DOCTOR OF PHILOSOPHY

Cognitive reserve, mood, and cognitive function in later life

Opdebeeck, Carol

Award date:
2015

Awarding institution:
Bangor University

Cognitive reserve, mood, and cognitive function in later life

Carol Opdebeeck

Thesis submitted to the School of Psychology, Bangor University, in fulfilment of the requirements for the degree of Doctor of Philosophy

October 2015

Acknowledgements

I am hugely grateful to Linda Clare for her support and encouragement throughout this process. Her advice and guidance has been invaluable and I feel extremely privileged to have been a part of her team and to have had the opportunity to learn from her. I am incredibly thankful to my second supervisors, Sharon Nelis and Catherine Quinn, who provided endless encouragement and advice, tirelessly supporting me throughout this process.

I would also like to thank the rest of the research team, Ant, Ola, Gill, Cat, Tam, Julie, and Sue, and past members and former officemates Kirstie, Lester, and Lexie. I am especially grateful to Ant for his advice on the meta-analysis and his patient responses to my never-ending questions, to Gill for her help in screening articles for both the systematic review and meta-analysis, and to Sue, my longest standing officemate who provided support and sometimes, some much-needed distraction.

I am extremely grateful to my supportive family and friends who have provided so much encouragement and support over the years. I am especially grateful to my parents, without whom none of this would have been possible.

I would like to thank the older people who participated in the studies throughout this thesis. They were a joy to meet and work with, and served to confirm why I wanted to work in research with older people. They made me look forward to my retirement and all the possibilities that come with this period of life.

Last, but not least, I am eternally grateful to Kevin. He has tirelessly supported me throughout my academic career, as a sounding board for my ideas, a foil to my increasing levels of anxiety, and in helping me to remember to live my life throughout it all.

Table of Contents

List of tables

List of figures

Summary

Background: Cognitive reserve (CR) is the concept that was proposed to account for the incongruity in the associations between levels of neuropathology and cognitive function. It is difficult to directly assess CR and so it is frequently indicated by those activities thought to increase it – educational level, occupational complexity, and/or engagement in cognitively-stimulating activities. The evidence regarding the associations and inter-relationships between CR, mood, and cognitive function is conflicting. Previous research has focused on individual proxy measures of CR in investigating these associations; this thesis introduces a novel element by considering CR in terms of multiple proxy measures from across the lifespan in attempting to clarify these complex associations.

Method: A meta-analysis synthesised the association between CR and domains of cognitive function in healthy older people. To explore whether CR is associated with self-reported experience of depressive thoughts and symptoms a survey of older people was conducted. To assess whether CR moderated the association between mood and cognitive function, a systematic review of existing evidence and a second survey of older people were conducted. These relationships were then further examined in a large cohort study, representative of the English population aged over 65.

Results: Higher levels of the three most commonly used proxy measures of CR, individually and in combination, are all associated with better cognitive function and with decreased subclinical and clinical levels of mood disorders and associated thoughts. CR was found to moderate the associations between mood and cognition across the systematic review and both empirical studies; higher levels of depression and anxiety have greater negative associations with cognitive function in those with lower than higher levels of CR.

Conclusions: It is important to continue to build on CR throughout the lifespan in order to maintain cognitive and psychological function and to help mitigate against the negative effect that depression and anxiety can have on cognition.

Chapter 1

Introduction

1.1 Introduction

The world's ageing population is continuing to grow, with projections suggesting that the percentage of the population aged 60 and over will increase from 11.7% (841 million people) in 2013 to 21.1% of the population (2 billion people) in 2050 (United Nations, 2013). A recent report suggests that the ratio of those aged 20-64 to those aged 65+ will decrease from the current ratio of 8.5 to a ratio of 2.5 20-64 year olds for every person aged 65+ by 2050 (Raftery, Li, Ševčíková, Gerland, & Heilig, 2012). This worldwide increase in life expectancy is to be welcomed, but it comes with challenges, in that older people are more likely to experience health problems requiring care (Beard & Bloom, 2015; Lloyd-Sherlock, 2000). The cost of providing care for the older population in the UK is expected to increase from £7.8 billion in 2010/11 to £11.5 billion by 2020 (Age UK, 2014). Dementia and cognitive impairment are more prevalent in older age, account for a significant proportion of care expenditure for older people, and are associated with increased disability and mortality (Comas-Herrera, Northey, Wittenberg, Knapp, Bhattacharyya, & Burns, 2011; Di Carlo et al., 2000).

Dementia prevalence is estimated at 5-7% for those aged over 60 (Prince, Bryce, Albanese, Wimo, Ribeiro, & Ferri, 2013), and the prevalence of cognitive impairment in over 65s has been estimated to be as high as 18.6% (Jagger, Matthews, Lindesay, Robinson, Croft, & Brayne, 2009). However, recent research has demonstrated that the prevalence of dementia and cognitive impairment is decreasing, potentially due to improvements in health and lifestyle, which in turn reduce the levels of risk factors for cognitive impairment (Jagger et al., 2009; Matthews et al., 2013; Wu et al, 2015). However, the number of people with dementia is continuing to increase due to the higher number of people now living into advanced old age. In addition, we will continue to see greater numbers of people with cognitive decline and impairment, making the study of potentially modifiable factors associated with maintaining cognitive function in later life an important area of research.

Cognitive decline is not only seen in those with dementia; it is also frequently observed in those older people deemed to be relatively healthy (Salthouse, 2009; Singh-Manoux et al., 2011). Given the negative outcomes associated with cognitive impairment it is important to identify potentially modifiable factors associated with reduced cognitive function in older people, which may help to reduce the numbers with, or delay the onset of,

cognitive impairment. Several factors have been identified that help to maintain cognitive function, alongside factors that are associated with poorer cognitive function. One construct that has recently received significant attention is cognitive reserve (CR), which is believed to be enhanced by participation in cognitively-stimulating activities across the lifespan (Richards & Deary, 2005; Richards & Sacker, 2003; Whalley, Dick, & McNeill, 2006; Stern 2002; 2009; 2011). CR is a theoretical construct and as such cannot be directly assessed; rather it is most commonly indexed by those activities thought to increase it, namely educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities or a combination of these. CR is associated with better cognitive function, and with reduced risk of cognitive decline, mild cognitive impairment, and dementia (Fratiglioni & Wang, 2007; Harrison et al., 2015; Meng & D'Arcy, 2012; Valenzuela & Sachdev, 2006a; 2006b). However, there is still considerable debate as to how CR is best assessed, with growing argument that multiple life experiences should be considered, and regarding the strength of the associations of CR with different cognitive domains in healthy older people.

Conversely, lowered mood, in particular greater experience of depression and anxiety, is associated with poorer cognitive function, and a greater risk of cognitive decline and dementia (Beaudreau & O'Hara, 2008; 2009; Diniz, Butters, Albert, Dew, & Reynolds, 2013; Pietrzak et al., 2012; Steffens McQuoid, & Potter, 2014). However, the evidence is equivocal with large variations in the associations between mood and cognitive function with surprisingly little research to date on what may moderate this association. Participation in the kinds of cognitively-stimulating activities associated with CR is additionally associated with less experience of depression in older people (Adams, Leibbrandt, & Moon, 2011; Bjelland, Krokstad, Mykletun, Dahl, Tell, & Tambs, 2008; Glass, De Leon, Bassuk, & Berkman, 2006; Hong, Hasche, & Bowland, 2009; Jenkins, 2011; Ladin, 2008; Lorant, Deliège, Eaton, Robert, Philippot, & Ansseau 2003; Murrell, Salsman, & Meeks, 2003; Narushima, Liu, & Diestelkamp, 2013; Ross & Mirowsky, 2006; 2010). However, these studies have only assessed the association between individual proxy measures of CR and mood; no previous study has assessed the association between multiple proxy measures of CR and mood.

The aim of this thesis is to clarify the associations between CR, mood and cognitive function in healthy older people. Followed by an assessment of whether greater CR, as indicated by educational level, occupational complexity and engagement in cognitively-

stimulating leisure activities, moderates the association between mood and cognitive function, which may help explain the variation observed in studies of this association.

The following sections will introduce background information relevant for the studies presented in this thesis. First, I will give a brief background to ageing and cognitive function, the concept of CR will then be defined and explained, and the neuroscientific evidence to support the concept and methods of assessing CR will be discussed. Next, mood disorders will be introduced, and the associations and inter-relationships between mood, CR and cognitive function will be addressed. The research questions and methodology for this thesis will then be introduced followed by a summary of the content.

1.2 Ageing and cognitive function

Ageing is a deteriorative process in the biological sense, something that cannot be avoided; however, there are significant individual differences in both the physical and psychological aspects of ageing (Coleman & O'Hanlon, 2008). Some older people maintain good physical, cognitive, and mental health into advanced old age, while others experience significant decline. Although there are variations across many aspects of function, health, and well-being in older people this thesis will focus on investigating what may account for variations in cognitive function and mood and in the association between cognitive function and mood in community-dwelling older people.

Cognitive decline in later life has been viewed as a continuum with cognitively healthy older people at one end of the spectrum and dementia at the other, representing the extreme of cognitive ageing (Deary et al., 2009; van der Flier et al., 2005). Mild cognitive impairment (MCI) resides within this continuum and is often regarded as a transitional phase between age-appropriate cognitive function and pathological decline, however not all of those with MCI will develop dementia (Matthews, Stephan, McKeith, Bond, & Brayne, 2008). Mild cognitive impairment is usually indicated by scores of 1.5 standard deviations below the average on cognitive tests and dementia by scores of 3 standard deviations below the average. Cognitive decline is common in older people but is not an inevitable outcome of ageing; indeed, there are substantial individual differences in cognitive performance in later life (Deary et al., 2009; Lindeboom & Weinstein, 2004). For instance, Wilson and colleagues (2002a) found that some older people had sharp declines in cognition and some had gradual

decline, while others maintained the same level of cognition or even improved over the 6-year period of the study. Differences in levels of the neuropathology underlying cognitive decline and dementia account for some variation in cognitive performance; however, researchers have consistently noted an incongruity between neuropathology and cognitive performance.

Katzman and colleagues (1988) were some of the first to report on the observation that an individual may have considerable Alzheimer's disease pathology, specifically high levels of neurocortical plaques, but have performed on a par with those with the highest levels of cognitive functioning and no observable dementia neuropathology. Yet, other people with lower levels of pathology exhibited poorer cognitive performance prior to death (Katzman et al., 1988). This finding was replicated in the often-cited Nun Study, a longitudinal clinical and pathological study of 678 Catholic sisters (e.g. Snowdon, 1997; Snowdon, 2003). Findings from the Nun Study also indicated disparities between levels of neuropathology and cognitive performance, with stark examples of individual differences in the relationship between levels of pathology observed at autopsy and cognitive function prior to death. Such results led to growing interest in what may account for these disparities and the development of cognitive and brain reserve theories.

1.3 What is cognitive reserve?

CR is the concept that was proposed to account for the incongruity frequently observed in the association between neuropathology, detected through imaging and autopsy studies, and level of cognitive performance. Stern (2002) proposed that CR is "the ability to optimize or maximize performance through differential recruitment of brain networks, which perhaps reflect the use of alternate cognitive strategies" (p. 451). Similarly, Snowdon (2003) described CR as "the capacity of the brain to resist the expression of symptoms in the face of existing neuropathology" (p. 452). These two definitions reflect the active and passive models that have been proposed to explain CR (Stern 2002; 2009).

The passive model of reserve has been referred to as brain reserve and represents a threshold at which neuropathology or damage to the brain will result in observable clinical signs and symptoms (Stern, 2002). This model is based around the theory of brain reserve capacity (Satz, 1993) and predominantly refers to brain size or neuronal count. It suggests

that greater brain reserve is a protective factor whereas lower brain reserve is associated with increased vulnerability (Stern, 2002). Those with higher brain reserve can sustain more neuropathology or damage before symptoms become apparent than those with low brain reserve. The brain reserve model does not take individual differences in the processing of cognitive and functional tasks into account and assumes that there is a fixed point at which damage will become apparent, hence, it is termed a passive model by Stern (2002).

The active model of reserve best represents the concept of CR, which Stern (2002; 2009) suggests relates to the ability of cognitive systems to continue to operate effectively after sustaining disruption. In this sense, CR can be built upon through engaging in cognitively-stimulating activities such as education, cognitively complex occupations, or leisure activities that help build more efficient processing mechanisms and alternative pathways that can in turn allow the individual to sustain more brain injury before clinically observable signs appear (Stern, 2002; 2009). It should be noted here that, while most of the literature refers to the effects of CR in the context of neuropathology and injury, Stern (2002; 2009) also stressed the relevance of CR in explaining individual differences in cognitive performance in healthy older people. It is probable that those with higher levels of reserve have more efficient, capable, or flexible cognitive systems; this reserve then in turn helps people to compensate in the face of normal brain ageing as well as in neurodegenerative conditions such as dementia. The focus of this thesis will be on CR, assessed through those cognitive experiences across the lifespan that are thought to increase it, namely educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities. In the following sections, the neuroscientific evidence and methods of assessing CR will be discussed.

1.3.1 The neuroscientific evidence for cognitive reserve

As mentioned above the initial evidence to support the existence of CR comes from autopsy studies, which were the precursor to the development of the concept. Imaging studies have provided additional evidence of structural and functional differences in those with low and high levels of CR. Ageing does not necessarily result in cognitive impairment; however, ageing is associated with reductions in brain volumes, which are associated with reduced cognitive function in some older people (Enzinger et al., 2005; Fox & Schott, 2004; Raz et

al., 2004). Engagement in the cognitive activities, which are considered proxy measures of CR, is associated with differences in neural activation and even structure. In several studies involving younger participants intensive periods of study, learning new skills, and memory training have been associated with increased cortical volume (Draganski, Gaser, Busch, Shuierer, Bogdahn, & May, 2004; Draganski et al., 2006; Takeuchi et al., 2010). Similarly, in functional imaging studies, decreases in activation of cortical networks post-memory training have been noted, indicating more efficient use of neuronal networks (Erickson et al., 2007).

These findings have been replicated in older people. Higher levels of proxy measures of CR, including educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities, are associated with greater brain volume and reduced activation in task-related cortical networks (Bartrés-Faz & Arenaza-Urquijo, 2011; Bartrés-Faz et al., 2009; Christensen, Anstey, Leach, & McKinnon, 2008; Solé-Padullés et al., 2009). White matter lesions which appear as hyperintensities on magnetic reasonance images (MRI) have been associated with general and domain specific cognitive function and decline in neurologically-intact older people (Debette & Markus, 2010; Gunning-Dixon & Raz, 2000). In support of the CR theory, proxy measures of CR moderate the association between white matter hyperintensities and cognitive function in older people. For instance, the severity of white matter hyperintensities is more highly correlated with cognition and a greater risk of cognitive impairment in those with low education or low levels of engagement in cognitively-stimulating leisure activities than in those with high education or high levels of engagement (Brickman et al., 2011; Dufouil, Alpérovitch, & Tzourio, 2003; Mortamais et al., 2014; Saczynski et al., 2008). This evidence suggests that the CR theory is supported, not just through evidence of the associations between the proxy measures and cognitive function, in that it impacts upon the association between the structural and functional changes seen in ageing and cognitive function. The various methods of assessing CR will be addressed in the following section.

1.4 How cognitive reserve is assessed

As CR is a theoretical construct, it is not possible to measure it directly. Instead, proxy measures, which reflect the life experiences thought to increase reserve, are frequently used. CR is most frequently indexed by educational level, occupational complexity, and/or

cognitively-stimulating leisure activities. It is thought that these life experiences are likely to provide protection against the clinical manifestations of disease or decline (Siedlecki, Stern, Reuben, Sacco, Elkind, & Wright, 2009; Stern, 2011). This section will consider each of these proxy measures and the issues of assessing these experiences, individually and in combination.

1.4.1 Educational level

Educational level is the most commonly used proxy measure of CR, and reviews of the association generally concur that greater educational attainment is associated with better cognitive function and a reduced risk of cognitive decline and dementia (Anstey & Christensen, 2000; Chen, Lin, & Chen, 2009; Valenzuela & Sachdev, 2006a; 2006b). However, the evidence is equivocal within these reviews, and Plassman and colleagues (2010) reported no consistent association between education and cognitive decline. While there is disparity in the observed associations between educational level and cognition, the majority of the evidence would suggest that the association is moderate. Some of the disparity in the results of these studies may be due to the different cut-off levels used to differentiate between high and low education. However, both weak and strong associations between education and cognitive function have been found in more and less highly-educated samples (e.g. Acevedo, Lowenstein, Agrón, & Duara, 2007; Alvarado, Zunzunegui, Del Ser, & Beland, 2002; Inzelberg et al., 2007; O'Connor, Pollitt, Treasure, Brook, & Reiss, 1989). It seems improbable that there is a specific cut-off at which education becomes beneficial, but rather it is likely that any additional education helps to maintain cognitive function, as the majority of reviews have indicated that overall a higher educational level is associated with better cognitive function. In addition, the majority of the imaging and autopsy evidence that supports the CR theory comes from studies using educational level as the CR proxy measure, indicating that educational level is a robust proxy measure of CR.

Several researchers have recently proposed that reading ability may be a better indicator of educational level than years of education completed due to disparities in the quality of education (e.g. Fyffe, Mukherjee, Barnes, Manly, Bennett, & Crane, 2011; Manly, Jacobs, Touradji, Small, & Stern, 2002; Manly, Schupf, Tang, & Stern, 2005). However, reading ability could be adversely effected by confounds such as dyslexia or other learning

difficulties and educational level is more commonly assessed through years of education completed or level attained (e.g. secondary school, bachelor degree, etc.) due to the ease of assessment. For these reasons, in this thesis I have focused on educational level as assessed by years and courses completed.

1.4.2 Occupational complexity

A complex and challenging occupation is thought to increase an individual's CR and is frequently considered a proxy measure of CR (Stern, 2006). Similarly to the association seen between education and cognitive function, complex or cognitively demanding occupations have been related to better cognitive performance in older people, and to a reduced risk of dementia and cognitive decline (Then et al., 2014a; Valenzuela & Sachdev, 2006a; 2006b). However, the results have ranged from a moderate to strong positive association between occupation and general cognition (e.g. Frisoni, Rozzini, Bianchetti, & Trabucchi, 1993; Kesse-Guyot et al., 2013) to a weak or non-existent association between occupation and memory (e.g. Fritsch et al., 2007; Staff, Murray, Deary, & Whalley, 2004). There is little consensus as to how occupation is assessed across studies pertaining to CR. While many studies consider occupation in terms of social class indicators, Richards and Sacker (2003) suggest classification of occupation in terms of social class gives few clues as to the specific occupational skills that benefit cognitive function.

Andel, Kåreholt, Parker, Thorslund, and Gatz (2007) considered the main occupations of people aged 77+ in terms of complexity with data, people, and things while controlling for socioeconomic status (SES). They found that complexity of work with data remained a significant contributor to variance in cognitive performance after SES was accounted for. They suggested that while SES and complexity were highly correlated it is probable that the benefit of a complex occupation comes from intellectual stimulation rather than SES. However, it should be noted that coding individuals' main occupation by social class is common in the literature and when examined in this fashion, a higher social class shows benefits for cognitive function against lower social class (e.g. Foubert-Samier et al., 2012; Helmer et al., 2001; Kesse-Guyot et al. 2013; Li, Wu, & Sung, 2002). It is probable that while SES does not provide finer detail of the level of cognitive complexity required by the occupation, the higher social class rating reflects more complex occupations such as

professional or managerial occupations compared to lower social class ratings which perhaps reflect less cognitively demanding roles such as manual or unskilled occupations.

The majority of studies that assess the association between occupation and cognitive function consider only the occupation held for the longest period of an individual's working life. However, this may not reflect a significant proportion of the working life that could have been spent in either a more or less cognitively challenging role. It may be more beneficial to assess occupational complexity at multiple time points from an individual's working life in order to truly assess the benefits that occupation may have for cognition. One measure which has overcome this potential confound is the Lifetime of Experiences Questionnaire (Valenzuela & Sachdev, 2007) which assesses occupation in terms of 5 year increments across midlife (30-65) to account for changes in occupation during a substantial proportion of a person's working life. This measurement also takes managerial experience into account, which may be crucial given that previous research indicates an association of more complex work with people with better cognitive function and a lower risk of dementia (Andel et al., 2007; Correa Ribeiro, Lopes, & Lourenço, 2013; Karp et al., 2009; Smart, Gow, & Deary, 2014).

The variance in the methods used to assess occupation across studies may account for the conflicting evidence reported. Reviews that have attempted to collate the contradictory results have reported a moderately positive effect with more complex and challenging occupations associated with better cognitive function and less cognitive decline (Then et al., 2014a; Valenzuela and Sachdev, 2006a). In addition, occupation appears to provide additional benefit for cognitive function independently of that provided by education (Andel et al., 2007; Correa Ribeiro et al., 2013), suggesting that occupation may increase an individual's CR, over and above educational level.

1.4.3 Engagement in cognitively-stimulating leisure activities

Engagement in cognitively-stimulating leisure activities is another of the most commonly used proxy measures of CR. Greater engagement in such activities is associated with better cognitive performance in healthy older people, less risk of cognitive decline, and a reduced risk of dementia (Andel, Silverstein, & Kåreholt, 2015; Fratiglioni, Paillard-Borg, & Winblad, 2004: Saczynski et al., 2008; Valenzuela & Sachdev, 2006a; 2006b; Verghese et

al., 2003; R.S. Wilson, Barnes, & Bennett, 2003a). Similarly to the measurement of occupation, cognitively-stimulating leisure activities have been assessed in a wide variety of ways, with varying definitions of what constitutes a cognitive activity. These definitions of what constitutes participation in cognitively-stimulating activities have ranged from studies which have assessed participation in one activity, such as reading (e.g. Gallucci et al., 2009) to assessments of participation levels in 17 activities ranging from trips to the theatre to adult education classes (e.g. Gow, Avlund, & Mortensen, 2014). There is no conclusive evidence as to the importance of the type of activity, duration, or frequency of participation for the associations between cognitively-stimulating leisure activities and cognitive function. However, the evidence that does exist generally emphasises that it is the frequency and variation of the activities undertaken that are important (Eskes et al., 2010; Hertzog, Kramer, Wilson, & Lindenberger, 2008; Wilson, Scherr, Schneider, Tang, & Bennett, 2007).

Another aspect of the association that is unclear is the temporal relationship and whether greater emphasis should be placed on previous or current engagement in cognitively-stimulating leisure activities. A significant proportion of research has focused on measures of cognitively-stimulating leisure activity at a single time-point; however, it has been argued that there is a cumulative effect of cognitively-stimulating leisure activities across the lifespan (R.S. Wilson et al., 2003a; Wilson, Barnes, Krueger, Hoganson, Bienias, & Bennett, 2005). Additionally, it is probable that current levels of participation are influenced by the individual's health, including cognitive function, whereas activities undertaken in earlier life have a less bi-directional relationship (Scarmeas & Stern, 2003).

Another question to be addressed is whether engagement in cognitively-stimulating activities provides any beneficial effect on later life cognitive function above that provided by earlier life educational experiences. In attempts to address this question, researchers have noted that education and cognitively-stimulating leisure activities have different patterns of association with cognition (Jefferson et al., 2011; R.S Wilson et al., 2003a) and frequent cognitive activity compensates for lower education and less complex occupations (Andel et al., 2015; Lachman, Agrigoraei, Murphy, & Tun, 2010). This suggests that each proxy measure of CR provides a unique contribution to an individual's CR, potentially creating a cumulative effect across the lifespan.

1.4.4 Combining proxy measures of cognitive reserve

A common criticism regarding the use of individual proxy measures of CR relates to possible confounding factors. There is a growing argument that CR indicators should consider multiple life experiences, especially given that CR is not fixed through one experience but rather is a fluid construct that is built across the lifespan (Nucci, Mapelli, & Mondini, 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez, Torrellas, Martín, & Fernandez, 2011; Stern, 2009; Tucker & Stern, 2011; Whalley et al., 2006). It is probable that although the proxy measures of CR are at least somewhat inter-related they impart independent effects that accumulate across the lifespan (Tucker & Stern, 2011). In a large longitudinal cohort study, a combination of educational level, occupational complexity, and social engagement was associated with a decreased risk of dementia while individually these factors did not provide any protective effect, leading the authors to suggest that some enriching cognitive activity beyond education is required to provide a protective effect (Valenzuela, Brayne, Sachdev, Wilcock, & Matthews, 2011). Several measures which attempt to combine the most common proxy measures of CR into one measure have recently been developed; for example, the Lifetime of Experiences Questionnaire (Valenzuela & Sachdev, 2007) and the Cognitive Reserve Index Questionnaire (Nucci et al., 2011). In the formulation of these measures both sets of authors noted that the sub-scores for the different proxy measures of CR were not highly related, leading to the suggestion that they gather distinct information about an individual's cognitive lifestyle. As such, throughout this thesis CR is operationalised in terms of a combination of the three most common proxy measures of CR; educational level, occupational complexity, and engagement in cognitively-stimulating activities across the lifespan. The empirical chapters of this thesis are novel in considering the cumulative effects of the individual proxy measures across the lifespan as the indicator of CR in the associations investigated within these chapters.

