127-151.

Martin, G. M. (2004). Defeating dementia. *Nature, 431*, 247-248.

Martyr, A., & Clare, L. (2012). Executive function and activities of daily living in Alzheimer's disease: a correlational meta-analysis. *Dementia and Geriatric Cognitive Disorders, 33*, 189-203.

Masic, I., Sivic, S., Toromanovic, S., Borojevic, T., & Pandza, H. (2012). Social networks in improvement of health care. *Materia Socio-Medica, 24*, 48-53.

Masliah, E., & Salmon, D. P. (2016). When Cognitive Decline Becomes Pathology: From Normal Aging to Alzheimer's Disease. *Genes, Environment and Alzheimer's Disease,* 29-50.

Mathers, C. D., Stevens, G. A., Boerma, T., White, R. A., & Tobias, M. I. (2015). Causes of international increases in older age life expectancy. *The Lancet, 385*, 540-548.

Matthews, F. E., Arthur, A., Barnes, L. E., Bond, J., Jagger, C., Robinson, L., Brayne, C., & Medical Research Council Cognitive Function and Ageing Collaboration. (2013). A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II. *The Lancet, 382*, 1405-1412.

Matthews, F. E., Stephan, B. C., McKeith, I. G., Bond, J., Brayne, C., & Medical Research Council Cognitive Function and Ageing Study. (2008). Two-year progression from mild cognitive impairment to dementia: to what extent do different definitions agree? *Journal of the American Geriatrics Society, 56,* 1424-1433.

Mattos, M. K., Snitz, B. E., Lingler, J. H., Burke, L. E., Novosel, L. M., & Sereika, S. M. (2017). Older Rural-and Urban-Dwelling Appalachian Adults With Mild Cognitive Impairment. *The Journal of Rural Health, 33*, 208-216.

Mazzuco, S., Meggiolaro, S., Ongaro, F., & Toffolutti, V. (2016). Living arrangement and cognitive decline among older people in Europe. *Ageing and Society, 37,* 1-23.

McDermott, L. M., & Ebmeier, K. P. (2009). A meta-analysis of depression severity and cognitive function. *Journal of Affective Disorders, 119*, 1-8.

McDougall, F. A., Kvaal, K., Matthews, F. E., Paykel, E., Jones, P. B., Dewey, M. E., & Brayne, C. (2007). Prevalence of depression in older people in England and Wales: the MRC CFAS Study. *Psychological Medicine, 37*, 1787-1795.

McGue, M., & Christensen, K. (2007). Social activity and healthy aging: a study of aging Danish twins. *Twin Research and Human Genetics, 10*, 255-265.

McHugh Power, J., Lawlor, B. A., & Kee, F. (2017). Social support mediates the relationships between extraversion, neuroticism, and cognitive function in older adults. *Public Health, 147*, 144-152.

McHugh Power, J., Tang, J., Lawlor, B., Kenny, R. A., & Kee, F. (2018). Mediators of the relationship between social activities and cognitive function among older Irish adults: results from the Irish longitudinal study on ageing. *Aging & Mental Health, 22*, 129-134.

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Kawas, C. H., Klunk, W. E., Koroshetz, W. J., Manly, J. J., Mayeux, R., Mohs, R. C., Morris, J. C., Rossor, M. N., Scheltens, M. C., Thies, B., Weintraub, S., & Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia, 7*, 263-269.

Mendes de Leon, C. F., Glass, T. A., & Berkman, L. F. (2003). Social engagement and disability in a community population of older adults: the New Haven EPESE. *American Journal of Epidemiology, 147*, 633-642.

Middleton, L. E., & Yaffe, K. (2010). Targets for the prevention of dementia. *Journal of Alzheimer's Disease, 20*, 915-924.

Milne, A. (2010). Dementia screening and early diagnosis: The case for and against. *Health, Risk & Society, 12*, 65-76.

Minder, C. E., Müller, T., Gillmann, G., Beck, J. C., & Stuck, A. E. (2002). Subgroups of refusers in a disability prevention trial in older adults: baseline and follow-up analysis. *American journal of public health, 92,* 445-450.

Mitchell, A. J., & Shiri-Feshki, M. (2009). Rate of progression of mild cognitive impairment to dementia–meta-analysis of 41 robust inception cohort studies. *Acta Psychiatrica Scandinavica, 119*, 252-265.

Mittelman, M. S., Ferris, S. H., Steinberg, G., Shulman, E., Mackell, J. A., Ambinder, A., & Cohen, J. (1993). An intervention that delays institutionalization of Alzheimer's disease patients: treatment of spouse-caregivers. *The Gerontologist, 33,* 730-740.

Monastero, R., Palmer, K., Qiu, C., Winblad, B., & Fratiglioni, L. (2007). Heterogeneity in risk factors for cognitive impairment, no dementia: population-based longitudinal study from the Kungsholmen Project. *The American Journal of Geriatric Psychiatry, 15*, 60-69.

Mortimer, J. A., Ding, D., Borenstein, A. R., DeCarli, C., Guo, Q., Wu, Y., Qianhua, Z., & Chu, S. (2012). Changes in brain volume and cognition in a randomized trial of exercise and social interaction in a community-based sample of non-demented Chinese elders. *Journal of Alzheimer's Disease, 30*, 757-766.

Mortimer, J. A., Snowdon, D. A., & Markesbery, W. R. (2003). Head circumference, education and risk of dementia: findings from the Nun Study. *Journal of Clinical and Experimental Neuropsychology, 25*, 671-679.

Mousavi-Nasab, S. M., Kormi-Nouri, R., & Nilsson, L. G. (2014). Examination of the bidirectional influences of leisure activity and memory in old people: A dissociative effect on episodic memory. *British Journal of Psychology, 105*, 382-398.

Mousavi-Nasab, S. M., Kormi-Nouri, R., Sundström, A., & Nilsson, L. G. (2012). The effects of marital status on episodic and semantic memory in healthy middle-aged and old individuals. *Scandinavian Journal of Psychology, 53*, 1-8.

Murad, K., Goff Jr, D. C., Morgan, T. M., Burke, G. L., Bartz, T. M., Kizer, J. R., Chaudhry, S. I., Gottidiener, J. S., & Kitzman, D. W. (2015). Burden of comorbidities and functional and cognitive impairments in elderly patients at the initial diagnosis of heart failure and their impact on total mortality: the Cardiovascular Health Study. *Journal of the American College of Cardiology: Heart Failure, 3*, 542-550.

Murphy, M., & Grundy, E. (2003). Mothers with living children and children with living mothers: The role of fertility and mortality in the period 1911-2050. *Population Trends London, 112*, 36-45.

Nakano, Y., Baba, H., Maeshima, H., Kitajima, A., Sakai, Y., Baba, K., Suzuki, T., & Arai, H. (2008). Executive dysfunction in medicated, remitted state of major depression. *Journal of Affective Disorders, 111*, 46-51.

National Health Service England. (2015). Practical guide to healthy ageing. Accessed 01/09/2018: https://www.england.nhs.uk/wp-content/uploads/2015/09/hlthy-ageing-brochr.pdf

National Institute for Health and Care Excellence. (2015). Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset. Accessed 03/09/2018: https://www.nice.org.uk/guidance/ng16/resources/dementia-disability-and-frailty-in-later-life-midlife-approaches-to-delay-or-prevent-onset

National Research Council (2000). *The aging mind: Opportunities in cognitive research*. Washington, DC, USA: National Academy Press.

Nebes, R. D., Butters, M. A., Houck, P. R., Zmuda, M. D., Aizenstein, H., Pollock, B. G., Mulsant, B. H., & Reynolds, C. F. (2001). Dual-task performance in depressed geriatric patients. *Psychiatry Research, 102*, 139-151.

Nebes, R. D., Reynolds, C. F., Boada, F., Meltzer, C. C., Fukui, M. B., Saxton, J., Halligan, E. M., & DeKosky, S. T. (2002). Longitudinal increase in the volume of white matter hyper-intensities in late-onset depression. *International Journal of Geriatric Psychiatry, 17*, 526-530.

Nelson, L. A., Noonan, C. J., Goldberg, J., & Buchwald, D. S. (2013). Social engagement and physical and cognitive health among American Indian participants in the health and retirement study. *Journal of Cross-Cultural Gerontology, 28,* 453-463.

Newall, N. E., Chipperfield, J. G., & Bailis, D. S. (2014). Predicting stability and change in loneliness in later life. *Journal of Social and Personal Relationships, 31*, 335-351.

Ng, T. P., Niti, M., Chiam, P. C., & Kua, E. H. (2007). Ethnic and educational differences in cognitive test performance on mini-mental state examination in Asians. *The American Journal of Geriatric Psychiatry, 15*, 130-139.

Ngandu, T., Lehtisalo, J., Solomon, A., Levälahti, E., Ahtiluoto, S., Antikainen, R., Bäckman. L., Hänninen, T., Jula, A., Laatikainen, T., Lindström, J., Mangialasche, F., Paajanen, T., Pajala, S., Peltonen, M., Rauramaa, R., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto, J., Soininen, H., & Kivipelto, M. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *The Lancet, 385*, 2255-2263.

Nicholson Jr, N. R. (2009). Social isolation in older adults: an evolutionary concept analysis. *Journal of Advanced Nursing, 65,* 1342-1352.

Nishiguchi, S., Yamada, M., Sonoda, T., Kayama, H., Tanigawa, T., Yukutake, T., & Aoyama, T. (2013). Cognitive decline predicts long-term care insurance requirement certification in community-dwelling older Japanese adults: A prospective cohort study. *Dementia and Geriatric Cognitive Disorders Extra, 3,* 312-319.

Niti, M., Yap, K. B., Kua, E. H., Tan, C. H., & Ng, T. P. (2008). Physical, social and productive leisure activities, cognitive decline and interaction with APOE-ε4 genotype in Chinese older adults. *International Psychogeriatrics, 20*, 237-251.

Njegovan, V., Man-Son-Hing, M., Mitchell, S. L., & Molnar, F. J. (2001). The hierarchy of functional loss associated with cognitive decline in older persons. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56,* M638-M643.

Norton, S., Matthews, F. E., Barnes, D. E., Yaffe, K., & Brayne, C. (2014). Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *The Lancet Neurology, 13*, 788-794.

Nucci, M., Mapelli, D., & Mondini, S. (2012). Cognitive Reserve Index questionnaire (CRIq): a new instrument for measuring cognitive reserve. *Aging Clinical and Experimental Research, 24*, 218-226.

O'Bryant, S. E., Humphreys, J. D., Smith, G. E., Ivnik, R. J., Graff-Radford, N. R., Petersen, R. C., & Lucas, J. A. (2008). Detecting dementia with the mini-mental state examination in highly educated individuals. *Archives of Neurology, 65*, 963-967.

O'Luanaigh, C., O'connell, H., Chin, A. V., Hamilton, F., Coen, R., Walsh, C., Caokley, C., Cunningham, C., & Lawlor, B. A. (2012). Loneliness and cognition in older people: the Dublin Healthy Ageing study. *Aging & Mental Health, 16*, 347-352.

Obisesan, T. O., & Gillum, R. F. (2009). Cognitive function, social integration and mortality in a US national cohort study of older adults. *BioMed Central: Geriatrics, 9,* 33.

Office for National Statistics. (2018). Accessed 16/07/2018: https://www.statista.com/statistics/281616/people-living-alone-in-the-united-kingdom-uk-by-age-and-gender/

Okabayashi, H., Liang, J., Krause, N., Akiyama, H., & Sugisawa, H. (2004). Mental health among older adults in Japan: do sources of social support and negative interaction make a difference? *Social Science & Medicine, 59*, 2259-2270.

Okereke, O. I., & Grodstein, F. (2013). Phobic anxiety and cognitive performance over 4 years among community-dwelling older women in the Nurses' Health Study. *The American Journal of Geriatric Psychiatry, 21*, 1125-1134.

Olesen, S. C., & Berry, H. L. (2011). Community participation and mental health during retirement in community sample of Australians. *Aging & Mental Health, 15*, 186-197.

Oliveira, S. E., Esteves, F., & Carvalho, H. (2015). Clinical profiles of stigma experiences, self-esteem and social relationships among people with schizophrenia, depressive, and bipolar disorders. *Psychiatry Research, 229,* 167-173.

Opdebeeck, C., Martyr, A., & Clare, L. (2016). Cognitive reserve and cognitive function in healthy older people: a meta-analysis. *Aging, Neuropsychology, and Cognition, 23*, 40-60.

Opdebeeck, C., Matthews, F. E., Wu, Y. T., Woods, R. T., Brayne, C., & Clare, L. (2018). Cognitive reserve as a moderator of the negative association between mood and cognition: evidence from a population-representative cohort. *Psychological Medicine, 48*, 61-71.

Owen, A. M., Downes, J. J., Sahakian, B. J., Polkey, C. E., & Robbins, T. W. (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia, 28*, 1021-1034.

Ownby, R. L., Crocco, E., Acevedo, A., John, V., & Loewenstein, D. (2006). Depression and risk for Alzheimer disease: systematic review, meta-analysis, and meta-regression analysis. *Archives of General Psychiatry, 63*, 530-538.

Paillard-Borg, S., Fratiglioni, L., Winblad, B., & Wang, H. X. (2009). Leisure activities in late life in relation to dementia risk: principal component analysis. *Dementia and Geriatric Cognitive Disorders, 28*, 136-144.

Palmer, K., Berger, A. K., Monastero, R., Winblad, B., Bäckman, L., & Fratiglioni, L. (2007). Predictors of progression from mild cognitive impairment to Alzheimer disease. *Neurology, 68*, 1596-1602.

Pandya, S. Y., Clem, M. A., Silva, L. M., & Woon, F. L. (2016). Does mild cognitive impairment always lead to dementia? A review. *Journal of the Neurological Sciences, 369*, 57-62.

Panza, F., Capurso, C., D'introno, A., Colacicco, A. M., Zenzola, A., Menga, R., Pistoia, G., Santamato, A., Scafato, E., Gandin, C., Capurso, A., & Solfrizzi, V. (2008). Impact of depressive symptoms on the rate of progression to dementia in patients affected by mild cognitive impairment. The Italian Longitudinal Study on Aging. *International Journal of Geriatric Psychiatry, 23*, 726-734.

Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. *Annual Review of Psychology, 60*, 173-196.

Park, D. C., Lodi-Smith, J., Drew, L., Haber, S., Hebrank, A., Bischof, G. N., & Aamodt, W. (2014). The impact of sustained engagement on cognitive function in older adults: the synapse project. *Psychological Science, 25,* 103-112.

Park, H. L., O'Connell, J. E., & Thomson, R. G. (2003). A systematic review of cognitive decline in the general elderly population. *International Journal of Geriatric Psychiatry, 18*, 1121-1134.

Paúl, C., Ribeiro, O., & Santos, P. (2010). Cognitive impairment in old people living in the community. *Archives of Gerontology and Geriatrics, 51*, 121-124.

Pauly, T., Lay, J. C., Nater, U. M., Scott, S. B., & Hoppmann, C. A. (2017). How We Experience Being Alone: Age Differences in Affective and Biological Correlates of Momentary Solitude. *Gerontology, 63*, 55-66.

Peel, N., Bartlett, H., & McClure, R. (2004). Healthy ageing: how is it defined and measured? *Australasian Journal on Ageing, 23,* 115-119.

Peplau, L. A., & Caldwell, M. A. (1978). Loneliness: A cognitive analysis. *Essence, 2,* 207-220

Perese, E. F., & Wolf, M. (2005). Combatting loneliness among persons with severe mental illness: social network intervention, characteristics, effectiveness, and applicability. *Issues in Mental Health Nursing, 26*, 591-609.

Perry, B. L., & Pescosolido, B. A. (2012). Social network dynamics and biographical disruption: The case of "first-timers" with mental illness. *American Journal of Sociology, 118*, 134-175.

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine, 256*, 183-194.

Petersen, R. C., Caracciolo, B., Brayne, C., Gauthier, S., Jelic, V., & Fratiglioni, L. (2014). Mild cognitive impairment: a concept in evolution. *Journal of Internal Medicine, 275*, 214-228.

Petersen, R. C., Doody, R., Kurz, A., Mohs, R. C., Morris, J. C., Rabins, P. V., Ritchie, K., Rossor, M., Thal, L., & Winblad, B. (2001). Current concepts in mild cognitive impairment. *Archives of Neurology, 58*, 1985-1992.

Petersen, R. C., Roberts, R. O., Knopman, D. S., Boeve, B. F., Geda, Y. E., Ivnik, R. J., Smith, G. E., & Jack, C. R. (2009). Mild cognitive impairment: ten years later. *Archives of Neurology, 66*, 1447-1455.

Petersen, R. C., Stevens, J. C., Ganguli, M., Tangalos, E. G., Cummings, J. L., & DeKosky, S. T. (2001). Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology, 56*, 1133-1142.

Peterson, R. A., & Brown, S. P. (2005). On the use of beta coefficients in meta-analysis. *Journal of Applied Psychology, 90*, 175-181.

Phillipson, C., Bernard, M., Phillips, J., & Ogg, J. (1998). The family and community life of older people: household composition and social networks in three urban areas. *Ageing and Society, 18*, 259-289.

Phillipson, L., Magee, C., Jones, S., Reis, S., & Skaldzien, E. (2015). Dementia attitudes and help-seeking intentions: an investigation of responses to two scenarios of an experience of the early signs of dementia. *Aging & Mental Health, 19,* 968-977.

Pietrzak, R. H., Maruff, P., Woodward, M., Fredrickson, J., Fredrickson, A., Krystal, J. H., Southwick, S. M., & Darby, D. (2012). Mild worry symptoms predict decline in learning and memory in healthy older adults: a 2-year prospective cohort study. *The American Journal of Geriatric Psychiatry, 20*, 266-275.

Pietschnig, J., Penke, L., Wicherts, J. M., Zeiler, M., & Voracek, M. (2015). Meta-analysis of associations between human brain volume and intelligence differences: How strong are they and what do they mean? *Neuroscience & Biobehavioral Reviews, 57*, 411-432.

Pimouguet, C., Rizzuto, D., Schön, P., Shakersain, B., Angleman, S., Lagergren, M., Fratiglioni, L., & Xu, W. (2015). Impact of living alone on institutionalization and mortality: a population-based longitudinal study. *The European Journal of Public Health, 26*, 182-187.

Pinquart, M., & Forstmeier, S. (2012). Effects of reminiscence interventions on psychosocial outcomes: A meta-analysis. *Aging & Mental Health, 16,* 541-558.

Pinquart, M., Duberstein, P. R., & Lyness, J. M. (2007). Effects of psychotherapy and other behavioral interventions on clinically depressed older adults: a meta-analysis. *Aging & Mental Health, 11*, 645-657.

Pitkala, K. H., Routasalo, P., Kautiainen, H., Sintonen, H., & Tilvis, R. S. (2011). Effects of socially stimulating group intervention on lonely, older people's cognition: a randomized, controlled trial. *The American Journal of Geriatric Psychiatry, 19*, 654-663.

Plassman, B. L., Langa, K. M., Fisher, G. G., Heeringa, S. G., Weir, D. R., Ofstedal, M. B., Burke, J. R., Hurd, M. D., Potter, G. G., Rodgers, W. L., Steffens, D. C., McArdle, J. J., Willis, R. J., & Wallace, R. B. (2008). Prevalence of cognitive impairment without dementia in the United States. *Annals of Internal Medicine, 148,* 427-434.

Plassman, B. L., Williams, J. W., Burke, J. R., Holsinger, T., & Benjamin, S. (2010). Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Annals of Internal Medicine, 153*, 182-193.

Platt, B., Kadosh, K. C., & Lau, J. Y. (2013). The role of peer rejection in adolescent depression. *Depression and Anxiety, 30*, 809-821.

Plehn, K., Marcopulos, B. A., & McLain, C. A. (2004). The relationship between neuropsychological test performance, social functioning, and instrumental activities of daily living in a sample of rural older adults. *The Clinical Neuropsychologist, 18*, 101-113.

Portet, F., Ousset, P. J., Visser, P. J., Frisoni, G. B., Nobili, F., Scheltens, P., Vellas, B., & Touchon, J. (2006). Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's Disease. *Journal of Neurology, Neurosurgery & Psychiatry, 77*, 714-718.

Potvin, O., Bergua, V., Meillon, C., Le Goff, M., Bouisson, J., Dartigues, J. F., & Amieva, H. (2013). State anxiety and cognitive functioning in older adults. *The American Journal of Geriatric Psychiatry, 21,* 915-924.

Potvin, O., Forget, H., Grenier, S., Préville, M., & Hudon, C. (2011). Anxiety, Depression, and 1-Year Incident Cognitive Impairment in Community-Dwelling Older Adults. *Journal of the American Geriatrics Society, 59,* 1421-1428.

Potvin, O., Hudon, C., Forget, H., Grenier, S., Dubé, M., Lorrain, D., & Préville, M. (2012). Prevalence of psychiatric disorders in community-dwelling older men and women with cognitive impairment no dementia: results from the ESA study. *Aging & Mental Health, 16*, 218-227.