The proxy measures of CR are not just associated with better cognitive function and a reduced risk of cognitive decline, but are also individually associated with a reduced risk of depression (e.g. Adams et al., 2011; Bjelland et al., 2008; Jenkins, 2011; Narushima et al., 2013; Ross & Mirowsky, 2006; 2010). Conversely, depression is associated with poorer cognitive function and an increased risk of cognitive decline and dementia (e.g. Diniz et al., 2013; Pietrzak et al., 2012; Steffens et al., 2014). The following sections will address the prevalence and presentation of depression and anxiety in older people and the thought

processes associated with these mood disorders. Finally, the complicated associations between mood and cognitive function, and whether CR is associated with mood, or perhaps moderates the association between mood and cognitive function, will be discussed.

1.5 Mood in later life

Depression and anxiety are both relatively common mood disorders in later life. A large cohort study indicated that the prevalence rate of depression for people aged over 65 in the UK was 8.7% (McDougall et al, 2007) while an analysis of data from nine European cities indicated a prevalence rate of 12.3% for people aged over 65 and residing in the community (Copeland et al., 2004). The large variations observed in the prevalence rates for depression are potentially due to different diagnostic criteria, with one meta-analysis suggesting a prevalence of 7.2% for major depression and 17.1% for minor depressive disorders (Luppa et al., 2012). Lifetime prevalence of anxiety in community-dwelling older people is as high as 11%, with 4.6% experiencing anxiety within the 6 months prior to the study (Zhang, Norton, Carrière, Ritchie, Chaudieu, & Ancelin, 2015). The term ‘mood’ will be used to refer to both depression and anxiety throughout this thesis. In the following sections, the presentation of, and thought processes associated with, depression and anxiety will be introduced.

1.5.1 Depression

Depression broadly describes a syndrome that encompasses physical, affective, and cognitive manifestations. Under the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013; DSM-V) in order to be diagnosed with major depression, a person must present with either a depressed mood or a loss of interest or pleasure. In addition, they must have four of the following symptoms: significant weight loss or gain, insomnia or hyperinsomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to think or concentrate, or indecisiveness, and/or recurrent thoughts of death. For a diagnosis, these symptoms need to have been present over a 2-week period and cause significant distress or impairment in functioning. This would indicate a diagnosis of major depression, which would be less common than depressive disorders, as indicated above. Depressive disorders or

symptoms may have a negative impact on functioning but would not necessarily meet the criteria for a major depressive episode.

The cognitive vulnerability-stress theories of depression suggest that negative thought processes interact with recent life events and are important in the aetiology of depression. Beck (1967) first proposed this cognitive theory of depression and it is further supported by the hopelessness theory of depression (Abramson, Metalsky, & Alloy, 1989). Beck's cognitive model is one of the most longstanding and robust models of the psychology of depression and is based on the pervasive negative thought patterns observed in people with depression. People with high levels of depression were also observed to experience high levels of repetitive, negative automatic thoughts, a bias toward negative interpretations of their experiences, overgeneralisation of these negative thoughts, and a reduced ability to generate solutions to their problems (Beck, 2002). Abramson and colleagues (2002) suggest, in line with Beck's cognitive theory, that negative cognitive styles provide vulnerability to depression when people encounter negative life events. This in turn supports vulnerability-stress theories in which a negative thinking style provides a cognitive vulnerability to developing depression through the effect these negative thoughts have on the interpretation or processing of recent events (Abramson et al., 2002).

The negative thinking or depressive thoughts that provide a vulnerability to depression have been described as negative thoughts focusing on self, the world, and the future and are considered persistent trait variables that are relatively stable in comparison to levels of depressive symptoms (Beck, 2002; Evans, Heron, Lewis, Araya, & Wolke, 2005; Zauszniewski, 1997; Zauszniewski & Rong, 1999). Nolen-Hoeksema (1991) suggested that response style was associated with the maintenance of depression. In her theory, people who respond negatively to mild depressive symptoms by consistently ruminating have a greater risk of severe or prolonged depressive episodes than those who distract themselves from their mild negative mood. The maladaptive thinking process of rumination has been defined as 'repetitive and passive thinking about one's symptoms of depression and the possible causes and consequences' (Nolen-Hoeksema, 2004, p. 107). Martin and Tesser (1996) have defined rumination more broadly as 'a class of conscious thoughts that revolve around a common instrumental theme and that recur in the absence of immediate environmental demands requiring the thoughts' (p. 7). Additionally, in line with vulnerability-stress models, people with higher levels of rumination have an increased risk of developing depressive symptoms

following a stressful event (Nolen-Hoeksema & Morrow, 1991). More recently, in a review of rumination, Nolen-Hoeksema, Wisco, and Lyubomirsky (2008) suggested that rumination plays a strong role in increasing the risk of developing depression as well as its involvement in the maintenance of depression. Rumination has been closely related to depressive thoughts but focuses on perseverative thinking rather than on the specific content of the thoughts themselves (Nolen-Hoeksema et al., 2008). There is also significant evidence to support the argument that rumination, like negative thinking, is relatively stable in comparison to levels of depressive symptoms (Nolen-Hoeksema et al., 2008).

These theories and existing evidence indicate that both depressive thoughts and rumination style thinking lead to an increased risk of depression and maintenance of depression once it arises (Beck, 2002; Evans et al., 2005; Garnefski & Kraaij, 2006; Kraaij, Pruymboom, & Garnefski, 2002; Nolen-Hoeksema, 2000; Thomsen, 2006; Watkins, 2008). As depressive symptoms fluctuate, cross-sectional research can only capture those who are currently experiencing symptoms and not those who have experienced symptoms in the past or who may experience them in the future. Identifying factors associated with these thought processes should be an area of focus given that they increase the risk of experiencing depression and anxiety, both of which have negative outcomes in later life, such as increased loss of independence, disability, and frailty, in addition to their association with poorer cognitive function (Agüero-Torres, Thomas, Winblad, & Fratiglioni, 2002; Covinsky et al., 2010; Lenze et al., 2001; Mezuk, Edwards, Lohman, Choi, & Lapane, 2012; Reynolds, Haley, & Kozlenko, 2008).

The presentation of depression differs in older people with lower presence of dysphoria, fewer ideational symptoms (such as guilt or suicidal ideation), but with higher levels of somatic symptoms, such as weight loss or aches, feelings of anxiety, and cognitive dysfunction (Nordhus, 2008). In addition, an older person may experience subsyndromal levels of depressive symptoms that do not meet the criteria for clinical depression, but which can have a negative impact on cognitive function, and when experienced over a long period can precede an episode of major depression (Alexopoulos, 2005). Older people tend to underreport the severity and presence of depressive symptoms (Alexopoulos, 2005; Nordhus, 2008), suggesting that depression may be a more widespread problem in later life than the prevalence indicates. As such, the investigation of clinical depression and subsyndromal depressive symptoms in older people is an important area of research; in particular, further

understanding of factors associated with the risk of depression, and what may moderate the association between depression and cognitive function, in older people is needed.

1.5.2 Anxiety

Anxiety in later life can take several forms, including generalised anxiety disorder, panic disorder, social phobia, post-traumatic stress disorders, acute stress disorder, and anxiety disorder due to a general medical condition. Generalised anxiety disorder is the most common anxiety disorder in older people (Nordhus, 2008) and will be the focus of this section. The DSM-V criteria for generalised anxiety disorders specifies that for a diagnosis, the person should have had excessive anxiety or worry for at least 6 months, difficulty controlling the worry, and at least three of the following symptoms: restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension, and/or sleep disturbance. Nordhus (2008) suggested that anxiety in older people is composed of cognitive (worry and concentration difficulties), somatic (fatigue, muscle tension, and sleep disturbances), and emotional (restlessness and irritability) components. As with depression, anxiety symptoms are likely to be underreported in older people with low recognition in general practice, and it is probable that older people minimize the impairment caused by anxiety (Nordhus, 2008; Parmentier, García-Campayo, & Prieto, 2013).

Depression and anxiety frequently co-occur in older people at both clinical and subsyndromal symptom level (Beekman et al., 2000; Braam et al., 2014; Kasckow et al., 2013; Kvaal, McDougall, Brayne, Matthews, & Dewey, 2008). It is probable that they are closely related, with cognitive processes involved in anxiety as well as depression. Eysenck (1992) argues that external stimuli are cognitively appraised before an emotional reaction occurs and that people with anxiety have unrealistic, negative thoughts about themselves and their situations. This would suggest that negative thought processes influence a person's appraisals, in turn arousing anxiety. In support of this supposition, reviews have found that rumination is associated with an increased risk of anxiety as well as depression (Kirkegaard Thomsen, 2006; Nolen-Hoeksema et al., 2008). Indeed, rumination, while a distinct construct, has been closely associated with worry, a central component of anxiety (Kirkegaard Thomsen, 2006). Given that both anxiety and depression are associated with several negative outcomes in later life, at both the clinical and subsyndromal symptom level,

investigating the complicated associations of these mood states and their related thought processes with CR and cognitive function is of importance. Such research could help inform what may help maintain psychological health and mitigate the negative impact of mood on cognitive function in later life.

1.6 Mood and cognitive function in later life

Clinical depression and depressive symptoms, even at low levels, have been associated with poorer cognitive performance and an increased risk of cognitive decline and dementia (e.g. Diniz et al., 2013; Reppermund et al., 2011; Rosenberg, Mielke, Xue, & Carlson, 2010; Steffens et al., 2014; Wilson, de Leon, Bennett, Bienias, & Evans, 2004; Yates, Clare, & Woods, 2013). However, the evidence is mixed with other studies reporting no association between depression and cognitive function (e.g. Becker et al., 2009) or an association on some but not all aspects of the cognitive measures (e.g. Kizilbash, Vanderploeg, & Curtiss, 2002; Murphy & O'Leary, 2010). In addition, there is conflicting evidence and substantial debate as to whether depression is a risk factor for, prodromal to, or a symptom of cognitive impairment or dementia (e.g. Byers & Yaffe, 2011; Geerlings et al., 2000; Jorm, 2001; Paterniti, Verfie-Taillifer, Dufouil, & Alpérovitch, 2002; Richard et al., 2013; Wilson et al., 2002b; Yates, Clare, & Woods, 2015).

Several researchers have proposed that there may be a shared underlying mechanism for depression and cognitive decline or dementia (Byers & Yaffe, 2011; Korczyn & Halperin, 2009; Leonard, 2007). This is supported by the growing literature linking depression in later life with white matter hyperintensities, hippocampal atrophy, and decreases in total brain volume (Ballmaier et al., 2004; Elbejjani et al., 2015; Lampe et al., 2003; Nebes et al., 2001; O'Brien, Lloyd, McKeith, Gholkar, & Ferrier, 2004), all of which are associated with poorer cognitive performance. These pathological overlaps suggest that perhaps CR, which is protective against cognitive impairment and decline, may also be protective against depression in older people and could be of benefit in moderating the association between mood and cognitive function. This potential is supported in that CR has previously been observed to account for individual differences in cognitive function in a number of neurological disorders, such as Parkinson's disease and multiple sclerosis (e.g. Benedict,

Morrow, Weinstock Guttman, Cookfair, & Schretlen, 2010; Hindle et al., 2015; Hindle, Martyr, & Clare, 2014; Poletti, Emre, & Bonuccelli, 2011).

Fewer researchers have investigated the association between anxiety and cognitive function in older people. The available evidence suggests that, generally, higher levels of anxiety are also associated with poorer cognitive function in later life and a higher risk of cognitive decline and dementia (Beaudreau & O'Hara, 2008; Bierman, Comijs, Rijmen, Jonker, & Beekman, 2005; Gallacher et al., 2009). Yet, other studies report no association (e.g. Kizilbash et al., 2002; Yates et al., 2015) or an association in some but not all cognitive domains (e.g. Gallacher et al., 2009). There is a paucity of research into the association between brain structure or function and anxiety in later life, but there is some evidence that symptoms of anxiety are associated with brain structure. For instance, in Mohlman and colleagues (2009), worry symptoms were associated with prefrontal cortex volumes but not with brain volume in other regions; suggesting that there may be less overlap between structural correlates of anxiety and cognitive function than is the case for depression and cognitive function. The available evidence indicates that the association between anxiety and cognitive function is currently unclear although it is probable that there is a weaker association than that generally observed between depression and cognitive function. However, further investigation of the association between anxiety and cognitive function, and factors that may moderate any association, is required to elucidate the relationships.

Only a small amount of consideration has been given to the associations between the thought processes associated with lowered mood and cognitive functioning in later life. In the available evidence, rumination was related to poorer executive function (Davis & Nolen-Hoeksema, 2000) and the co-occurrence of rumination and depression resulted in greater cognitive deficits than depression alone (Lyubomirsky, Kasri, & Zehm, 2003). As anxiety, rumination, and depressive thoughts are highly associated with depression in later life it would follow that the associations are similar although perhaps not as evident as with depression. As there may be some shared mechanism underpinning both mood and cognitive dysfunction in older people it is of interest to investigate whether educational level, occupational complexity, and/or engagement in cognitively-stimulating leisure activities show similar associations with mood and the associated thought processes as they do with cognitive function in older people.

1.7 Mood and cognitive reserve

The individual proxy measures of CR have been associated with mood in later life but no study has previously assessed the association between a comprehensive indicator of CR and mood. Previously, higher levels of education and greater engagement in cognitively-stimulating leisure activities have been associated with fewer self-reported depressive symptoms and anxiety (Adams et al., 2011; Beekman et al., 1998; Bjelland et al., 2008; Glass et al., 2006; Hong et al., 2009; Jenkins, 2011; Ladin, 2008; Lorant et al., 2003; Murrell et al., 2003; Narushima et al., 2013; Ross & Mirowsky, 2006; 2010). Occupation has been closely linked with mood in those who are still currently working; people in less stimulating or non-managerial roles are more likely to report depressive symptoms or mental distress than those in more stimulating professional or managerial roles (e.g. Fan, Bonauto, Foley, Anderson, Yragui, & Silverstein, 2012; Zimmerman, Christakis, & Vander Stoep, 2004). The findings regarding whether a person's occupation is associated with his/her experience of depression or anxiety in later life to date are equivocal with no evidence available for a UK cohort. In one study, traditionally less complex primary lifetime occupations were associated with higher levels of depression in two out of six cities in Latin America and the Caribbean (Alvarado, Zunzunegui, Béland, Sicotte, & Tellechea, 2007). In another study, there was no association between the last occupation of participants and later life depression (Lindesay, Briggs, & Murphy, 1989). However, Lindesay and colleagues did not consider whether the participants had previously held more complex or higher status occupations and neither study considered that the participants may have held varying roles across their working life. In addition, it has yet to be considered whether proxy measures of CR, either individually or in combination, are associated with those thought processes, such as rumination and depressive thoughts, which are probable contributors to the risk of developing depression and to maintaining depression once it has arisen.

There is conflicting evidence regarding the association between mood and cognitive function meaning it is probable that other factors moderate this association. As the pathology, that frequently underlies mood and cognitive function overlaps and as CR is associated with both mood and cognitive function, CR may also moderate the association between mood and cognitive function in older people.

1.7.1 Accounting for the variance in the associations between mood and cognition

Currently the evidence regarding whether CR moderates the association between mood and cognitive function is mixed. Several studies have reported beneficial effects, with smaller negative associations, or no negative associations, between mood and cognition in those with higher levels of CR (Pálsson, Aevarsson, & Skoog, 1999; Pálsson et al., 2001; Wight, Aneshensel & Seeman, 2002). Yet others have reported greater negative associations in those with higher CR (Geerlings et al. 2000; O'Shea et al., 2015). The majority of studies focus on the effects of education alone and do not consider a comprehensive indicator of CR. However, research encompassing multiple proxy measures may be important in clarifying whether CR moderates the association between mood and cognitive function because, as evidenced above, the individual proxy measures of CR contribute uniquely and dynamically to an individual's CR. If CR is associated with better cognitive function and reduced levels of depressive symptoms, or plays a moderating role in the negative association between mood and cognitive function, it would add weight to the importance of developing interventions that aim to build an individual's CR to maintain both cognitive function and well-being in later life.

1.8 Aims of the thesis and research questions

The aim of this thesis was to explore the associations and inter-relationships of proxy measures of CR, individually and through measures that combine them, with cognitive function and mood in later life.

The following research questions were addressed in this thesis:

1) Do the three key proxy measures of cognitive reserve, educational level, occupational complexity/status, and engagement in cognitively-stimulating leisure activities, and indices which combine these three measures, differ in their association with cognitive function in healthy older people?

2) Are the three key proxy measures of cognitive reserve, individually or in combination, associated with depressive symptoms and related thoughts in later life?

3) Does cognitive reserve, as indicated by individual proxy measures of cognitive reserve or measures that combine the three key proxy measures, moderate the association between mood and cognitive function in older people?

1.9 Research Methodology

In this section, the design and methodology of the studies presented in this thesis are briefly described.

Prior to empirical examination, research question one was addressed by conducting a meta-analysis of cross-sectional studies to synthesise the evidence on the associations between proxy measures of CR and cognitive function in healthy older people. In addition, the three empirical studies also address the association between CR and cognitive function.

Research question two was addressed with newly-collected cross-sectional data from a sample of 206 community-dwelling older people, which assessed the association of depressive thoughts and symptoms with cognitive reserve.

Research question three extended the findings from the meta-analysis and research question two by assessing whether CR moderates the association between mood and cognitive function and was assessed via three separate studies. In the first study, existing research on whether CR moderates the association between depression or anxiety and cognitive function in older people was collated through a systematic review. The second study that addressed this research question utilised newly-collected cross-sectional data from a sample of 236 community-dwelling older people, which comprised a different sample to that used in the study addressing research question two. The last study to address this research question utilised data from the second enumeration of the Medical Research Council Cognitive Function and Ageing Study (CFAS II), which allowed the findings of the above study to be tested in a large cohort sample that is weighted to be representative of the population of England.

1.9.1 Ethical approvals

Ethical approval was obtained for both of the studies conducted for this thesis from Bangor University School of Psychology Ethics Committee, details of which can be found in Appendix A. Ethical approval for CFAS was obtained locally at all participating sites from 1991; details of the approvals obtained for CFAS II can be found in Appendix B. Access to the CFAS II dataset was obtained by completing a data request application form which was approved by the CFAS team. Confirmation of this approval was provided in the form of a data transfer agreement (see appendix C). Participants for all studies were provided with information sheets and gave written informed consent (see Appendices D-F).

1.9.2 Participant recruitment

The data from the two newly-collected samples of healthy older people (research questions two and three) were collected partly by me with contributions from a group of MSc students carrying out their master's research project. Both studies included additional measures not presented in this thesis. For both studies, healthy older people were recruited using a purposive snowball sampling method from local community groups, church groups, active retirement groups, and AgeWell centres, and through responses to flyers advertising the studies (Appendix G), in locations across the UK and Republic of Ireland. For the study that addressed research question two, 206 people aged over 65 were recruited, and for the study that addressed research question three, 236 people aged over 60 were recruited. I contributed to designing the studies, selecting the measures for both masters' projects, and to supervising the students, including training them in the administration of the battery. In addition, I managed the two datasets and conducted all analyses within this thesis.

The data for Chapter 6 of the thesis came from CFAS II, CFAS and CFAS II will be briefly described below. The original CFAS study began in 1989 with sites in six centres across England and Wales – Cambridgeshire, Gwynedd, Newcastle, Nottingham, Oxford, and Liverpool. The initial aim of CFAS was to assess the prevalence and incidence of dementia and associated conditions in England and Wales and to assess if these differ across the UK. The CFAS team additionally sought to assess the service needs and degree of disability of people with dementia, the risk factors associated with developing dementia, and the

progression of disease. The study involved comprehensive interviews to assess mental, physical, and cognitive health, and biological measures including blood and saliva samples for a subsample of the cohort. In total over 13,000 people aged over 65 participated in the first enumeration of CFAS. In order to allow for comparison across cohorts, the CFAS II and CFAS Wales studies began in 2008 and 2010 respectively in a subset of the sites involved in the original study – Cambridgeshire, Nottingham, and Newcastle are sites for CFAS II and Gwynedd and Swansea are the sites for CFAS Wales. As this thesis utilises data from CFAS II, the following descriptions will be limited to this arm of the study.

Wave 1 of CFAS II data collection was completed in 2011. Participants were identified through general practice records and introductory letters from the general practitioner (Appendix H) were sent to potential participants. Each study centre was required to provide 2,500 participants with equal numbers of those aged 65 to 75 and those aged 75-85. Oversampling was used to allow for losses due to participant/carer refusals, ineligibility, or incorrect registration information. The introductory letter was followed by a visit from a named researcher. Informed consent was sought and procedures in full compliance with the UK Mental Capacity Act, 2005 were implemented in the event of impaired capacity. Interviewers visited participants up to three times to complete the assessments. A total of 7,762 people aged over 65 completed Wave 1 of CFAS II. The full questionnaires are available from cfas.ac.uk. A subset of the measures completed is considered in this thesis and will be outlined in the relevant chapter.

1.10 Structure of the thesis

The thesis consists of seven chapters: the general introduction, a meta-analysis, a systematic review, three empirical chapters, and the general discussion, which synthesises the evidence obtained in the studies in order to answer the research questions on which the thesis focuses. The meta-analysis, systematic review, and empirical chapters are presented in the format of journal articles. Versions of chapters two, four and five have been accepted for publication in peer reviewed academic journals and chapter three has been submitted for publication (see below for details). These have been reformatted for inclusion in the thesis but are substantially similar to the published versions. The chapters comprise individual studies but across the chapters, the work focuses on the same research area, and involves the same or

similar assessment measures; therefore, there will be some duplication in the introduction and method sections of the individual chapters. The following is a summary of the content of each chapter:

Chapter 2 – Cognitive reserve and cognitive function in healthy older people a meta-analysis.

Chapter 2 presents the results of a meta-analytic investigation of the association between the three key proxy measures of CR – educational level, occupational complexity, and/or engagement in cognitively-stimulating leisure activities – and cognitive function in healthy older people across several cognitive domains. The review provides an overview of the inconsistency in the methods used in assessing proxy measures of CR and the differences in the associations between individual and combined proxy measures across different cognitive domains. The meta-analyses synthesises information from a wide variety of cognitive measures from 135 studies. The findings suggest that there are small to moderate associations between the three key proxy measures of CR, individually and in combination, and cognitive function, with the greatest variation across cognitive domains being evident for occupation and engagement in cognitively-stimulating leisure activities.

Chapter 3 – Is cognitive reserve associated with depressive thoughts and self-reported depressive symptoms in later life?

Chapter 3 presents an empirical study that assessed the association between the three key proxy measures of CR, individually and in combination, and depressive thoughts and symptoms in people aged over 65. This study utilised a comprehensive measure of cognitive activity across the lifespan, indicating that greater CR, especially engagement in cognitively-stimulating leisure activities in later life, was associated with lower levels of both depressive thoughts and symptoms in older people. A path analysis model illustrated that earlier life experiences had an indirect effect on depressive thoughts and symptoms through later life experiences, in contrast to the direct associations noted between earlier life experiences and cognitive function in the meta-analysis. This model demonstrates the importance of a lifespan perspective in explaining the associations between proxy measures of CR and depressive symptoms and thoughts in later life.

Chapter 4 – Does cognitive reserve moderate the association between mood and cognitive function? A systematic review

Chapter 4 presents the results of a systematic review examining whether proxy measures of CR moderate the association between mood and cognitive function in later life. The review provides an overview of the existing research and identifies the incongruities in the methods and results of the existing research in this area. The disparities in the results allowed for a tentative conclusion, that CR is a beneficial moderator of the negative association between mood and cognitive function. This review also highlights the need for studies that utilise measures that combine multiple proxy measures of CR to assess whether CR moderates the association between mood and cognitive function.

Chapter 5 - How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life?

Chapter 5 built upon the findings from the systematic review by examining whether the associations of depressive symptoms, anxiety, and rumination with cognitive function differ in those with lower and higher CR, utilising a comprehensive measure of cognitive activity across the lifespan. This instrument provided a detailed proxy measure of CR that included the three key components. The findings indicated that rumination was not associated with cognitive function while higher levels of depressive symptoms and anxiety were associated with poorer cognitive performance in those with lower but not higher CR. It should be noted, that the published version of Chapter 5 is included in the preceding meta-analysis and systematic review as this paper was accepted for publication prior to the final systematic searches being conducted.

Chapter 6 – The role of cognitive reserve in the association between mood and cognitive function in a nationally representative cohort

Chapter 6 utilised data from the second Cognitive Function and Ageing Study (CFAS II) to investigate whether CR, indicated by a combination of the three key proxy measures, moderated the association between mood and cognitive function in a large cohort study, weighted to be representative of people aged over 65 in England. This study allowed participants to be grouped into those with no mood disorder, a sub-threshold mood disorder,

or a clinically relevant mood disorder. The findings from this study support those from Chapter 5 and extend them in that the presence of a clinically relevant mood disorder had a much larger negative association with cognitive function in those with lower CR than in those with higher CR.