Powell, J., Lewis, P. A., Roberts, N., García-Fiñana, M., & Dunbar, R. I. M. (2012). Orbital prefrontal cortex volume predicts social network size: an imaging study of individual differences in humans. *Proceedings of the Royal Society of London B: Biological Sciences, 279*, 2157-2162.

Prince, M. J., Harwood, R. H., Blizard, R. A., Thomas, A., & Mann, A. H. (1997). Social support deficits, loneliness and life events as risk factors for depression in old age. The Gospel Oak Project VI. *Psychological Medicine, 27*, 323-332.

Prince, M. J., Wimo, A., Guerchet, M., Ali, G., Wu, Y., & Prina, M. (2015). World Alzheimer Report 2015: the global impact of dementia: an analysis of prevalence, incidence, cost and trends. Accessed 03/07/2018: https://www.alz.co.uk/research/WorldAlzheimerReport2015.pdf

Prince, M., Comas-Herrera, A., Knapp, M., Guerchet, M., & Karagiannidou, M. (2016). World Alzheimer report 2016: improving healthcare for people living with dementia: coverage, quality and costs now and in the future. Accessed 27/06/2018: http://eprints.lse.ac.uk/67858/1/Comas-Herrera_World%20Alzheimer%20report_2016.pdf

Rabbitt, P., Diggle, P., Smith, D., Holland, F., & McInnes, L. (2001). Identifying and separating the effects of practice and of cognitive ageing during a large longitudinal study of elderly community residents. *Neuropsychologia, 39,* 532-543.

Rait, G., Morley, M., Burns, A., Baldwin, R., Chew-Graham, C., & St Leger, A. S. (2000). Screening for cognitive impairment in older African-Caribbeans. *Psychological Medicine, 30,* 957-963.

Rapp, M. A., Schnaider-Beeri, M., Grossman, H. T., Sano, M., Perl, D. P., Purohit, D. P., Gorman, J. M., & Haroutunian, V. (2006). Increased hippocampal plaques and tangles in patients with Alzheimer disease with a lifetime history of major depression. *Archives of General Psychiatry, 63,* 161-167.

Reisberg, B., Ferris, S. H., de Leon, M. J., Franssen, E. S. E., Kluger, A., Mir, P., Borenstein, J., George, A. E., Shulman, E., Steinberg, G., & Cohen, J. (1988). Stage-specific behavioral, cognitive, and in vivo changes in community residing subjects with age-associated memory impairment and primary degenerative dementia of the Alzheimer type. *Drug Development Research, 15*, 101-114.

Reynolds, C. F., Dew, M. A., Pollock, B. G., Mulsant, B. H., Frank, E., Miller, M. D., Houk, P. R., Mazumdar, S., Butters, M. A., Stack, J. A., Schlernitzauer, M. A., Whyte, E. M., Gildengers, A., Karp, J., Lenze, E., Szanto, K., Bensasi, S., & Kupfer, D. J. (2006). Maintenance treatment of major depression in old age. *New England Journal of Medicine, 354,* 1130-1138.

Reynolds, C. F., Frank, E., Perel, J. M., Imber, S. D., Cornes, C., Miller, M. D., Mazumdar, S., Houck, P., Dew, M. A., Stack, J. A., Pollock, B. G., & Kupfer, D. J. (1999). Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression: a randomized controlled trial in patients older than 59 years. *Journal of the American Medical Association, 281,* 39-45.

Riboli, E. (1992). Nutrition and cancer: background and rationale of the European Prospective Investigation into Cancer and Nutrition (EPIC). *Annuals of Oncology, 3,* 783-791.

Richard, E., Reitz, C., Honig, L. H., Schupf, N., Tang, M. X., Manly, J. J., Mayeux, R., Devanand, D., & Luchsinger, J. A. (2013). Late-life depression, mild cognitive impairment, and dementia. *Journal of the American Medical Association: Neurology, 70,* 383-389.

Richards, M., & Deary, I. J. (2005). A life course approach to cognitive reserve: a model for cognitive aging and development? *Annals of Neurology, 58*, 617-622.

Richards, M., & Sacker, A. (2003). Lifetime antecedents of cognitive reserve. *Journal of Clinical and Experimental Neuropsychology, 25,* 614-624.

Rizzuto, D., & Fratiglioni, L. (2014). Lifestyle factors related to mortality and survival: a mini-review. *Gerontology, 60*, 327-335.

Roberts, R. O., Cha, R. H., Mielke, M. M., Geda, Y. E., Boeve, B. F., Machulda, M. M., Knopman, D. S., & Petersen, R. C. (2015). Risk and protective factors for cognitive impairment in persons aged 85 years and older. *Neurology, 84*, 1854-1861.

Rock, P. L., Roiser, J. P., Riedel, W. J., & Blackwell, A. D. (2014). Cognitive impairment in depression: a systematic review and meta-analysis. *Psychological Medicine, 44*, 2029-2040.

Rodríguez, J. L. S., Torrellas, C., Martín, J., & Fernandez, M. J. (2011). Cognitive reserve and lifestyle in Spanish individuals with sporadic Alzheimer's disease. *American Journal of Alzheimer's Disease & Other Dementias, 26,* 542-554.

Rook, K. S. (2003). Exposure and reactivity to negative social exchanges: A preliminary investigation using daily diary data. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 58,* P100-P111.

Rose, E. J., & Ebmeier, K. P. (2006). Pattern of impaired working memory during major depression. *Journal of Affective Disorders, 90,* 149-161.

Rose, G. A. (1962). The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bulletin of the World Health Organization, 27*, 645-658.

Ross, G. W., Abbott, R. D., Petrovitch, H., Masaki, K. H., Murdaugh, C., Trockman, C., Curb, J. D., & White, L. R. (1997). Frequency and characteristics of silent dementia among elderly Japanese-American men:

the Honolulu-Asia Aging Study. *Journal of the American Medical Association: Neurology*, 277, 800-805.

Rosso, A. L., Taylor, J. A., Tabb, L. P., & Michael, Y. L. (2013). Mobility, disability, and social engagement in older adults. *Journal of Aging and Health, 25*, 617-637.

Roth, M., Tym, E., Mountjoy, C. Q., Huppert, F. A., Hendrie, H., Verma, S., & Goddard, R. (1986). CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *The British Journal of Psychiatry, 149*, 698-709.

Routasalo, P. E., Tilvis, R. S., Kautiainen, H., & Pitkala, K. H. (2009). Effects of psychosocial group rehabilitation on social functioning, loneliness and well-being of lonely, older people: randomized controlled trial. *Journal of Advanced Nursing, 65*, 297-305.

Rowe, J. W., & Kahn, R. L. (1997). Successful aging. *The Gerontologist, 37*, 433-440.

Royall, D. R., Palmer, R., Chiodo, L. K., & Polk, M. J. (2005). Normal rates of cognitive change in successful aging: the freedom house study. *Journal of the International Neuropsychological Society, 11*, 899-909.

Saczynski, J. S., Pfeifer, L. A., Masaki, K., Korf, E. S., Laurin, D., White, L., & Launer, L. J. (2006). The effect of social engagement on incident dementia The Honolulu-Asia Aging Study. *American Journal of Epidemiology, 163,* 433-440.

Salthouse, T. A. (2010a). Selective review of cognitive aging. *Journal of the International Neuropsychological Society, 16*, 754-760.

Salthouse, T. A. (2010b). Influence of age on practice effects in longitudinal neurocognitive change. *Neuropsychology, 24*, 563-572.

Sani, F., Herrera, M., Wakefield, J. R., Boroch, O., & Gulyas, C. (2012). Comparing social contact and group identification as predictors of mental health. *British Journal of Social Psychology, 51*, 781-790.

Santini, Z. I., Koyanagi, A., Tyrovolas, S., Haro, J. M., Donovan, R. J., Nielsen, L., & Koushede, V. (2017). The protective properties of Act-Belong-Commit indicators against incident depression, anxiety, and cognitive impairment among older Irish adults: findings from a prospective community-based study. *Experimental Gerontology, 91*, 79-87.

Santini, Z. I., Koyanagi, A., Tyrovolas, S., Mason, C., & Haro, J. M. (2015). The association between social relationships and depression: a systematic review. *Journal of Affective Disorders, 175*, 53-65.

Satz, P. (1993). Brain reserve capacity on symptom onset after brain injury: a formulation and review of evidence for threshold theory. *Neuropsychology, 7*, 273-295.

Schafer, M. H. (2013). Structural advantages of good health in old age: Investigating the health-begets-position hypothesis with a full social network. *Research on Aging, 35*, 348-370.

Scharf, T. (2002). *Growing older in socially deprived areas: Social exclusion in later life*. London, UK: Help the Aged.

Scharf, T., & Smith, A. E. (2004). *Older people in urban neighbourhoods: addressing the risk of social exclusion in later life*. London, UK: Ashgate, 162-179.

Scharf, T., Phillipson, C., & Smith, A. E. (2004). *Poverty and social exclusion: growing older in deprived urban neighbourhoods.* Maidenhead, UK: Open University Press, 81-106.

Schnittker, J. (2007). Look (closely) at all the lonely people: Age and the social psychology of social support. *Journal of Aging and Health, 19*, 659-682.

Schöllgen, I., Huxhold, O., Schüz, B., & Tesch-Römer, C. (2011). Resources for health: differential effects of optimistic self-beliefs and social support according to socioeconomic status. *Health Psychology, 30*, 326-335.

Schultz, S. A., Larson, J., Oh, J., Koscik, R., Dowling, M. N., Gallagher, C. L., Carlsson, C. M., Rowley, H. A., Bendlin, B. B., Asthana, S., Hermann, B. P., Johnson, S. C., Sager, M., LaRue, A., & Okonkwo, O. C. (2015). Participation in cognitively-stimulating activities is associated with brain structure and cognitive function in preclinical Alzheimer's disease. *Brain Imaging and Behavior, 9,* 729-736.

Schwingel, A., Niti, M. M., Tang, C., & Ng, T. P. (2009). Continued work employment and volunteerism and mental well-being of older adults: Singapore longitudinal ageing studies. *Age and Ageing, 38*, 531-537.

Seeman, T. E., & Berkman, L. F. (1988). Structural characteristics of social networks and their relationship with social support in the elderly: who provides support? *Social Science & Medicine, 26,* 737-749.

Seeman, T. E., Lusignolo, T. M., Albert, M., & Berkman, L. (2001). Social relationships, social support, and patterns of cognitive aging in healthy, high-functioning older adults: MacArthur studies of successful aging. *Health Psychology, 20*, 243-255.

Segrin, C. (2000). Social skills deficits associated with depression. *Clinical Psychology Review, 20*, 379-403.

Seshadri, S., Beiser, A., Au, R., Wolf, P. A., Evans, D. A., Wilson, R. S., Peterson, R. C., Knopman, D. S., Rocca, W. A., & Corrada, M. M. (2011). Operationalizing diagnostic criteria for Alzheimer's disease and other age-related cognitive impairment—Part 2. *Alzheimer's & Dementia, 7*, 35-52.

Shankar, A., Hamer, M., McMunn, A., & Steptoe, A. (2013). Social isolation and loneliness: relationships with cognitive function during 4 years of follow-up in the English Longitudinal Study of Ageing. *Psychosomatic Medicine, 75,* 161-170.

Shatenstein, B., Ferland, G., Belleville, S., Gray-Donald, K., Kergoat, M. J., Morais, J., Gaudrea, P., Payette, H., & Greenwood, C. (2012). Diet quality and cognition among older adults from the NuAge study. *Experimental Gerontology, 47*, 353-360.

Shaw, B. A., Fors, S., Fritzell, J., Lennartsoon, C., & Agahi, N. (2017). Who lives alone during old age? Trends in the social and functional disadvantages of Sweden's solitary living older adults. *Research on Aging, 39*, 1-24.

Shin, S. H., Kim, G., & Park, S. (2018). Widowhood Status as a Risk Factor for Cognitive Decline among Older Adults. *The American Journal of Geriatric Psychiatry, 26*, 778-787.

Shouse, J. N., Rowe, S. V., & Mast, B. T. (2013). Depression and cognitive functioning as predictors of social network size. *Clinical Gerontologist, 36*, 147-161.

Siedlecki, K. L., Stern, Y., Reuben, A., Sacco, R. L., Elkind, M. S., & Wright, C. B. (2009). Construct validity of cognitive reserve in a multiethnic cohort: The Northern Manhattan Study. *Journal of the International Neuropsychological Society, 15,* 558-569.

Simning, A., Conwell, Y., & van Wijngaarden, E. (2014). Cognitive impairment in public housing residents living in Western New York. *Social Psychiatry and Psychiatric Epidemiology, 49*, 477-485.

Singh-Manoux, A., Richards, M., & Marmot, M. (2003). Leisure activities and cognitive function in middle age: evidence from the Whitehall II study. *Journal of Epidemiology and Community Health, 57,* 907-913.

Sinoff, G., & Werner, P. (2003). Anxiety disorder and accompanying subjective memory loss in the elderly as a predictor of future cognitive decline. *International Journal of Geriatric Psychiatry, 18*, 951-959.

Small, B. J., Dixon, R. A., McArdle, J. J., & Grimm, K. J. (2012). Do changes in lifestyle engagement moderate cognitive decline in normal aging? Evidence from the Victoria Longitudinal Study. *Neuropsychology, 26*, 144-155.

Small, B. J., Fratiglioni, L., Viitanen, M., Winblad, B., & Bäckman, L. (2000). The course of cognitive impairment in preclinical Alzheimer disease: three-and 6-year follow-up of a population-based sample. *Archives of Neurology, 57*, 839-844.

Smith, G., Chandler, M., Locke, D. E., Fields, J., Phatak, V., Crook, J., Hanna, S., Lunde, A., Morris, M., Graff-Radford, M., Hughes, C. A., Lepore, S., Cuc, A., Caselli, M., Hurst, D., Wethe, J., Francone, A., Eilertsen, J., Lucas, P., Hoffman Synder, C., Kuang, L. A., Becker, M., Dean, P., Diehl, N., Lofquist, M., Vanderhook, S., Myles, D., & Cochran, D. (2017). Behavioral interventions to prevent or delay dementia: Protocol for a randomized comparative effectiveness study. *Journal of Medical Internet Research: Research Protocols, 6*, e223.

Smith, T. F., & Hirdes, J. P. (2009). Predicting social isolation among geriatric psychiatry patients. *International Psychogeriatrics, 21*, 50-59.

Sonnenberg, C.M., Deeg, D.J., van Tilburg, T.G., Vink, D., Stek, M.L., & Beekman, A.T. (2013). Gender differences in the relation between depression and social support in later life. *International Psychogeriatrics, 25,* 61-70.

Spijker, J., & MacInnes, J. (2013). 'Population ageing: the time bomb that isn't?' *British Medical Journal, 347*, f6598.

Stephan, B. C., Savva, G. M., Brayne, C., Bond, J., McKeith, I. G., & Matthews, F. E. (2010). Optimizing mild cognitive impairment for discriminating dementia risk in the general older population. *The American Journal of Geriatric Psychiatry, 18*, 662-673.

Stephan, B., Matthews, F. E., McKeith, I. G., Bond, J., & Brayne, C. (2007). Early cognitive change in the general population: how do different definitions work? *Journal of the American Geriatrics Society, 55,* 1534-1540.

Stepler, R. (2016). Smaller share of women ages 65 and older are living alone: More are living with spouse or children. Washington, DC, USA: Pew Research Centre. Accessed 10/08/2018: http://www.pewsocialtrends.org/2016/02/18/smaller-share-of-women-ages-65-and-older-are-living-alone/

Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013). Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences, 110*, 5797-5801.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society, 8,* 448-460.

Stern, Y. (2009). Cognitive reserve. *Neuropsychologia, 47,* 2015-2028.

Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *The Lancet Neurology, 11*, 1006-1012.

Stern, Y., Alexander, G. E., Prohovnik, I., & Mayeux, R. (1992). Inverse relationship between education and parietotemporal perfusion deficit in Alzheimer's disease. *Annals of Neurology, 32,* 371-375.

Stern, Y., Gurland, B., Tatemichi, T. K., Tang, M. X., Wilder, D., & Mayeux, R. (1994). Influence of education and occupation on the incidence of Alzheimer's disease. *Journal of the American Medical Association, 271*, 1004-1010.

Stessman, J., Rottenberg, Y., Shimshilashvili, I., Ein-Mor, E., & Jacobs, J. M. (2014). Loneliness, health, and longevity. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 69*, 744-750.

Stoykova, R., Matharan, F., Dartigues, J. F., & Amieva, H. (2011). Impact of social network on cognitive performances and age-related cognitive decline across a 20-year follow-up. *International Psychogeriatrics, 23*, 1405-1412.

Suurmeijer, T. P., Sonderen, F. V., Krol, B., Doeglas, D. M., Heuvel, W. V. D., & Sanderman, R. (2005). The relationship between personality, supportive transactions and support satisfaction, and mental health of patients with early rheumatoid arthritis. Results from the Dutch part of the EURIDISS study. *Social Indicators Research, 73*, 179-197.

Takagi, D., Kondo, K., & Kawachi, I. (2013). Social participation and mental health: moderating effects of gender, social role and rurality. *BioMed Central: Public Health, 13,* 701.

Tervo, S., Kivipelto, M., Hänninen, T., Vanhanen, M., Hallikainen, M., Mannermaa, A., & Soininen, H. (2004). Incidence and risk factors for mild cognitive impairment: a population-based three-year follow-up study of cognitively healthy elderly subjects. *Dementia and Geriatric Cognitive Disorders, 17*, 196-203.

The New Policy Institute. (2006). Accessed 16/07/2018: https://www.jrf.org.uk/file/37100/download?token=bN3pYj78&filetype=summary

Thoits, P. A. (2011). Mechanisms linking social ties and support to physical and mental health. *Journal of Health and Social Behavior, 52*, 145-161.

Thomas, P. A. (2011a). Gender, social engagement, and limitations in late life. *Social Science & Medicine, 73*, 1428-1435.

Thomas, P. A. (2011b). Trajectories of social engagement and limitations in late life. *Journal of Health and Social Behavior, 52*, 430-443.

Tilvis, R. S., Kähönen-Väre, M. H., Jolkkonen, J., Valvanne, J., Pitkala, K. H., & Strandberg, T. E. (2004). Predictors of cognitive decline and mortality of aged people over a 10-year period. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 59,* M268-M274.

Tinetti, M. E., McAvay, G. J., Chang, S. S., Newman, A. B., Fitzpatrick, A. L., Fried, T. R., & Peduzzi, P. N. (2011). Contribution of multiple chronic conditions to universal health outcomes. *Journal of the American Geriatrics Society, 59*, 1686-1691.

Toepoel, V. (2013). Ageing, leisure, and social connectedness: how could leisure help reduce social isolation of older people? *Social Indicators Research, 113*, 355-372.

Tolea, M. I., & Galvin, J. E. (2016). Relationship between Mobility Dysfunction Staging and Global Cognitive Performance. *Alzheimer Disease and Associated Disorders, 30*, 230-236.

Tomaka, J., Thompson, S., & Palacios, R. (2006). The relation of social isolation, loneliness, and social support to disease outcomes among the elderly. *Journal of Aging and Health, 18,* 359-384.

Tomaszewski, W. (2013). Living environment, social participation and wellbeing in older age: the relevance of housing and local area disadvantage. *Journal of Population Ageing, 6*, 119-156.

Tomioka, K., Kurumatani, N., & Hosoi, H. (2016). Social participation and cognitive decline among community-dwelling older adults: a community-based longitudinal study. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *73,* 799-806.

Tov, W., Nai, Z. L., & Lee, H. W. (2016). Extraversion and agreeableness: Divergent routes to daily satisfaction with social relationships. *Journal of Personality, 84*, 121-134.

Townsend, P. (1957). *The family life of old people: an inquiry in East London*. London, UK: Routledge & Paul.

Trivedi, M. H., Morris, D. W., Pan, J. Y., Grannemann, B. D., & Rush, A. J. (2005). What moderator characteristics are associated with better prognosis for depression? *Neuropsychiatric Disease and Treatment, 1,* 51-57.

Tschanz, J. T., Welsh-Bohmer, K. A., Lyketsos, C. G., Corcoran, C., Green, R. C., Hayden, K., Norton, M. C., Zandi, P. P., Toone, L., West, N. A., & Breitner, J. C. S. (2006). Conversion to dementia from mild cognitive disorder The Cache County Study. *Neurology, 67,* 229-234.

Tse, W. S., & Bond, A. J. (2004). The Impact of Depression on Social Skills: A Review. *Journal of Nervous and Mental Disease 192*, 260-268.

Tucker, A., & Stern, Y. (2011). Cognitive reserve in aging. *Current Alzheimer Research, 8*, 354-360.

Tunstall, J. (1966). *Old and alone: A sociological study of old people*. London, UK: Routledge & Paul.

Turner, R. J., & Marino, F. (1994). Social support and social structure: A descriptive epidemiology. *Journal of Health and Social Behavior, 35,* 193-212.

Uchino, B. N. (2006). Social support and health: a review of physiological processes potentially underlying links to disease outcomes. *Journal of Behavioral Medicine, 29,* 377-387.

Udell, J. A., Steg, P. G., Scirica, B. M., Smith, S. C., Ohman, E. M., Eagle, K. A., Goto, S., Cho, J. I., & Deepak, L. B. (2012). Living alone and cardiovascular risk in outpatients at risk of or with atherothrombosis. *Archives of Internal Medicine, 172*, 1086-1095.

Umberson, D., & Montez, J. K. (2010). Social relationships and health a flashpoint for health policy. *Journal of Health and Social Behavior, 51,* S54-S66.

United Nations: Department of Economic and Social Affairs Population Division. (2015). World population ageing. Accessed 22/08/2018: http://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015_Report.pdf

Unverzagt, F. W., Gao, S., Baiyewu, O., Ogunniyi, A. O., Gureje, O., Perkins, A., Emsley, C. L., Dickens, J., Evns, R., Musick, B., Hall, K. S., Hui, H. C., & Hendrie, H. C. (2001). Prevalence of cognitive impairment data from the Indianapolis study of health and aging. *Neurology, 57*, 1655-1662.

Vable, A. M., Subramanian, S. V., Rist, P. M., & Glymour, M. M. (2015). Does the "widowhood effect" precede spousal bereavement? Results from a nationally representative sample of older adults. *The American Journal of Geriatric Psychiatry, 23*, 283-292.

Valenzuela, M. J., & Sachdev, P. (2007). Assessment of complex mental activity across the lifespan: development of the Lifetime of Experiences Questionnaire (LEQ). *Psychological Medicine, 37*, 1015-1025.

Valenzuela, M. J., Matthews, F. E., Brayne, C., Ince, P., Halliday, G., Kril, J. J., Dalton, M. A., Richardson, K., Forster, G., & Sachdev, P. S. (2012). Multiple biological pathways link cognitive lifestyle to protection from dementia. *Biological Psychiatry, 71*, 783-791.

Valenzuela, M., Brayne, C., Sachdev, P., Wilcock, G., & Matthews. F. (2011). Cognitive lifestyle and long-term risk of dementia and survival after diagnosis in a multicenter population-based cohort. *American Journal of Epidemiology, 173,* 1004-1012.

van Baarsen, B., Snijders, T. A., Smit, J. H., & van Duijn, M. A. (2001). Lonely but not alone: Emotional isolation and social isolation as two distinct dimensions of loneliness in older people. *Educational and Psychological Measurement, 61*, 119-135.

van Beijsterveldt, C. E. M., van Boxtel, M. P. J., Bosma, H., Houx, P. J., Buntinx, F. J. V. M., & Jolles, J. (2002). Predictors of attrition in a longitudinal cognitive aging study: The Maastricht Aging Study (MAAS). *Journal of Clinical Epidemiology, 55*, 216-223.

van Gelder, B. M., Tijhuis, M., Kalmijn, S., Giampaoli, S., Nissinen, A., & Kromhout, D. (2006). Marital status and living situation during a 5-year period are associated with a subsequent 10-year cognitive decline in older men: the FINE Study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 61,* P213-P219.

Van Ness, P. H., & Kasl, S. V. (2003). Religion and cognitive dysfunction in an elderly cohort. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 58*, S21-S29.

Van Praag, H., Shubert, T., Zhao, C., & Gage, F. H. (2005). Exercise enhances learning and hippocampal neurogenesis in aged mice. *Journal of Neuroscience, 25*, 8680-8685.

van Schaik, A., van Marwijk, H., Adèr, H., van Dyck, R., de Haan, M., Penninx, B., van der Kooij. K., van Hout, H., & Beekman, A. (2006). Interpersonal psychotherapy for elderly patients in primary care. The *American Journal of Geriatric Psychiatry, 14*, 777-786.

van Tilburg, T. (1995). *Delineation of the social network and differences in network size*. Amsterdam, Netherlands: University Press, 83-96.

Vanderhorst, R. K., & McLaren, S. (2005). Social relationships as predictors of depression and suicidal ideation in older adults. *Aging & Mental Health, 9*, 517-525.

Victor, C. R., Scambler, S. J., Bowling, A. N. N., & Bond, J. (2005). The prevalence of, and risk factors for, loneliness in later life: a survey of older people in Great Britain. *Ageing and Society, 25*, 357-375.

Victor, C., Scambler, S., & Bond, J. (2008). *The social world of older people: Understanding loneliness and social isolation in later life.* Maidenhead, UK: McGraw-Hill Education.

Victor, C., Scambler, S., Bond, J., & Bowling, A. (2000). Being alone in later life: loneliness, social isolation and living alone. *Reviews in Clinical Gerontology, 10*, 407-417.

Vidarsdottir, H., Fang, F., Chang, M., Aspelund, T., Fall, K., Jonsdottir, M. K., Jonsson, P. V., Cotch, M. F., Harris, T. B., Launer, L. J., Gudnason, V., & Valdimarsdottir, U. (2014). Spousal loss and cognitive function in later life: A 25-year follow-up in the AGES-Reykjavik study. *American Journal of Epidemiology, 179,* 674-683.

Von Der Heide, R., Vyas, G., & Olson, I. R. (2014). The social network-network: size is predicted by brain structure and function in the amygdala and paralimbic regions. *Social Cognitive and Affective Neuroscience, 9,* 1962-1972.

Wai, S. T., & Bond, A. J. (2004). Relationship between baseline cortisol, social functioning and depression: a mediation analysis. *Psychiatry Research, 126*, 197-201.

Wang, B., He, P., & Dong, B. (2015). Associations between social networks, social contacts, and cognitive function among Chinese nonagenarians/centenarians. *Archives of Gerontology and Geriatrics, 60,* 522-527.

Wang, H. X., Jin, Y., Hendrie, H. C., Liang, C., Yang, L., Cheng, Y., Unverzagt, F. W., Ma, F., Hall, K. S., Murrell Ping Li, J. R., Bian, J., P, J., Gao, S., & Kritchevsky, S. (2013). Late life leisure activities and risk of cognitive decline. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 68,* 205-213.

Wang, H. X., Karp, A., Winblad, B., & Fratiglioni, L. (2002). Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. *American Journal of Epidemiology, 155,* 1081-1087.

Wang, H. X., Xu, W., & Pei, J. J. (2012). Leisure activities, cognition and dementia. *Biochimica et Biophysica Acta: Molecular Basis of Disease, 1822*, 482-491.

Wang, J. Y. J., Zhou, D. H. D., Li, J., Zhang, M., Deng, J., Tang, M., Gao, C., Li, J., Lian, Y., & Chen, M. (2006). Leisure activity and risk of cognitive impairment: the Chongqing aging study. *Neurology, 66*, 911-913.

Ward, A., Arrighi, H. M., Michels, S., & Cedarbaum, J. M. (2012) Mild cognitive impairment: disparity of incidence and prevalence estimates. *Alzheimer's and Dementia, 8*, 14-21.

Wasay, M., Grisold, W., Carroll, W., & Shakir, R. (2016). World Brain Day 2016: celebrating brain health in an ageing population. *The Lancet Neurology, 15*, 1008.

Watson, P. J., & Andrews, P. W. (2002). Toward a revised evolutionary adaptationist analysis of depression: The social navigation hypothesis. *Journal of Affective Disorders, 72,* 1-14.

Weden, M. M., Carpiano, R. M., & Robert, S. A. (2008). Subjective and objective neighborhood characteristics and adult health. *Social Science & Medicine, 66*, 1256-1270.

Weightman, M. J., Air, T. M., & Baune, B. T. (2014). A review of the role of social cognition in major depressive disorder. *Frontiers in Psychiatry, 5*, 179.

Weiss, R.S. (1973). *Loneliness: The experience of emotional and social isolation*. Cambridge, UK: Massachusetts Institute of Technology Press.

Wen, M., Hawkley, L. C., & Cacioppo, J. T. (2006). Objective and perceived neighborhood environment, individual SES and psychosocial factors, and self-rated health: An analysis of older adults in Cook County, Illinois. *Social Science & Medicine, 63*, 2575-2590.

Wenger, G. C. (1989). *Support networks in old age: Constructing a typology*. London, UK: Routledge.

Wenger, G. C. (1997). Social networks and the prediction of elderly people at risk. *Aging & Mental Health, 1,* 311-320

Wenger, G. C., & Burholt, V. (2004). Changes in Levels of Social Isolation and Loneliness among Older People in a Rural Area: A Twenty–Year Longitudinal Study. *Canadian Journal on Aging, 23*, 115-127.

Wenger, G. C., Davies, R., Shahtahmasebi, S., & Scott, A. (1996). Social isolation and loneliness in old age: review and model refinement. *Ageing & Society, 16*, 333-358.

Wesnes, K., & Pincock, C. (2002). Practice effects on cognitive tasks: a major problem? *The Lancet Neurology, 1*, 473.

Whalley, L. J., Dick, F. D., & McNeill, G. (2006). A life-course approach to the aetiology of late-onset dementias. *The Lancet Neurology, 5*, 87-96.

Wharton, S. B., Brayne, C., Savva, G. M., Matthews, F. E., Forster, G., Simpson, J., Lace, G., & Ince, P. G. (2011). Epidemiological neuropathology: the MRC cognitive function and aging study experience. *Journal of Alzheimer's Disease, 25*, 359-372.

Wilkinson, R. G., & Marmot, M. (2003). *Social determinants of health: the solid facts*. Copenhagen, Denmark: World Health Organization.

Willerman, L., Schultz, R., Rutledge, J. N., & Bigler, E. D. (1991). In vivo brain size and intelligence. *Intelligence, 15,* 223-228.

Williams, J. W., Plassman, B. L., Burke, J., Holsinger, T., & Benjamin, S. (2010). Preventing Alzheimer's disease and cognitive decline. *Evidence Report/Technology Assessment, 193*, 1-727.

Williams, P., Barclay, L., & Schmied, V. (2004). Defining social support in context: a necessary step in improving research, intervention, and practice. *Qualitative Health Research, 14*, 942-960.

Williams, R. J., Tse, T., Harlan, W. R., & Zarin, D. A. (2010). Registration of observational studies: is it time? *Canadian Medical Association Journal, 182,* 1638-1642.

Wilson, K., Mottram, P. G., & Vassilas, C. (2008). Psychotherapeutic treatments for older depressed people. *Cochrane database of systematic reviews.* CD004853

Wilson, R. S., Beckett, L. A., Barnes, L. L., Schneider, J. A., Bach, J., Evans, D. A., & Bennett, D. A. (2002). Individual differences in rates of change in cognitive abilities of older persons. *Psychology and Aging, 17*, 179-193.

Wilson, R. S., Begeny, C. T., Boyle, P. A., Schneider, J. A., & Bennett, D. A. (2011). Vulnerability to stress, anxiety, and development of dementia in old age. *The American Journal of Geriatric Psychiatry, 19*, 327-334.

Wilson, R. S., Boyle, P. A., James, B. D., Leurgans, S. E., Buchman, A. S., & Bennett, D. A. (2015). Negative social interactions and risk of mild cognitive impairment in old age. *Neuropsychology, 29*, 561-570.

Wilson, R. S., De Leon, C. F. M., Barnes, L. L., Schneider, J. A., Bienias, J. L., Evans, D. A., & Bennett, D. A. (2002). Participation in cognitively stimulating activities and risk of incident Alzheimer disease. *Journal of the American Medical Association, 287*, 742-748.

Wilson, R. S., Evans, D. A., Bienias, J. L., De Leon, C. M., Schneider, J. A., & Bennett, D. A. (2003). Proneness to psychological distress is associated with risk of Alzheimer's disease. *Neurology, 61*, 1479-1485.

Wilson, R. S., Krueger, K. R., Arnold, S. E., Schneider, J. A., Kelly, J. F., Barnes, L. L., Tang, Y., & Bennett, D. A. (2007). Loneliness and risk of Alzheimer disease. *Archives of General Psychiatry, 64*, 234-240.

Wilson, R. S., Schneider, J. A., Boyle, P. A., Arnold, S. E., Tang, Y., & Bennett, D. A. (2007). Chronic distress and incidence of mild cognitive impairment. *Neurology, 68*, 2085-2092.

Wimo, A., Guerchet, M., Ali, G. C., Wu, Y. T., Prina, A. M., Winblad, B., Jonsson, L., Liu, Z., & Prince, M. (2017). The worldwide costs of dementia 2015 and comparisons with 2010. *Alzheimer's & Dementia, 13,* 1-7.

Winblad, B., Amouyel, P., Andrieu, S., Ballard, C., Brayne, C., Brodaty, H., Cedazo-Minquez, A., Dubois, B., Edvardsson, D., Feldman, H., Fratiglioni, L., Frisoni, G. B., Gauthier, S., Georges, J., Graff, C., Iqbal, K., Jessen, F., Johansson, G., Jönsson, L., Kivipelto, M., Knapp, M., Mangialasche, F., Melis, R., Nordberg, A., Rikkert, M. O., Qiu, C., Sakmar, T. P., Scheltens, P., Schneider, L. S., Sperling, R., Tjernberg, L. O., Waldemar, G., Wimo, A., & Zetterberg, H. (2016). Defeating Alzheimer's disease and other dementias: a priority for European science and society. *The Lancet Neurology, 15*, 455-532.

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., Wahlund, L. O., Nordberg, A., Backman, L., Albert, M., Almkvist, O., Arai, H., Basun H., Blennow, K., De Leon, M., DeCarli, C., Erkinjuntti, T., Giacobini, E., Graff, C., Hardy, J., Jack, C., Jorm, A., Ritchie, K., van Duijn, C., & Petersen, R. C. (2004). Mild cognitive impairment–beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *Journal of Internal Medicine, 256*, 240-246.

Windle, G., Markland, D. A., & Woods, R. T. (2008). Examination of a theoretical model of psychological resilience in older age. *Aging and Mental Health, 12,* 285-292.

Wirth, M., Haase, C. M., Villeneuve, S., Vogel, J., & Jagust, W. J. (2014). Neuroprotective pathways: lifestyle activity, brain pathology, and cognition in cognitively normal older adults. *Neurobiology of Aging, 35*, 1873-1882.

Wolff, J. L., Starfield, B., & Anderson, G. (2002). Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Archives of Internal Medicine, 162*, 2269-2276.

Woodruff, B. K., Stonnington, C. M., Locke, D. E., Hentz, J. G., Dueck, A. C., Wojtulewicz, L. B., Geda, Y. E., & Caselli, R. J. (2014). Paradoxical impact of widowhood on incidence of dementia in subjects with Mild cognitive impairment. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 10,* P617.

World Health Organization. (2015). World report on ageing and health. Accessed 03/07/2018: http://apps.who.int/iris/bitstream/handle/10665/186463/9789240694811_eng.pdf;jsessionid=C5EF848FB1145D4E9A66D8428D5D5E2F?sequence=1

World Health Organization. (2015). World report on ageing and health. Accessed 01/09/2018: http://apps.who.int/iris/bitstream/handle/10665/186463/9789240694811_eng.pdf;jsessionid=9143C14D8675E9F5D1A4B15A12836562?sequence=1

Wouters, H., van Gool, W. A., Schmand, B., Zwinderman, A. H., & Lindeboom, R. (2010). Three sides of the same coin: measuring global cognitive impairment with the MMSE, ADAS-cog and CAMCOG. *International Journal of Geriatric Psychiatry, 25,* 770-779.

Wrzus, C., Hänel, M., Wagner, J., & Neyer, F. J. (2013). Social network changes and life events across the life span: a meta-analysis. *Psychological Bulletin, 139*, 53-80.

Wu, Y. T., Fratiglioni, L., Matthews, F. E., Lobo, A., Breteler, M. M., Skoog, I., & Brayne, C. (2016). Dementia in Western Europe: epidemiological evidence and implications for policy making. *The Lancet Neurology, 15,* 116-124.

Wu, Y. T., Teale, J., Matthews, F. E., Brayne, C., Woods, B., Clare, L., & Ageing Study Wales research team. (2016). Lifestyle factors, cognitive reserve, and cognitive function: results from the Cognitive Function and Ageing Study Wales, a population-based cohort. *The Lancet, 388*, S114.

Xu, M., Thomas, P. A., & Umberson, D. (2015). Marital Quality and Cognitive Limitations in Late Life. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *71,* 165-176.

Yaacob, S. N., Juhari, R., Talib, M. A., & Uba, I. (2017). Loneliness, stress, self-esteem and depression among Malaysian adolescents. *Jurnal Kemanusiaan, 7*, 85-95.

Yaffe, K., & Hoang, T. (2013). Nonpharmacologic treatment and prevention strategies for dementia. *Continuum: Lifelong Learning in Neurology, 19*, 372-381.

Yaffe, K., Fiocco, A. J., Lindquist, K., Vittinghoff, E., Simonsick, E. M., Newman, A. B., Satterfield, S., Rosano, C., Rubin, S. M., Ayonayon, H. N., & Harris, T. B. (2009). Predictors of maintaining cognitive function in older adults The Health ABC Study. *Neurology, 72*, 2029-2035.

Yates, J. A., Clare, L., & Woods, R. T. (2017). “You’ve got a friend in me”: can social networks mediate the relationship between mood and MCI? *BioMed Central: Geriatrics, 17*, 144.

Yeh, S. C. J., & Liu, Y. Y. (2003). Influence of social support on cognitive function in the elderly. *BioMed Central: Health Services Research, 3*, 9.

Yen, C. H., Yeh, C. J., Wang, C. C., Liao, W. C., Chen, S. C., Chen, C. C., L. J., Lai, T., Lin, H., Lee, S., & Lee, M. C. (2010). Determinants of cognitive impairment over time among the elderly in Taiwan: results of the national longitudinal study. *Archives of Gerontology and Geriatrics, 50*, S53-S57.

Yochim, B. P., Mueller, A. E., & Segal, D. L. (2013). Late life anxiety is associated with decreased memory and executive functioning in community dwelling older adults. *Journal of Anxiety Disorders, 27*, 567-575.

Zhang, Z. (2006). Gender differentials in cognitive impairment and decline of the oldest old in China. The *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 61,* S107-S115.

Zhao, E., Tranovich, M. J., & Wright, V. J. (2014). The role of mobility as a protective factor of cognitive functioning in aging adults: a review. *Sports Health, 6*, 63-69.

Zou, L. Q., Yang, Z. Y., Wang, Y., Lui, S. S., Chen, A. T., Cheung, E. F., & Chan, R. C. (2016). What does the nose know? Olfactory function predicts social network size in human. *Scientific Reports, 6,* 25026.

Zunzunegui, M. V., Alvarado, B. E., Del Ser, T., & Otero, A. (2003). Social networks, social integration, and social engagement determine cognitive decline in community-dwelling Spanish older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 58*, S93-S100.

Appendices

Appendix A: CFAS-Wales data access form

CFAS Wales notification for requests to undertake additional projects, analysis of the data or a bolt on study during the project phase

Related document:
http://cfaswales.bangor.ac.uk/documents/Protocolforrequeststousedatadraft1i.pdf

Proposed title of research:
Social isolation, social engagement, cognitive reserve and cognition in later life.
Investigator name(s):
Isobel Evans, Linda Clare, Yu-Tzu Wu, Julia Teale, Carol Brayne, Fiona Matthews, Bob Woods; others to be decided as appropriate.
Names of collaborators and Organisation(s)
n/a
Proposed funder:
n/a
Amount requested (if known) or amount available from funder:
n/a
Proposed duration (start date/end date):
n/a
Summary of proposed research (250 words):
Background: There is conflicting evidence regarding the relationship between social isolation and cognition in later life. Some research suggests that social isolation is associated with impaired cognition, and that social engagement is protective against cognitive decline. Conversely, other studies suggest no such relationship. Furthermore, although some previous studies conclude that social engagement may be protective against cognitive decline in later life, it is unclear by what mechanism social engagement contributes to cognitive reserve. It is also unclear whether there are any specific features of social engagement that are optimal for cognitive health. Understanding more about the relationship between social isolation, social engagement, cognitive reserve and cognition will help to determine whether these potentially modifiable lifestyle factors are implicated in cognitive health in later life. Potentially vulnerable groups of older people may experience social isolation and social engagement differently to healthy older people. Therefore, it would be useful to examine these potentially vulnerable groups separately to determine whether social engagement and isolation influence cognitive reserve and cognition differently in these groups compared to older people within the healthy population. Overall, these analyses may be used to inform the development of interventions to reduce social isolation in later life.

Aims:
(1) To examine the relationship of social isolation and social engagement with cognitive reserve and cognition in community dwelling older people without cognitive impairment in CFAS Wales at Time 1.