Chapter 7 – General discussion

The final chapter synthesises the results from the meta-analysis, systematic review, and empirical studies and discusses the findings in the context of the research questions, existing research and the implications of these findings.

1.11 Dissemination of findings

A version of Chapter 2 has been published in *Aging, Neuropsychology, and Cognition.*

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. doi: 10.1080/13825585.2015.1041450

A version of Chapter 3 has been accepted for publication in the *European Journal of Ageing*

Opdebeeck, C., Quinn, C., Nelis, S.M., & Clare, L. (2015). Is cognitive lifestyle associated with depressive thoughts and self-reported depressive symptoms in later life? *European Journal of Ageing.* Advance online publication. doi: 10.1007/s10433-015-0359-7

A version of Chapter 4 has been published in *Reviews in Clinical Gerontology*

Opdebeeck, C., Quinn, C., Nelis, S.M., & Clare, L. (2015). Does cognitive reserve moderate the association between mood and cognition? A systematic review. *Reviews in Clinical Gerontology, 25,* 181-193. doi: 10.1017/S0959259815000155

A version of Chapter 5 has been published in *Aging & Mental Health.*

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (2015). How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life? *Aging & Mental Health, 19*, 705-712. doi: 10.1080/13607863.2014.962005

A version of Chapter 6 in being prepared for publication

Opdebeeck, C., Matthews, F. E., Woods, R. T., & Clare, L. (in preparation). The role of cognitive reserve in the association between mood and cognitive function in a nationally representative cohort.

A number of presentations have been made based on the findings from the data included in the thesis:

Opdebeeck, C., Quinn, C., Nelis, S.M., & Clare, L. (July, 2015). *Is cognitive lifestyle associated with depressive thoughts and self-reported depressive symptoms in later life?* Paper presented at the 44th British Society of Gerontology conference, Newcastle, UK.

Opdebeeck, C., Quinn, C., Nelis, S.M., & Clare, L. (April, 2015). *The interrelationship between cognitive reserve, depressive cognitions and symptoms, and cognition in later life.* Poster presented at the International Association of Gerontology and Geriatrics European Region conference, Dublin, Ireland.

Opdebeeck, C., Marty, A., Clare, L. (April, 2015). *Cognitive reserve and cognitive function in healthy older people: a meta-analysis.* Poster presented at the International Association of Gerontology and Geriatrics European Region conference, Dublin, Ireland.

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (February, 2015). *How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life?* Paper presented at the NEURODEM Cymru conference, Bangor, UK.

Opdebeeck, C., Martyr, A., & Clare, L. (July, 2014). *Cognitive reserve and cognitive function: a meta-analysis.* Poster presented at the Alzheimer's Association International Conference, Copenhagen, Denmark

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (November, 2013). *Mood, thinking style and cognition in later life: the impact of cognitive reserve*. Poster presented at the Gerontological Society of America conference, New Orleans, USA.

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (July, 2013). *Mood, thinking style and cognition in later life: the impact of cognitive reserve*. Paper presented at the Psychology Postgraduate Affairs Group Conference, Lancaster, UK.

1.12 Conclusion

Although there is significant evidence that CR is associated with better cognitive function and a reduced risk of dementia, the evidence regarding the associations between the key proxy measures and different cognitive domains is unclear. This thesis will aim to clarify these associations through a meta-analysis. This is important as any differential associations could help emphasise which proxy measure of CR is most important in maintaining different domains of cognitive function or whether they are of equal importance. Individual proxy measures of CR, in particular educational level and engagement in cognitively-stimulating leisure activities, are associated with depressive symptoms. However, addressing the question as to whether a singular proxy measure is of most importance or whether they interact with one another may provide additional information on the importance of the different components of CR in maintaining psychological as well as cognitive health in later life.

The associations between mood and cognitive function are equivocal, with little explanation to date on factors that may moderate this association. Previous research, which has considered whether proxy measures of CR moderate the association between mood and cognitive function have utilised singular proxy measures, with no consideration of whether a combination of experiences accumulated across the lifespan moderates the mood-cognition association. This thesis aims to address this gap in order to clarify whether CR may help to explain the variance in the associations between mood and cognitive function.

Chapter 2

Cognitive reserve and cognitive function in healthy older people: A meta-analysis

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. doi: 10.1080/13825585.2015.1041450

2.1 Abstract

Background: Cognitive reserve (CR) is associated with better cognitive function in later life but the associations between proxy measures of CR and cognition vary across studies and cognitive domains. This meta-analysis aimed to assess the relationship between cognitive reserve and cognition in multiple domains (memory, executive function, visuospatial ability, and language) in community-dwelling older people.

Method: CR was considered in terms of three key proxy measures - educational level, occupational complexity, and engagement in cognitively-stimulating activities – individually and in combination. Existing literature on the association between these proxy measures of CR and cognitive function was searched and the studies were screened for inclusion.

Results: One-hundred and thirty-five studies representing 128,328 participants were included. Of these, 109 used a measure of education, 19 used a measure of occupation, 31 used a measure of participation in cognitively-stimulating activities, and six used a combination of these proxy measures. All three proxy measures, individually and in combination, had a modest positive association with cognition; occupational complexity and cognitive activities showed the most variation across cognitive domains.

Conclusion: The results indicate that higher levels of CR are consistently associated with better cognitive function in community-dwelling older people but that the proxy measures differ in their associations with cognitive performance by domain. This supports the view that the commonly-used proxy measures of CR share an underlying process but that each additionally provides a unique contribution to CR.

2.2 Introduction

The concept of cognitive reserve (CR) was developed to explain the repeated finding that the amount of observed brain pathology or damage does not always correspond with the clinical presentation of an associated condition. In some older people, despite the presence of considerable brain pathology, there may be no clinically-observable signs or symptoms of disease (Mortimer, Snowdon, & Markesbery, 2003). CR has also been referred to as 'behavioural brain reserve' by some researchers (e.g. Valenzuela & Sachdev, 2006a; 2006b), as it is suggested that certain behaviours or experiences lead to increased reserve. In this meta-analysis the term 'cognitive reserve' will be employed as it is the more frequently-used of these two terms describing active reserve. The lifestyle factors underpinning CR are potentially amenable to modification and hence, in principle, they could provide a basis for preventive intervention (Tucker & Stern, 2011).

As CR cannot be directly measured, it is commonly indexed by those experiences and activities thought to increase it. The most commonly-used proxy measures are educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities. Cognitively-stimulating activities are those leisure pursuits that involve cognitive effort, such as reading, attending further education classes, doing crosswords or Sudoku, or playing games such as bridge etc. (Aartsen, Smits, van Tilburg, Knipscheer, & Deeg, 2002; Mousavi-Nasab, Kormi-Nouri, & Nilsson, 2014; Wilson et al., 1999). A number of cross-sectional studies have observed a relationship between the most common indicators of CR and cognitive function in generally healthy older people but, as will be discussed below, there are variations in these findings, as well as methodological issues relating to the way in which CR has been assessed.

Cross-sectional results have varied across studies examining the relationship between educational level as a proxy measure of CR and aspects of cognitive function in older people. These results have ranged from a strong correlation between education and measures of memory (e.g. Angel, Fay, Bouazzaoui, Baudouin, & Isingrini, 2010; Arbuckle, Gold, & Andres, 1986; Lee, Lee, &Yang, 2012) to a weak correlation between education and executive function (e.g. Jefferson et al., 2011; Lee et al., 2012; Mueller, Raymond, & Yochim, 2013); suggesting that the relationship of this proxy measure with cognitive function differs according to the cognitive domain assessed. Educational level itself has also been

assessed using various methods in different studies; for example, indices include years of education (Albert & Teresi, 1999), levels of education categorised into multiple groups ranging from no formal education to greater than 12 years (Mathuranath et al., 2007), and categories yielded by dichotomising education into lower and higher levels (Van Exel et al., 2001). The main difficulty with employing education as a proxy measure of CR is that the nature, intensity and content of education differ across nationalities and social groups. Indeed, it has been suggested that literacy may be a better indicator of educational attainment (e.g. Manly et al., 2005; Manly, Touradji, Tang, & Stern, 2003). Due to the relative ease of obtaining details about the extent of education, educational level is still more commonly-used than literacy in assessing educational attainment, and therefore educational level was the proxy measure selected for consideration in this meta-analysis.

Similarly, studies evaluating the relationship between occupational complexity as a proxy measure of CR and cognitive function in later life have yielded findings ranging from a weak correlation with memory (e.g. Fritsch et al., 2007; Leung et al., 2010) to a moderate correlation with executive function (e.g. Foubert-Samier et al., 2012). These findings suggest that the relationship of this proxy measure with cognitive function also varies by domain. Occupational complexity is also reported in a number of different ways; for example, Forstmeier and Maercker (2008) classified occupational complexity into motivational abilities and cognitive abilities, while Correa Ribeiro and colleagues (2013) coded occupations according to their complexity with data, people, and things.

It has been noted that engagement in cognitively-stimulating leisure activities provides a strong contribution to CR, with physical and social activities playing a smaller role in relation to late life cognitive function (Marioni, van den Hout, Valenzuela, Brayne, & Matthews, 2012); hence cognitively-stimulating activities and their relationship to cognitive function are considered as a proxy measure of CR in this meta-analysis. Discrepancies between findings on the nature of this relationship can also be seen in relation to different domains of cognitive function, with small, non-significant correlations between engagement in cognitively-stimulating leisure activities and memory (e.g. Lin, Friedman, Quinn, Chen, & Mapstone, 2012; Murphy & O'Leary, 2009) but moderate correlations between this proxy measure and executive function (e.g. Eskes et al., 2010; Lin et al., 2012; Newson & Kemps, 2005). A further issue arises in that a variety of measures to assess these activities, from details of the diversity and duration of current activities (Eskes et al., 2010) to scores on

questionnaires about cognitive activities across the lifespan such as that developed by R.S Wilson and colleagues (2003a) have been employed.

It has been suggested that using only one proxy measure of CR does not provide a complete picture, as CR is a fluid construct resulting from a combination of experiences and activities over the course of an individual's life (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern 2011; Whalley et al., 2006). It is doubtful whether one proxy alone constitutes a complete measure of CR, given that CR is derived from a combination of experiences and exposures across the lifespan. A number of measures combine these factors to give an index of an individual's overall CR, such as the Lifetime of Experiences Questionnaire (LEQ; Valenzuela & Sachdev, 2007) and the Cognitive Reserve Index Questionnaire (CRIq; Nucci et al., 2011), which may help in standardising the assessment of CR across studies. A fourth indicator of CR which has been considered by some is verbal IQ. However, this was not included as a proxy measure of CR in this meta-analysis as measures of verbal ability are frequently used as measures of cognition rather than as a proxy measure of CR (e.g. Anstey, Hofer, & Luszcz, 2003; Parisi, Stine-Morrow, Noh, & Morrow, 2009; Welsh-Bohmer et al., 2009).

The fluidity of CR suggests that it could be difficult to assess fully in younger people who have yet to obtain the effects of occupational complexity across their working lives. Hence, it is more salient to focus on people over the age of 60 who have had the opportunity to build their CR through education, occupation, and engagement in cognitively-stimulating activities over a number of years.

In summary, many cross-sectional studies assess proxy measures of CR, in particular educational level, occupational complexity, and/or participation in cognitively-stimulating leisure activities, and their relationship with cognitive function yet there is some discrepancy in the results and with regard to the patterns of association with different cognitive domains. Discrepancies in the way in which CR is indexed could account for some of the variance in findings and make synthesising the available information difficult; an indication of how each of the most commonly-used proxy measures of CR, and those measures which combine these proxies are related to cognitive function is needed. Furthermore, it is currently unclear how these proxy measures relate to different domains of cognition in a non-clinical population.

To date there is no meta-analysis or systematic review available that summarises the relationships between multiple proxy measures of CR and performance in different cognitive domains in healthy older people. Previous reviews of CR have tended to focus on the association between proxy measures of CR and incidence of dementia or take a narrative approach rather than a systematic review of the topic (e.g. La Rue, 2010; Richards & Deary, 2005; Scarmeas & Stern, 2003; Stern, 2002; 2006; 2009). Other reviews have focused only on a single proxy measure of CR and overall cognitive function (e.g. Bielak, 2010; Then et al., 2014a). These reviews have generally reported that a reduction in the risk of dementia and better cognitive function are associated with greater educational level, occupational complexity and engagement in cognitively-stimulating leisure activities. The present review aims to address the gap in the literature via meta-analytic methods, which avoid the bias associated with narrative reviews (Lyman & Kuderer, 2005). While it is now widely accepted that life experiences such as educational level, occupational complexity and participation in cognitively-stimulating leisure activities are associated with cognitive function, this meta-analysis adds to the literature by considering multiple proxy measures of CR and examining their association with cognitive function in different domains. It is becoming increasingly common for studies to consider the role of CR in healthy ageing, and yet no cohesive quantitative report on these studies is currently available. Specifically, this meta-analysis set out to assess how the different proxy measures of CR are employed by researchers, whether single proxy measures or combinations of these, and what the similarities and differences between these proxy measures and their associations with cognitive function in healthy older people are. The focus here is solely on cross-sectional studies assessing the relationship between proxy measures of CR and cognitive function, as previous reviews have considered the association between CR and both cognitive decline and incidence of dementia (e.g. Valenzuela & Sachdev, 2006a; 2006b). These reviews found a beneficial effect of the life experiences associated with CR, in that higher levels of these experiences resulted in less cognitive decline and reduced incidence of dementia. However, neither of these reviews considered cross-sectional studies of CR and cognitive function in different cognitive domains in healthy older people.

In this meta-analysis we set out to review and synthesise the information on the most common proxy measures of CR, namely educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities, and their relationship with different domains of cognitive function, in generally healthy people aged over 60 years who do not

have cognitive impairment or dementia. This age group was selected since individuals over 60 have had time to build CR across their life and the cognitive decline sometimes associated with ageing may begin to present itself, resulting in more variability in cognitive function within these individuals (Salthouse, 2009).

The specific aim of this meta-analysis was to collate the results of existing literature to answer the following research questions:

1. What are the similarities and differences in the relationships of each individual proxy measure of CR, specifically educational level, occupational complexity, engagement in cognitively-stimulating activities, and of indices which combine these proxies into a single measure, with cognitive function in healthy older people?

2. Do the nature and strength of these relationships differ across different domains of cognitive function?

2.3 Method

2.3.1 Literature search strategy

In order to identify studies investigating the relationship between cognitive function and CR, assessed using one of the key proxy measures or a combination of CR proxy measures, a search was conducted of the electronic databases ScienceDirect, PubMed, PsycInfo, and CINAHL on 21/11/2014. Each database was searched for (a) 'cognitive OR cognition OR memory OR executive OR visuospatial OR language OR reserve OR lifetime' in the title. The results of this search were then cross-matched with (b) '"cognitive reserve" OR "brain reserve" OR education* OR occupation* OR activit* OR leisure OR literacy' AND (c) 'old* OR later life OR elder* OR aged OR aging OR ageing OR nondemented' in the title, abstract, or keywords. The reference sections of included studies were searched for additional papers not identified in the initial search.

2.3.2 Inclusion and exclusion criteria

Studies were included if (a) at least 80% of participants were aged over 60 or the information for those aged over 60 was reported separately, (b) a proxy measure of CR, specifically educational level, occupational complexity, cognitively-stimulating leisure activities, or a combination of these was used, and (c) a cross-sectional outcome measure of cognitive function was reported.

Studies were excluded if (a) more than 20% of the sample consisted of people with a neurological disorder or a disorder which may affect cognitive functioning (e.g. dementia, multiple sclerosis, Parkinson's disease, HIV, or traumatic brain injury), (b) an outcome of dementia or mild cognitive impairment incidence was used, or participants were grouped into those with or without cognitive impairment, as this does not allow for assessment of cognitive function as a continuous variable in generally healthy people, or (c) the authors reported a biological or pathological proxy measure or outcome only.

2.3.3 Procedure

A summary of the procedure for selecting studies for inclusion can be seen in Figure 2.1. The searches identified 15,742 titles of which 10,330 were unique. The titles were evaluated in relation to the inclusion criteria by the lead author and those clearly unrelated to later life (e.g. related to children, animals, autism, or dyslexia) were excluded. The remainder (>50%) were screened by a second reviewer. The two reviewers achieved 99% agreement on inclusion/exclusion and where there was disagreement the title was retained for abstract screening. At this point 9,710 articles were discarded as they did not meet the inclusion criteria; the primary reasons were that these studies focused solely on animals, children, or clinical populations. Six hundred and twenty abstracts were then evaluated by two reviewers working independently. The reviewers achieved 81% agreement on inclusion/exclusion with disagreements discussed and full text retrieved when agreement could not be reached. After abstract screening 275 articles were discarded as they did not meet inclusion criteria; the primary reason was that these studies used no measure of either the required CR proxy measures or cognitive function.

The full texts of the remaining 345 articles were retrieved and the method and results sections evaluated against the inclusion criteria. This process yielded 128 articles, including four PhD theses, which satisfied the inclusion criteria and provided statistical information that could be included in the meta-analysis. Authors of eight of these studies were contacted to request additional statistical information, but only three responded. As a result, conservative estimates of the p-values given in the studies were used to calculate an effect size for four of these studies; for instance where $p < .05$ was reported, the p value .049 was used (Brewster et. al., 2014; Le Carrett et al., 2003; Rexroth et al., 2014; Welsh-Bohmer et al., 2009). Morgan, Marsiske, and Whitfield (2007) provided a range of correlation values for the relationship between educational level and cognitive function, consequently the lowest value was taken to provide a conservative estimate of the effect size. Additionally, it was not possible to contact the authors of one article that reported only statistically significant correlation values (Denney & Thissen, 1983). In this instance, a value of zero was used for the non-significant associations.

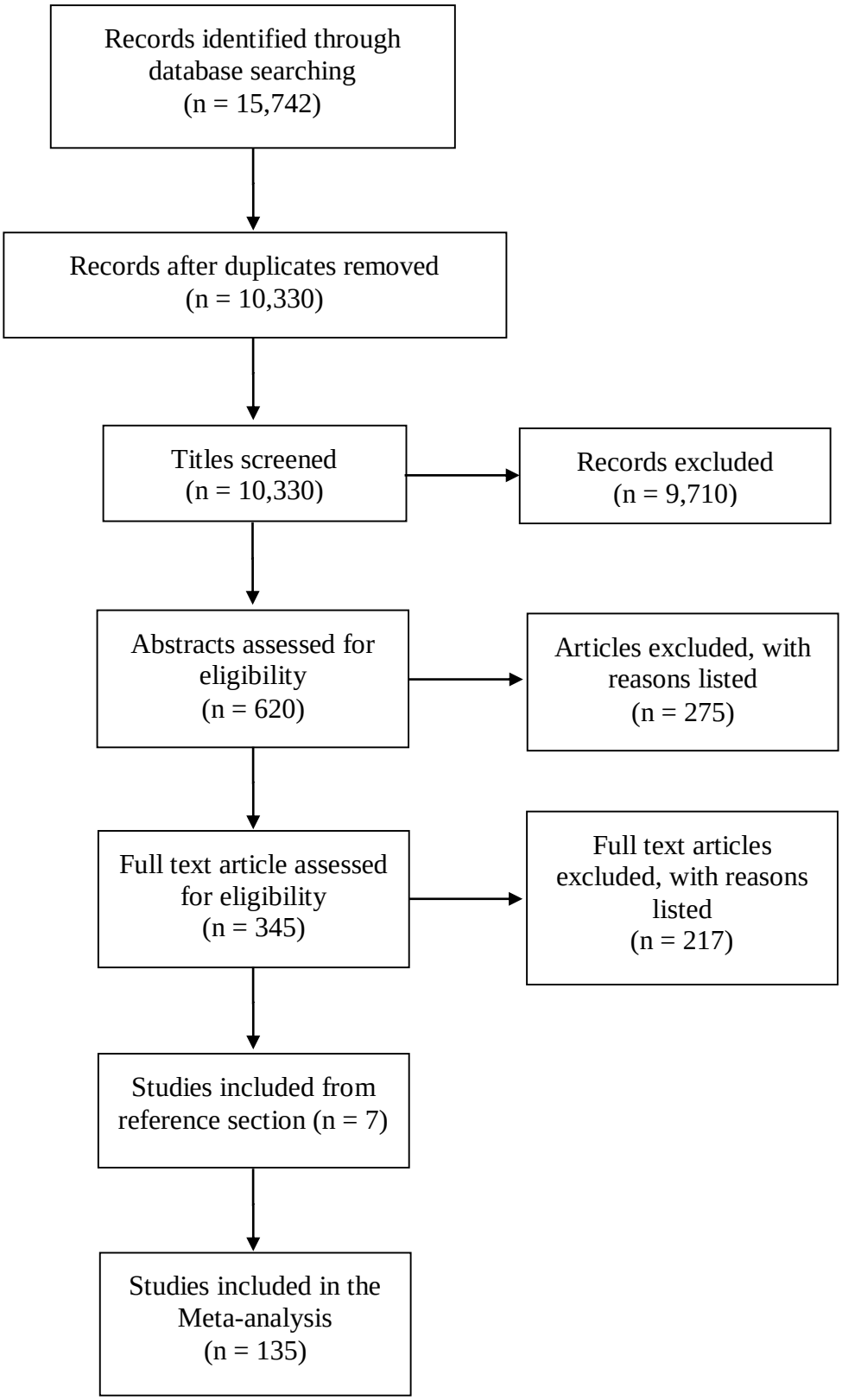


Figure 2.1. Study selection process

The 217 studies rejected at this stage were primarily excluded for the following reasons: they reported results for dementia/cognitive impairment outcomes or clinical samples (k = 19); they reported longitudinal research only (k = 50); more than 20% of the sample were aged under 60 (k = 54); the study did not include a required CR proxy measure, objective cognitive function outcome, or report specific results (k = 42); or it was not possible to retrieve the full text (three book chapters, one PhD thesis, and two journal articles). Multiple reports from the sample were dealt with in the following ways. Decisions on which study to include were based on the sample size, with those with a greater sample size reported, or on the number of cognitive domains assessed. For example the study by Ganguli and colleagues (2010) was included as they reported the association between education and five cognitive domains from the Monongahela-Youghiogheny Healthy Aging Team study for 1,413 participants while that by Snitz and colleagues (2009) was excluded as they reported two cognitive domains for 1,866 participants from the same sample. When reports from the same sample provided separate analyses relating to different proxy measures all the relevant reports were included. For example, Hultsch, Hammer, and Small (1993) and Zahodne and colleagues (2011) both utilised data from the Victoria Longitudinal Study reporting engagement in cognitively-stimulating activities and education respectively and their association with cognitive function; therefore they were both included in the analyses for the separate proxy measures. Table 2.1 provides information on the sample size, CR proxy measure and cognitive domain assessed by each included study. The Supplementary Table (Appendix I) gives a complete list of the included studies by the proxy measure of CR used and includes additional information on the samples for each study reported by the authors of that study and the measures used to assess the different cognitive domains. Searching the reference sections of the included studies yielded seven additional studies that satisfied the inclusion criteria and provided appropriate statistical information.