(2) To examine the relationship of social isolation and social engagement with cognitive reserve and cognition in potentially vulnerable groups of older people in CFAS Wales at Time 1.

Method:

Aim 1:
We will use regression analysis to examine the cross-sectional relationships between (a) social isolation, cognitive reserve and cognition and (b) social engagement, cognitive reserve and cognition.

Social isolation can be assessed by considering the participant's social network, social support, social engagement and loneliness. Social network is covered by questions asking about the number of children, siblings, other relatives and friends the participant has contact with, the frequency of contact, and the proximity (in miles) of these contacts (Q59-66.1, 76-76.2, 77, 90-91). Availability of social support from friends and relatives is also covered in a number of these questions (Q66.2-66.3, 76.3-76.4, 553-558). Social engagement can be assessed through questions asking about paid or unpaid work post-retirement, attendance at meetings, community, or social groups, and the type of activities engaged with (Q43-44, 58, 67-68.1). An indication of the individual's satisfaction with his/her level of social engagement is also available (Q80). Living situation (Q27-37), marital status (Q4-5) and current accommodation (Q6-9, 659) may be used to further characterise the sample and provide additional insight into social connectedness. There are also questions available to measure loneliness (Q211-214).

Cognitive reserve will be assessed using a combination of educational level (Q40-42), occupational complexity (Q43-50), and cognitive activity (Q69-75). This combined proxy measure is under development to determine the appropriate weights to be assigned to each component.

Cognitive function will be assessed using the CAMCOG (Q266-373).

Individuals who are currently depressed (Q99-135) or living in an institution (Q9) will be excluded from this analysis. We will control for age (Q11-15, plus age at interview from extra variables dataset) and physical limitations associated with health (Q189-190, 405-422, 427-433, 439-440, 450-478, 482-483, 531), mobility (Q559), and frailty (Q188, 632) in the analyses. We will also consider ability to carry out activities of daily living (ADLs) to further characterise the sample (Q532-552).

Aim 2:
Further sub-group analyses will be conducted to examine the impact of social isolation on cognitive reserve and cognition in potentially vulnerable groups of older people. These analyses can be divided into four main themes as follows:

(1) Mental health: This will consider differences in the relationship between social isolation and cognition for individuals with and without a history of, or current symptoms of, psychosis (Q216-265), depression (Q99-135), or anxiety (Q82-98). Analyses will also be conducted for individuals with high or low self-esteem (Q373.6-373.13), interpersonal control (Q373.14-373.18), and self-efficacy (Q373.19-373.24).

(2) Living situation: This will consider the effects of a range of living situations that may create contexts that hinder social engagement, for example individuals living alone (Q27-35), living in remote rural or urban areas or areas characterised by high rates of crime (derived from the participant's postcode available in the extra variables dataset), or individuals who have relocated post-retirement (Q36-37), who are currently living in an

institution (Q6-9, 659), or who have recently experienced bereavement (Q61, 485-490), or individuals who report low life satisfaction (Q373.1-373.5, 56).

(3) Sociodemographic attributes: This will consider a range of sociodemographic features that may influence the association between social isolation and cognition. Individuals from a lower socioeconomic group (available in the additional extra variables dataset), or with fewer years of education (Q40-42), the oldest-old (Q11-15, plus age at interview from the additional variables dataset), individuals with a physical disability or long term health condition (Q189-190, 405-422, 427-433, 439-440, 450-478, 482-483, 531), or those defined as frail (Q188, 632), or with mobility issues (Q559) will be considered.

(4) Impaired cognitive health: This will consider differences between individuals with and without cognitive impairment (Q266-373) or dementia (derived from AGECAT diagnosis, available in the extra variables dataset).

Research aims/objectives/research questions:

(1) To examine the relationship of social isolation and social engagement with cognitive reserve and cognition in community dwelling older people without cognitive impairment in CFAS Wales at Time 1.

(2) To examine the relationship of social isolation and social engagement with cognitive reserve and cognition in potentially vulnerable groups of older people in CFAS Wales at Time 1.

Which measures do you need to undertake the research? PLEASE LIST

Variables required from the participant interview:

For social factors:

- Marital status: Q4-5
- Current accommodation: Q6-9, 659
- Living situation: Q27-37
- Social network: Q59-66.1, 76-76.2, 77, 90-91
- Social support: Q66.2-66.3, 76.3-76.4, 553-558
- Social engagement: Q43-44, 58, 67-68.1, 80
- Loneliness: Q211-214

For cognitive reserve:

- Educational level: Q40-42
- Occupational complexity: Q43-50
- Cognitive activity: Q69-75

For cognition:

- Cognitive function: Q266-373

Variables for sub-group analysis/ exclusion/ confounds:

- Age: Q11-15
- Physical health variables
    - Diabetes: Q409-411
    - Stroke: Q189-190, 418-422
    - Cancer: Q405-408
    - Parkinson's disease: Q412-417
    - Epilepsy: Q427-428
    - Head injury: Q429-433

- Arthritis: Q439-440
- Hearing: Q450-458
- Eyesight: Q459-460
- Gait speed test and balance: Q461-477
- Encephalitis: Q478
- Other medical problems: Q482-483
- Physical limitations associated with health conditions: Q531

- Life satisfaction: Q373.1-373.5, 561
- Self-esteem: Q373.6-373.13
- Interpersonal control: Q373.14-373.18
- Self-efficacy: Q373.19-373.24
- Anxiety: Q82-98
- Depression: Q99-135
- Mental state: Q216-265
- Interviewer observations of mental state: Q598-605, 640-644, 649-654
- Bereavement: Q61, 485-490
- Mobility: Q559
- Frailty: Q188, 632
- ADL's: Q532-552

To characterise the sample:

- Ethnicity: Q38-39

Variables required from the extra variables dataset:

- Gender
- Age at interview
- All diagnostic information from AGECAT
- Diagnosis variable (dx: normal, anxiety, depression, dementia)
- Social class
- Socioeconomic group
- Centre location (Gwynedd or Swansea)
- Participant postcode

We are requesting participants' postcodes in order to determine whether they reside in a rural or urban location, or in an area characterised by high levels of crime. This will enable us to determine whether there are differences in level of social connectedness among those living in these different types of location.

Does this proposal require new/additional interviewing/contacting participants during the project duration? If so, what is the proposed sample size? PLEASE DESCRIBE THE PROPOSED SAMPLE
n/a
How does this additional interviewing link directly to, and augment the main project?
n/a
Who will undertake the data analysis?
Isobel Evans, Yu-Tzu Wu, Linda Clare

Publication and dissemination – Please detail how disseminate the findings of your proposed study:
Thesis chapter, journal article
Authorship and acknowledgement: Please refer to the CFAS Wales publication policy
Authorship: Exact order of authorship will be decided based on contribution, but the investigators listed above will (subject to contribution) be the co-authors 'on behalf of the CFAS-Wales research team'. Acknowledgement: This study draws on the CFAS-Wales data set, version xxx. The CFAS Wales study was funded by the ESRC (RES-060-25-0060) and HEFCW as 'Maintaining function and well-being in later life: a longitudinal cohort study', (Principal Investigators: R.T Woods, L. Clare, G. Windle, V. Burholt, J. Philips, C. Brayne, C. McCracken, K. Bennett, F. Matthews). We are grateful to the Health and Care Research Wales Clinical Research Centre for their assistance in tracing participants and in interviewing and in collecting blood samples, and to general practices in the study areas for their cooperation.

Appendix B: CFAS-Wales data agreement

CFASCYMRU
GWEITHREDIAD GWYBYDDOL A HENEIDDIO
CFASWALES
COGNITIVE FUNCTION AND AGEING

UNDERTAKING FOR USERS OF CFAS WALES DATA

All use of the CFAS Wales data should be in agreement with the conditions as specified below:

(1) **Purpose:** To use the materials only for the purposes of non-commercial research or teaching specified in the accompanying application and to seek the approval of the CFAS Wales management team for any other proposed use.

(2) **Confidentiality:** To act at all times so as to preserve the confidentiality of individuals and institutions recorded in the materials. In particular I undertake not to attempt or to use the materials to derive information relating to an identified individual or institution nor to claim to have done so.

(3) **Report of progress:** For projects of more than one year, a short (one side A4) progress report for the CFAS Wales management team is requested, counted from the day of data application acknowledgement and approval.

(4) **Acknowledgement:** To acknowledge in any publication, whether printed, electronic or broadcast, based wholly or in part on such materials, the ESRC Maintaining Function and Well-Being Study (CFAS Wales) (**see publication policy for agreed form of acknowledgement**). A declaration to be included in any such work that those who carried out the original data collection and analysis hold no responsibility for the further analysis or interpretation.

(5) **Publications(1):** All publications must conform to the CFAS Wales Publications Policy agreed form of authorship and acknowledgements, see: http://cfaswales.bangor.ac.uk/documents/CFASWalesPUBPOLICYFINALv.119thMarch13.pdf

To deposit with the CFAS Wales study administrator two copies of any published work, conference presentation or report based wholly or in part on such materials.

(6) **Publications(2):** To distribute an abstract to the CFAS Wales management team ***prior to submission*** of any proposed publications, conference/seminar presentations or reports, to allow the CFAS Wales team to comment on and approve papers using CFAS Wales data. To quote the dataset version number in all such papers.

(7) **Publications (3):** The CFAS Wales management team will not accept or approve any publication, conference presentation or report containing findings which were not previously proposed in the data application. For analyses which have not followed the objectives set out in the original data request application, the investigator/researcher should seek approval of their new objectives from the CFAS Wales management team (i.e. through a new data request application).

(8) **Copyright:** Not to distribute copies of the materials to others, nor to make copies of them except as necessary to carry out the purpose specified (see Clause 1).

(9) **Access to others:** To store the data securely, and to restrict access to the data contained in or derived from the materials (including tables and summary statistics) only to registered users who have received permission from CFAS Wales for the specified purpose; or in the case of teaching, to give access only to students who have signed the Students' Undertaking on Conditions of Use Form, a copy of which will be provided to the CFAS Wales Study Manager by the end of June each year in which the specified data have been used.

(10) **Derived dataset: deposit:** At the conclusion of the proposed research (or at any time at the request of the CFAS Wales management team) to deposit in the CFAS Wales data archive for eventual study archiving, on a suitable medium and at own expense, any new datasets which have been derived from the materials supplied or which have been created by the combination of the data supplied with other data. The deposit of the derived datasets will include sufficient explanatory documentation to enable the new data files to be accessible to others and programmes detailing how derived data were created.

(11) **Errors:** To notify CFAS Wales of any errors discovered in the materials.

(12) **Charges:** To meet agreed charges for the supply of materials.

(13) **Liability:** To accept that the CFAS Wales management team bear no legal responsibility for the accuracy or comprehensiveness of the materials.

(14) **Completion:** To inform CFAS Wales of the completion of the project specified in this application. Should publications not arise immediately from a PhD project, the student may make an application to use the data for revisions.

(15) **Destruction of data:** After the data has been deposited and verified by the CFAS Wales data archive (see Clause 10), except where an application has been received to use the data for a further project, to destroy or erase irrecoverably all complete, partial or derived copies of the data which have been made available for this application on completion of the specified project and to inform CFAS Wales Management team that this has been done.

I agree to comply with this agreement, and understand that any breeches will result in CFAS Wales informing my institution, funding agency and the ESRC

Signed: .....

Name (Block Capitals) ISOBEL EVANS

Date: 26-4-16

The completed form should be sent to:

Dr. Gill Windle

DSDC Wales

Ardudwy, Bangor University, Normal Site, Holyhead Road, Bangor, Gwynedd

g.windle@bangor.ac.uk

Appendix C: PROTECT participant information sheet for social connections study

Participant Information Sheet: Social connections in later life

Version 1.0: Date 2/11/17

Invitation to take part in a research study

We would like to invite you to take part in a research study. Before you decide if you would like to take part in the study, we would like you to read the information below to understand why the research is being done and what it will involve for you.

Please take time to read the following information carefully and discuss it with family or friends if you wish. If you have any questions about anything that you read, you can contact a member of the study team (details at the end of the information sheet).

It is important for you to understand that you do not have to take part in this study. If you do decide to take part, you are free to withdraw at any time. If you decide to take part we will ask you to confirm that you have read and understood this information and tick the box indicating you agree to take part.

What is the purpose of the study?

This study aims to ask you some questions about your social relationships and the types of activities that you do in your spare time. We would like to get a better understanding of how social relationships may influence health in later life and particularly how social lifestyle may influence cognitive function. The study is being led by the University of Exeter.

Why have I been invited?

We are inviting adults over the age of 60 from across the UK to take part in this study. All the adults invited to take part are already part of the Platform for Research Online to investigate Cognition and Genetics in Ageing (PROTECT). We are looking for at least 5,000 people to join the study. In order to participate, you will also need to have the ability to use a computer or device like a smartphone or tablet with internet access.

If you have an established diagnosis of dementia from your doctor then unfortunately you will not be eligible for this study.

Do I have to take part?

It is up to you whether or not to join the study. This information sheet aims to inform you about the study in order to help you decide if you would like to take part or not. If you agree to take part, you will then need to read and sign a consent form on the website. You will then be redirected to begin the questionnaires. You are free to withdraw from the study at any time, without giving a reason.

What will happen if I take part?

We will ask you to complete four questionnaires that ask about your social relationships and activities that you take part in during your spare time. These questions should take no more than

approximately 20 minutes to complete. Once you have completed and successfully submitted the questionnaires, your time on this short study will end.

All the information we collect will be kept anonymous and confidential. We will keep all data for 10 years after the study has finished. We will then destroy it.

The University of Exeter Psychology Research Ethics Committee has approved this research (Ref number: eCLESPsy000045) and the research will be covered by normal insurance policies at The University of Exeter.

What are the possible benefits and risks of taking part?

There are no risks associated with taking part in this study. You will simply be asked to answer questions.

The main advantage of this research is that all participants will be taking part in an important research study that will provide us with valuable knowledge about social relationships in later life.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time without giving a reason. You can do this through the 'I wish to withdraw' link on the website or by contacting us on the study helpline. If someone develops dementia and loses the capacity to make decisions independently about their involvement in the study, they would then be withdrawn from the study. For legal reasons we will retain the name and participant ID of any withdrawn participants to ensure we have a record of your consent when you registered. We will retain all anonymised data that we have collected up to the point you withdraw. This includes all anonymised data from questionnaires.

Will my taking part in this study be kept confidential?

Research data will be collected online through the PROTECT website. All data will be stored securely according to the Data Protection Act (1998) and the security procedures in place at King's College London and the NIHR Bioresource. The study database will not include your name, just a study number. Your data will be completely anonymised and it will not be possible to identify you. All anonymised data will be transferred to Exeter University and stored securely according to the Data Protection Act (1998).

What will happen at the end of the study?

The results of the study will be published in a scientific journal. We will provide you with a lay summary of our findings in the form of a newsletter. The findings will also be available on the PROTECT website. The information collected is totally confidential and no individuals will be identified in any publications.

What if there is a problem?

If you have any concern about any aspect of this study 'social connections in later life', please do not hesitate to contact the lead study investigator: Isobel Evans (email: i.evans@exeter.ac.uk, telephone: 01392 724696).

In the event of technical issues or general queries regarding the PROTECT study, please continue to contact the PROTECT team on 0207 848 8183 or via email on admin@protectstudy.org.uk

Appendix D: PROTECT participant consent form for social connections study

Consent Form for Participants: Version 1.0, Date: 09/01/2018

Social Connections in Later Life

Please read the below statements carefully and tick all boxes found in this form.

1. I am aged 60 or older, live in the UK and have access to a computer and the internet. ☐

2. I confirm that I have read and understand the participant information sheet (version 1.0) dated 02/11/2017 for the above study. I have had the opportunity to consider the information, seek clarification and understand my involvement in the study. ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected. ☐

4. I understand that relevant data collected during the study may be looked at by individuals representing the research team at Exeter University or from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data. ☐

5. I agree for anonymous data from this study to be used by other researchers in the future. ☐

6. In the event that I lose capacity to consent during the period of this research I understand that I will immediately be withdrawn from the study. ☐

7. If I choose to withdraw or lose the capacity to consent as described in point 6, I understand that all anonymous data collected prior to my withdrawal will be retained and included in the study. ☐

8. I understand that all data will be stored in a way complying with the provisions of the Data Protection Act. ☐

9. I agree to take part in the above study. ☐

_____ _____

Name of Participant Date

Appendix E: PROTECT study ethics application

Ethics application to the University of Exeter Psychology Ethics Committee

Main application submitted: 29/08/2017

Summary

Title	Perceived social isolation in later life
Application type	Student
Project supervisor	Linda Clare
Campus	Streatham
Applicant	Isobel Evans
Applicant declaration	I confirm I have read the University of Exeter 'Good Practice in the Conduct of Research' code of practice.
Has your project been externally ethically reviewed?	No
Estimated start date	04/09/2017 (duration 8 months)
Is the project externally funded?	Yes (Alzheimer's Society)
Lay summary	There is evidence to suggest that being socially isolated is associated with a range of negative health outcomes, including poor cognitive function in later life (Kuiper et al. 2016). Evidence suggests that a high number of social contacts and more frequent social interaction leads to better cognitive outcomes (e.g. Barnes et al. 2004; Shankar et al. 2013). However, findings are inconsistent and some studies do not report this association (e.g. Hughes et al. 2008; Simning et al. 2014). One reason for this inconsistency may be that measures of isolation are typically standardised and focus on quantitative features of social networks. This is approach is objective and does not consider the individual's personal feelings of isolation and perceptions of their social network. Measures classify participants as isolated or not based on cut-points that determine whether the amount of social contact an individual has is sufficient or not. This is problematic as some individuals may prefer less contact than implied by selected cut-points and are still able to function sufficiently with this level of contact, yet are classified as isolated. It is also important to consider different personal (e.g. mental health, personality) and environmental or social factors (e.g. cultural and social capital) that may influence perceptions of social isolation. This study aims to (1) consider how scores on standardised measures of social isolation compare to subjective appraisals of isolation, (2) identify whether there are differences in standardised measures of isolation and perceived isolation in their prediction of cognitive function, and (3) consider what factors (i.e. person and environment) may influence perceived social isolation. These aims will be explored using the PROTECT study, an ongoing longitudinal study of people ≥50. Participants complete an online annual assessment and questionnaires to assess constructs of interest will be embedded into the annual assessment.

Location

Where will your research take place	Within the United Kingdom
Please provide details of your research location(s)	The aims will be assessed using the PROTECT study, an existing ongoing longitudinal study. The study collects questionnaire data from participants annually using an online platform – therefore participants are able to complete all aspects of the study online. The PROTECT study is co-ordinated by researchers from King's College London and the University of Exeter Medical School.

Details

Is the application linked to a previous application?	No
Has your project been peer reviewed by any of the following?	Research team / group members: YES External peer review: NO
Does your project involve:	Humans: YES Animals: NO
Does this study involve human samples?	NO
Track type	B

Questions

Human aspects	
I am familiar with the BPS Guidelines for ethical practices in psychological research (and have discussed them with other researchers involved in the project.)	YES
Communication and consent	
Will you describe the main research procedures to participants in advance, so that they are informed in advance about what to expect?	YES
Will you tell participants that their participation is voluntary?	YES
Will you obtain written consent for participation?	YES
If the research is observational, will you ask participants for their consent to being observed?	N/A
Will you tell participants that they may withdraw from the research at any time and for any reason?	YES
With questionnaires, will you give participants the option of omitting questions they do not want to answer?	YES
Will you tell participants that their data will be treated with full confidentiality and that, if published, it will not be identifiable as theirs?	YES
Will you debrief participants at the end of their participation (i.e. give them a brief explanation of the study)?	YES
Possible harms	
Will your project involve deliberately misleading participants in any way?	NO
Is there a realistic risk of any participants experiencing either physical or psychological distress or discomfort?	NO

Vulnerable groups *Does your project involve*:	
Children under 18 years of age	NO
People with learning or communication difficulties	NO
Participants who are unable to give informed consent	NO
Any member of the research team or participants are members of the Armed Forces or their dependents	NO
Those at risk of psychological distress or otherwise vulnerable	NO
People in custody or on probation	NO
People engaged in illegal activities (e.g. drug taking)	NO
NHS patients or social care service users	NO
Data protection and storage	
Will you ensure participant data is kept confidential	YES
Will data be stored securely	YES
Will you inform participants about how the data collected from them will be used	YES
Will you retain collected data for a specified period (e.g. five years)	YES
Will you inform participants of this data retention period	YES
I am satisfied that the research study is compliant with the Data Protection Act 1998, and that necessary arrangements have been made with regard to the storage and processing of participants' personal information and generally, to ensure confidentiality of such data supplied and generated in the course of the research.	YES

Statement

Research methodology	The aims will be assessed using the PROTECT study, an ongoing longitudinal study. Participants complete annual follow-up assessments in the autumn of each year. Permission has been granted by the study co-ordinator (Prof. Clive Ballard) to embed a series of questionnaires into the annual assessment in order to examine my aims. I am able to access results of measures that have already been assessed in previous waves of PROTECT data collection. This includes measures of cognitive function and mental health. A description of the PROTECT study design is provided below and details of participant recruitment are provided in the 'research participants section'. The PROTECT study commenced in November 2015. The study length is anticipated to be ten years, with an initial two years for recruitment and a further eight years follow-up. The target population for the study is healthy adults, ≥50, who reside in the community. Data is collected using an online platform in which participants can log in to the site and complete questionnaires and assessments. Participants initially provided consent to complete a baseline assessment in 2015 and are then invited to complete a follow-up assessment each year. Consent of participation is obtained at each yearly assessment. In the 2017 annual assessment, questionnaires will be embedded that assess the aims of my study. These questionnaires will include the following: a standardised measure of social isolation (the Lubben Social Network Scale–6), a set of questions taken from existing longitudinal studies to assess perceived social isolation, a measure of personality (the MINI-IPIP), and measures of social and cultural capital. The questionnaire can be found in the supporting documents, along with a description of each questionnaire.