Table 2.1: Studies included, the cognitive reserve proxy measure and cognitive domains assessed

Authors	N	CR proxy measure	Cognitive domains
Aartsen et al. (2002)	3,107	Education	Screening measure, memory, working memory, executive function, and general cognition
Acevedo et al. (2007)	89	Education	Memory, working memory, executive function, language, and visuospatial ability
Aiken-Morgan et al. (2010)	449	Education	Screening measure, memory, working memory, executive function, and general cognition
Al Hazzouri et al. (2011)	7,042	Education	General cognition
Albert & Teresi (1999)	161	Education	Screening measure
Alvarado et al. (2002)	557	Education and occupation	General cognition
Andel et al. (2015)	810	Education, occupation, and cognitive activity	Screening measure
Angel et al. (2010)	28	Education	Memory
Anstey et al. (2003)	1,823	Education	Memory and executive function
Arbuckle et al. (1986)	285	Education and cognitive activity	Memory
Ardila et al. (2000)	250	Education	Memory, executive function, visuospatial ability, and language
Ashley (2008)	63	Education and cognitive activity	Executive function and general cognition
Barnes et al. (2004)	664	Education	Screening measure, memory, and executive function
Barnes et al. (2006)	108	Education and cognitive activity	General cognition
Barnes et al. (2011)	6,158	Education	General cognition

Beatty et al. (2003)	634	Education	Memory, executive function, language, visuospatial ability, and general cognition
Brand (2003)	94	Cognitive activity	Memory
Brewster et al. (2014)	333	Cognitive activity	Memory and executive function
Capitani et al. (1996)	220	Education	Memory, executive function, and general cognition
Carmelli et al. (1995)	522	Education	Screening measure
Christensen et.al (1996)	703-852	Education	Screening measure and memory
Christensen et al. (2009)	472	Education	Memory and executive function
Christofoletti et al. (2007)	116	Education	Memory, executive function, and language
Constaintinidou et al. (2012)	359	Education	Executive function, visuospatial ability, and language
Correa-Ribeiro et al. (2013)	624	Education and occupation	Screening measure
Davey et al. (2013)	244	Education	Screening measure, memory, and executive function
de Araújo Carvalho et al. (2009)	333	Education	Language
de Oliveira-Wachholz et al. (2011)	67	Education	Screening measure, memory, working memory, executive function, and language
de Souza-Talarico et al. (2007)	40	Education	Working memory and executive function
Denney & Thissen (1983)	115	Education	Executive function, language, and general cognition
Diehl et al. (1995)	62	Education	Working memory, executive function, and general cognition

Dorbath et al. (2013)	64	Education	Executive function
Duff et al. (2013)	576	Education	Screening measure
Elias et al. (1997)	1,002	Education	Memory, working memory, executive function, visuospatial ability
Eskes et al. (2010)	42	Cognitive activity	Memory, executive function, language, and visuospatial ability
Ferreira et al. (2015)	3,515	Education and cognitive activity	Memory, working memory, and language
Fillenbaum et al. (1988)	1,637	Education	Screening measure
Finkel et al. (2009)	565	Occupation	Memory, executive function, and visuospatial ability
Fisk et al. (1995)	361	Education	Screening measure
Forstmeier & Maercker (2008)	147	Occupation	General cognition
Foubert-Samier et al. (2012)	331	Education, occupation, and cognitive activity	Executive function
Fournet et al. (2012)	445	Education	Memory and working memory
Frisoni et al. (1993)	524	Occupation	Screening measure
Fritsch et al. (2007)	349	Education, occupation, and cognitive activity	Screening measure, memory, executive function, language, and visuospatial ability
Galluci et al. (2009)	668	Cognitive activity	Screening measure
Ganguli et al. (2010)	1413	Education	Memory, executive function, language, and visuospatial ability
Gilhooly et al. (2007)	145	Cognitive activity	Executive function
Giogkaraki et al. (2013)	383	Education	Memory, executive function, and visuospatial ability

Giordano et al. (2012)	288	Education	Screening measure, memory, working memory, executive function, and visuospatial ability
Glymour et al. (2005)	5,726	Education	General cognition
Gonzales (2013)	90	Combination	Screening measure
Gonzalez et al. (2013)	8,833	Education	Screening measure
Gow, Avlund, & Mortensen (2014)	576	Cognitive activity	Executive function
Gow, Avlund & Mortensen (2012)	425	Occupation	General cognition
Gow, Corley et al. (2012)	778	Cognitive activity	Memory and executive function
Hashimoto et al. (2006)	155	Education	Executive function and visuospatial ability
Hassing et al. (1998)	80	Education	Screening measure and memory
Hill, Whalin et al. (1995)	253	Education and cognitive activity	Memory
Ho & Chan (2005)	204	Education and cognitive activity	General cognition
Hultsch et al. (1993)	484	Cognitive activity	Memory, working memory, executive function, and language
Inouye et al. (1993)	1,182	Education	Memory, executive function, language, and visuospatial ability
Inzelberg et al. (2007)	260	Education	Screening measure
Jefferson et al. (2011)	951	Education and cognitive activity	Memory, working memory, executive function, and general cognition
Kaplan et al. (2009)	95	Education	Memory, executive function, and visuospatial ability
Kempler et al. (1998)	317	Education	Executive function

Kesse-Guyot et al. (2013)	3083	Educational and occupation	General cognition
Kilander et al. (1997)	504	Education	General cognition
Kim et al. (2011)	3157	Education	Screening measure
Lang et al. (2008)	2,397	Education	General cognition
Le Carrett et al. (2003)	1,022	Education and occupation	Screening measure
Lee, Lee, & Yang (2012)	50	Education	Memory and executive function
Leggett et al. (2013)	489	Education	Screening measure
Leung et al. (2010)	512	Education and occupation	Screening measure, memory, working memory, and executive function
Li et al. (2013)	52	Education	Working memory and executive function
Lin et al. (2012)	342	Cognitive activity	Memory and executive function
Lin et al. (2007)	58	Education	Executive function
Linderberger & Baltes (1997)	516	Education and occupation	General cognition
Luszcz (1992)	119	Education	Screening measure, memory, executive function, and general cognition
Mangione et al. (1993)	472	Education and occupation	Screening measure
Mathuranath et al. (2007)	488	Education	Screening measure
Matioli et al. (2008)	83	Education	Screening measure, memory, and executive function
Maurer (2011)	3,069	Education	Screening measure
McCarty et al. (1982)	172	Education	Memory and visuospatial ability

Mejia et al. (1998)	60	Education	Memory and executive function
Milan et al. (2004)	226	Education	Screening measure
Mitrushina et al. (1989)	156	Education	Language
Morgan et al. (2007)	162	Education	Screening measure, memory, and executive function
Mousavi-Nasab et al. (2014)	794	Education	Memory
Mueller et al. (2013)	44	Education and cognitive activity	Memory and executive function
Mulgrew et al. (1999)	1360	Education	Screening measure
Mungas et al. (2005)	497	Education	Memory, working memory, executive function, language, and visuospatial ability
Murayama et al. (2013)	118	Education	Memory
Murden et al. (1991)	94	Education	Screening measure
Murphy & O'Leary (2009)	99	Education and cognitive activity	Memory
Newson & Kemps (2005)	755	Cognitive activity	Memory, executive function, and language
Opdebeeck et al. (2015a; Chapter 5 of the thesis)	236	Combination	Screening measure, memory, and executive function
O'Connor et al. (1989)	1,822	Education	Screening measure
O'Shea et al. (2015)	3,484	Education	Memory, executive function, language, and visuospatial ability
Parisi et al. (2009)	189	Education and cognitive activity	Working memory, executive function, visuospatial ability, and general cognition
Parslow et al. (2006)	2,522	Cognitive activity	Executive function
Paula et al. (2013)	60	Education	Executive function

Pedersen et al. (1996)	580	Education	Screening measure and general cognition
Petersen et al. (1992)	161	Education	Memory and executive function
Plassman et al. (1995)	930	Education	Screening measure
Plumet et al. (2005)	49	Education	Executive function
Portin et al. (1995)	389	Education	Memory, working memory, executive function, and visuospatial ability
Potter et al. (2006)	3,880	Occupation	Screening measure
Puccioni & Vallesi (2012a)	17	Education and combination	Executive function
Puccioni &Vallesi (2012b)	23	Education and combination	Executive function
Rexroth et al. (2014)	2,782	Education	Memory and executive function
Ritchie et al. (2013)	1,628	Education	Executive function
Saczynski et al. (2008)	1,787	Cognitive activity	Memory and executive function
Scherr et al. (1988)	3,603	Education and occupation	Memory and executive function
Schmand et al. (1997)	4,051	Education	Screening measure
Senanarong et al. (2001)	3,177	Education	Screening measure
Sheres (2002)	77	Cognitive activity	General cognition
Smart et al. (2014)	1,066	Occupation	Memory, executive function, and general cognition
Smits et al. (1995)	115	Education and cognitive activity	Memory, executive function, and general cognition
Staff et al. (2004)	99	Occupation	Memory and general cognition
Then et al. (2014b)	422	Education and occupation	Screening measure
Unversagt et al. (1996)	83	Education	Screening measure, memory, executive function, and language

Van der Linden et al. (1997)	48	Education	Memory
van Exel et al. (2001)	446	Education	Memory and executive function
van Hooren et al. (2007)	576	Education	Memory and executive function
Vaughan et al. (2014)	393	Education and cognitive activity	General cognition
Vemuri et al. (2014)	1,995	Cognitive activity and combination	General cognition
Welsh-Bohmer et al. (2009)	507	Education	Memory, executive function, language, and visuospatial ability
Wiederholt et al. (1993)	1,692	Education	Screening measure, memory, executive function, visuospatial ability, and general cognition
Wilson et al. (1999)	6,162	Cognitive activity	General cognition
Wirth et al. (2014)	92	Cognitive activity	Global cognition
Yao et al. (2009)	1,000	Education	Screening measure
Zahodne et al. (2011)	1,014	Education	Memory, working memory, and executive function
Zahodne et al. (2014)	487	Education	Memory, working memory, and executive function
Zhou et al. (2014)	172	Education	Screening measure
Zimmerman et al. (2012)	549	Education	Memory, working memory, executive function, and visuospatial ability

Effect sizes for the relationship between the relevant proxy measure of CR and the cognitive function domain calculated from the statistical information provided for each individual study are presented in the Supplementary Table (Appendix I). The r effect size was utilised in this meta-analysis to represent the strength of the associations and is interpreted in respect to Cohen (1992). Studies were grouped according to the proxy measure of CR used, whether this was educational level, occupational complexity, engagement in cognitively-stimulating activities, or a combination of these. When a study used more than one CR proxy measure, it was listed in all relevant groups.

Measures assessing cognitive function were grouped into different domains using criteria provided by Lezak (1995) and on descriptions given by the studies that had utilised the measure. The Supplementary Table provides details of the specific tests employed in each study (see Appendix I). Cognitive screening measures commonly used with older people, including the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and the Telephone Inventory for Cognitive Status (TICS; Welsh, Breitner, & Magruder-Habib, 1993), were grouped together to give an indication of the relationship between proxy measures of CR and continuous scores on these measures. The memory domain included tests of episodic, logical, and semantic memory. Working memory was analysed separately as it has been considered as relating to both memory and executive function (Lezak, 1995). The executive function domain comprised specific tests measuring aspects of executive function including processing speed, attention, and verbal fluency (Lezak, 1995; Martyr & Clare, 2012). Visuospatial ability encompassed tests relating to visual search, figure copying, and line orientation. While Raven's Progressive Matrices (Raven, 1960) were incorporated into composite scores for visuospatial ability by two studies (Aiken-Morgan, Sims, & Whitfield, 2010; Jefferson et al., 2011) it has more commonly been described as a measure of fluid intelligence or general cognitive ability (e.g. Aartsen et al., 2002; Luszcz, 1992; Staff et al., 2004). Therefore, this measure was included in overall cognitive function analyses only. While a number of studies used the Spot-the-Word test (Baddeley, Emslie, & Nimmo-Smith, 1993) as a measure of language ability this was not included in this analysis as it is commonly used to assess verbal intelligence and it is not sensitive to age-related cognitive decline. The National Adult Reading Test (NART; Nelson, 1982) was excluded for the same reasons. Where studies had used confirmatory factor analysis to combine tests into specific domains, these domains were accepted as employed in the original study (e.g. Kaplan et al., 2009; Zahodne et al., 2011). To assess the associations between the proxy measures of CR

and general cognitive function all the tests of cognitive function were then grouped under each proxy measure to give an indication of these relationships. Forest Plot Viewer (Boyles, Harris, Rooney, & Thayer, 2011) was used to create a forest plot, which provides a visual representation of the weight of each effect size and allows for a comparison between the effects of the individual CR proxy measures in relation to each included cognitive domain.

2.3.4 Statistical analysis

The Comprehensive Meta-Analysis 2 (Borenstein, Hedges, Higgins, & Rothstein, 2005) software package was used to convert the individual correlation coefficients presented in the included studies into combined *r* effect sizes. This software uses Fisher's Z transformations and also calculates average z-scores, *p* values, 95% confidence intervals for the collective effect sizes, indices of between-study heterogeneity, and Rosenthal's fail-safe N for each analysis with three or more included studies. Between-study heterogeneity was assessed using an index of inconsistency (I^2; Higgins, Thompson, Deeks, & Altman, 2003). The I^2 statistic gives a percentage indicating the degree of heterogeneity in relation to total variation in observed effects and is not sensitive to the effect size or the number of studies included (Borenstein, Hedges, Higgins, & Rothstein, 2009). The fail-safe N provides the number of missing studies with a mean effect of zero that if added to the analysis would yield a statistically non-significant overall effect (Borenstein et al., 2005). It has been suggested that a fail-safe N can give an indication of the stability of the analyses where stability is indicated when the fail-safe N = 5k + 10 (Carson, Schriesheim, & Kinicki, 1990). Where *t* or *F* statistics, mean scores, or *p* values were reported, the program converted these to the *r* effect size. The *r* effect size makes use of the correlation coefficient to allow for evaluations of the relationship between two continuous variables in a number of studies (Borenstein et al., 2009). Standardised betas were converted to *r* effect sizes using the formula reported by Peterson & Brown (2005). A random effects model was used to calculate the effect size as the included studies were heterogeneous in their methods of assessing CR and cognitive function (DerSimonian & Laird, 1986). The random effects model allows for differences in the true effect size between studies (Borenstein et al., 2009). Holm-Bonferroni corrections were applied in the case of multiple analyses utilising each proxy of CR. These corrections were used to reduce the likelihood of making the errors associated with standard Bonferroni

corrections, errors such as not finding a significant association when one exists (Nakagawa, 2004).

Analyses were carried out to assess the relationship of each of the three most common proxy measures of CR, and combinations of these proxy measures, with the different domains of cognitive function, including cognitive screening measures, memory, executive function, visuospatial abilities, and language. Additional analyses assessed the relationship of all the measures of cognitive function employed in order to give an indication of the proxy measure's relationship with overall cognitive function. Studies reporting the relationship of cognitive function to more than one proxy measure of CR were included in the relevant analyses for each proxy. For those studies that included more than one outcome for a given cognitive domain or for multiple domains when they were analysed together, the Comprehensive Meta-Analysis 2 software program was instructed to average the within-study correlations to correct for violations of independence, so that all available data could be included in the analysis. Where more than 10 studies were included in the analysis a meta-regression was conducted to assess whether age was a moderator of the association between the CR proxy measure and cognition.

2.4 Results

The search identified 135 studies with a total of 128,238 unique participants. Of these, 109 used a measure of education (n = 111,683), 19 used a measure of occupational complexity (n = 18,167), 31 used a measure of participation in cognitively-stimulating leisure activities (n = 24,554), and six studies used composites of the key proxy measures of CR (n = 2,799). Of the studies evaluating educational level, 57 studies used years of education, 16 dichotomised educational levels into low and high, and 36 classified education into different levels. Of the studies evaluating occupational complexity, 15 used the individual's primary occupation, three the last occupation held, and one the participant's highest obtained occupation. A number of different classification systems were employed to grade the occupation for its complexity (see Supplementary Table, Appendix I). Of the studies evaluating engagement in cognitively-stimulating activities, 24 gave an indication of participation in the given activities currently or within the last year, five gave an indication of participation across the lifespan, and two assessed participation in cognitive activities earlier in life only (adolescence and

mid-life). Of the studies evaluating composites of the proxy measures of CR, four combined the three proxy measures of CR considered in this meta-analysis and two combined education and occupation. The Supplementary Table gives further details of the various ways in which each proxy measure was operationalized in the studies.

As can be seen in Tables 2.2a-d, heterogeneity ranged from low to high for the analyses, and this is further discussed below in relation to each set of analyses. The levels of heterogeneity observed indicate that the included studies differed substantially in their variance, which supported the use of the random effects model.

Figure 2.2 shows the effect sizes and associated confidence intervals for the relationship between the individual and combined proxy measures of CR and the domains of cognitive function assessed. This forest plot demonstrates that the largest confidence intervals were found in relationships between education and language ability and engagement in cognitively-stimulating activities and cognitive screening measures, visuospatial ability, and language. Overall, none of the confidence intervals passed below zero indicating generally consistent positive associations between the proxy measures of CR and performance across different cognitive domains.

2.4.1 Educational level and cognitive function

The relationships of educational level with cognition were assessed in relation to cognitive screening measures, memory, working memory, executive function, visuospatial ability, language, and a combination of all the tests of cognition employed (see Table 2.2a). Twelve studies combined a number of different tests into a measure of global cognitive function. These studies were included in the analysis of overall cognitive function and educational level but could not be analysed within any of the specific domains.

Table 2.2a. Results for the meta-analyses of the associations between educational level and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity Q	Df(Q)	p	I-squared	Fail safe N
Screening	41	51,644	.314	.278-.349	16.10	**<.001**	1091.88	60	**<.001**	94.51	13,640
Memory	53	34,560	.230	.196-.263	13.12	**<.001**	466.89	55	**<.001**	88.22	6,640
Working	18	11,311	.235	.169-.298	6.84	**<.001**	191.63	18	**<.001**	90.61	1,996
Executive	57	33,552	.291	.249-.331	13.15	**<.001**	838.41	60	**<.001**	92.84	9,839
Visuospatial	18	13,091	.287	.212-.358	7.26	**<.001**	333.06	18	**<.001**	94.60	4,735
Language	16	12,033	.314	.177-.440	4.35	**<.001**	832.14	15	**<.001**	98.20	4,265
General	108	111,683	.295	.268-.322	20.25	**<.001**	2835.12	133	**<.001**	95.31	18,415

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. P values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

The random effects meta-analysis in Table 2.2a indicated that the estimated effect sizes for the relationship of education with all the cognitive domains were significant, though small to medium. All the results remained significant after Holm-Bonferroni corrections were applied. The fail-safe Ns indicate that a substantial number of additional studies would be required to reduce the estimated effect size to non-significant indicating good stability of the results. There was, however, a high level of heterogeneity in all of the domains, particularly for screening measures, language, and overall cognition. The high levels of heterogeneity could be due to the variation in the associations reported in the different studies or the differences in sample sizes (e.g. Unverzagt et al. (1996) report a strong association between the MMSE and education with a sample size of 83, while Schmand et al. (1997) report a weak association between the MMSE and education with a sample size of 4,051). Alternatively, the high levels of heterogeneity could be due to the vast number of different measures of cognitive function included in the analysis of the association between education and overall cognitive function. Age was found to be a significant moderator for the association between education and screening measures (z = -3.13, p = .002), working memory (z = -5.23, p < .001), executive function (z = -6.30, p < .001), language (z = -7.56, p < .001), and overall cognition (z = -3.32, p = .001) but not for memory or visuospatial ability. This indicates that age did not moderate the association between education and performance in these two cognitive domains.

2.4.2 Occupational complexity and cognitive function

The relationships between occupational complexity and cognitive screening measures, two separate domains of cognitive function (memory and executive function) and overall cognitive function were assessed (see Table 2.2b). One study assessed the association between occupational complexity and working memory (Leung et al. 2010), reporting a small association between the two variables (r = .11). One study assessed the association between occupational complexity and visuospatial ability (Finkel, Andel, Gatz, & Pedersen, 2009), reporting a small association between the two variables (r = .20). Six studies gave a score for general cognitive function on the basis of several tests. These studies were only included in the analysis of the overall relationship of occupational complexity with all the tests of cognitive function.

The strongest estimated effects were shown for the screening measures and overall cognitive function, with occupation having a close to moderate association with these outcomes. All other analyses, while significant, showed small associations between occupation and the cognitive domains assessed. The fail-safe Ns indicate that a large number of additional studies would be required to make the association between screening measures and overall cognition and occupation non-significant. Smaller but still stable fail-safe Ns were found for memory and executive function, which is to be expected given the small estimated effect size for these two domains. All the analyses showed a high index of heterogeneity, indicating considerable variance between studies and supporting the use of the random effects model. Age was found to be a significant moderator for the association between occupation and overall cognition (z = -2.05, p = .041) which was the only occupational complexity analysis with more than 10 included studies.

2.4.3 Cognitively-stimulating leisure activities and cognitive function

Engagement in cognitively-stimulating leisure activities was assessed in relation to screening measures, memory, working memory, executive function, visuospatial ability, and language and to overall cognitive functioning (see Table 2.2c). Seven studies which combined a number of different tests into a measure of global cognitive function were only included in the analyses assessing cognitive function in general. The estimated effect sizes for the relationships between engagement in cognitively-stimulating leisure activities and screening measures, executive function, and overall cognitive function were moderate while the other associations were small, especially for working memory. All the associations remained significant after Holm-Bonferroni corrections were applied. The association between engagement in cognitively-stimulating leisure activities and visuospatial ability should be viewed tentatively due to the small number of studies available for inclusion in this analysis. The fail-safe Ns indicated that a large number of studies would be required to bring the estimated effect size for memory, executive function, and general cognitive function below significance. However, the fail-safe N for the association between working memory and engagement in cognitively-stimulating activities indicates that the significance of this result is not stable; although, this is to be expected given the magnitude of the estimated effect size.

Table 2.2b. Results for the meta-analyses of the associations between occupational complexity and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity Q	Df(Q)	p	I-squared	Fail safe N
Screening	9	8,245	.239	.142-.332	4.72	**< .001**	144.40	8	**< .001**	94.46	991
Memory	7	5,930	.141	.073-.208	4.05	**<.001**	35.15	6	**<.001**	82.93	163
Executive	8	8,143	.138	.076-.199	4.35	**<.001**	41.95	6	**<.001**	85.70	215
General	19	18,167	.247	.187-.304	7.90	**<.001**	284.18	18	**<.001**	93.66	4,371

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. p values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

Table 2.2c. Results for the meta-analyses of the associations between engagement in cognitively-stimulating leisure activities and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity				
							Q	Df(Q)	p	I-squared	Fail safe N
Screening	4	2,504	.265	.115-.403	3.41	**.001**	44.91	3	**<.000**	93.32	167
Memory	16	10,226	.204	.148-.259	6.96	**<.001**	98.37	15	**<.000**	84.75	1,131
Working	4	5,139	.077	.024-.130	2.85	**.004**	6.87	3	.076	56.30	18
Executive	17	9,796	.257	.217-.297	12.16	**<.001**	61.61	17	**<.001**	72.41	2,542
Visuospatial	2	231	.172	.043-.295	2.61	**.009**	0.09	1	.762	0	N/A
Language	4	4,796	.174	.072-.272	3.34	**.001**	19.11	3	**<.001**	84.30	73
General	31	24,554	.264	.212-.315	9.51	**<.001**	496.33	31	**<.001**	93.75	10,151

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. p values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

Levels of heterogeneity were generally lower than those for education and occupation, although heterogeneity remained high for cognitively-stimulating leisure activities and screening measures, memory, language, and overall cognition. This indicates a high level of variance between the studies, supporting the use of the random effects model. Age was found to be a significant moderator for the association between engagement in cognitively-stimulating activities and overall cognition ($z = -3.47$, $p < .001$) but not for memory or executive function. This indicates that age did not moderate the association between education and performance in these two cognitive domains.

2.4.4 Composites of cognitive reserve proxy measures and cognitive function

Composites of CR proxy measures were assessed in relation to screening measures, executive function, and overall cognitive function (see Table 2.2d). Only one study assessed a composite measure of CR and memory (Opdebeeck, Nelis, Quinn, & Clare, 2015a, this is the published version of Chapter 5 of this thesis), reporting a moderate association between the two variables ($r = .344$). The estimated effect sizes for the associations of the two individual domains and overall cognitive function with the composite CR proxy measures were moderate and remained significant after Holm-Bonferroni corrections were applied. The fail-safe N for screening measures was small which is to be expected given that only three studies were included in this analysis, while for executive function and overall cognitive function it was adequate given the small number of studies included and both indicated stability in the results. Levels of heterogeneity were low for instruments that combined different proxy measures of CR and their association with screening measures but were high with overall cognitive function, supporting the use of the random effects model.

Table 2.2d. Results for the meta-analyses of the associations between measures that combined proxy measures of cognitive reserve and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity				
							Q	Df(Q)	p	I-squared	Fail safe N
Screening	3	815	.274	.213-.340	8.09	**<.001**	1.17	2	.557	0	41
Executive	4	1,714	.314	.182-.435	4.51	**<.001**	7.58	3	.059	60.40	85
General	6	2,799	.315	.227-.398	6.70	**<.001**	17.32	5	**.006**	71.13	335

Note: screening, cognitive status screening measures; Executive, executive function; General, overall cognitive function. p values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

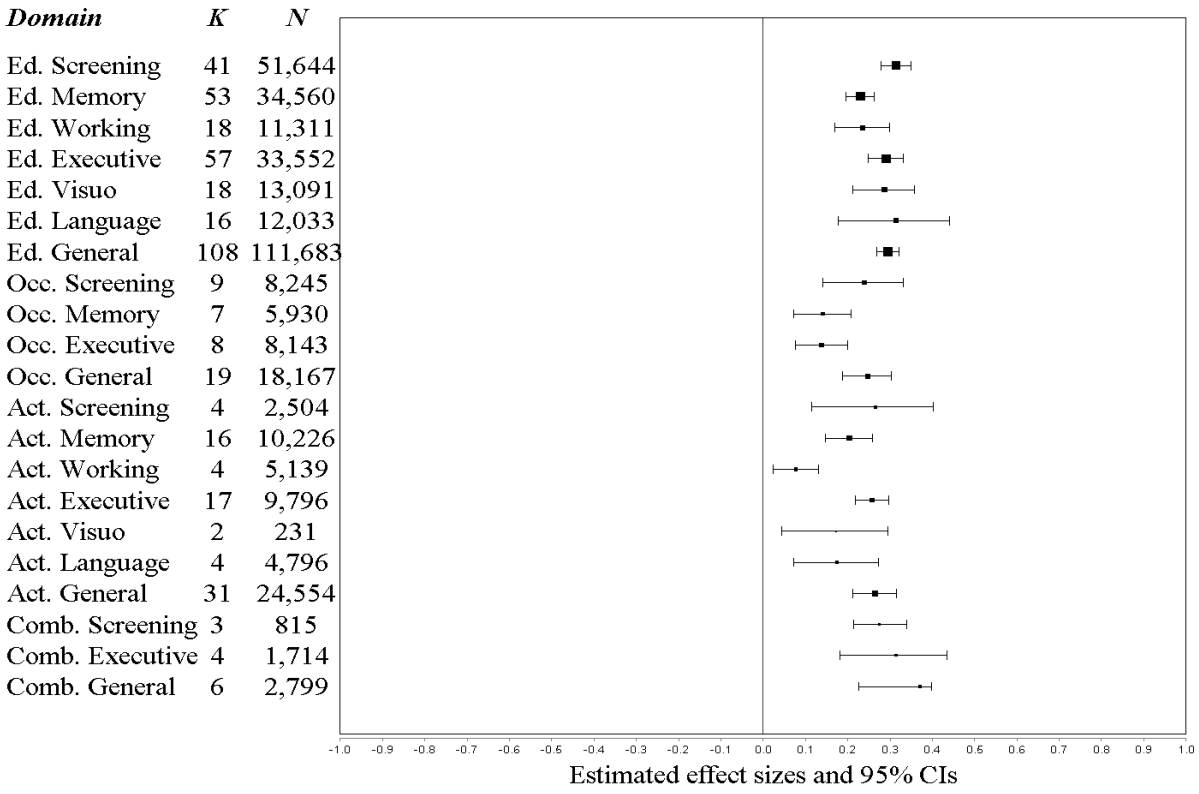


Figure 2.2. Forest plot of the effect sizes for each cognitive reserve proxy measure and each cognitive domain.

Note: Ed., educational level; Occ., occupational complexity; Act., cognitively-stimulating leisure activities; Comb., combined cognitive reserve proxy measures; Screening, cognitive status screening measures; Executive, executive function; Visuo., visuospatial abilities; General, overall cognitive function.

2.5 Discussion

This random effects meta-analytic study aimed to investigate the relationship of the three most commonly-used proxy measures of CR - educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities - and measures which combine these proxy measures with a number of cognitive domains in later life. To the best of our knowledge this meta-analysis is the first to synthesise the available cross-sectional statistical information from studies investigating these relationships in a healthy population.

The first aim of this meta-analysis was to investigate the similarities and differences in the associations of educational level, occupational complexity, engagement in cognitively-stimulating activities, and measures which combine these proxy measures of CR with cognitive function in later life. The meta-analyses showed positive significant relationships between overall cognitive function and the three individual and combined proxy measures of CR. There were moderate associations between measures that combined the proxy measures of CR and education and cognitive function and small associations between engagement in cognitively-stimulating leisure activities and occupational complexity and cognition. Overall, the results are consistent with the findings of previous reviews and studies which showed a modest association of individual and combined CR proxy measures with reduced cognitive decline and incidence of dementia (Marioni et al., 2012; Valenzuela et al., 2011; Valenzuela & Sachdev, 2006a; 2006b; 2007). Previous studies have shown large variations in the relationships between educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities and cognitive function (e.g. Barnes, Tager, Satariano, & Yaffe, 2004; Ferreira, Owen, Mohan, Corbett, & Ballard, 2015; Fritsch et al., 2007; Smart, Gow, & Deary, 2014; Smits, van Rijsselt, Jonker, & Deeg, 1995). One explanation for this variability between studies may be due to the variations in the measures used to assess these proxy measures of CR, for example current versus past participation in cognitively-stimulating leisure activities (Fritsch et al., 2007; Smits et al., 1995). The results of this meta-analysis indicate that the three proxy measures of CR and measures that combine these are positively associated with cognitive function in later life.

The second aim of this meta-analysis was to address whether the strength of these relationships differ across different domains of cognitive function. Measures that combined different proxy measures of CR and educational level showed the smallest variation in their relationships with different domains of cognitive function. All these relationships were positive, with moderate or marginally below moderate estimated effect sizes, and statistically significant. Both higher educational level alone and in combination with more complex occupational experience, and greater participation in cognitively-stimulating activities were related to better performance on cognitive tests in all the domains assessed. The relationships between the different cognitive domains and occupational complexity and engagement in cognitively-stimulating leisure activities had greater levels of variability with estimated effect sizes ranging from negligible to close to moderate. This could have been due to the greater variations in how these proxy measures were assessed, which meant that the studies included

in the meta-analyses differed more widely in their results than the combined CR proxy measures and educational level studies. However, it could also suggest that these proxy measures differ in their association with cognitive function on the basis of the domain assessed. Until there is a standard method for classifying occupational complexity used across a number of studies, and agreement as to whether current activity levels or activity across the lifetime are crucial for building CR, it will be difficult to assess the true nature of these relationships. It should also be noted that each of the individual CR proxy measures assess experiences that are salient at different time points across the lifespan, with the majority of education primarily experienced early in life, occupational benefits in mid-life, and engagement in cognitively-stimulating activities predominantly experienced in late-life. It is probable that early life experiences are closely related to the quality of later experiences, for example, educational level is likely related to occupational complexity. Therefore, the individual proxy measures may not be fully orthogonal. Measures that combine the different CR proxy measures go some way to overcoming these issues. The similarities and differences in the patterns of association between the individual and combined proxy measures of CR and function across cognitive domains in later life is consistent with the suggestion that experiences across the lifespan affect cognitive function in combination as well as individually. Indeed, the findings suggest that a combination of experiences across the lifespan increases CR and may partly explain the differences in cognition observed (e.g. Nucci et al., 2011; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern, 2011).

The small to moderate effect sizes found in this meta-analysis should be considered a conservative estimate of the relationships between the different proxy measures of CR and the included domains of cognitive function. The findings may have been affected by the differences in the methods used for each proxy measure of CR and the different neuropsychological tests adopted. In a number of studies correlation coefficients were not provided and the available statistics had to be converted to correlation coefficients, with conservative estimates taken in certain studies (Brewster et al., 2014; Morgan et al., 2007; Le Carrett et al., 2003; Rexroth et al., 2014; Welsh-Bohmer et al., 2009); these should be viewed as estimates of the relevant effect sizes and may have reduced the size of the effects. This is especially true where the *p*-value and sample size had to be used as a gross estimate of the effect size as it is probable that the association was under-estimated in those studies with a large sample size due to the conservative effect size estimated by the meta-analysis software, two of these studies had a sample size of over 500 and two had a sample size of over 1,000.

However, including these studies, even with conservative estimates, is less of a limitation than excluding them. There may also be some non-independence of the analyses for the different proxy measures in that 25 studies reported that given cognitive domains were associated with more than one proxy measure of CR. However, this may add further weight to the argument that the different proxy measures of CR are differently associated with cognition (R.S. Wilson et al., 2003a). Given that age was a significant moderator of a number of the associations between the CR proxy measures and cognitive function, it is possible that age plays a role in the associations. However, it should be noted that the associations with age are likely to be confounded by cohort effects. In addition, cohort effects may account for some of the variance in associations of the different CR proxy measures with cognitive function in that other confounders associated with different cohorts such as ethnicity, generational differences, or area of residence may account for differing levels of the variance in cognitive function explained by CR proxy measures; however, it was not possible to control for this potential confound.

This meta-analysis was limited to published articles and PhD theses. Consequently there may be a bias toward studies which found a relationship between the proxy measures of CR and cognitive function. However, it should be noted that a number of studies provided statistically non-significant findings that were included in the analyses (e.g. Diehl et al., 1995; Eskes et al., 2010; Jefferson et al., 2011; van Hooren et al., 2007). Additionally, the fail-safe Ns suggest that for the majority of analyses a large number of non-significant, unpublished studies would be required to reduce the estimated effect size to non-significance. A common criticism of meta-analytic studies is that they ignore differences across the included studies (Borenstein et al., 2009). This may be an issue here, in that the proxy measures of CR are assessed in a variety of ways; however, combining studies makes it possible to address broader questions and with larger samples than can usually be obtained by individual studies. Additionally, there were large differences between the sample sizes in the included studies, but the random effects meta-analysis accounts for these differences; therefore, studies with large effect sizes but small samples are unlikely to have biased the results (e.g. Angel et al., 2010; Foubert-Samier et al., 2012; Unverzagt et al., 1996).

It should be noted that while all the estimated effect sizes of the associations were significant, the relationship between engagement in cognitively-stimulating activities and working memory was very small and those of occupational complexity and all the individual

domains assessed except for screening measures were small. This indicates that these proxy measures may show a weaker relationship with certain domains than educational level or measures which combine these proxies, although not with cognitive function overall; however, the number of studies included in these analyses were small so this conclusion may change as more studies investigate this relationship. One of the major limitations with assessing these relationships relates to the varying ways in which CR is indexed in different studies for occupational complexity and engagement in stimulating leisure activities. This can be noted in the high levels of heterogeneity generally seen in these analyses and could partly explain the variability seen between individual studies. Additionally, activities other than those usually included in measures of leisure activities may be classed as cognitively-stimulating, such as those undertaken in a work environment, and this may confound the associations between cognitively-stimulating leisure activities and cognitive function when this CR proxy measure is taken alone. Little can be done to rectify this until a general consensus on how to assess CR is reached. Until then, studies that use a single proxy measure to indicate CR may be better described simply as focusing on the relationship between that proxy measure, for example educational level, and cognitive function, rather than reflecting CR per se.

When considering the idea that CR is associated with better cognitive functioning in later life, it is important to note that we cannot be certain about the causal direction of this relationship. As Salthouse (2006) argues, the associations may be due to preserved differentiation, with the observed variations in cognitive function reflecting innate abilities rather than lifetime experiences. However, there are no known reasons not to engage in experiences and activities that are stimulating and enjoyable (Salthouse, 2006). Indeed, engaging in the cognitively-stimulating life experiences thought to increase CR has been shown to enhance levels of cognitive functioning in later life and slow cognitive ageing (Hertzog et al., 2008). Other researchers have also noted that exposure to stimulating life experiences may enhance cognitive ability throughout the lifespan (Richards & Sacker, 2003; Rutter, 1985; Schaie, 1996).

The similarities and differences in the associations between the proxy measures considered here and cognitive function across different domains supports the theory that CR is based on a lifetime of exposures (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern 2011; Whalley et

al., 2006). As such, when assessing CR without measures of pathology multiple life experiences should be taken into account. Measures specifically designed to assess the experiences associated with CR, which give an overall score taking account of different life periods and experiences, could help standardise the assessment of the relationship between CR and cognitive function. For example, the LEQ (Valenzuela & Sachdev, 2007; Valenzuela et al., 2013) uses a weighting system to give equal importance to education, occupational complexity, and participation in cognitively-stimulating leisure activities in building CR across the lifespan and provides a score which combines these experiences in different periods of life. The CRIq (Nucci et al., 2011) is another measure specifically designed to assess the experiences associated with CR. The CRIq also attempts to incorporate the influence of educational level, occupational complexity, and engagement in cognitively-stimulating, social, and physical leisure activities. While the CRIq incorporates three distinct sections that can be combined to give an overall score, the sections are not weighted to allow for an even contribution of these experiences to CR as is the case with the LEQ. As these proxy measures have similar relationships with cognitive function there is likely to be significant overlap between them; it would seem prudent to give them equal weighting in their contribution to an overall score indexing CR. The results from the construction of the CRIq indicate that the three most commonly-used proxy measures are only moderately linked (Nucci et al., 2011). Indeed, R.S. Wilson and colleagues (2003a) noted that there may be different patterns of association between cognitive function and educational level and engagement in cognitively-stimulating activities. These findings all support the view that the commonly-used proxy measures of CR – educational level, occupational complexity, and engagement in cognitively-stimulating activities - share an underlying process but that each additionally provides a unique contribution to an individual's CR.

This meta-analytic study of the relationship between the three most commonly-used proxy measures of CR and cognitive function supports the supposition that indices of CR are related to cognitive function in a number of different domains, although the associations found were modest. The results are consistent with the recent suggestion that a standardised index of CR, which encompasses multiple proxy measures, is required to more comprehensively investigate the relationship between this concept and cognitive function in healthy and clinical populations. Future research should employ measures such as the LEQ or the CRIq that give an indication of CR based on a lifetime of exposures in order to more accurately assess the relationship between CR and cognitive function. A further

understanding of this relationship would aid in establishing which lifestyle changes could help delay cognitive decline and the onset of dementia.

Chapter 3

Is cognitive reserve associated with depressive thoughts and self-reported depressive symptoms in later life?

Opdebeeck, C., Quinn, C., Nelis, S.M., & Clare, L. (2015). Is cognitive lifestyle associated with depressive thoughts and self-reported depressive symptoms in later life? *European Journal of Ageing.* Advance online publication. doi: 10.1007/s10433-015-0359-7

3.1 Abstract

Background: Key components of cognitive reserve (CR) are educational attainment, occupational complexity and engagement in cognitively-stimulating leisure activities. Each of these factors is associated with experiencing fewer depressive symptoms in later life, but no study to date has examined the relationship between a measure that combines these key components of CR and depressive symptoms. This task is made more complex because relatively few older participants in cross-sectional studies will be currently experiencing depression. However, many more will show evidence of a depressive thinking style that predisposes them towards depression. This study aimed to investigate the extent to which CR and its individual components are associated with depressive thoughts and symptoms.

Method: Two hundred and six community-dwelling participants aged 65+ completed measures of depressive thoughts and symptoms and CR.

Results: Correlational analysis indicated that each of the individual lifestyle factors - education, occupational complexity, and activities in young adulthood, mid-life, and later life - and the combined components score were positively associated with each other and negatively with depressive symptoms, while all except education were negatively associated with depressive thoughts. CR explained 4.6% of the variance in depressive thoughts and 10.2% of the variance in depressive symptoms.

Conclusion: The association of greater participation in cognitive activities, especially in later life, with fewer depressive symptoms and thoughts suggests that preventive interventions aimed at increasing participation in cognitively-stimulating leisure activity could be beneficial in decreasing the risk of experiencing depressive thoughts and symptoms in later life.

3.2 Introduction

Depressive symptoms in later life are associated with a number of negative outcomes. Late-life depression can lead to increased disability, frailty, and loss of independence in older age (Agüero-Torres et al., 2002; Covinsky et al., 2010; Lenze et al., 2001; Mezuk et al., 2012; Reynolds et al., 2008). In addition, the experience of depression in later life is associated with poorer cognitive function and increased risk of developing cognitive impairment and dementia (Reppermund et al., 2011; Dotson, Beydoun, & Zonderman, 2010; Yates et al., 2013). However, the association between depression and cognitive impairment and dementia is complex and it currently remains unclear whether depression is a risk factor for dementia, or a prodromal symptom, or whether there is some underlying mechanism that is shared between depression and dementia (Byers & Yaffe, 2011; Korczyn & Halperin, 2009; Leonard, 2007). Given the negative outcomes associated with depression and its complex association with late life cognitive ability, it is of interest to investigate potentially modifiable factors that are associated with increased risk of both depression and cognitive impairment or dementia in later life.

While the prevalence of depression in later life is high, cross-sectional research generally only captures those who are currently experiencing depressive symptoms, and not those who have experienced depressive symptoms in the past or who may experience them in the future (Crawford, Henry, Crombie, & Taylor, 2001). However, thought processes related to lowered mood, such as negative thoughts or depressive cognitions focusing on self, the world and the future, are thought to increase the risk of experiencing a depressive episode in both younger and older people, and these are more persistent trait variables (Beck, 2002; Evans et al., 2005; Zauszniewski, 1997; Zauszniewski & Rong, 1999). Depressive symptoms refer to those symptoms observed in clinically-diagnosed depression, and this term is frequently used when symptoms are assessed via a screening tool which cannot provide a clinical diagnosis of depression. The experience of mild depressive symptoms and the depressive thought patterns associated with depression are likely to be more common in community-dwelling older people than clinically-diagnosed depression (Beekman, Copeland, & Prince, 1999). These depressive symptoms and thought patterns, like clinical depression, are associated with cognitive impairment and functional disabilities (Vinkers, Gussekloo, Stek, Westendorp, & van der Mast, 2004; R.S. Wilson et al., 2003b; Yen, Rebok, Gallo, Jones, & Tennstedt, 2011; Zauszniewski & Rong, 1999). Therefore, it is important to

consider potentially modifiable factors associated not just with clinically diagnosed depression but also with mild depressive symptoms and those depressive thoughts that may in turn increase the risk of experiencing an episode of clinical depression. One such construct may be cognitive reserve (CR).

Higher levels of CR are related to better cognition in later life and a reduced risk of cognitive impairment and dementia (Foubert-Samier et al., 2012; Stern, 2009; Tucker & Stern, 2011; Valenzuela & Sachdev, 2006a; 2006b). As several researchers have proposed that there may be a shared underlying mechanism for both dementia and depression in later life (Byers & Yaffe, 2011; Korczyn & Halperin, 2009; Leonard, 2007), CR could also help to protect against the experience of depressive symptoms and depressive thoughts. In Paulson, Bowen, and Lichtenberg (2014), a higher level of education was protective against the negative effects of cerebrovascular burden on levels of depressive symptoms at baseline. A recent review of the neurobiology of later life depression argued the case for CR as a protective factor against late-life depression but suggested that further research is required (Weisenbach & Kumar, 2014).

There is consensus from previous research that higher educational level and greater participation in leisure activities are associated with fewer depressive symptoms in later life (Adams et al., 2011; Bjelland et al., 2008; Glass et al., 2006; Hong et al., 2009; Jenkins, 2011; Ladin, 2008; Lorant et al., 2003; Murrell et al., 2003; Narushima et al., 2013; Ross & Mirowsky, 2006; 2010). Fewer studies have assessed the relationship between holding a higher status or more cognitively complex occupation and depressive symptoms in later life, and to date findings are mixed, perhaps partly due to methodological differences (e.g. Alvarado et al., 2007; Lindesay et al., 1989). The associations of education, cognitively-stimulating leisure activity, and occupation with depressive thoughts, which are likely to increase the risk of experiencing a depressive episode, have not been investigated previously. Additionally, no study to date has combined these key components of CR to assess the associations between experiences at different life stages and depressive symptoms in older people.

The current evidence indicates that education and cognitively-stimulating leisure activities are more consistently associated with levels of depressive symptoms than occupation. However, the association between occupational level and depressive symptoms in older people has not been investigated to the same extent, and no previous study has

assessed the associations between any of these proxy measures of CR and depressive thoughts. It is important to consider a lifespan perspective as it is probable that, rather than any one of these three components of CR acting in isolation, they interact and accumulate across the lifespan to affect mood and cognition in later life. However, there is no evidence to date as to whether lifetime CR or an individual proxy measure of CR from one life-stage is of greater importance in explaining variance in depressive thoughts or symptoms in older people and whether proximal or distal factors are more relevant.

The paucity of current evidence regarding the association of educational level, occupational complexity and engagement in cognitive activity with depressive thoughts makes it difficult to predict the strength of any associations. As depressive thoughts are highly associated with depression, which is known to be negatively associated with these factors, a negative association can be hypothesised, although it is probable that these negative thoughts are more pervasive and consistent than depressive symptoms or episodes and therefore it is possible that CR exerts a smaller influence on depressive thoughts. It should also be noted that a number of other factors not considered here may influence the level of depressive symptoms in later life, most notably adverse life events, illness, or bereavement (Bruce, 2002; Cole & Dendukuri, 2003). However, the purpose of the current study was to assess the extent to which CR, built across the lifespan, which has previously been associated with better cognitive function and a reduced risk of dementia, is associated with depressive thoughts and symptoms in older people. The study had two specific aims:

1. To assess whether a validated measure of participation in cognitively-stimulating activities across the lifespan, yielding a CR proxy score, accounts for a significant amount of variance in depressive thoughts and symptoms in community-dwelling older people.

2. To investigate whether there was a cumulative effect, through direct or indirect pathways, of the key individual proxy measures of CR, namely education, occupational complexity, and participation in cognitively-stimulating leisure activities at different times across the lifespan, in accounting for variance in depressive thoughts and symptoms in later life.

3.3 Method

3.3.1 Design

This study was a cross-sectional observational study involving self-report questionnaires and a brief cognitive assessment. There was no incentive provided but participants could opt to receive follow-up information regarding the results of the study. Ethical approval for the research was granted by the School of Psychology Ethics and Research Committee at Bangor University (Appendix A).

3.3.2 Participants

The inclusion criteria required that participants should be over 65 years of age and in good health according to self-report, with no self-reported history of neurological disorder, psychosis, or cognitive impairment. An a priori power analysis (Cohen, 1992) indicated that a minimum sample size of 107 would provide sufficient power to detect a medium effect at $\alpha = .05$. Two-hundred and seven healthy, community-dwelling older people were recruited. Trained researchers met with participants at either their own home or the university for a single testing session during which the self-completion questionnaires were completed and the Lifetime of Experiences Questionnaire and neuropsychological assessment were administered. One participant chose to withdraw at the time of testing and is not included in the analyses.

3.3.3 Measures

Demographic and background details recorded were age, gender, and self-reported current illnesses (see Table 3.1).

3.3.3.1 Depressive thoughts assessment

Depressive thoughts were assessed using the Depressive Cognitions Scale (DCS; Zauszniewski, 1995), an 8-item self-rating questionnaire designed to measure thinking styles associated with depression (see Appendix J). Each item reflects one of the key themes occurring in depressive cognitions (helplessness, hopelessness, purposelessness, worthlessness, powerlessness, loneliness, emptiness, and meaninglessness). Scores can range from 0-40, with higher scores indicating a higher level of depressive cognitions. Scores of 0-6 indicate normal levels of depressive cognitions, while scores of 7-40 indicate serious depressive cognitions and a greater risk of depression (Zauszniewski & Bekhet, 2012). The test is valid and reliable, with Cronbach's alpha ranging from .75 to .88 across diverse populations (Zauszniewski & Bekhet, 2011) and of .88 in the current study.

3.3.3.2 Depressive symptoms assessment

Levels of depression were assessed using the Geriatric Depression Scale (15-item short form; GDS-15; Yesavage & Sheikh, 1986). This measure is a screening instrument that assesses depressive symptoms in older people through 15 self-report questions with yes/no responses (see Appendix K). A lower score suggests fewer depressive symptoms. Scores of 0-4 indicate no evidence of depression, scores of 5-9 indicate possible mild depression, and scores of 10-15 indicate possible moderate to severe depression (Alden, Austin, & Sturgeon, 1989). The GDS-15 has good internal consistency, with a Cronbach's alpha of .83 in previous research (Chiang, Green, & Cox, 2009) and .72 in the current study. It has good test-retest reliability and is valid against other clinical measures of depression (Yesavage & Sheikh, 1986).

3.3.3.3 Cognitive reserve assessment

The Lifetime of Experiences Questionnaire (LEQ; Valenzuela & Sachdev, 2007) yields a cognitive lifestyle score that reflects engagement in complex cognitive activity across the lifespan (see Appendix L). It was developed as a means of quantifying the key life experiences thought to contribute to CR, specifically education, occupational complexity and engagement in leisure activities. The LEQ covers three life stages (young adulthood, mid-life,

and later life). The section for each life-stage contains both age-specific and general questions. The scores for the specific questions relating to each life stage are weighted to allow for an equal contribution of experiences from across the lifespan. The general questions are the same for all life-stages and assess the average frequency with which participants engaged in seven activities (e.g. playing a musical instrument, reading, and travel). The scores for these questions are added to the scores for the age-specific questions. Higher scores indicate a more active cognitive lifestyle, considered to be associated with higher CR. The young adulthood score comprises scores regarding the level of education attained prior to the age of 30 and scores for the general questions. The mid-life score comprises scores for occupational complexity and education undertaken between the ages of 30 and 65 (or retirement) and scores for the general questions. Occupation type is scored in five-year increments from the age of 30 to 65; in this study, occupation was rated using Office for National Statistics (2010) classifications. The final occupational complexity score also comprises scores for managerial experience, which is thought to increase the complexity or challenge of the occupation.

The later life section comprises scores for the general questions and for frequency of engagement in activities specific to this time of life (e.g. frequency of charity/volunteer work, membership of social clubs or groups, methods of seeking information about the world, number of different types of material read). Additional scores are given for any formal education or paid work undertaken in later life. Reports on the reliability of the measure suggest that it is variable, with Cronbach's alpha ranging from .43 to .84 (Valenzuela & Sachdev, 2007). This is to be expected given that the measure assesses a number of life experiences that are not necessarily theoretically or conceptually related; indeed, the LEQ is designed to assess a wide variety of unrelated activities to capture the types of activity undertaken by different people. The LEQ has high construct validity, concurrent validity and clinical validity as well as good test-retest reliability (Valenzuela & Sachdev, 2007).

3.3.3.4 Cognitive function assessment

The Addenbrooke's Cognitive Examination III (ACE-III; Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013) was used to characterise the sample in terms of cognitive function. The ACE-III is a cognitive screening tool that assesses five cognitive domains: attention and

orientation, memory, verbal fluency, language, and visuospatial skills. The ACE-III is highly correlated with its previous version, the ACE-R, which incorporated the Mini Mental State Examination (Folstein et al., 1975) and was shown to have high specificity and sensitivity (Hsieh et al., 2013). The maximum total score is 100, with higher scores indicating better performance. In the current study, the ACE-III had good reliability with a Cronbach's alpha of .78.