	Full details of the PROTECT protocol can be found in the supporting documents.
Research participants	This section provides an overview of how participants were initially recruited for the PROTECT study. It then provides detail of the procedures for the annual follow-up assessment. *Initial recruitment to PROTECT:* Participants were recruited through several channels. The study was promoted through communication channels at King's College London (KCL), the Biomedical Research Centre at KCL, the University of Exeter and the Royal Devon and Exeter NHS Trust. This included publicity through the media and University press partners, and online content. The study was also advertised on the Department of Health 'Join Dementia Research' website. People ≥50 who were participants in existing cohort studies and completed trials hosted by KCL and Exeter were contacted with study information and invited to register online if they wished to participate. Finally, leaflets were placed in GP surgeries and memory clinics. Potential participants were directed to the study website (http://www.protectstudy.org.uk/consent.aspx). The information webpage (http://www.protectstudy.org.uk/StudyInfoSheet/ProtectStudyInfoSheet_v16_20170214.pdf) includes detailed information about the purpose and aims of the study, what the participant can expect if they agree to take part in the study, possible risks and benefits from taking part, the right to withdraw from the study, how their data will be kept confidential, what will happen at the end of the study, and finally contact details if participants have further questions or concerns (information sheet can be found in the supporting documents). After reading the information leaflet, participants decided whether they wanted to consent to take part in the study and could register online (https://www.protectstudy.org.uk/register.aspx). The study recruited approximately 5,000 people ≥50. Both male and female participants were recruited. Inclusion criteria for participation was as follows: aged over 50, residing in the UK, living in the community, and have access to a computer and the internet. Participants with an established diagnosis of dementia or cognitive impairment were not eligible to participate. Most participants completed baseline assessments in October and November 2015. *Annual assessments:* Participants were invited to complete a follow-up assessment by email exactly one year after they completed their baseline assessment (October/ November 2016). If participants wished to complete this assessment, they were invited to log in to the site and again provide consent. Participants were made aware of their right to withdraw from the study or stop completing the questionnaire at any time. This procedure will be followed for each annual assessment. In the upcoming annual assessment, questionnaires assessing concepts of interest for the current research project will be embedded into the existing annual questionnaire for PROTECT.
Ethical considerations	*Sensitive questions about social relationships:* Participants may feel some discomfort when answering questions about their social relationships. If participants are dissatisfied with their social relationships, they may find it difficult to answer the questions and may find it an uncomfortable experience. However, participants do not have to answer these questions if they feel uncomfortable in doing so and this will be made clear to them in the information sheet prior to the questionnaire beginning. In

	addition, the questions are not too probing and will not cause significant psychological distress or discomfort. *Data protection procedures:* All participants have a unique ID number. Personal data is collected on a separate database from non-personal data and can be matched using the participant ID number. Personal databases are held separately by King's College London and the University of Exeter, dictated by the recruitment route taken by the participant. All databases are password protected and located on University shared drives which only the study team at that University have access to. The data is held on the Universities' servers which are not accessible by anyone outside the organisations. Non-personal data is stored in two independent databases at the two sites in King's College London and the University of Exeter. This data is accessible for import to either site to enable the creation of a full database for analysis purposes. Data generated through the Wesnes Online Cognitive Test (measure of cognitive function that already exists as a measure in PROTECT) is stored in a secure server and transferred to the host site via a regular encrypted transfer. Data is also stored online on Google Cloud to provide a back-up database (https://cloud.google.com/terms/data-processing-terms). Raw data (not including personal details) is stored in encrypted form, subject ISO/IEC 27001:2005 Certification. Only core study team members have access to personal data through the electronic database. This includes the Chief Investigator, study co-ordinators, and IT specialist. Once data has been collected, colleagues from the PROTECT team are able to extract relevant data requested by researchers and prepare this to be sent anonymously. *Benefits of participation:* The main benefit of participation is that the PROTECT study is an important piece of research that will provide valuable knowledge about how the brain works as we get older. Participants will receive information letters about the study and updates about research regarding the prevention of dementia and poor cognitive function in later life. There are no financial inducements, participants take part in the study voluntarily. Participants will receive feedback in the form of a newsletter following the completion of the study. This newsletter will contain a lay summary of the findings from the study. This information will also be available on the PROTECT website.
Researcher experience	I have previously completed work using the Cognitive Function and Ageing Study – Wales (CFAS-Wales), a large-scale database aiming to answer key questions about lifestyles and cognitive health in later life. I have successfully handled this data and have understood the importance of storing this data in a confidential manner. I have also successfully conducted analyses using this data. The data from PROTECT will be in a similar form to data from CFAS-Wales and so I will be able to draw upon my existing skills for handling and analysing large datasets.

Supporting files

- Main PROTECT protocol
- Main PROTECT study information sheet
- Social connections questionnaire to be uploaded
- Social connections study protocol
- Social connections participant information sheet
- Social connections consent form

Amendments:

22/09/2017	Response to ethics committee on data: I can confirm that once I receive the data from the co-ordinators at Kings College London, I will not be able to link the data with any participant's personal details. Information about the provision of support information, such as befriending, will be included in the annual emails and information sheets which update participants about the study.
14/11/2017	Rather than adding the proposed questionnaires to the annual assessment of the PROTECT study, participants who have signed up to the PROTECT study will be emailed and invited to take part in a study 'social connections in later life'. The email will contain a short summary of the questionnaires and a link that will direct them to an information sheet (attached in files). Participants will have the opportunity to read the information sheet and then if they consent to take part in the study they must tick a box that will state 'I agree to take part in this study 'social connections in later life'.
09/01/2018	It has now been decided that we will ask participants to provide consent using a more extensive consent form rather than one single tick box. This form is attached (social connections in later life consent form) and the participant will see the form and sign and date this electronically before starting the questionnaires.

Appendix F: Letter of approval for PROTECT study from University of Exeter Psychology Ethics Committee

CLES – Psychology
Psychology
College of Life and Environmental Sciences
University of Exeter
Washington Singer Building
Perry Road
Exeter
EX4 4QG
Web: www.exeter.ac.uk

CLES – Psychology Ethics Committee

Dear Isobel Evans

Ethics application - eCLESPsy000045

Perceived social isolation in later life.

Your project has been reviewed by the CLES – Psychology Ethics Committee and has received a Favourable opinion.

The Committee has made the following comments about your application:

Linda Clare commented,

You are required to re-submit for full review/confirm that comments have been addressed before you begin your research.

If you have any further queries, please contact your Ethics Officer.

Yours sincerely

Date: 02/10/2017

CLES – Psychology Ethics Committee

Appendix G: Social connections questionnaires administered to the PROTECT cohort

Lubben Social Network Scale-6

This questionnaire asks you about your relationships with family and friends.

***FAMILY**: Considering the people to whom you are related by birth, marriage, adoption, etc...*

1. How many relatives do you see or hear from at least once a month?

0 = none 1 = one 2 = two 3 = three or four 4 = five through eight 5 = nine or more

2. How many relatives do you feel at ease with that you can talk about private matters?

0 = none 1 = one 2 = two 3 = three or four 4 = five through eight 5 = nine or more

3. How many relatives do you feel close to such that you could call on them for help?

0 = none 1 = one 2 = two 3 = three or four 4 = five through eight 5 = nine or more

***FRIENDSHIPS**: Considering all of your friends including those who live in your neighbourhood*

4. How many of your friends do you see or hear from at least once a month?

0 = none 1 = one 2 = two 3 = three or four 4 = five through eight 5 = nine or more

5. How many friends do you feel at ease with that you can talk about private matters?

0 = none 1 = one 2 = two 3 = three or four 4 = five through eight 5 = nine or more

6. How many friends do you feel close to such that you could call on them for help?

0 = none 1 = one 2 = two 3 = three or four 4 = five through eight 5 = nine or more

Satisfaction with social contact

This questionnaire asks how you feel about your relationships with others.

1. Do you feel you need more people to talk with?

Yes (1)/ no (0)

2. Do you feel you need to spend more time with friends/family?

Yes (1)/ no (0)

3. Do you feel you need more advice about important matters?

Yes (1)/ no (0)

4. Do you feel you need more help and support?

Yes (1)/ no (0)

5. How do you feel about your life in terms of family relationships?

Terrible/ Unhappy/ Mostly dissatisfied/ Mixed/ Mostly satisfied/ Pleased/ Delighted

6. How do you feel about your life in terms of friendships?

Terrible/ Unhappy/ Mostly dissatisfied/ Mixed/ Mostly satisfied/ Pleased/ Delighted

7. In general, do you get out and about as much as you would like to?

Yes (1)/ no (0)

8. Are you satisfied with the amount of contact you have with family and friends?

Yes (1)/ no (0)

Personality

These questions measure your personality. You will see 20 statements and will be asked to evaluate the extent to which you agree with them. Please answer honestly with regard to how you see yourself in the present moment. There are no incorrect answers.

1. In general I am the life of the party.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

2. In general I sympathize with others' feelings.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

3. In general I get chores done right away.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

4. In general I have frequent mood swings.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

5. In general I have a vivid imagination.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

6. In general I don't talk a lot.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

7. In general I am not interested in other people's problems.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

8. In general I often forget to put things back in their proper place.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

9. In general I am relaxed most of the time.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

10. In general I am not interested in abstract ideas.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

11. In general I talk to a lot of different people at parties.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

12. In general I feel others' emotions.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

13. In general I like order.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

14. In general I get upset easily.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

15. In general I have difficulty understanding abstract ideas.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

16. In general I keep in the background.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

17. In general I am not really interested in others.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

18. In general I make a mess of things.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

19. In general I seldom feel blue.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

20. In general I do not have a good imagination.

Strongly disagree/ somewhat disagree/ neither agree nor disagree/ somewhat agree/ strongly agree

Social capital

We would now like to ask you some questions about social capital. Social capital refers to the networks of relationships among people who live in a particular society, enabling that society to function effectively.

1. How satisfied are you with your neighbourhood as a place to live?

Very dissatisfied/ fairly dissatisfied/ neither satisfied nor dissatisfied/ slightly satisfied/ very satisfied/ don't know

2. Suppose you lost your purse or wallet containing your address details, and it was found in the street by someone living in this neighbourhood. How likely is it that it would be returned to your home with nothing missing?

Very likely/ quite likely/ not very likely/ not at all likely/ don't know

3. How much of a problem are people being drunk or rowdy in public places in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

4. How much of a problem is rubbish or litter lying around in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

5. How much of a problem are vandalism, graffiti, and other deliberate damage to property or vehicles in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

6. How much of a problem are people using or dealing drugs in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

7. How much of a problem are people being attacked or harassed because of their skin colour, ethnic origin, or religion in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

8. How much of a problem are teenagers hanging around on the street in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

9. How much of a problem are troublesome neighbours in your neighbourhood?

Very big problem/ fairly big problem / not a very big problem/ not a problem at all/ it happens but it's not a problem/ don't know

10. In your neighbourhood to what extent do you agree or disagree that people are willing to help their neighbours?

Strongly disagree/ slightly disagree/ neither agree nor disagree/ slightly agree/ strongly agree/ don't know or no opinion

11. In the last 12 months have you taken any of the following actions in attempt to solve a problem affecting the local area? (Please select all that apply)
    - *Contacted a local radio station, television station, or newspaper*
    - *Contacted the appropriate organisation to deal with the problem, e.g. council*
    - *Contacted a local councillor or Member of Parliament*
    - *Attended a public meeting or neighbourhood forum to discuss local issues*

- *Attended a tenants' or local residents' group*
- *Attended a protest meeting or joined an action group*
- *Helped organise a petition on a local issue*
- *No local problems*
- *None of the above*
- *Don't know*

We would now like to ask you some questions about the social activities you do in your spare time.

12. How often do you speak to relatives on the phone?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

13. How often do you write a letter or note to relatives?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

14. How often do you text or email relatives, or use the internet to talk to relatives (e.g. FaceTime, Skype, chatrooms)?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

15. How often do you speak to friends on the phone?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

16. How often do you write a letter or not to friends?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

17. How often do you text or email friends, or use the internet to talk to friends (e.g. FaceTime, Skype, chatrooms)?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

18. How often do you speak to neighbours?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

19. How often do you meet up with relatives who are not living with you?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

20. How often do you meet up with friends?

On most days/ once or twice a week/ once or twice a month/ less often than once a month/ never/ don't know

21. During the last 12 months have you given any unpaid help to any groups, clubs, or organisations in any of the ways listed below? (Please select all that apply)
    - *Raising or handling money/ taking part in sponsored events*
    - *Leading the group/ member of a committee*
    - *Organising or helping to run an activity or event*
    - *Visiting people*
    - *Befriending or mentoring people*
    - *Giving advice/ information/ counselling*
    - *Secretarial, admin, or clerical work*
    - *Providing transport/ driving*
    - *Representing (e.g. addressing meetings, leading a delegation, talking to a council official)*
    - *Campaigning*
    - *Other practical help (e.g. helping out at school, religious group, shopping)*
    - *Any other help*
    - *None of the above*
    - *Don't know*

Cultural activities

We would now like to ask you some questions about some more activities you may do in your spare time.

22. How often do you go to the cinema?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

23. How often do you go to museums?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

24. How often do you go to pubs?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

25. How often do you go to rock concerts?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

26. How often do you go to the opera?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

27. How often do you go to bingo?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

28. How often do you go to orchestral or choral concerts?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

29. How often do you go to stately homes or historic sites?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

30. How often do you go to musicals?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

31. How often do you go to the theatre?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

32. How often do you go to art galleries?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

33. How often do you go to night clubs?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

34. How often do you go somewhere to eat out?

At least once a week/ less often but at least once a month/ less often but at least several times a year/ once a year or less/ never

Appendix H: PROTECT data access form

Application for Access to PROTECT Study Data and / or samples

Title of project	Social isolation in later life
Principal Investigator	Isobel Evans
Organization and Department (full contact details)	Centre for Research in Ageing and Cognitive Health (REACH), University of Exeter Medical School, South Cloisters, Heavitree Road, Exeter, EX1 2LU.
Co-investigators (Please highlight any existing PROTECT investigators)	Professor Linda Clare
Primary contact for study	Name: Isobel Evans Address: University of Exeter Medical School, South Cloisters, Heavitree Road, Exeter, EX1 2LU. Email: i.evans@exeter.ac.uk Tel: n/a
Start and completion dates	Start Date: October 2017 Expected completion Date: September 2018
Source of funding	Alzheimer's Society

What is being requested? (Place a **X** in all that apply)	**Participant characteristics**	
	Sample Size	**Full sample**
	Participant characteristics (Provide as much detail on required participants as possible)	
	Anonymised Datasets	

			Baseline	**Follow-up**
	Full PROTECT Dataset			
	Partial PROTECT Dataset	Demographics	X	X
		Medical History		
		Lifestyle	**X**	**X**
		Cognitive Test Package 1 (PROTECT)	**X**	**X**
		Cognitive Test Package 2 (CogTrack)*	**X**	**X**
		IQCode		
		IADL		
		Mental Health Questionnaire (full)	**X**	**X**
		Mental Health Questionnaire (partial – please specify which sections):	**X**	**X**
		Mild Behaviour impairment Scale		
		Pain short-form		
		Sleep		
		Fertility / menopause		
	Genetic Data / Samples			
	Genotype / GWAS Data			
	Access to extracted DNA samples			
	Personal details and re-contact			
	Personal details data (please specify)			
	Re-contact of participants for nested PROTECT study e.g. addition of new assessment or email distribution of survey etc			

	Re-contact of participants for separate study e.g. identification of participants for clinical trial	
Study Aims & Objectives Please outline the aims of your study	(1) To determine how scores on standardised measures of social isolation compare to subjective appraisals of social isolation (2) To determine whether there are differences in standardised measures of social isolation and perceived social isolation in their prediction of cognitive function. (3) To determine whether personal (mental health, personality) or social and environmental factors (social and cultural capital) may influence perceived social isolation.	
Brief Description of Project (If access to personal details or genetic data is required please include study protocol)	There is evidence to suggest that being socially isolated is associated with a range of negative health outcomes, including poor cognitive function in later life (Kuiper et al. 2016). Evidence suggests that a high number of social contacts and more frequent social interaction leads to better cognitive outcomes (e.g. Barnes et al. 2004; Shankar et al. 2013). However, findings are inconsistent and some studies do not report this association (e.g. Hughes et al. 2008; Simning et al. 2014). One reason for this inconsistency may be that measures of isolation are typically standardised and focus on quantitative features of social networks. This is approach is objective and does not consider the individual's personal feelings of isolation and perceptions of their social network. Measures classify participants as isolated or not based on cut-points that determine whether the amount of social contact an individual has is sufficient or not. This is problematic as some individuals may prefer less contact than implied by selected cut-points and are still able to function sufficiently with this level of contact, yet are classified as isolated. It is also important to consider different personal (e.g. mental health, personality) and environmental or social factors (e.g. cultural and social capital) that may influence perceptions of social isolation.	
Ethical approval status (Some data requests may fall within the existing PROTECT approvals. If in doubt please contact a PROTECT administrator to discuss)		**Tick relevant box**
	No additional approval required (please justify)	
	Ethics submission in process Anticipated date of approval: REC: R&D dept: Reference number: (Please attach confirmation of sponsorship)	
	Ethical approval confirmed	X

	Date of approval: 26-9-17, confirmed by the University of Exeter Psychology Ethics Committee. REC: R&D dept: Reference number: HRA approval required?: (Please attach letter of approval from REC and HRA if appropriate)	
Justification for request Please provide rationale for the data or samples requested above, including: 1. Sample size 2. Participant characteristics 3. Data type **4.** Sample type **5.** New study or assessment If relevant provide a clear justification for requests that include both access participants with specific genotypes and personal details, including any plans to disclose genetic information and how this will be managed.	I require the whole sample as I would like to assess my aims using a large database in order to gain the most accurate and population representative results. I require the participant characteristics so that I can comprehensively report the participant characteristics in my results. I require these additional questions to be added to the PROTECT study as they are not currently assessed. These questions will also add to the database as they encompass questions on lifestyle, including social activity, social isolation, cultural capital, and other personal characteristics such as personality.	
Involvement of PROTECT Investigators If you expect to require support from PROTECT investigators please give details. This may include: - Managing participant contact through PROTECT - Technical support for PROTECT website, incl new assessments - Statistical support - Data management	I do not require a great deal of support from PROTECT investigators. I anticipate the only support I need will be getting the data sent to me.	
Budget		

Do you have budget available to support this request? Please provide details This is particularly relevant to requests that require active involvement of PROTECT investigators or amendments to PROTECT study assessments	
Further Information Please provide any further relevant information	

Key information for applicants

- Use of PROTECT data is subject to full ethical approval. Some requests may fall under existing PROTECT approvals. Please contact the study administrator to discuss further
- This application will be reviewed by the PROTECT Strategy Group to ensure the request is appropriate to the data, and does not conflict with existing research and analyses within the PROTECT portfolio
- GWAS data will be released as summary data only (list of markers with effect size / overall frequency of requested alleles per marker) and will not include individual-level genetic data
- The PROTECT investigators ask that any publications or outputs arising from the use of PROTECT data include authorship for PROTECT investigators and acknowledgement of PROTECT support and funders.
- CogTrack™ is provided by a third party. Use of this data may be subject to additional cost.

Document to be submitted to maria.megalogeni@kcl.ac.uk

Questions regarding this process should be directed to maria.megalogeni@kcl.ac.uk and zunera.2.khan@kcl.ac.uk in the first instance**.**

Appendix I: PROTECT data agreement

PROTECT data usage agreement

I agree to comply with the following terms covering both genetic and phenotype data:

1. PROTECT data must be stored securely according to the Data Protection Act (1998) and the security procedures in place at your institution of residence.

2. Data from PROTECT is only to be used for non-commercial purposes.

3. PROTECT data is not to be transferred to, or used by, any other person or organisation other than those listed in the application proposal.

4. Usage of the data is strictly limited to addressing the hypotheses/research questions defined in the project proposal. Any broadening of scope of research must be discussed with the PROTECT study team and cannot proceed without their authorisation.

5. Any outputs of research involving PROTECT data including but not limited to conference presentations, journal publications and posters must include acknowledgement to funders of PROTECT and the PROTECT study team, and make use of the PROTECT logo where fitting (please liaise with PROTECT team for details).

6. Any output must adhere to any authorship agreements made between you and the PROTECT team.

7. Once your project has finished you must permanently delete the PROTECT data.

Data usage agreement: PROTECT-hosted measures

I agree to comply with the following terms:

1. All data generated through measures hosted on the PROTECT platform, can be accessed and used freely by the PROTECT study team.

Please sign below to confirm your agreement to the above terms:

Name Signed

Isobel Evans

Date

20-11-17

Appendix J: Full search terms used to search databases for the systematic review

Table J. *Full search terms used in databases for the systematic review.*

Step	Terms
1	Title OR Abstract: social* isolat* OR social* engage* OR social* activ* OR social* disconnect* OR social participation OR social relationship* OR social* integrat* OR social network* OR social tie* OR network* OR social contact* OR social* connect* OR active lifestyle OR engaged lifestyle OR social interaction OR social components
2	Title OR Abstract: cognit* OR cognitive reserve OR cognit* lifestyle OR cognit* health* OR cognit* activ* OR cognit* function* OR cognit* impair* OR cognitive decline OR cognitive performance OR cognitive status OR cognit* abilit*
3	Title OR Abstract: "late* life" OR old* OR elder* OR age* OR aging
4	#1 AND #2 AND #3

Appendix K: Quality measure for assessing articles included in the systematic review

Each question scores either 1 (poor), 2 (fair), or 3 (very good). Scores are summed and range from 14–42 with higher scores indicating greater methodological quality.

Aims

1. Aims/objectives clearly described?

Study population

2. Characteristics of participants clearly described (inclusion/exclusion criteria)?
3. Adequate description of participants (including age, gender, and cognitive status)?
4. Characteristics of participants lost to follow-up considered?
5. Cohort representative of the general population?

Method

6. Clear the number of years participants were followed up for?
7. Number of participants included in final analysis clear?
8. Follow-up of participants long enough to detect cognitive change (at least 2 years)?

Measures

9. Standardised measures of social isolation used and scoring method clearly outlined?
10. Standardised cognitive measure used and scoring method outlined?

Results and analysis

11. Statistical methods used appropriate?
12. Adequate adjustment for confounding variables?
13. Main findings clearly outlined?
14. Can results be applied to a general population?

Appendix L: Forest plots for the sub-analyses for aspects of social isolation and cognitive function

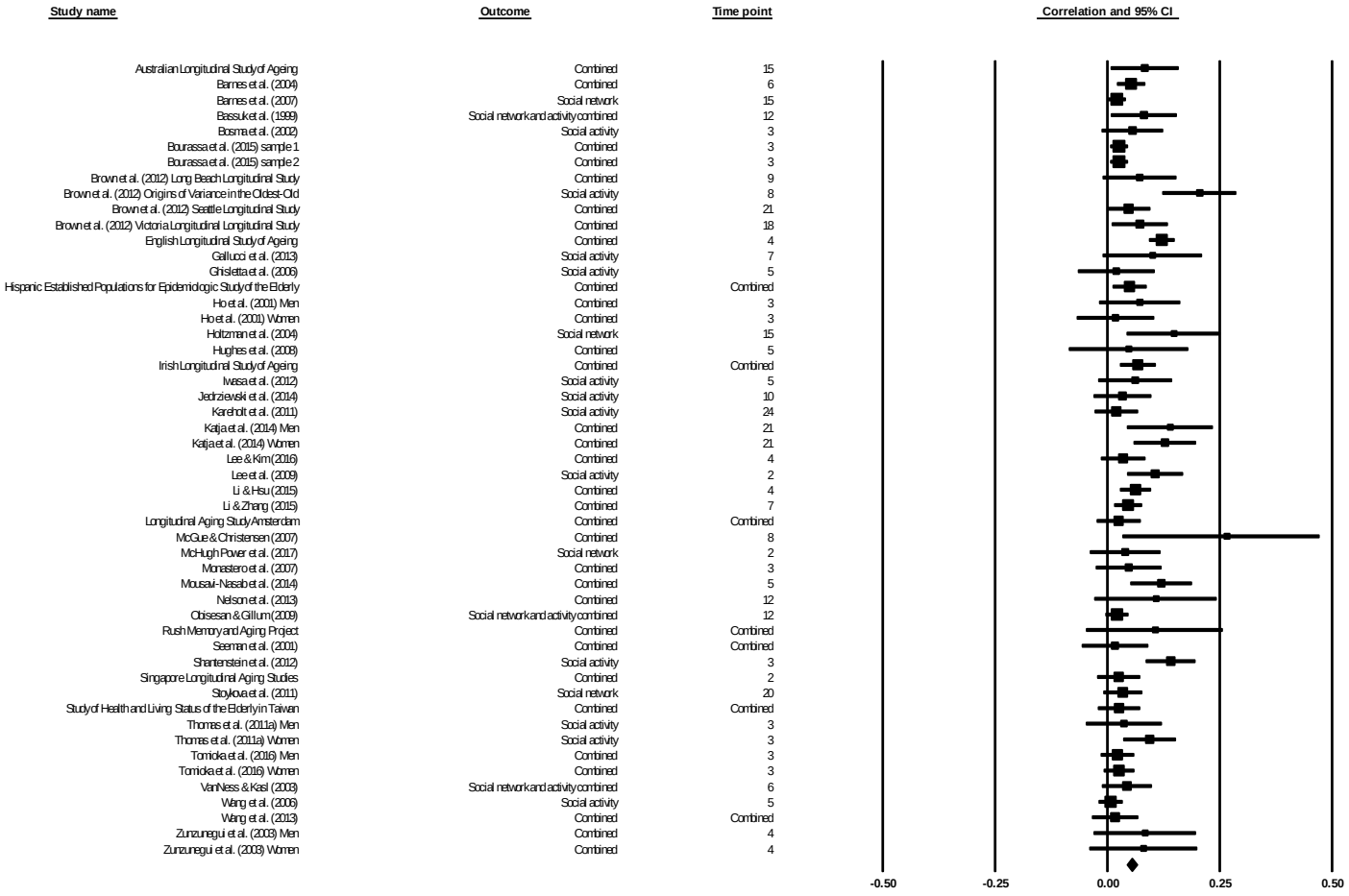


Figure L.1. Forest plot of the positive association between all social measures and all cognitive measures.

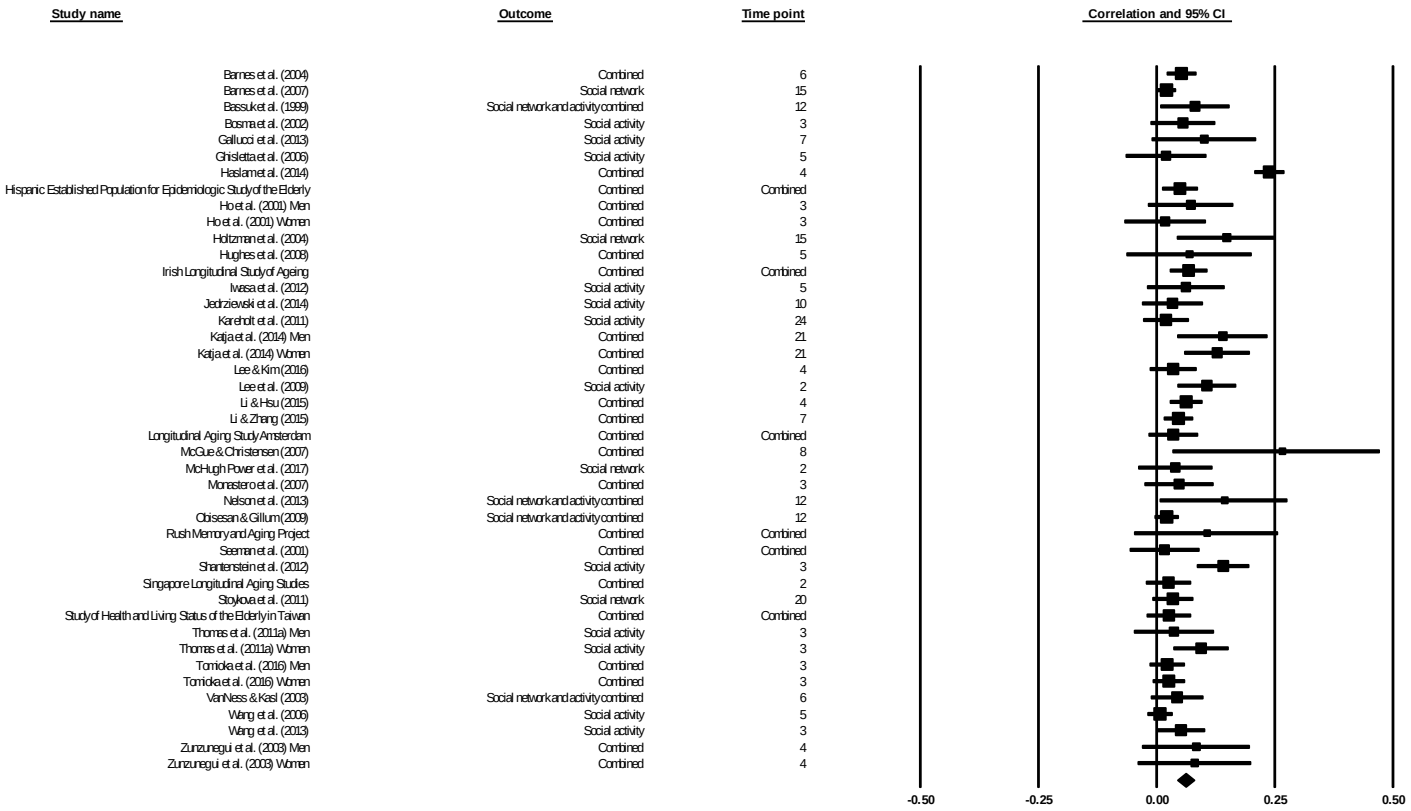


Figure L.2. Forest plot of the positive association between all social measures and global measures of cognitive function.

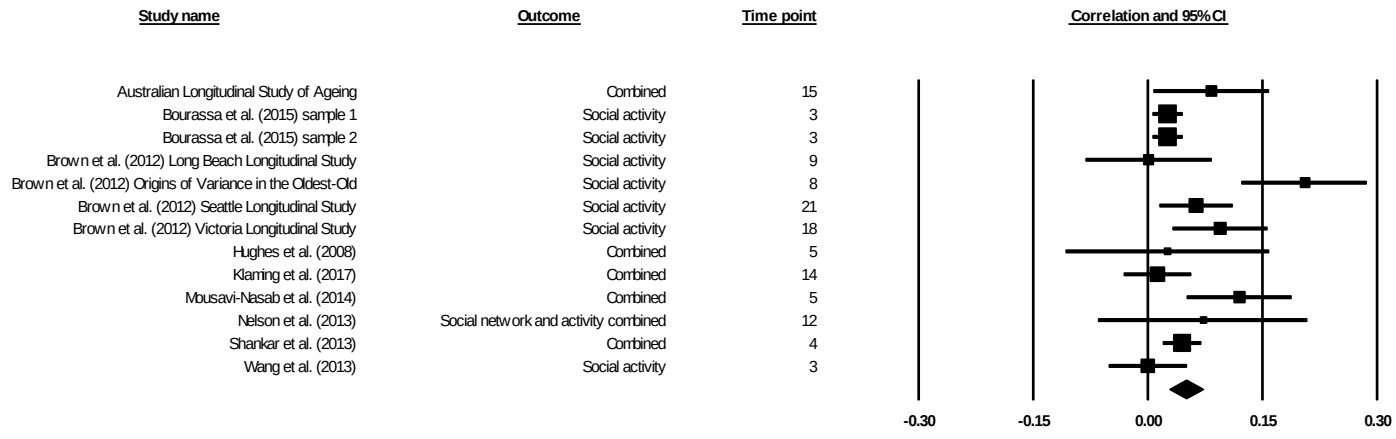


Figure L.3. Forest plot of the positive association between all social measures and memory.

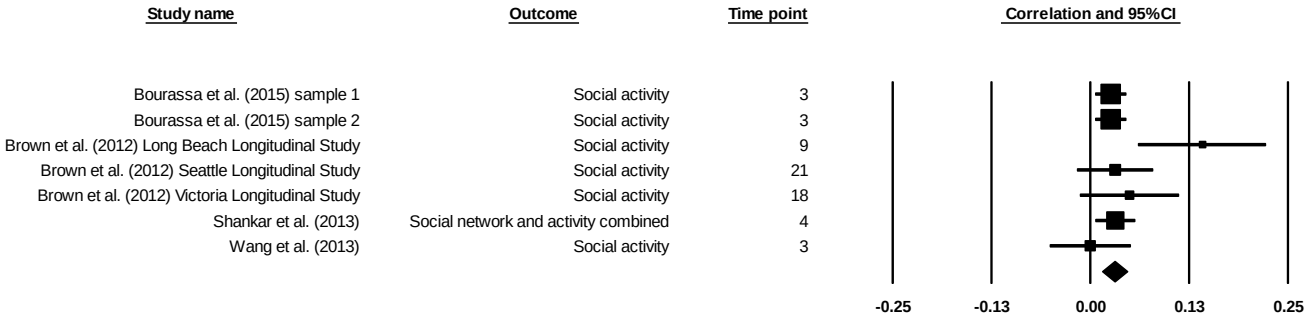


Figure L.4. Forest plot of the positive association between all social measures and executive function.

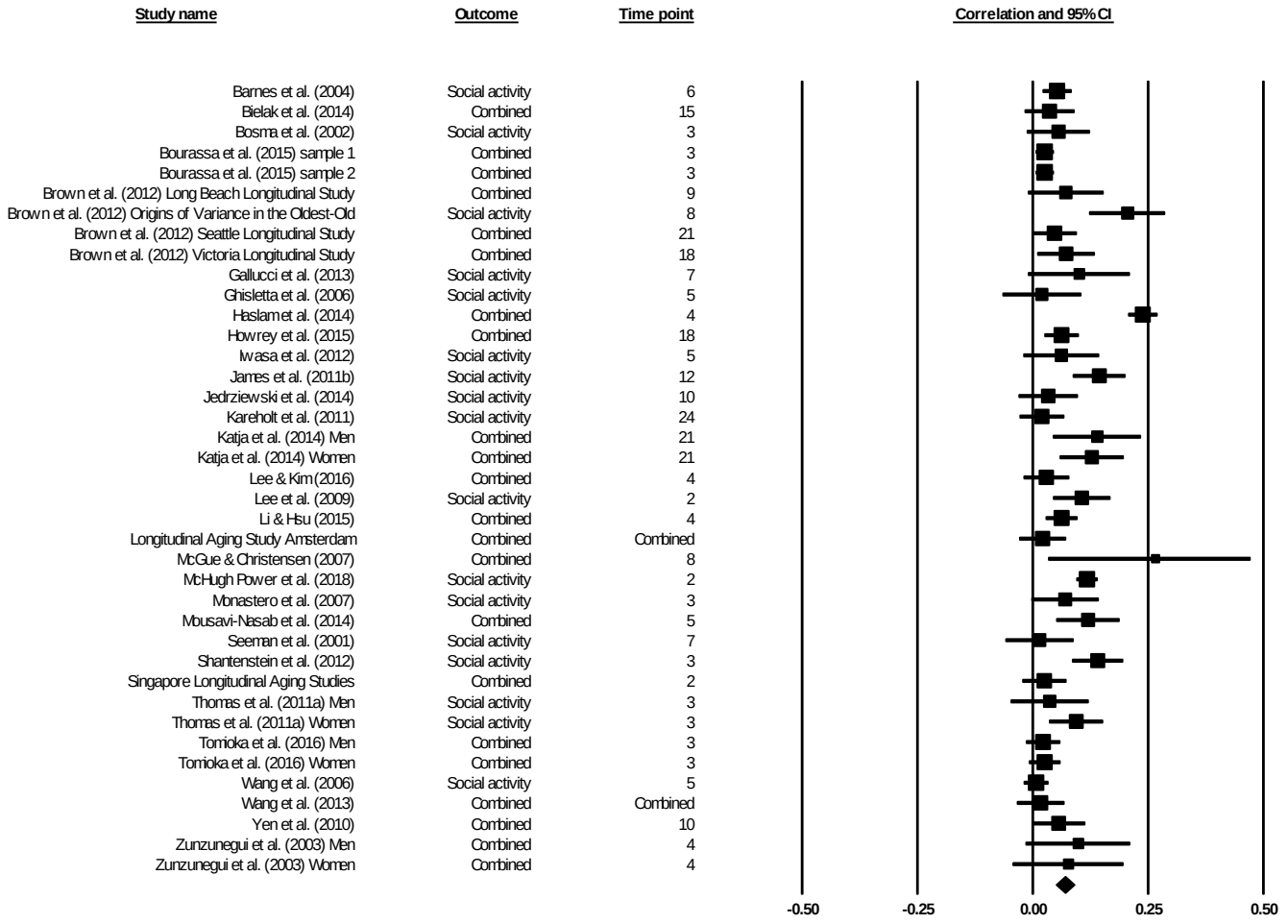


Figure L.5. Forest plot of the positive association between all measures of social activity and all cognitive measures.

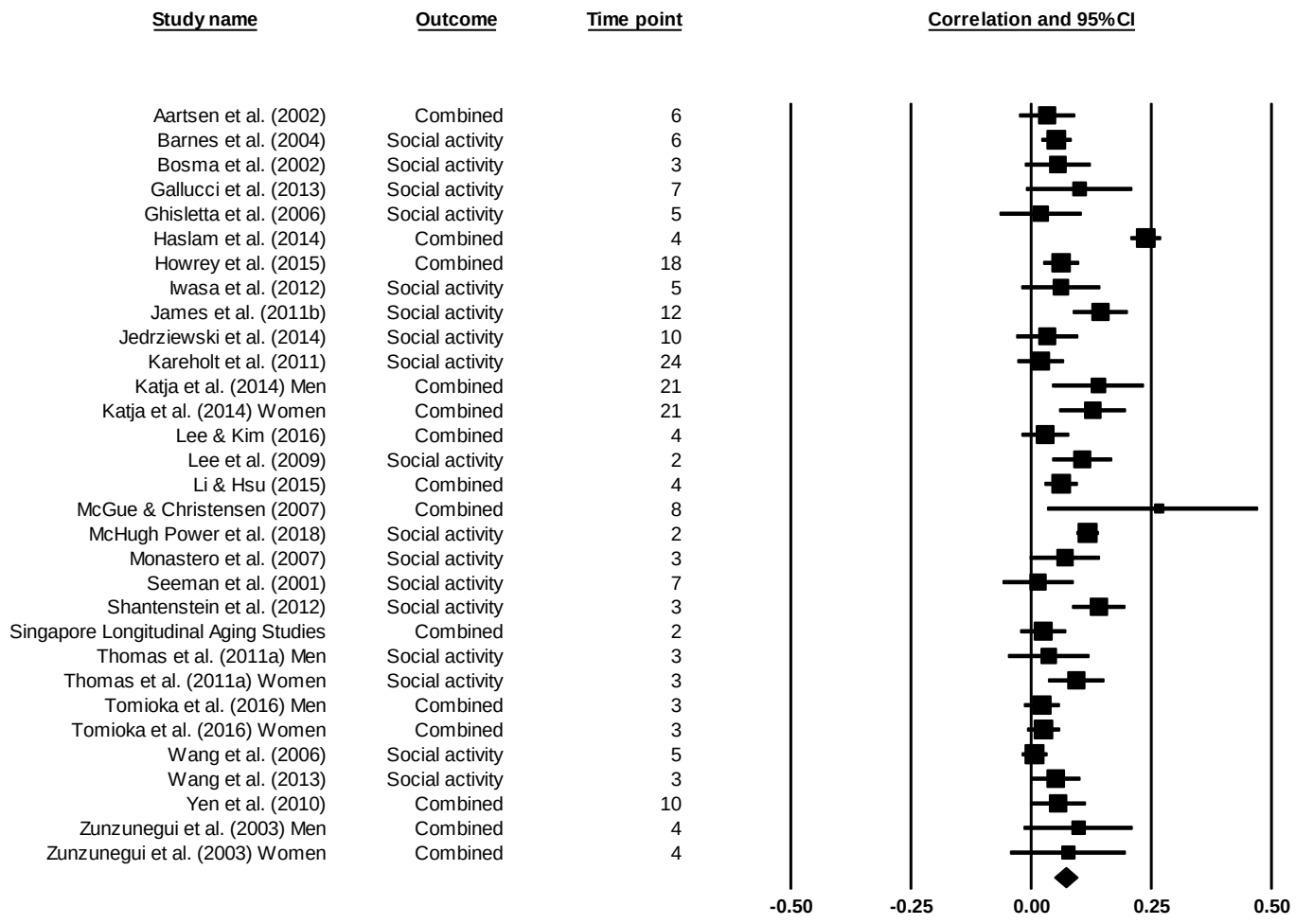


Figure L.6. Forest plot of the positive association between all measures of social activity and global measures of cognitive function.