3.3.4 Data analysis

Data were analysed using SPSS v.20. Pearson's r correlations were calculated to investigate associations between the variables. Simple regression analyses were used to address the first aim of this study and indicate whether CR, as indicated by a validated measure of participation in complex mental activities across the lifespan, accounted for a significant amount of variance in depressive thoughts and symptoms. Details of participants' years of education, cognitively-stimulating activities undertaken in young adulthood and mid-life, the total occupational complexity scores from age 30-65, and later life activity scores were taken from the LEQ to allow for an assessment of the cumulative effects of life experiences. Hierarchical multiple regressions were then conducted to assess whether there was a cumulative effect of activity engagement across the lifespan on the amount of variance in depressive thoughts and depressive symptoms that was accounted for. Taking depressive thoughts and depressive symptoms separately, in each case variables reflecting activity engagement at different stages of the lifespan were entered sequentially into the regression model. Factors reflecting engagement in complex mental activity in young adulthood - years of education and activities - were entered first, occupational complexity scores and activities undertaken in mid-life were added in the second step, and a score for participation in activities in later life was added in the third and final step. Finally, a parsimonious path analysis was conducted using AMOS v.22, with only the significant pathways between variables included, to demonstrate the additive effect of cognitive reserve proxy measures from across the lifespan on depressive thoughts and symptoms. Chi squared, the comparative fit index (CFI), and the root mean square error of approximation (RMSEA) were taken as indices of the fit of the model to the data.

All regression analyses are reported using adjusted R^2. Collinearity statistics were examined to ensure there were no issues of multicollinearity in the hierarchical regressions. There were no significant differences between males and females in either levels of depressive cognitions or self-reported experience of depressive symptoms, and therefore gender was not added as a covariate in the analysis. Similarly, age or cognitive function did not add significantly to any of the regression models and resulted in very minor changes in standardised beta values, and these are therefore not reported in these analyses.

3.4 Results

Participants were 206 community-dwelling older people. Demographic details and the most commonly reported medical conditions are shown in Table 3.1. Scores for all questionnaire measures are shown in Table 3.2. Thirty-eight per cent (n = 78) of participants reported clinical levels of depressive thoughts while 8% (n = 17) reported mild levels of depressive symptoms and 1% (n = 2) reported moderate to severe levels of depressive symptoms. As participants could not be divided into equal-sized groupings by levels of depressive thoughts or symptoms, both depressive thoughts and symptoms were considered as continuous variables, with higher scores on the DCS indicating higher experience of depressive thoughts and higher scores on the GDS indicating greater experience of the symptoms associated with depression.

Table 3.1: Demographic information (n = 206)

	N/Mean	Range
Gender		
Male	68 (33%)	
Female	138 (67%)	
Age	72.79 (6.46)	65-93
Education (years)	14.31 (3.91)	2-27.5
Marital status		
Married	122 (59.2%)	
Never married/divorced	26 (12.6%)	
Widowed	58 (28.2%)	
No. of current illnesses	1.08 (1.03)	0-5
Most common medical conditions reported		
Arthritis/osteoporosis	46 (22.3%)	
High/low blood pressure	38 (18.4%)	
Diabetes	19 (9.2%)	
Heart problem	14 (6.8%)	
Stomach problem	11 (5.3%)	
Thyroid problem	10 (4.9%)	
High cholesterol	7 (3.4%)	

Table 3.2: Means, standard deviations, and range of scores for all measures (N = 206)

	Possible Range	Mean (SD)	Min-Max
Depressive Cognitions (DCS)	0 - 40	5.80 (5.16)	0 - 34
Depressive Symptoms (GDS)	0 - 15	1.63 (2.01)	0 - 12
LEQ (CR) Total	0 - ∞	101.99 (22.43)	44.20 - 159.60
LEQ Young adulthood activities	0 - 35	20.20 (4.62)	7 - 31
LEQ Occupation	0 - ∞	55.25 (22.28)	13 - 95
LEQ Mid-life activities	0 - 35	20.62 (4.12)	8 - 30
LEQ Late-life activities	0 - ∞	45.54 (8.04)	26 - 65
ACE-III	0-100	90.66 (6.62)	63 - 100

Note: DCS, Depressive Cognitions Scale; GDS, Geriatric Depression Scale; LEQ (CR), Lifetime of Experiences Questionnaire (CR); ACE-III, Addenbrooke's Cognitive Examination III; for the LEQ and ACE-III a higher score indicates a better score. For depressive symptoms and depressive cognitions a higher score indicates greater symptoms.
∞ - no max score available

Pearson's r correlations between variables are summarised in Table 3.3. There were significant small to moderate negative correlations between depressive thoughts and the total CR proxy score (LEQ), young adulthood activities, occupational complexity scores, mid-life activities, and later life activities. Depressive symptoms had significant moderate negative correlations with the total CR proxy score (LEQ) and later life activities, and small, but significant, negative correlations with all the remaining individual CR proxy measures and cognitive function. Additionally, there were significant small to moderate positive correlations between all the CR proxy measures, individually and in combination, and cognitive function.

As the independent variables were moderately to strongly correlated, collinearity statistics were examined. Tolerance and the Variance Inflation Factors (VIF) were all within accepted limits indicating that there were no issues of multicollinearity in the following regression analyses (Robinson & Schumacker, 2009).

In relation to the first aim of this study, the total CR proxy score from the LEQ accounted for 4.6% of the variance in depressive thoughts ($F = 10.85$, $p = .001$) with a standardised beta coefficient of -.225, suggesting that higher CR was associated with lower levels of depressive thoughts. The total CR proxy score accounted for 10.2% of the variance in self-reported experience of depressive symptoms ($F = 24.32$, $p < .001$) with a standardised beta coefficient of -.326, suggesting that higher CR was associated with experiencing fewer depressive symptoms.

In relation to the second aim of the study, the hierarchical regressions indicated that as scores for elements of the CR proxy score at each life stage were added to the model a greater amount of variance was explained; however, not all predictors were independently significant (Table 3.4).

With regards to depressive thoughts, in the first step education and young adulthood activities together explained 4.3% of the variance, with only activities an independently significant predictor of depressive thoughts. The addition of mid-life experiences did not result in a significant *F* change but did increase the variance explained to 6.1%; only occupational complexity was an independently significant predictor of depressive thoughts at this stage. The full model accounted for 11.3% of the variance in depressive thoughts ($F = 6.20$, $p < .001$). However, it is probable that most of this variance was accounted for by later life activities, the only independently significant predictor of depressive thoughts in the full model.

Table 3.3: Correlations between depressive symptoms, depressive cognitions, variables representing engagement in cognitive activity across the lifespan, and cognitive function

	DCS	GDS	LEQ (CR)	Education	Young adulthood activities	Occupation	Mid-life activities	Later life activities	Cognition (ACE-III)
DCS	..	.618**	-.225**	-.035	-.226**	-.183**	-.220**	-.338**	.030
GDS		..	-.326**	-.168*	-.183**	-.250**	-.256**	-.393**	-.221**
LEQ (CR)			..	.695**	.687**	.683**	.682**	.715**	.452**
Education				..	.315**	.453**	.213**	.312**	.480**
Young adult activities					..	.266**	.705**	.529**	.152*
Occupation						..	.280**	.366**	.253**
Mid-life activities							..	.656**	.183**
Later life activities								..	.300**
Cognition (ACE-III)									..

*indicates significant at $p < .05$ ** indicates significant at $p < .01$

Note: DCS, Depressive Cognitions Scale; GDS, Geriatric Depression Scale; LEQ (CR), Lifetime of Experiences Questionnaire (CR); ACE-III, Addenbrooke's Cognitive Examination III

Table 3.4: Hierarchical regression analyses for depressive thoughts and depressive symptoms

	Depressive thoughts					Depressive symptoms				
	β	t	ΔR^2	R^2 Change	F change	β	t	ΔR^2	R^2 Change	F change
Step 1			.043**	.052	5.59**			.038**	.047	5.00**
Education	.039	0.55				-.123	-1.70			
Young adult activities	-.228***	-3.30				-.144*	-1.99			
Step 2			.061**	.027	2.91			.085***	.056	6.30**
Education	.102	1.30				-.058	-0.75			
Young adult activities	-.155	-1.57				.038	-0.39			
Occupation	-.161*	-2.06				-.172*	-2.27			
Mid-life activities	-.084	-0.86				-.223*	-2.34			
Step 3			.113***	.056	12.80***			.150***	.068	16.32***
Education	.135	1.77				-.020	-0.28			
Young adult activities	-.117	-1.21				.079	0.84			
Occupation	-.111	-1.44				-.118	-1.59			
Mid-life activities	.066	0.64				-.053	-0.53			
Later life activities	-.318***	-3.58				-.352***	-4.04			

* indicates $p < .05$ ** indicates $p < .01$ *** indicates $p < .001$

With regards to self-reported experience of depressive symptoms, addition of the elements of the CR proxy score for each life stage significantly increased the amount of variance explained by the model. As was the case for depressive thoughts, only young adulthood activities were an independently significant predictor of depressive symptoms in the first step, with 3.8% of variance explained. In the second step, there was an increase to 8.5% in the variance accounted for, with both occupational complexity scores and mid-life activities emerging as independently significant predictors of depressive symptoms. The full model accounted for 15% of the variance in depressive symptoms ($F = 8.22$, $p < .001$). However, as with depressive thoughts, only later life activities were an independently significant predictor of depressive symptoms in the full model. This indicates that greater engagement in activities in later life is associated with less depressive thoughts and symptoms.

Figure 3.1 demonstrates the path analysis model that illustrates the interrelationships between the individual components of CR and the direct and indirect associations with depressive thoughts and symptoms. The model also demonstrates the strong association between depressive thoughts and depressive symptoms. The model indicates that education and activities in early life interact and contribute to occupation and activities in mid-life that in turn interact and contribute to later life activities that have a direct negative effect on depressive thoughts and symptoms. The models for both depressive thoughts and symptoms show good fit to the data (depressive thoughts: $\chi^2 = 11.76$, df = 6, $p = .068$; CFI = .983; RMSEA = .068; depressive symptoms, $\chi^2 = 10.90$, df = 6, $p = .092$; CFI = .986; RMSEA = .063, p = .089).

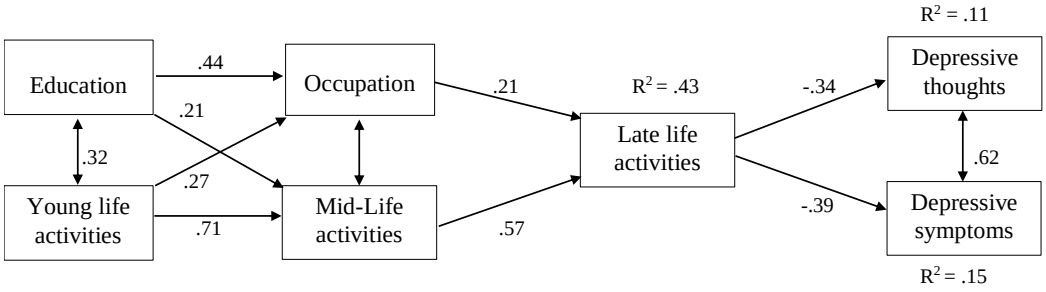


Figure 3.1. Path analysis model illustrating the significant pathways between individual components of the cognitive reserve proxy measure to depressive thoughts and symptoms

3.5 Discussion

The first aim of the current study was to assess whether CR, indicated by a validated measure of participation in cognitively-stimulating activities across the lifespan, accounts for a significant amount of variance in depressive thoughts and symptoms in community-dwelling older people. The results indicate that there was a small negative association of CR with depressive thoughts and a moderate negative association with depressive symptoms, in that higher levels of CR were associated with fewer depressive thoughts and symptoms. The second aim of the current study was to assess whether there was a cumulative effect of the individual components of CR, namely education, occupational complexity, and participation in cognitively-stimulating leisure activities at different times across the lifespan, in accounting for variance in depressive thoughts and symptoms. The results indicate that the percentage of variance accounted for in both thoughts and symptoms increased with the addition of the elements of the CR proxy score for each life stage into the model. However, only engagement in cognitive activities in later life was an independently significant predictor for both depressive thoughts and symptoms in the full model. This suggests that the association between current activity participation, a more proximal life experience, and depressive thoughts and symptoms outweighs any association with earlier, more distal, life experiences. The path analysis model specifies the direct pathways between early life experiences and mid-life experiences, and from mid-life experiences to late-life activities. This contribution of early and mid-life experiences to later activity, and the associations found between early and mid-life experiences and depressive thoughts and symptoms in the correlation analysis and in the regressions before later life activities were added, suggests that these early life experiences do still contribute to depressive thoughts and symptoms in later life. These inter-relationships also demonstrate the importance of considering these associations in the context of a lifespan perspective. Additionally, it is possible that the current level of participation in activities has a reciprocal relationship with the current level of depressive thoughts and symptoms, whereas it is less probable that the associations with earlier life experiences are bi-directional given that these experiences occurred a long time before the assessment of depressive thoughts and symptoms.

The amount of variance in both depressive thoughts and symptoms explained by CR, using the established measure of lifetime cognitive activity, was lower than that explained by summing the amount explained by each of the individual elements that the measure purports

to assess. It is probable that this is an artefact of the scoring methods for this measure, which give an equal weighting to experiences in young, mid, and later life (Valenzuela & Sachdev, 2007); when the experiences were considered individually, later life cognitive activities had the strongest association with depressive thoughts and symptoms. However, for future research that seeks to understand the association of CR, which is thought to be accumulated throughout life (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern 2011; Whalley et al., 2006), with mood and well-being in later life, the total score on this validated measure of lifetime experiences offers a useful index of the key life experiences thought to increase CR.

The results of the current study were similar to those of previous research in that all of the proxy measures of CR were associated with depressive symptoms in later life (e.g. Adams et al,, 2011; Alvarado et al., 2007; Bjelland et al., 2008; Glass et al., 2006; Hong et al., 2009; Jenkins, 2011; Ladin, 2008; Lorant et al., 2003; Murrell et al., 2003; Narushima et al., 2013; Ross & Mirowsky, 2006; 2010). However, several previous studies have noted an independent association of education with depressive symptoms in later life when other life experiences are accounted for (Bjelland et al., 2008; Ladin, 2008; Ross & Mirowsky, 2006), which was not the case in the current study. Education showed a small negative association with depressive symptoms and was not an independently significant predictor of either depressive thoughts or symptoms when other life experiences were considered. This is the first study to date to examine, through a lifespan perspective, how proxy measures of CR from throughout life are related to depressive thoughts and symptoms individually and in combination with each other. The results of the current study suggest that there is an indirect positive pathway between early and mid-life proxy measures of CR and depressive thoughts and symptoms through current life experiences. While this is the first study to focus on the cognitive activities thought to increase CR, it is well established that earlier life experiences such as childhood socioeconomic status have an indirect pathway to later life depression through experiences in mid- and later life (e.g. Bjelland et al., 2008; Blane, Webb, Wahrendorf, Neutveli,, 2012; Murrell et al., 2003; Platts, Webb, Zins, Goldberg, Netuveli, 2015; Ross & Mirowsky, 2010). The suggestion that there may be a common pathological process underlying depression and dementia (e.g. Byers & Yaffe, 2011; Korczyn & Halperin, 2009; Leonard, 2007) could help to explain why indicators of CR are associated with fewer depressive symptoms and thoughts as well as a reduced risk of cognitive decline and dementia. Further research utilising samples with clinically diagnosed depression and

imaging methods to assess structural and functional commonalities is needed to determine whether this is the case.

While the current study suggests that CR, as indicated by lifetime cognitive activity, is associated with less experience of depressive thoughts and symptoms in later life as well as better cognitive health, there are some limitations to be considered. The primary limitation of this study is that participants were required to retrospectively recall their levels of activity, which may not give a fully accurate indication of the activities they participated in. Additionally, those who have more depressive thoughts or symptoms may have a more negative view of their past and may fail to accurately identify all the activities they have undertaken. Future research could adopt longitudinal designs making it possible to utilise objective as well as self-report measures. As participants were drawn from the community and were self-selecting it may not be possible to fully generalise the results to the whole community-dwelling population, as those with lower levels of participation and higher levels of depressive thoughts and symptoms may not have been willing to participate. However, this is a criticism that could be levelled at many studies of community-dwelling older people. The participants in this study had low levels of depressive symptoms and consequently it is not possible to determine whether higher levels of CR are associated with less clinical depression. Future studies could help elucidate the results by assessing the associations in those with clinical depression. However, while depression was rare, depressive thoughts were more frequently observed and these are thought to increase the risk of depression (Beck, 2002; Evans et al., 2005; Zauszniewski, 1997; Zauszniewski & Rong, 1999). The negative associations of these negative thoughts with occupational complexity and engagement in cognitive activities across the lifespan provide evidence that there may be a role for CR in the thought processes associated with depression. It should also be noted that the associations between the key proxy measures of CR and depressive thoughts and symptoms were modest and there may be a number of other factors that play a greater role in the experience of depressive thoughts and symptoms in later life, such as health, bereavement, and low socioeconomic status (Alexopoulos, 2005; Blazer, 2003; Schoevers et al., 2006).

The associations seen in this sample of community-dwelling older people between greater participation in the cognitive activities that increase CR, especially in later life, and fewer depressive thoughts and symptoms suggest that preventive interventions aimed at increasing participation in cognitively-stimulating activity could be beneficial in decreasing

the risk of depression in later life. There are benefits of physical activity interventions on depressive symptoms and clinical depression in older people (Blake, Mo, Malik, & Thomas, 2009); similar intervention strategies could be utilised to investigate the effect of increasing cognitive activity on depression. As it has previously been demonstrated that CR is also of value in maintaining cognitive health in later life, any increase in the activities associated with building CR could have manifold benefits for older people in helping to maintain both cognitive and psychological well-being.

Chapter 4

Does cognitive reserve moderate the association between mood and cognition? A systematic review

Opdebeeck, C., Quinn, C., Nelis, S.M., & Clare, L. (2015). Does cognitive reserve moderate the association between mood and cognition? A systematic review. *Reviews in Clinical Gerontology, 25,* 181-193. doi: 10.1017/S0959259815000155

4.1 Abstract

Background: The evidence regarding the association of depression and anxiety with cognitive function is conflicting, suggesting the involvement of moderating factors. This systematic review aimed to assess whether cognitive reserve (CR) moderates the association of depression and anxiety with cognitive function in older people.

Method: CR was considered in terms of the three key proxy measures – educational level, occupation, and engagement in cognitively-stimulating leisure activities –individually and in combination. The existing literature was systematically searched and studies screened for inclusion.

Results: Sixteen studies representing 37,101 participants were included in the review. Of these, 13 used a measure of education, one used a measure of occupation, two used a measure of participation in cognitively-stimulating activities, and one used a combination of these CR proxy measures. The methodology and findings of the included studies were mixed; however, in general, CR moderated the association between mood and cognition.

Conclusion: There was a greater negative association between mood and cognition in those with low CR than in those with high CR in the majority of the included studies. This demonstrates that having higher levels of CR can indirectly, as well as directly, benefit cognitive function in later life; however, further research utilising multiple proxy measures of CR is required to elucidate the associations.

4.2 Introduction

Investigations of the associations between depression, anxiety and cognitive function have provided conflicting evidence regarding the direction and strength of these relationships. Most studies have found that greater levels of depression and/or anxiety are associated with poorer cognitive performance and a greater risk of cognitive decline, mild cognitive impairment, and dementia (Beaudreau & O'Hara, 2008; 2009; Diniz et al., 2013; Reppermund et al., 2011; Steffens et al., 2014; Yates et al., 2013). However, other studies have found no association between depression or anxiety and cognitive function (Becker et al., 2009; de Bruijn et al., 2014). While differences in the methods of assessing mood and cognition may account for some of the variation, it is possible that other psychosocial factors moderate the association between mood and cognition.

Several previous reviews have assessed the associations between cognition and either depression or anxiety in older people (e.g. Beaudreau & O'Hara, 2008; Kindermann & Brown, 1997). While overall these reviews have reported that those with depression or anxiety have poorer cognitive performance than those without a mood disorder, the individual studies included in the reviews have shown mixed results. For instance, in the 40 studies included in the Kindermann and Brown (1997) review, the effect of depression on cognition ranged from a strong negative effect to a moderate positive effect. Examination of potential moderators of the association indicated a significant difference by education; when the depressed and non-depressed groups were well-matched on education there was a weaker negative effect of depression on cognition. This may suggest that educational level, a commonly used proxy measure of cognitive reserve (CR), plays a role in the association between depression and cognition.

CR is a theoretical construct and as such cannot be directly measured; therefore, it is frequently assessed in terms of the cognitive activities thought to increase it, most commonly educational level, complex occupational activity, and engagement in cognitive activities. Higher levels of these proxy measures of CR are associated with better cognitive function in community-dwelling older people, people with Parkinson's disease, HIV, multiple sclerosis, and traumatic brain injury, and with a reduced risk of cognitive decline and dementia (Benedict et al., 2010; Foley et al., 2012; Hindle et al., 2014: Kesler, Adams, Blasey, & Bigler, 2003; Valenzuela & Sachdev, 2006a; 2006b). In addition, greater educational level

and participation in cognitively-stimulating leisure activities in later life are associated with less risk of experiencing depression and lower scores on measures of depressive symptoms (Adams et al., 2011; Bjelland et al., 2008; Glass et al., 2006; Hong et al., 2009; Jenkins, 2011; Ladin, 2008; Lorant et al., 2003; Murrell et al., 2003; Narushima et al., 2013; Ross & Mirowsky, 2006; 2010). A number of studies have noted that mood disorders, most commonly depression, are associated with reduced brain volume and increased hippocampal atrophy (Ballmaier et al., 2004; Elbejjani et al., 2015; Lampe et al., 2003), both of which are associated in turn with poorer cognitive performance in older people (e.g. Sandu et al., 2014). This evidence supports the proposition that depression and cognitive impairment share an underlying mechanism (Byers & Yaffe, 2011; Korczyn & Halperin, 2009; Leonard, 2007). As CR is thought to help maintain cognitive function through increasing resistance to neuropathology, it may be reasonable to hypothesise that proxy measures of CR may also account for some of the variance in findings regarding the associations between mood and cognition, playing a moderating role.

To date, however, evidence about the possible moderating role of CR in the association between mood and cognition has been conflicting. In several studies, negative associations between mood and cognition have been found in those with lower but not higher levels of CR (e.g. Pálsson et al., 1999; 2001). In others there was a negative mood-cognition association in those with higher but not lower levels of CR (e.g. O'Shea et al., 2015), and in yet other studies there was no moderating effect of CR (e.g. Bhalla et al., 2005). Given these apparent variations in the available evidence, we aimed to systematically review the existing studies to try to establish whether CR, indicated by educational level, occupational complexity, and/or engagement in cognitively-stimulating leisure activities, acts as a moderator in the association between mood and cognition in older people. The review was limited to studies that investigated whether CR, assessed by proxy measures, moderated the association between mood and cognitive function, impairment, or decline in older people without dementia or other neurodegenerative conditions; including specific clinical groups, such as those with dementia, would have risked confounding the results.

4.3 Method

4.3.1 Literature search strategy

In order to identify studies assessing whether CR moderates the association between mood and cognition in later life, a search was conducted of the electronic databases ScienceDirect, PubMed, PsycInfo, and CINAHL on 19/03/2015. Each database was searched for the terms (a) 'cognitive OR cognition' AND (b) 'depress* OR mood OR anxiety' AND (c) '"cognitive reserve" OR "brain reserve" OR educat* OR occupation* OR activ* OR leisure' AND (d) 'old* OR later life OR elder* OR aging OR ageing' in the title, abstract, or keywords. The reference sections of included studies were searched for additional papers not identified in the initial search.

4.3.2 Inclusion and exclusion criteria

Studies were included in this systematic review if (a) at least 80% of participants were aged over 60 or the information for those aged over 60 was reported separately, (b) at least 80% of participants were community-dwelling older people, (c) a proxy measure of CR, specifically educational level, occupational status, cognitively-stimulating leisure activities, or a combination of these was used, (d) a standardised measure of depression or level of self-reported depressive symptoms was used, and (e) a cross-sectional or longitudinal outcome measure of cognitive function was reported.

Studies were excluded if (a) more than 10% of the sample consisted of people with a neurological disorder or a disorder which may affect cognitive functioning (e.g. dementia, multiple sclerosis, Parkinson's disease, HIV, traumatic brain injury, or stroke), (b) the study was an intervention or randomised controlled trial, and (c) the authors reported a biological or pathological proxy measure or outcome only.