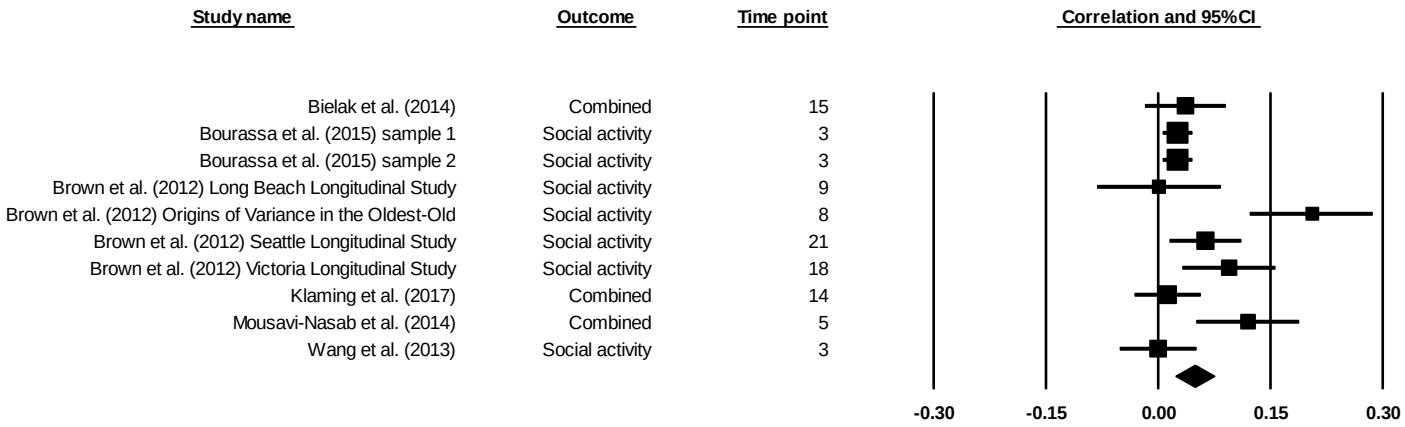


Figure L.7. Forest plot of the positive association between all measures of social activity and memory.

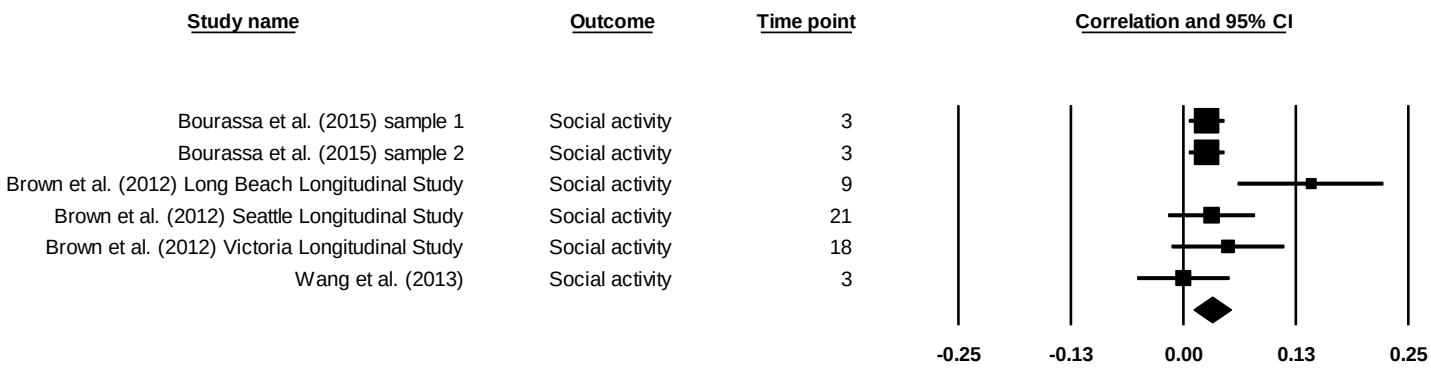


Figure L.8. Forest plot of the positive association between all measures of social activity and executive function.

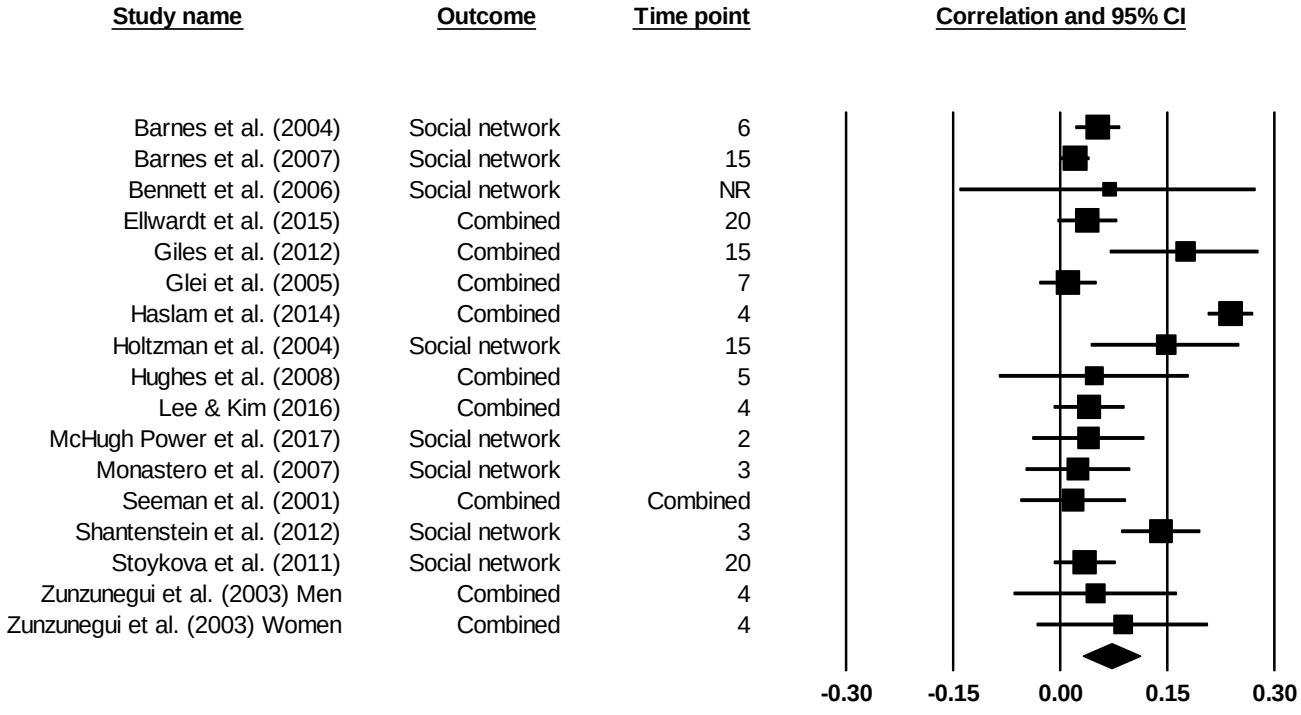


Figure L.9. Forest plot of the positive association between all measures of social network and all measures of cognitive function.

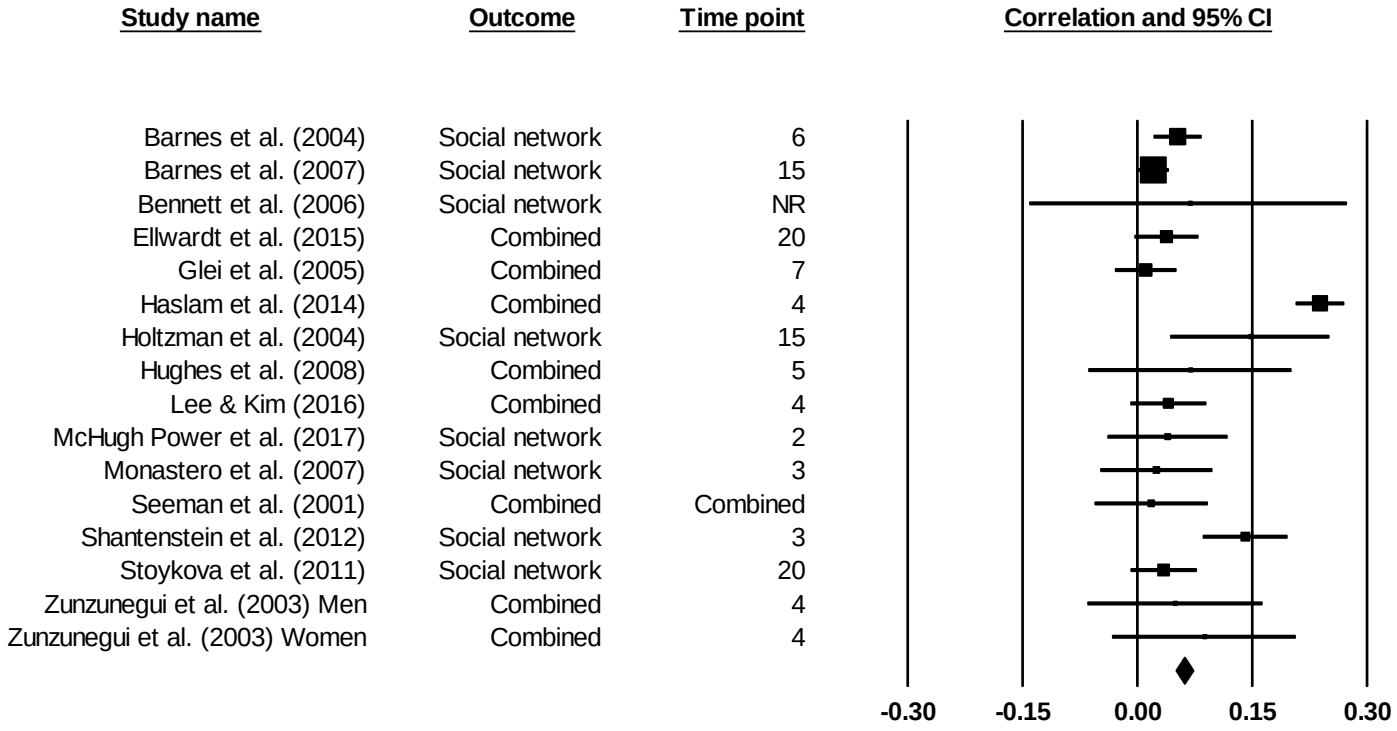


Figure L.10. Forest plot of the positive association between all measures of social network and global measures of cognitive function.

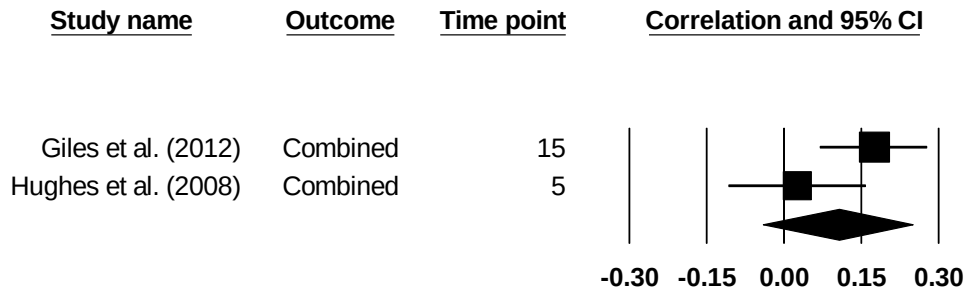


Figure L.11. Forest plot of the positive association between all measures of social network and memory.

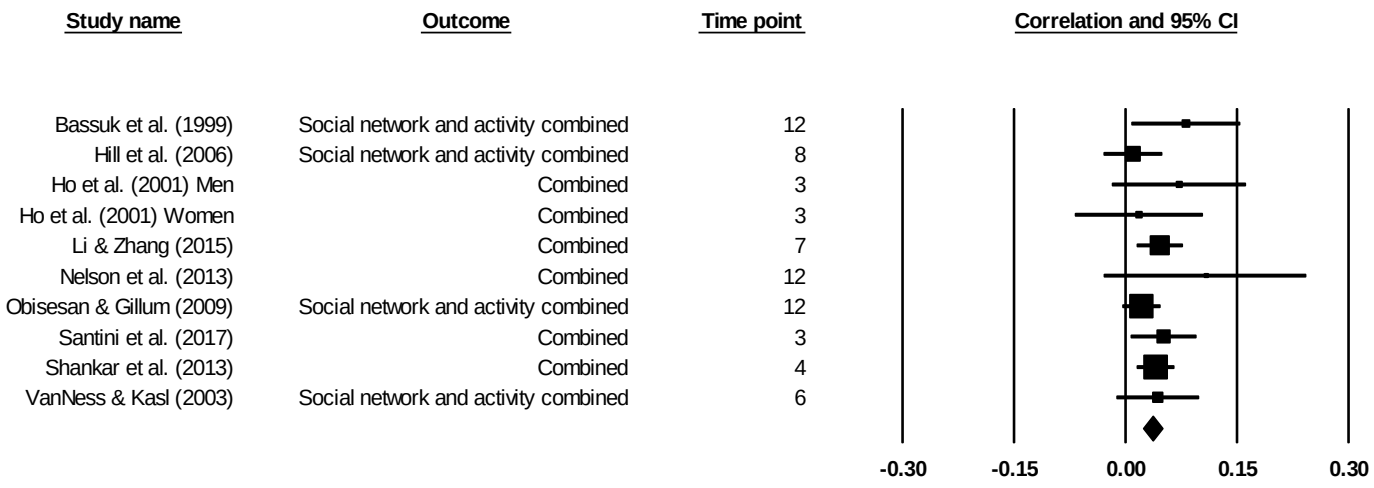


Figure L.12. Forest plot of the positive association between all measures that combine social activity and social networks and all cognitive measures.

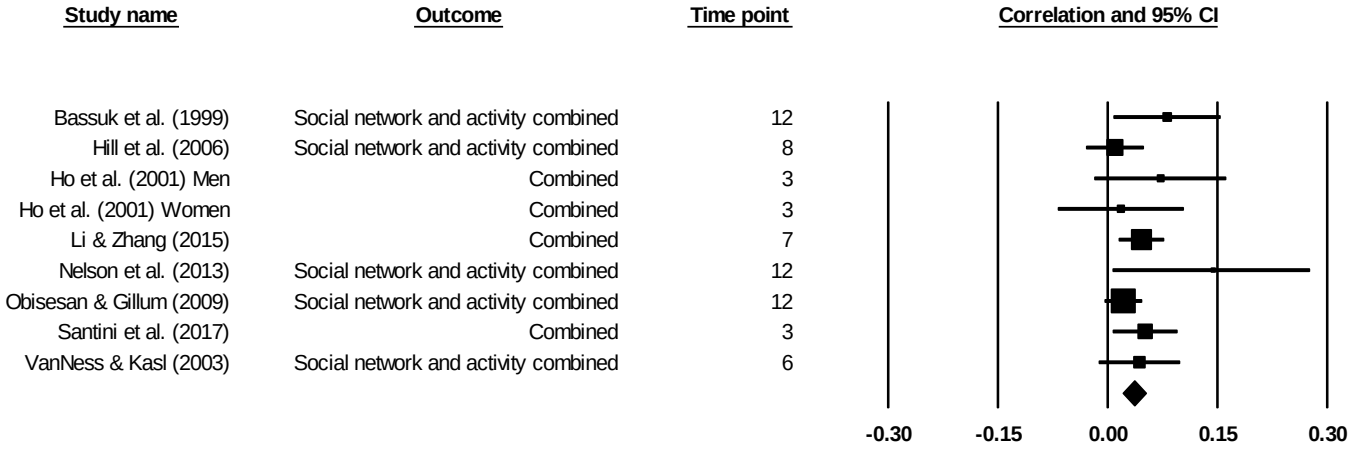


Figure L.13. Forest plot of the positive association between all measures that combine social activity and social networks and global measures of cognitive function.

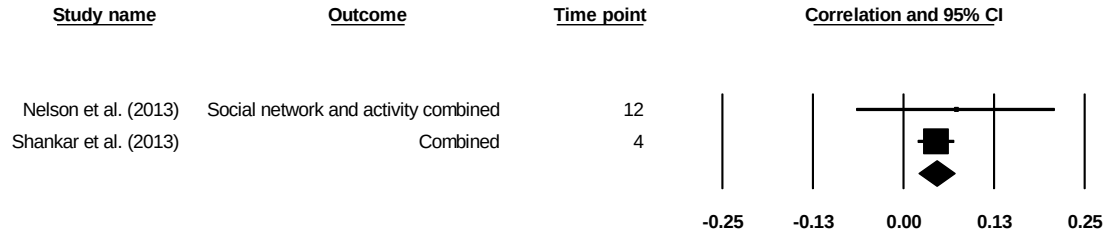


Figure L.14. Forest plot of the positive association between all measures that combine social activity and social networks and memory.

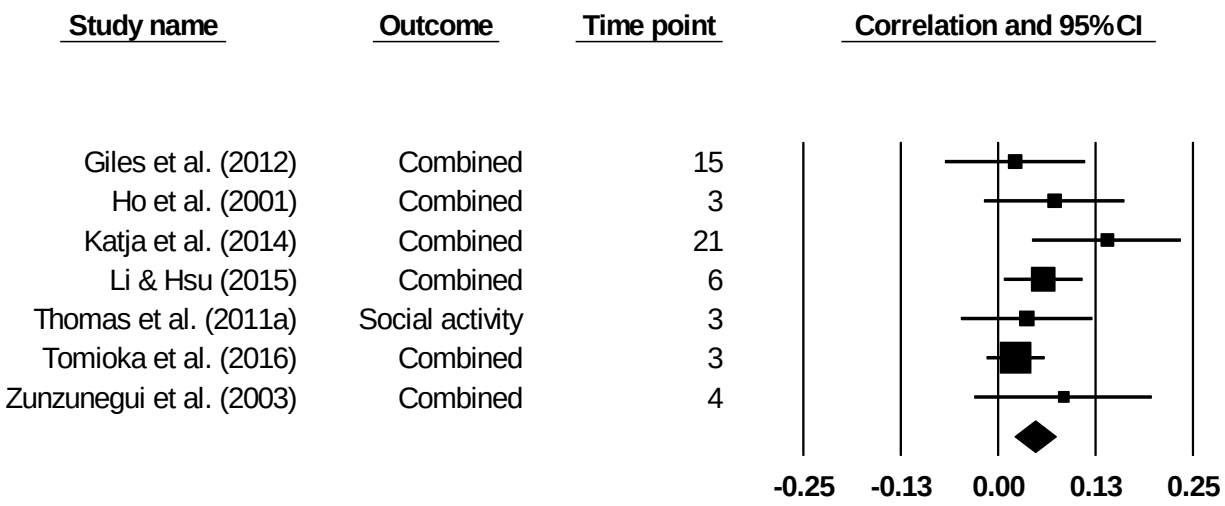


Figure L.15. Forest plot of the positive association between all social measures and all cognitive measures for men.

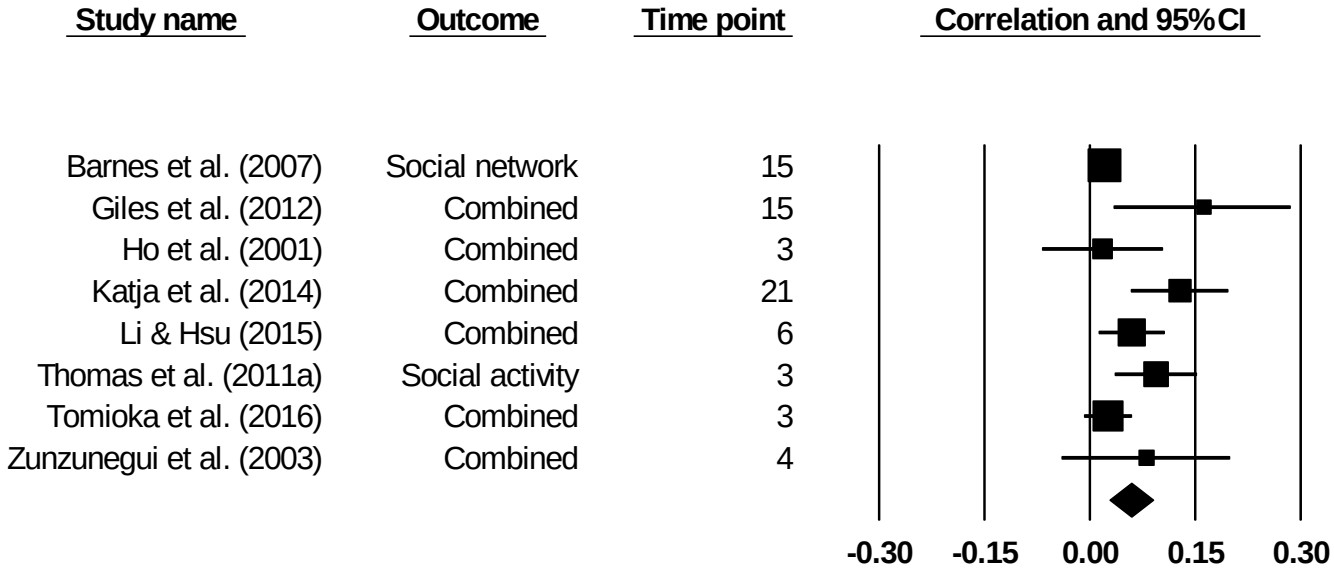


Figure L.16. Forest plot of the positive association between all social measures and all cognitive measures for women.