4.3.3 Procedure

A summary of the procedure for selecting studies for inclusion can be seen in Figure 4.1. The searches identified 3,877 unique titles that were evaluated in relation to the inclusion criteria, and those clearly unrelated to later life (e.g. child, animal, or autism studies) were excluded. The remainder of the titles (k = 2,625) were independently screened by two reviewers. The two reviewers achieved 98% agreement on inclusion/exclusion; where there was disagreement the title was retained for abstract screening. The primary reasons for exclusion after title screening were that the study focused solely on children, adolescents, animals, or clinical populations. The lead author and second reviewer independently screened the abstracts of the remaining articles. The reviewers achieved 92% agreement on the inclusion/exclusion of articles. Where agreement could not be reached, the full text was retrieved for screening. The primary reasons for exclusion after abstract screening were that the study did not utilise a measure of CR, depression or anxiety, or cognition.

Full texts were retrieved for the remaining 130 articles and the method and results sections were evaluated against the inclusion criteria. This resulted in 15 articles that satisfied the inclusion criteria. The articles rejected at this stage were primarily rejected because more than 20% of the population was from a clinical sample or aged under 60 (k = 13), there was no proxy measure of CR or mood measure (k = 10), there was no cognition measure (k = 19), or the study did not consider whether a proxy measure of CR moderated the association between mood and cognition (k = 69). In the majority of studies that did not assess any moderation effect analyses were adjusted for the CR proxy measure or mood measure only. Searching the reference sections of the included studies resulted in the inclusion of one additional study.

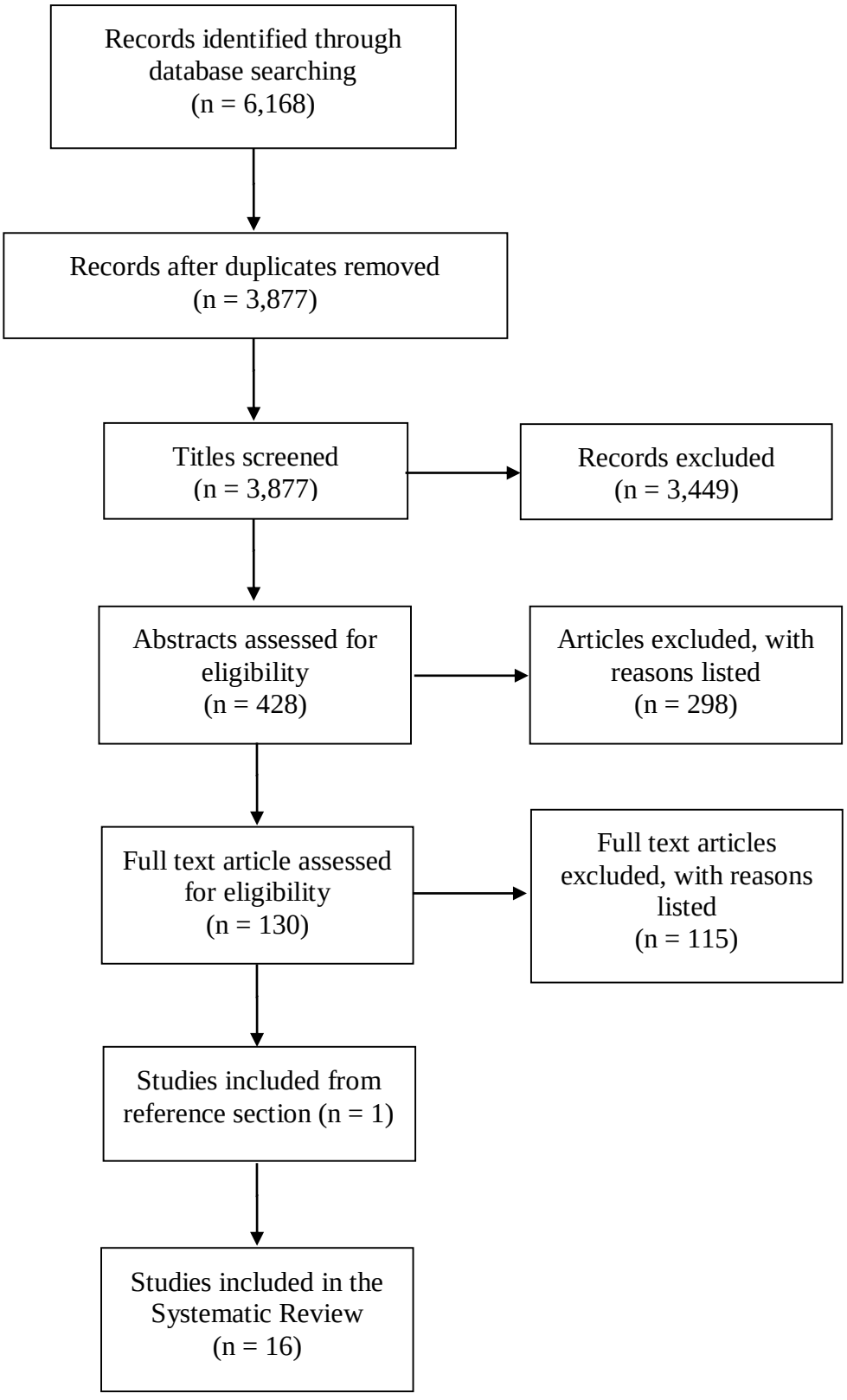


Figure 4.1. Study selection process

4.4 Results

The search identified 16 studies with a total of 37,101 unique participants. The vast majority of the studies assessed whether educational level moderated the association between depression and cognitive function or decline (k = 12), with one study examining whether educational level moderated the association between anxiety and cognition (Potvin et al., 2013). Only one study considered whether occupation, using an occupation-based measure of social class, acted as a moderator of the depression-cognition association (Gale, Allerhand, & Deary, 2012). Two studies considered whether religious attendance, suggested by the authors of both studies to be a cognitive activity that contributes to CR, moderated the depression-cognition association (Corsentino, Collins, Sachs-Ericsson, & Blazer, 2009; Reyes-Ortiz et al., 2008). Only one study combined the three key indicators of CR, education, occupation, and cognitive activity, and assessed whether the association of depressive symptoms and anxiety with cognition differed in those with low and high CR (Opdebeeck et al., 2015a, this is the published version of Chapter 5 of this thesis). Table 4.1 provides details of the sample, proxy measure of CR, mood and cognitive function measures, and outcome for each of the included studies. The majority of the studies considered only educational level as a potential moderator, and only two studies assessed whether the proxy measure of CR moderated the association between anxiety and cognition. The following results are grouped by whether the proxy measures of CR moderated the association between mood and cognition or not, with those studies which found no moderation effect discussed first.

Table 4.1: Studies included in the systematic review, with demographic details, cognitive reserve proxy, mood and cognitive function measures, and outcome details, grouped by reported moderation effect found

Author	Study aim	Participants and demographic details	CR, mood, and cognition measures	Outcome
Studies in which cognitive reserve was not a moderator of the mood-cognition association				
Bhalla et al. (2005)	To assess whether educational level influences the association between cognition and depression	159 aged 59+ 115 with depression 44 without	Education grouped as low and high Depression – none or clinically diagnosed Executive function, memory, and language ability	There was no moderation effect of education on the depression-cognition association.
Wilson et al. (2004)	To assess whether depressive symptoms predict cognitive decline (Interaction secondary)	6,158 at baseline aged 65-101 CHAP	Education in years Depressive symptoms – 10-item CES-D General cognitive function	There was no moderation effect of education on the depression-cognition association.
Studies in which cognitive reserve was a beneficial moderator of the mood-cognition association				
Fuhrer et al. (1992)	To assess factors associated with the co-occurrence of depression and cognitive impairment	2,792 aged 65+ PAQUID	Education grouped as no school/primary without diploma to baccalaureate or university Depression - CES-D (cut-off = 17 for males and 23 for females)	Lower education was associated with a greater likelihood of experiencing cognitive impairment and depression than depression alone in women of

			Cognitive impairment - scores of <24 on MMSE	all ages and men aged 75-84 but not in men aged 65-74 or 85+
Opdebeeck et al. (2015a; Chapter 5 of the thesis)	To assess whether cognitive reserve moderates the association between mood and cognition	236 aged 60+ (mean age = 70.86)	Education, occupation, and cognitive activity in combination (Lifetime of Experiences Questionnaire) Depressive symptoms and anxiety - HADS Memory and verbal fluency	Higher cognitive reserve positively moderated the association between depression and cognitive performance on all tasks and anxiety and cognitive performance on the memory tasks
Pálsson et al. (1999)	To assess the associations between depression, cognition, and brain atrophy (Interaction secondary)	268 aged 65+ 59 with depression 209 without depression	Education dichotomised into 6 years or less and >6 years Depression – none, major, or dysthymic disorder General cognitive function	Higher educational level positively moderated the association between depression and cognitive performance on the MMSE
Pálsson et al. (2001)	To assess the associations between depression, cognition, and brain atrophy in women (Interaction secondary)	421 women aged 70-74 206 without, 159 with previous depression, and	Education dichotomised into 6 years or less and >6 years Depression – none, major, or dysthymic disorder General cognitive function	Higher educational level positively moderated the association between depression and cognitive performance on the MMSE

		56 with current major depression or dysthymia		
Reyes-Ortiz et al. (2008)	To assess whether the association between depressive symptoms and cognition is modified by church attendance	2,759 Mexican Americans (mean age = 72.7)	Church attendance dichotomised into frequent attenders and infrequent attenders Depression - CES-D (cut-off score = 16) General cognitive function	Frequent attendance positively moderated the negative association between mood and cognition
Wight et al. (2002)	To assess the association between educational attainment and training on cognition (Interaction secondary)	1,839 men aged 69-83	Education in years Depressive symptoms – CES-D General cognitive function	Education positively moderated the association between depressive symptoms and cognition
Studies in which cognitive reserve was a negative moderator of the mood-cognition association				
Geerlings et al. (2000)	To assess whether depression is associated with risk of cognitive decline and depression (Interaction secondary)	3,147 aged 65+ AMSTEL 2,399 aged 55+ LASA	Education in years and dichotomised into lower and higher at 8 years in both samples AMSTEL – Depression - GMS-AGECAT LASA – Depression - CES-D	In both samples educational level negatively moderated the depression-cognition association. Depression increased the risk of AD and cognitive decline in

			AMSTEL – outcome of clinical Alzheimer's disease LASA – Cognitive decline (MMSE decline of 3+)	those with high but not low education
O'Shea et al. (2015)	To assess whether cognitive reserve moderates the association between depressive symptoms and cognition	3,484 (mean age = 76.07) WHICAP	Education in years Depressive symptoms - 10-item CES-D Memory, executive function, visuospatial ability and language	Higher educational level negatively moderated the depression-cognition association
Santos et al. (2014)	To assess the association between depressive symptoms and cognitive and the role of covariates	1,051 aged 50+	Education grouped as <4 years, 4 years, and >5 years Depressive symptoms – GDS Cognition categorised into general and executive function, processing speed, and memory	Higher educational level negatively moderated the depression-cognition association in the general executive and memory domains and mixed moderation effects on processing speed
Studies with mixed moderation effects				
Avila et al. (2009)	To assess the influence of education and depression on cognition	110 aged 60+ 59 with depression 51 without	Education dichotomised into low and high Depression – none, dysthymic, or major	Higher education positively moderated the association between depression and

			General cognitive function, processing speed, executive function, and memory	cognitive performance on some but not all tasks
Corsentino et al. (2009)	To assess the effect of gender and depressive symptoms on the association between religious attendance and cognitive decline	2,792 aged 65+ PAQUID	Religious attendance dichotomised into frequent and infrequent attenders Depression - modified version of the CES-D General cognitive function	Frequent attendance positively moderated the negative association between mood and cognition in females but not males.
Gale et al. (2012)	To assess the association between depressive symptoms and cognition and the role of confounds	8,611 aged 50+ ELSA – those aged 60-80 and 80-90 were analysed separately	Age at which participants left education and occupation grouped from unskilled manual to professional Depression - 8-item CES-D (cut-off score of 4) General cognitive function	Occupation positively moderated the association between depression and cognitive performance in the 80-90 year old age group only. There was no moderation effect of education on the depression cognition association.
Moraes et al. (2010)	To assess the association between health and demographic variables and cognition by level of schooling	2,712 grouped as those under 75 and those aged 75+	Education grouped as no formal education, 1-4 years, and 5 years+ Depression – 10-item measure similar to the GDS General cognitive function	Depression entered alongside 15 other covariates. Depression was a significant predictor of cognition in those aged < 75

				with no or 1-4 years of schooling only.
Potvin et al. (2013)	To assess the relationship between state anxiety and performance on cognition (Interaction secondary)	955 aged 65+	Education grouped as no diploma, primary diploma, or secondary/university Anxiety - state anxiety subscale of the French version of the State-Trait Anxiety Inventory Y-version General cognitive function, semantic verbal fluency, short-term visual memory, information processing, episodic memory, working memory	Short-term memory performance increased with moderate and high levels of anxiety in comparison to no anxiety in those with low education but not high education. There were no significant moderation effect of education in the other domains

Note: CHAP, Chicago Health and Aging Project; CES-D, Centre for Epidemiological Studies Depression Scale; PAQUID, Personnes Agées Quid; MMSE, Mini Mental State Exam; HADS, Hospital Anxiety and Depression Scale; AMSTEL, Amsterdam Study of the Elderly; LASA, Longitudinal Aging Study Amsterdam; GMS-AGECAT, Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy; GDS, Geriatric Depression Scale; WHICAP, Washington Heights/Hamilton Heights Inwood Columbia Aging Project; ELSA, English Longitudinal Study of Aging.

4.4.1 Studies in which cognitive reserve was not a moderator of the mood-cognition association

Two studies reported that although there was a main effect of depression on cognitive performance there was no difference in the associations between depression and cognition according to the educational level of participants across all the cognitive function measures employed (Bhalla et al., 2005; Wilson et al., 2004). In Bhalla and colleagues (2005), the level of education was relatively homogenous and there were few participants with lower levels of education; this lack of variability could account for why there was no moderation effect of educational level on the association between depression and cognitive function. However, Wilson and colleagues (2004) included participants with a wide range of education and still noted no moderation effect; indeed, these two studies employed very different methodologies, as can be seen from Table 4.1. Bhalla and colleagues (2005) suggested that a possible explanation for these results is that lowered mood might overwrite the protective effect of education on cognitive performance. However, this was not the case in the following set of studies.

4.4.2 Studies in which cognitive reserve was a moderator of the mood-cognition association

Nine studies found that proxy measures of CR moderated the association between mood and cognition in older people across different cognitive function measures. In six of these nine studies, the negative association between mood and cognitive function was stronger in those with lower than higher levels of CR. Of these six studies, four utilised educational level (Fuhrer, Antonucci, & Dartigues, 1992; Pálsson et al., 1999; Pálsson et al., 2001; Wight et al., 2002), one considered religious attendance as a cognitively-stimulating leisure activity (Reyes-Ortiz et al. 2008), and one combined educational level, occupational complexity, and engagement in cognitive leisure activities to provide an overall indicator of CR (Opdebeeck et al., 2015a). In all of these studies, having a higher level of CR, indicated by one or a combination of the three key proxy measures, appeared to be somewhat protective against the observed negative main effect of clinical depression or depressive symptoms on cognitive function. In addition, in the one study that included a measure of anxiety, higher levels of anxiety were associated with poorer performance on memory tasks in those with lower levels

but not higher levels of CR (Opdebeeck et al., 2015a). Three of these studies made some effort to match the CR groups for levels of depression (Opdebeeck et al., 2015a; Pálsson et al., 1999; 2001). This could be an important factor in explaining differences in the observed associations given that previous research has suggested that higher levels of education, occupational complexity, and engagement in cognitive activities are associated with reduced risk of experiencing clinical depression and lower scores on measures of depressive symptoms.

In contrast, the three other studies that observed that a proxy measure of CR acted as a moderator of the association between mood and cognitive function found the opposite effect (Geerlings et al., 2000; O'Shea et al., 2015; Santos et al., 2014). In these three studies, higher levels of depressive symptoms had a stronger association with poorer cognitive function or greater cognitive decline in those with higher educational level than in those with lower educational level. O'Shea and colleagues suggested that these results could be due to the higher level of cognition seen in those with higher education, indicating that those individuals have more to lose whereas those with lower education were already performing at a lower level regardless of depressive symptoms. However, this explanation does not correspond with results from the six studies that noted a stronger negative association in those with lower levels of the proxy measures of CR than those with higher levels. All of these studies varied considerably in their methodology (see Table 4.1), making it difficult to account for the opposing results.

4.4.3 Studies with mixed moderation effects

Five studies reported that proxy measures of CR moderated the association between mood and cognition in some but not all of the groups or cognitive domains assessed (Avila et al., 2009; Corsentino et al., 2009; Gale et al., 2012; Moraes, Pinto, Lopes, Litvoc, & Bottino, 2010; Potvin et al., 2013). In all but one of these studies, depressive symptoms had a stronger association with cognitive function in those with higher than lower levels of the proxy measure of CR assessed in at least one age or gender group or for one of the cognitive measures assessed (see Table 4.1; Avila et al., 2009; Corsentino et al., 2009; Gale et al., 2012; Moraes et al., 2010). These studies varied considerably in their methodology. For instance, Avila and colleagues (2009) assessed whether there was a significant interaction

between education and depressive symptoms on 16 different cognitive measures across multiple domains while Corsentino and colleagues (2009) focused on differences in the associations by age group. Moraes and colleagues (2010) grouped participants by age and educational level and regressed depression alongside 15 other covariates on cognitive function, making it difficult to disentangle the results. One study reported mixed results when considering the associations with anxiety, with better performance on one of the seven cognitive measures employed in those with moderate and high levels of anxiety in comparison to those with no anxiety in the lower but not in the higher education group (Potvin et al., 2013). Avila and colleagues (2009) suggest the mixed moderation effects may be due to differences in the domains assessed and measures used. Those instruments wherein education moderated the association might be more sensitive to the effects of education; this could explain why there was an interaction on some measures and not others. However, this explanation does not account for the differences between groups of participants or, why some studies report a main effect of education but not an interaction. The variation in the methodology of these studies makes it difficult to form a cohesive picture of the results; however, the majority of the significant findings indicated that depression has a stronger negative association with cognition in those with lower levels than in those with higher levels of education, occupation based social class, or attendance at religious activities.

4.5 Discussion

This study is the first to systematically review the evidence as to whether proxy measures of CR moderate the association between depression or anxiety and cognitive function in older people. The 16 studies identified by this review were disparate in their methodology and findings. Of the 15 studies that assessed whether individual or combined proxy measures of CR influence the association between clinical levels of depression or low levels of depressive symptoms and cognition, most suggested that CR is beneficial. People with higher levels of CR, indicated by educational level, more frequent religious attendance, or a combination of the three most common proxy measures, had better cognitive functioning regardless of depression level than those with lower CR. In addition, in several of these studies, higher levels of depression were significantly associated with poorer cognitive function in those with lower but not higher levels of CR. This evidence suggests that CR may go at least some way towards moderating the negative association between depression and cognition. However,

opposing findings were reported by five studies, ranging from no association to an association between depression and cognitive function in those with higher CR only. Additionally, in four other studies, the proxy measures of CR moderated the association between mood and cognition positively for some cognitive measures or some participant groups but not for all. The following sections will consider possible explanations for the disparate findings, discuss limitations of the review, and draw conclusions from the available evidence.

There was significant variation across studies in the proxy measures of CR, the measures of mood employed, and the methods of assessing cognitive function. We will address the variance in the methods employed to assess each of these complex and multi-faceted constructs in turn. The vast majority of studies considered only one commonly-used proxy measure of CR, with educational level the most frequent proxy measure employed. The average levels of education of participants in the individual studies ranged from very low levels (e.g. Avila et al., 2009) to very high levels (e.g. Bhalla et al., 2005) with no trend for similar education levels to show the same direction of moderation of the association between mood and cognitive function. Only one study considered a measure of occupational status as an independent moderator, and the only cognitive activity measure employed was religious attendance, utilised by two studies. These three studies all found that these measures were beneficial moderators of the association between depressive symptoms and cognitive function; however, the small number of studies makes it difficult to draw definitive conclusions about these specific proxy measures of CR. Only one study considered CR in terms of a proxy measure that combines educational level, occupational complexity, and engagement in cognitively-stimulating activities across the lifespan. However, it has recently been suggested that CR is not static but rather results from a lifetime of exposure to cognitively-stimulating experiences (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern 2011; Whalley et al., 2006). To fully assess whether CR moderates the association between mood and cognitive function it would seem prudent to include measures that evaluate a lifetime of experiences rather than assessing education, occupation, or engagement in cognitive activities individually.

The measures of depression also varied considerably; most notably some measures considered the differences between those with clinically diagnosed major depression and

those with no depression while others considered depressive symptoms on a continuous scale designed to assess the level of symptoms, which does not provide a clinical diagnosis. Measures of depressive symptoms are very different from clinically-diagnosed depression; clinical depression requiring intervention is likely to exert a much stronger influence on functioning than mild levels of depressive symptoms in community-dwelling older people. As such, we could reasonably have expected differences in the moderation effect of proxy measures of CR on the association of clinical depression with cognition and of depressive symptoms with cognition. However, there was no trend for proxy measures of CR to show the same direction of moderation on the association between either type of depression measurement and cognitive function.

The methods of assessing cognitive function also varied considerably, from brief tests of general cognition such as the Mini-Mental State Examination (Folstein et al., 1975) and more in depth neuropsychological assessment across multiple cognitive domains to measures of cognitive decline over time. Education has been differentially associated with different cognitive domains in several previous studies (e.g. Davey et al., 2013; Leibovici, Ritchie, Ledésert, & Touchon, 1996; Leung et al., 2010; Mueller et al., 2013; Zahodne, Nowinski, Gershon, & Manly, 2014). Additionally, in a recent meta-analysis each of the three proxy measures of CR varied in its associations with different domains of cognitive functioning (Opdebeeck, Martyr, & Clare, 2015b, this is the published version of Chapter 2 of this thesis). However, this cannot explain the variations observed in this review, as there was no consistency in moderation effects according to cognitive domain assessed, or in those studies that considered general cognitive function measures only. Without any consistency in the samples or methods of studies which showed a beneficial moderation effect of higher CR levels on the negative association between mood and cognition it is difficult to say why some studies report this finding while others found no moderation effect or indeed an opposing effect. However, as the majority of studies showed a beneficial moderation effect it seems reasonable to tentatively conclude that in general having higher levels of CR may reduce the negative effects that depression exerts on cognitive function.

There may, however, be several possible confounds which result in the disparities between the moderation effects noted in the studies. The most notable of these may be cohort affects. There were significant cohort differences, including generational, geographical, and racial differences. For instance, regarding geographical difference, four of the six studies that

reported a beneficial moderation effect of CR on the association between mood and cognition were conducted in Europe. In contrast, both studies in which there was no moderation effect were conducted in the US. The aims of the studies also varied, with some setting out to specifically assess whether proxy measures of CR moderate the association between mood and cognitive function whereas for others the moderation effect analysis was secondary to the main aim of the study (see Table 4.1). However, studies which considered the moderation effect as the main aim of the study are represented among those reporting each type of effect or no effect, as are studies in which assessing the moderation effect was secondary to the main aim. In sum, while there were a number of possible confounds, ranging from methodological differences to differences in study aims, none of these appear to relate to specific types of moderation effect.

Due to the disparate methodology used in the studies included in this review it was not possible to carry out a meta-analysis that can avoid the bias associated with narrative reviews (Lyman & Kuderer, 2005). However, meta-analytic methods ignore differences across studies (Borenstein et al., 2009); given the large variations seen in the relatively small number of studies available on this topic, a narrative systematic review was in any case deemed more appropriate. One of the major limitations of this review is our inability to address whether proxy measures of CR moderate the association between anxiety and cognitive function. This was unavoidable as only two studies assessed whether the association between anxiety and cognition differed according to level of CR, suggesting that this area has been under-researched to date. Given the heterogeneity of the methods employed and the results of these two studies, the question of whether proxy measures of CR, individually or in combination, moderate the association between anxiety and cognitive function remains unanswered.

CR appears to moderate the negative effect that many neurological conditions and injuries have on cognitive function (Benedict et al., 2010; Foley et al., 2012; Hindle et al., 2014: Kesler et al., 2003) and perhaps further investigation may provide greater support for the supposition that it can also moderate the negative effect that mood disorders may have on cognition. If this is the case, it provides extra incentive to encourage people to engage in the activities that are associated with higher levels of CR across the lifespan. It is not possible to give a definitive answer to the research question posed by this review until more studies, using consistent methods to assess CR across varied samples of older people, have

investigated whether CR moderates the association between mood and cognitive function in later life. However, the current evidence assessed in this review suggests that we can tentatively conclude that CR is a beneficial moderator of the negative associations between mood and cognitive function.

Chapter 5

How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life?

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (2015). How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life? *Aging & Mental Health, 19,* 705-712. doi: 10.1080/13607863.2014.962005

5.1 Abstract

Background: Higher levels of cognitive reserve (CR) are associated with better cognitive function in later life. In contrast, depressive symptoms, anxiety, and rumination are associated with diminished cognitive function. There has been limited research to date examining the influence of CR on the relationship between mood and cognitive function, and results are inconsistent. The aim of this study was to investigate the role a comprehensive indicator of CR plays in the relationships between mood, rumination, and cognitive function in later life.