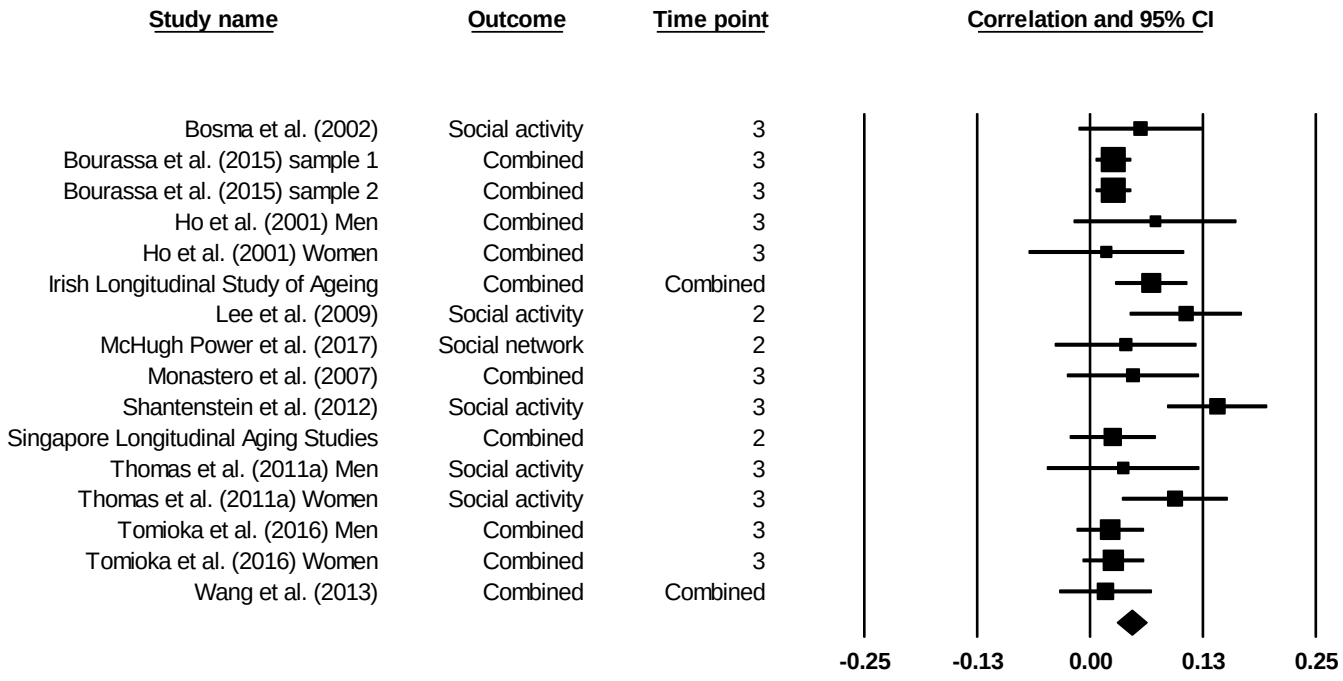


Figure L.17. Forest plot of the positive association between all social measures and all cognitive measures for studies with a follow-up of 2-3 years.

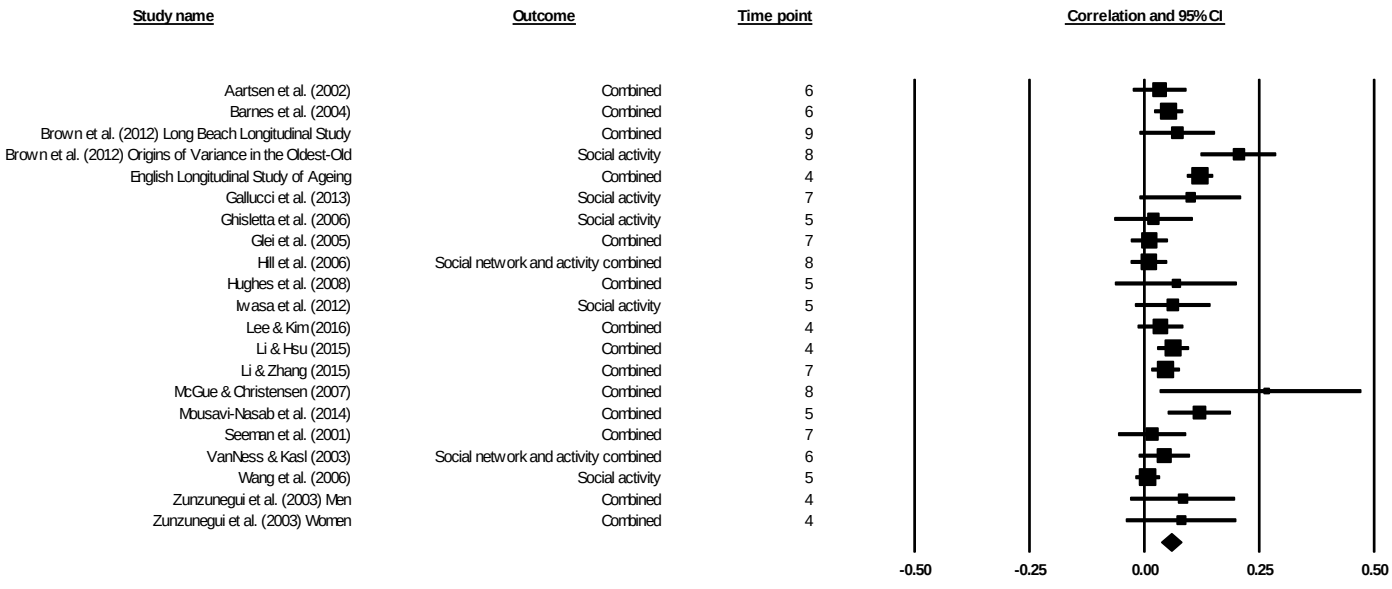


Figure L.18. Forest plot of the positive association between all social measures and all cognitive measures for studies with a follow-up of 3-9 years.

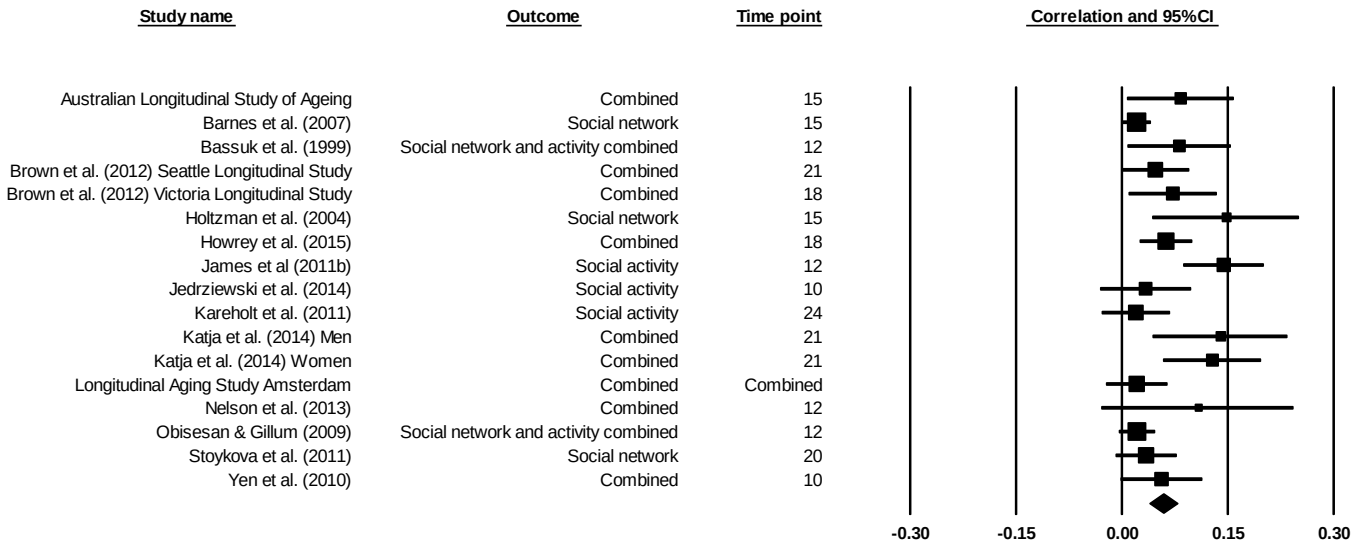


Figure L.19. Forest plot of the positive association between all social measures and all cognitive measures for studies with a follow-up of 10-24 years.

Appendix M: Reducing heterogeneity by removing articles from the meta-analysis

Heterogeneity was considerably reduced by removing two articles with large effect sizes and sample sizes (Haslam et al. 2014; McHugh Power et al. 2018) and a third article with a large effect size and a moderate sample size (Brown et al. 2012 OCTO). The large effect sizes reported by these articles accounts for a large proportion of heterogeneity as seen by a reduction in I^2 values after excluding these articles.

Table M. *Random effects meta-analysis and sub-analyses for aspects of social isolation and cognitive function excluding Haslam et al. (2014)[a], McHugh Power et al. (2018)[b], and Brown et al. OCTO (2012)[c].*

	n	k	*r*	95% CI	*p*	Heterogeneity		
						Q	Q *p*	I^2
All social measures								
All cognitive measures [a b c]	101,321	50	.045	.036, .054	<.001	75.450	.009	35.06
Global measures [a b]	70,282	42	.048	.037, .058	<.001	64.086	.012	36.02
Memory [c]	34,706	12	.039	.023, .056	<.001	18.164	.078	39.44
Social activity								
All cognitive measures [a b c]	67,032	36	.053	.041, .066	<.001	75.224	<.001	53.47
Global measures [a b]	41,406	29	.058	.043, .073	<001	59.710	<.001	53.11
Memory [c]	28,575	9	.036	.017, .055	<.001	15.231	.055	47.48
Social network								
All cognitive measures [a]	26,624	16	.050	.029, .071	<.001	30.353	.011	50.58
Global measures [a]	26,271	15	.045	.026, .064	<.001	24.141	.044	42.01
All social measures and all cognitive measures								
Follow-up time								
2-3 years [b]	38,090	16	.044	.028, .060	<.001	27.496	.025	45.45
4-9 years [a c]	35,898	20	.040	.027, .053	<.001	24.940	.163	23.82

Appendix N: Funnel plots displaying publication bias in the meta-analysis

The results of the meta-analysis may be slightly overestimated due to publication bias (Figure N). Egger's test for: (A) all social and all cognitive measures (b = 1.52, 95% CI: .746, 2.285, p <.001), (B) all social and global cognitive measures (b = 1.25, 95% CI: -.014, 2.638, p = .076), (C) all social and memory measures (b = 1.46, 95% CI: -.214, 3.129, p = .081), and (D) all social and executive function measures (b = 1.31, 95% CI: -1.141, 3.759, p = .228). This finding is unsurprising and suggests that studies with a smaller sample size that do not find a significant association between aspects of social isolation and cognitive function are less likely to be reported in the literature.

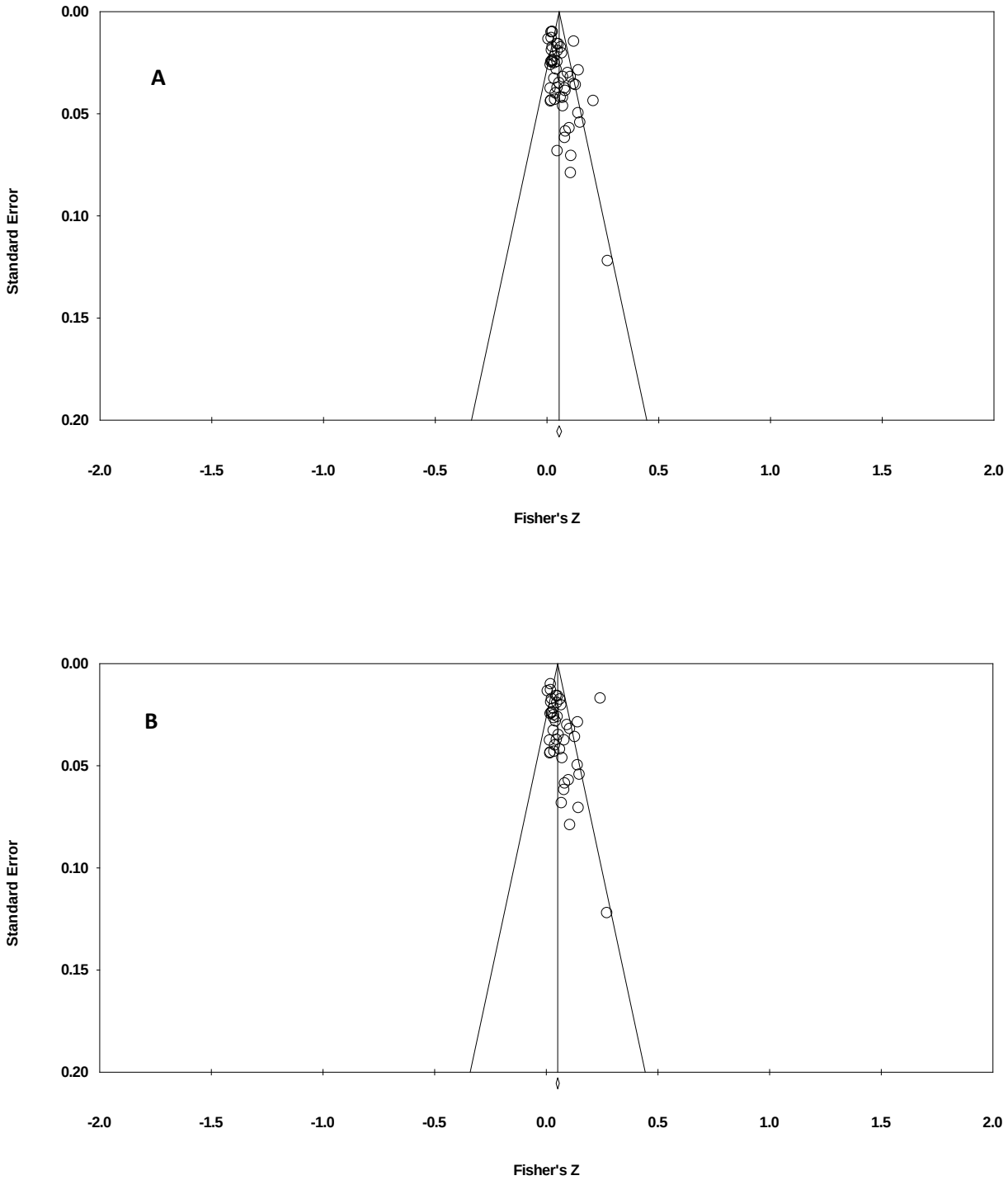
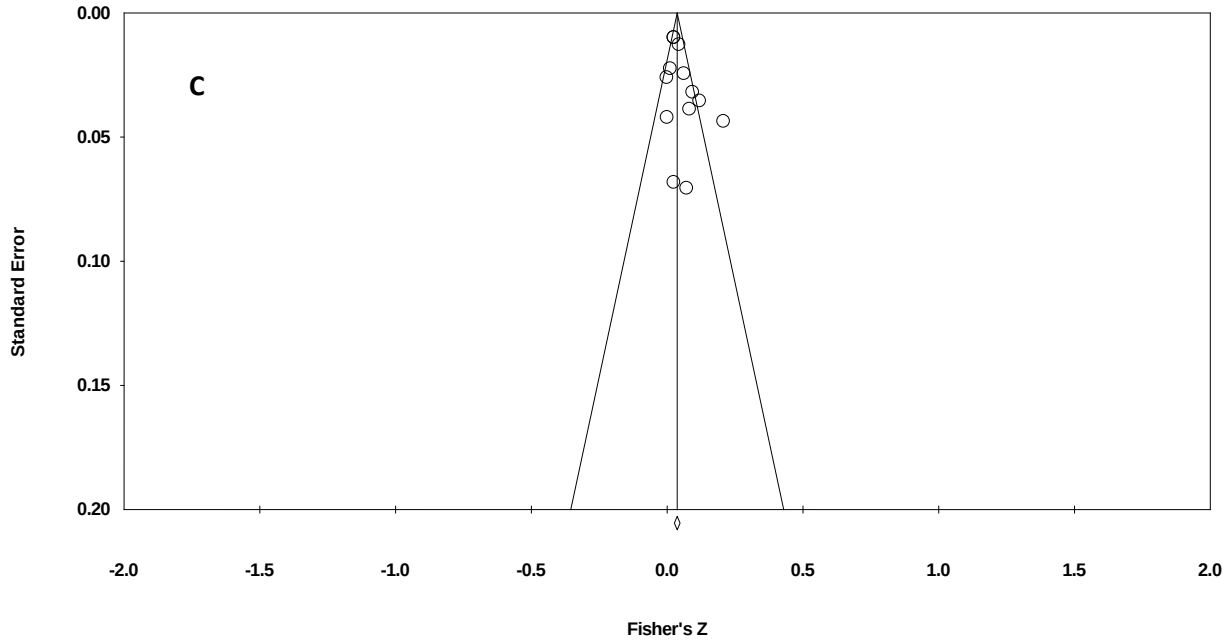


Figure N. Funnel plots for (A) all social and all cognitive measures, and (B) all social and global cognitive measures.



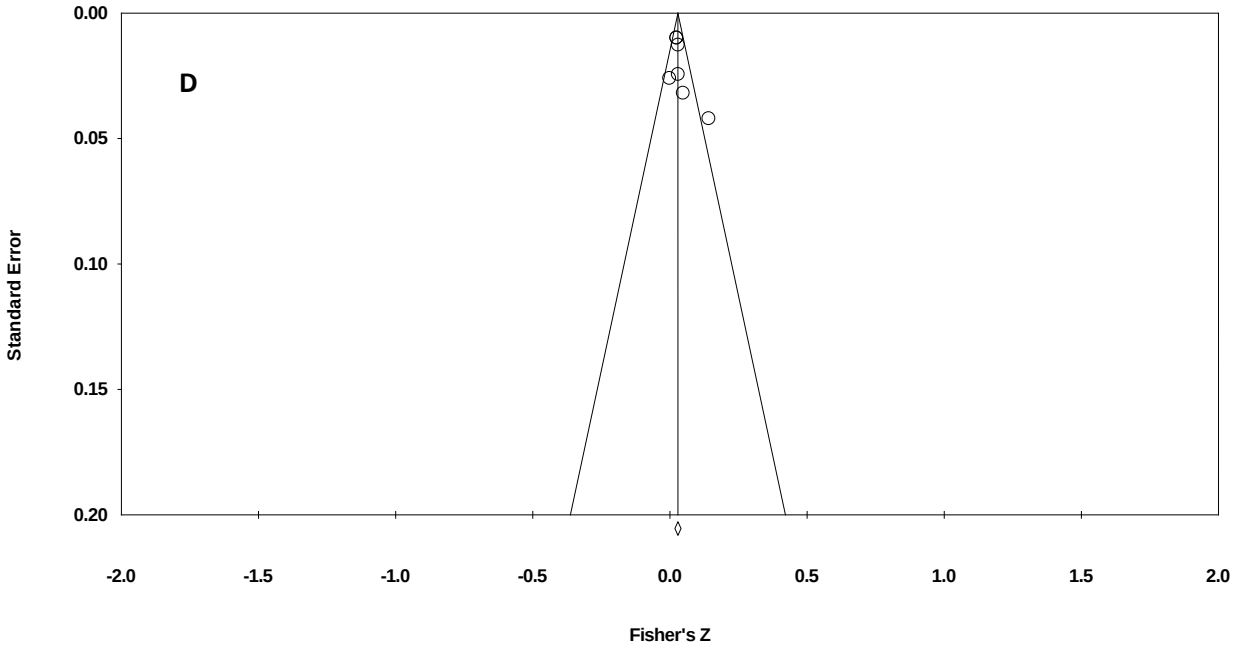


Figure N. Funnel plots for (C) all social and memory measures, and (D) all social and executive function measures.