Method: Two hundred and thirty-six healthy people aged 60+ completed measures of CR, depression, anxiety, rumination, recall, and verbal fluency. Participants were dichotomised at the median into those with lower and higher levels of CR.

Results: CR, mood, and rumination together accounted for between 13% and 15.6% of the variance in scores on the cognitive tasks in the sample as a whole. Mood and rumination explained a significant amount of variance in cognitive test scores in those with lower levels of CR, but not in those with higher levels of CR. The way in which mood and rumination are related to cognitive function differs depending on the individual's level of CR.

Conclusion: These results support the view that it is important to continue to build on CR as people move into later life in order to maintain cognitive health, both directly and in the event of lowered mood.

5.2 Introduction

Improvements in health care, standards of living, and nutrition mean that people are living longer lives than ever before, and the world's ageing population is increasing at a rapid rate. It is expected that the percentage of the population over 65 in Europe will increase from 17.1% in 2008 to 30% in 2030 (Giannakouris, 2010). With age there is often a decrease in cognitive ability even in those older people deemed healthy (Salthouse, 2009; Singh-Manoux et al., 2011); this decline can have wide-ranging implications for the quality of life of the individual concerned, his or her family, society, and the economy (Comas-Herrera, Wittenberg, Pickard, & Knapp, 2007; Gaugler, Duval, Anderson, & Kane, 2007). This makes the study of modifiable factors related to cognition in later life an important area of research (Stern, 2009; Tucker & Stern, 2011).

Cognitive reserve (CR), thought to be a result of engagement in cognitively-stimulating experiences throughout the lifespan, is related to variability in cognitive function in later life, and can help individuals cope more effectively with the brain changes frequently seen in normal ageing (e.g. Richards & Deary, 2005; Stern, 2009; Whalley et al., 2006). It has been related to better cognitive function in healthy older people in both longitudinal and cross-sectional research (Jefferson et al., 2011; Nucci et al., 2011; Valenzuela & Sachdev, 2006a). Whereas greater CR is related to better cognitive function, depression, anxiety and rumination are related to reduced cognitive ability in later life (e.g. Bierman et al., 2005; Davis & Nolen-Hoeksema, 2000; Reppermund et al., 2011). To date research addressing the question of whether higher CR may reduce the influence of depressive symptoms and related psychological factors on cognitive function in later life remains limited, and findings are inconsistent.

CR is most commonly indexed by educational level, occupational complexity, engagement in cognitively-stimulating leisure activities, or a combination of all three (Stern, 2009). Higher educational level, more cognitively complex occupations, and participation in cognitively-stimulating leisure activities have repeatedly been associated with better performance on measures of cognitive function (Angel et al., 2010; Fritsch et al., 2007; Jefferson et al., 2011; Kaplan et al., 2009; Potter, Helms, & Plassman, 2008; R.S. Wilson et al., 2003a). A number of recent studies have created measures which combine these experiences to give an indication of an individual's level of CR and noted that higher scores

on these measures are related to better cognitive function and less cognitive decline (Nucci et al., 2011; Valenzuela & Sachdev, 2007). While CR has been shown to moderate the association between pathology and cognitive function, studies to date have only considered the role that a single proxy of CR, such as educational level, may play in the association between mood and cognitive function.

A negative association between depressive symptoms and cognitive function in healthy older people is well-established (e.g. Reppermund et al., 2011; Rosenberg et al., 2010). Depression has also been associated with an increased risk of mild cognitive impairment and dementia (e.g. Dotson et al., 2010; Goveas, Espeland, Woods, Wassertheil-Smoller, & Kotchen, 2011; Yates et al., 2013). However, other studies have found no effect of mood on cognitive function (e.g. Becker et al., 2009; Kizilbash et al., 2002), raising the question of what may moderate the association and account for the variation in findings. Those studies that have examined the relationship between indicators of CR, mood, and cognitive function have focused solely on one single proxy of CR, either education or engagement in cognitively-stimulating activities and have yielded mixed results. For example, one study reported a relationship between depression and risk of Alzheimer's disease only in those with higher levels of education (Geerlings et al., 2000); while others have found that there was an association between depression and cognitive function in those with a lower educational level only (Pálsson et al., 1999; 2001). Yet other studies have reported no influence of education or engagement in cognitively-stimulating activities on the relationship between depression and cognitive function (Bhalla et al., 2005; Wilson et al., 2004). No study to date has used a combined measure of CR, which might provide a more comprehensive index.

Older people with higher levels of anxiety tend to score lower on cognitive function assessments (Bierman, et al., 2005; Gallacher et al., 2009). Additionally, Porter and colleagues (2003) suggested that anxiety impacts on performance in cognitive assessments, resulting in an overestimation of the severity of any cognitive decline. Anxiety may occur without depression but it frequently occurs alongside depression in older people (Beekman et al., 2000; Kvaal et al., 2008). Only one previous study has assessed whether CR, considered in terms of educational level, moderates the association between anxiety and cognitive function (Potvin et al., 2013). In this study, higher levels of anxiety were associated with better memory performance in those with low levels of education but not in those with high

levels of education, with no other effects of education on the association between anxiety and cognitive function. This would appear contrary to evidence that suggests that anxiety has a negative effect on cognitive function, which could be explained by the generally low levels of anxiety in this sample. In addition, Potvin and colleagues did not examine whether any of the other commonly-used proxy measures of CR moderated the association between anxiety and cognitive function.

Rumination or ruminative thinking is commonly associated with both depression and anxiety (Garnefski & Kraaij, 2006; Nolen-Hoeksema, 2000; Thomsen, 2006; Watkins, 2008) and has been specifically linked with late-life depression (Kraaij et al., 2002). Rumination is a maladaptive thought process that has been related to deficits in cognitive function in that ruminators tend to perform worse on tests of executive function than non-ruminators (Davis & Nolen-Hoeksema, 2000), and when rumination occurs alongside depressive symptoms cognitive deficits increase (Lyubomirsky et al., 2003). Whether levels of CR play any role in the relationships that have been previously observed between anxiety, rumination and cognitive function remains to be established.

As depression, anxiety, rumination, and CR are all potentially modifiable factors, understanding more about their impact and the relationships between them may contribute to knowledge about maintenance of cognitive health in later life. The specific aims of this study were:

1. To assess whether CR, depressive symptoms, anxiety, and rumination explained a significant amount of variance in cognitive function in a sample of community-dwelling older people.

2. To investigate whether the relationships between depressive symptoms, anxiety, rumination and cognitive function differed between people with low and high levels of CR in later life.

5.3 Method

5.3.1 Design

This study was a cross-sectional questionnaire survey with a brief neuropsychological assessment. There was no incentive provided but participants could opt to receive follow-up information regarding the results of the study. Ethical approval for the research was granted by the School of Psychology Ethics and Research Committee at Bangor University (Appendix A).

5.3.2 Participants

The study sample consisted of 236 participants aged over 60. An a priori power analysis using the procedure outlined by Cohen (1992) was conducted to estimate the sample size required to detect a medium effect at $\alpha = .05$. This indicated that a minimum sample size of 214 would provide sufficient power when the sample was divided into two groups consisting of those with lower and higher CR. The inclusion criteria for this study required that participants should be over 60 years of age and in good health according to self-report, with no history of neurological disorder, depression, psychosis, or cognitive impairment. Trained researchers met with participants at either their own home or the university for a single testing session during which the self-completion questionnaires were completed and the Lifetime of Experiences Questionnaire and neuropsychological assessment were administered.

5.3.3 Measures

Demographic and background details elicited were age, gender, and a self-rating of perceived health and memory ability in relation to others of the same age.

5.3.3.1 Cognitive reserve assessment

The Lifetime of Experiences Questionnaire (Valenzuela & Sachdev, 2007) was used to give an indication of participants' level of CR (Appendix L). It was developed as a means of quantifying the life experiences thought to contribute to CR, specifically education, occupation and engagement in leisure activities. In this study, occupation was rated using Office for National Statistics (2010) classifications. The LEQ covers three life stages (young adulthood, mid-life and late life). The scores for the specific questions relating to each life stage are then weighted to allow for an equal contribution of experiences from across the lifespan. Higher scores indicate higher levels of CR. Reports on the reliability of the measure suggest that reliability is variable (Cronbach's alpha = .43 - .84; Valenzuela & Sachdev, 2007); this is to be expected given that the measure assesses a number of life experiences that are not necessarily theoretically or conceptually related. The LEQ has high construct validity, concurrent validity and clinical validity as well as good test-retest reliability (Valenzuela & Sachdev, 2007).

5.3.3.2 Mood assessment

Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS; Snaith & Zigmond, 1994). Possible scores on this scale range from 0-21 for each of the two sub-scales covering anxiety and depression, with higher scores indicating more severe symptoms. The scale is a widely used and well-accepted measure, validated for use in the general population and with older people (Bjelland, Dahl, Haug, & Neckelmann, 2002; Dennis, Boddington, & Funnel, 2007; Spinhoven, Ormel, Sloekers, & Kempen, 1997). The scale has good internal reliability for anxiety (Cronbach's alpha = .80 - .84) and depression (Cronbach's alpha = .71 - .86), and good to very good concurrent validity (Bjelland et al., 2002; Spinhoven et al., 1997). The Cronbach's alpha for anxiety and depression in the current study were .81 and .71 respectively.

The Ruminative Response Scale – Short form (RRS; Davis & Nolen-Hoeksema, 2000) consists of ten self-report items, with higher scores indicating greater rumination (Appendix M). The RRS short form has high internal reliability when used with older people, with a Cronbach's alpha of .85 (von Hippel, Vasey, Gonda, & Stern, 2008) and .84 in the

current study. Davis and Nolen-Hoeksema (2000) reported a strong correlation with the full 22-item version of the RRS (r = .93).

5.3.3.3 Cognitive assessment

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) is a cognitive screening test designed to detect mild cognitive impairment (MCI) with 11 sub-scores for different domains of cognition. As this test is a brief screening measure it was used to characterise the sample in the current study. Cronbach's alpha for the MoCA is .84 for internal reliability, it has a test-retest reliability of .92 and it has strong concurrent validity with the Mini Mental State Examination, r = .87 (Nasreddine et al., 2005). In the current study the Cronbach's alpha was .68, indicating acceptable reliability.

To assess memory, the immediate and delayed recall components of the Rivermead Behavioural Memory Test Version 2 (RBMT-2; B.A. Wilson, Cockburn, & Baddeley, 2003) short story recall subtest were used. Participants are read a short story and asked to recall it immediately and to recall it again after a 20-minute delay. Scoring is based on the number of ideas correctly recalled with a maximum raw score of 21. The raw scores rather than the profile score were used in the current study as these provide a greater range of possible scores.

The FAS Phonemic Fluency Test (Spreen & Strauss, 1991) was used to assess phonemic fluency, which is regarded as a measure of executive function. In this test participants are asked to name as many words beginning with a specified letter, in this case each of F, A and S, as they can in 60 seconds. A minimum score of 12-15 per letter is suggestive of normal functioning. Psychometric properties for the FAS Verbal Fluency Test are good, with a Cronbach's Alpha of .83 in previous research and .90 in the current study, and test-retest reliability of .74 (Tombaugh, Kozak, & Rees, 1999).

5.3.4 Data analysis

SPSS version 20 was used to analyse the data. For the sample as a whole, forced entry multiple regression analyses were carried out for each of the three cognitive tests of interest -

immediate recall, delayed recall, and verbal fluency - with CR, depressive symptoms, anxiety symptoms and rumination as the predictor variables, in order to assess whether these predictors explained a significant amount of variance in cognitive performance. The sample was then split at the median into lower and higher CR groups. The median score was expected to be similar to that found by Valenzuela and colleagues (2013) of 97.4 and 89.1 for male and female participants respectively. Pearson's r correlations were calculated to investigate associations between variables. Forced entry multiple regressions were conducted to assess whether the amount of variance in cognitive performance explained by depressive and anxiety symptoms and rumination differed in those with high and low CR. Collinearity statistics were examined to ensure there were no issues of multicollinearity in the hierarchical regressions.

5.4 Results

Participants were 236 healthy older people, 146 females and 90 males, with a mean age of 70.86 years (*S.D.* = 7.66, range 60 – 92) and a mean of 12.91 years of formal education (*S.D.* = 3.15, range 8 – 23). One participant who completed the measures was excluded due to a very low score of 16 achieved on the Montreal Cognitive Assessment indicating possible impairment. In the case of one male and one female participant, scores for the depression and anxiety measures were not available as these participants declined to complete these measures, and these were considered as missing values in the relevant analyses. Table 5.1 gives a summary of characteristics for the sample as a whole and for the two subgroups consisting of those with high and low CR. The significant differences in performance on the cognitive function tests between those who had high and low CR were expected due to the established association between CR and cognitive function in later life.

As the independent variables were moderately to strongly correlated, collinearity statistics were examined for each regression analysis. Tolerance and the Variance Inflation Factors (VIF) were all within accepted limits indicating that there were no issues of multicollinearity in the following regression analyses (Robinson & Schumacker, 2009).

Table 5.1: Means, standard deviations, and alpha coefficients of all measures for the whole sample (N = 236) and the low (n = 118) and high (n = 118) cognitive reserve groups

		Full Sample		Low CR	High CR	p-values for
	Possible Range	Mean (SD)	Min-Max	Mean (SD)	Mean (SD)	differences
LEQ (CR)	0 - ∞	89.78 (20.07)	30.60-138.80	73.54 (11.12)	106.02 (12.37)	$p < .001$
Immediate Recall	0 - 21	6.57 (2.71)	0.5-15	5.88 (2.67)	7.27 (2.58)	$p < .001$
Delayed Recall	-1 - 21	5.47 (2.72)	-1-15.5	4.70 (2.71)	6.23 (2.51)	$p < .001$
FAS	0 - ∞	39.84 (13.74)	8-80	34.76 (12.22)	44.92 (13.34)	$p < .001$
MoCA	0 - 30	25.97 (2.82)	18-30	25.23 (3.07)	26.72 (2.34)	$p < .001$
Depressive Symptoms	0 - 21	2.78 (2.41)	0-12	3.35 (2.68)	2.21 (1.96)	$p < .001$
Anxiety	0 - 21	5.61 (3.44)	0-18	6.12 (3.73)	5.09 (3.06)	$p = .033$*
Rumination	10 - 40	16.33 (4.74)	10-33	16.46 (5.15)	16.21 (4.31)	$p = .527$

*Indicates that the result was not significant after controlling for multiple comparisons using the Holm-Bonferroni method.

Note: CR, cognitive reserve; LEQ (CR), Lifetime of Experiences Questionnaire; MoCA, Montreal Cognitive Assessment; FAS, verbal fluency; for all cognitive function variables a higher score indicates a better score. For depression, anxiety and rumination a higher score indicates greater symptoms.

Multiple forced entry regression analyses indicated that CR, depressive symptoms, anxiety, and rumination, using adjusted R^2, accounted for 13% of the variance in immediate recall ($F = 9.67$, $p < .001$), 14.8% of the variance in delayed recall ($F = 11.11$, $p < .001$), and 15.6 % of the variance in verbal fluency ($F = 11.75$, $p < .001$) in the sample as a whole. CR was an independently significant predictor for immediate recall ($\beta = .285$), delayed recall ($\beta = .311$), and verbal fluency ($\beta = .364$), all $p < .001$. Depressive symptoms were an independently significant predictor for immediate ($\beta = -.186$) and delayed recall ($\beta = -.215$), both $p < .01$. Additionally, depressive symptoms showed a trend towards significance as an independent predictor for verbal fluency ($\beta = -.135$, $p = .058$).

The sample was divided into lower and higher CR by dichotomising the sample at the LEQ median of 87.90. Pearson's r correlations between variables in the low and high CR groups are summarised in Table 5.2. There were significant negative correlations between depressive symptoms and immediate recall, delayed recall, and verbal fluency, and between anxiety and immediate recall and delayed recall, in the group with lower CR. There were no significant correlations between depressive symptoms or anxiety and cognitive function in the higher CR group. Rumination was not significantly correlated with scores on any of the cognitive tests in either CR group.

Depressive symptoms, anxiety, and rumination explained 8.8% of the variance in immediate recall, 8.2% of the variance in delayed recall, and 8.4% of the variance in verbal fluency in the lower CR group. Depressive symptoms were an independently significant predictor of variance for immediate recall, delayed recall, and verbal fluency in the lower CR group, all $p < .01$. Rumination was an independently significant predictor of verbal fluency in the group with lower CR (Table 5.3). The predictor variables did not explain a significant amount of variance for scores on any of the cognitive tests in the higher CR group (Table 5.3).

Table 5.2: Correlations between variables for the low cognitive reserve and high cognitive reserve groups

	LEQ (CR)	Immediate Recall	Delayed recall	FAS	Depression	Anxiety	Rumination
LEQ (CR)	--	.275**	.261**	.142	-.104	-.143	-.051
Immediate Recall	.189*	--	.860**	.295**	-.301**	-.229*	-.016
Delayed Recall	.216*	.824 **	..	.324**	-.293**	-.187*	.017
FAS	.186*	.238**	.153	..	-.233*	.008	.115
Depression	-.023	-.076	-.067	.079	..	.506**	.357**
Anxiety	-.105	.022	.098	.011	.399**	..	.370**
Rumination	.183*	-.050	.031	.055	.288*	.469**	..

** indicates significant at $p < .01$

*indicates significant at $p < .05$

Note: High cognitive reserve group correlations are to the left of the table; low cognitive reserve group correlations are to the right. LEQ (CR), Lifetime of Experiences Questionnaire (CR); FAS, verbal fluency

Table 5.3: Regression analyses for immediate recall, delayed recall, and verbal fluency by low and high cognitive reserve

Low cognitive reserve	Immediate recall		Delayed recall		Verbal fluency	
R_a^2 for model	.088		.082		.084	
	β	p	β	p	β	p
Depressive symptoms	-.278	.009**	-.300	.005**	-.356	.001**
Anxiety	-.134	.207	-.089	.403	.094	.378
Rumination	.124	.206	.146	.140	.211	.033*
High cognitive reserve	Immediate recall		Delayed recall		Verbal fluency	
R_a^2 for model	-.014		-.003		-.017	
	β	p	β	p	β	p
Depressive symptoms	-.096	.352	-.126	.221	.082	.427
Anxiety	.090	.421	.149	.180	-.047	.672
Rumination	-.064	-.602	-.002	.984	.054	.614

** indicates significant at $p < .01$

*indicates significant at $p < .05$

As Table 5.1 shows, there was a significant difference between the high and low CR groups in level of depressive symptoms; therefore matched samples were identified based on level of depressive symptoms for the high and low CR groups (n = 85 for low CR and n = 85 for high CR). This was done to ensure that this difference in depressive symptoms was not confounding the results. In the matched samples analysis, there were significant negative associations between depressive symptoms and immediate (r = -.283) and delayed recall (r = -.311) in the low CR group. However, the correlation between depressive symptoms and verbal fluency was no longer significant (r = -.174). There were still no significant correlations between depressive symptoms and cognitive test scores in the high CR group in the matched samples analysis.

Multiple regression analyses conducted with the depression matched samples showed that depressive symptoms, anxiety, and rumination explained 5.2% of the variance in immediate recall, 6.6% of the variance in delayed recall, and 7.9% of the variance in verbal fluency in the lower CR group. Depressive symptoms were still an independently significant predictor for immediate recall (β = -.266), delayed recall (β = -.317), and verbal fluency (β = -.320) in the lower CR group (all $p < .05$). The predictor variables did not explain a significant amount of variance for scores on any of the cognitive tests in the higher CR group in the depression matched sample.

5.5 Discussion

The first aim of the current study was to assess the level of variance in cognitive function explained by CR, depressive symptoms, anxiety, and rumination in community-dwelling older people. The results indicate that these variables predicted a significant proportion of variance in both memory and verbal fluency, with CR an independently significant predictor of all the tests of cognitive function, and depression an independently significant predictor of performance on the memory components. The second aim of this study was to assess whether the relationship of depressive symptoms, anxiety and rumination with cognitive function differs in those with low and high CR. The results indicate that the relationship of mood and rumination with cognitive function does differ in those with low and high CR in this sample of community dwelling older people, with associations found in the low but not the high CR group.

While there are no specific norms available for the LEQ the median found in the current study is similar to that reported by Valenzuela and colleagues (2013), indicating that the division used in the current study represents the lower and higher 50th percentile range of scores found in previous research. When the participants were split into two groups, according to their level of CR, there was a relationship between depressive symptoms and cognitive function only in those with lower levels of CR. Anxiety was related to performance on immediate and delayed recall in the group with lower CR and rumination was an independently significant predictor of verbal fluency in the lower CR group only. However, it should be noted that the association between rumination and verbal fluency in the multiple regression was positive, suggesting that those with higher levels of rumination performed better on this task. This result is the opposite of what would be expected given that previous research suggests that rumination is associated with reduced cognitive function (Davis & Nolen-Hoeksema, 2000; Lyubomirsky et al., 2003). This could indicate that despite the moderate positive association between depressive symptoms and rumination found in this study, these two factors influence performance on verbal fluency, a measure of executive function, in differing manners.

The level of depressive symptoms was low in this study, as would be expected in a sample of community-dwelling healthy older people (Crawford et al., 2001). However, despite the low levels of depressive symptoms, depression scores still provided an independent contribution to the proportion of variance explained for the memory tasks in the sample as a whole and for all the cognitive tasks in the low CR group. These results along with previous research suggest that even low levels of depressive symptoms may affect cognitive function in later life (Murphy & O'Leary, 2010; Vinkers et al., 2004; R.S. Wilson et al., 2003b; Yen et al., 2011). This indicates that it is important to consider the influence of depressive symptoms on cognitive function even in older people who do not have clinical levels of depression.

Several previous studies on this topic have found that single indicators of CR, specifically education and engagement in cognitively-stimulating activities, do not influence the relationship between depressive symptoms and cognitive function (e.g. Bhalla et al. 2005, Wilson et al., 2004). The current results contradict these findings, and one possible explanation is that the differing results could be due to the more extensive assessment of participants' CR in the present study. This study made use of a measure that combines the

three most common proxy measures of CR rather than using a single proxy, for example educational level, as most previous studies have done, which could allow for a more accurate indication of an individual's level of CR. Additionally, the associations between anxiety, rumination and cognitive function in the lower CR group found in this study, and the previously established relationships between anxiety, rumination and cognitive function (Bierman et al., 2005; Davis & Nolen-Hoeksema, 2000; Gallacher et al., 2009; Lyubomirsky et al., 2003), suggest that these relationships in association with CR warrant further investigation. Future studies which include a more comprehensive indicator of CR such as the LEQ, and a more in-depth assessment of cognitive function, could help elucidate the pathways involved in these relationships.

There are some limitations to this study that should be considered. In particular, the neuropsychological assessment was kept brief to limit the burden on participants. It would be beneficial for a future study to include a more extensive neuropsychological assessment to gain a greater insight into these relationships. The Ruminative Response Scale –Short form (Davis & Nolen-Hoeksema, 2000) used in this study to assess rumination is specifically related to depressive mood in that participants are asked to respond to the questions based on what they do when they are feeling down, sad, or depressed. Rumination is a maladaptive thought process that is related to depression but not limited to occurring alongside it. A future study could make use of a more general rumination scale in order to assess the relationship between rumination and cognitive function without limiting it to depressive rumination. The group that was lower in CR had significantly more depressive symptoms than those with higher levels of CR. However, additional analyses utilising matched samples showed that the associations remained significant when the two CR groups were matched on depressive symptoms, apart from the correlation between depressive symptoms and verbal fluency in those with lower CR. This loss of significance could be the result of a reduction in power caused by creating matched samples and hence reducing the sample size. Additionally, as expected, those with lower CR scored significantly lower on recall and verbal fluency than those with higher CR. This could suggest that depressive symptoms, anxiety, and rumination exert more of an influence on cognition in those with lower cognitive function, rather than merely in those with lower CR. It was not possible to create low and high CR groups matched for cognitive function while retaining an adequate sample size, so this remains unclear. Finally, the current study can show only associations between mood, CR and cognitive function, rather than indicating the direction of causation, although previous longitudinal

studies have shown that depressive symptoms do lead to a decrease in cognitive function (Geerlings et al., 2000; van Hooren et al., 2005; R.S. Wilson et al. 2003b). However, it is also possible that lower cognitive function leads to increased depressive symptoms in some people (Paterniti et al., 2002; Stewart, 2004). Nevertheless, even if this is the case, it remains apparent that it is important to build CR to maintain cognitive function in later life.

In summary, having higher CR appeared to mitigate the association between depressive symptoms, anxiety, and cognitive function in this sample. This, together with previous findings showing that CR can help delay cognitive decline, highlights the importance of CR in maintaining cognitive functioning in later life, not only in relation to resilience against neuropathology, but also in relation to the effects of psychological adversity.

Chapter 6

The role of cognitive reserve in the association between mood and cognitive function in a nationally representative cohort

Opdebeeck, C., Matthews, F. E., Woods, R. T., & Clare, L. (in preparation). The role of cognitive reserve in the association between mood and cognitive function in a nationally representative cohort.

6.1 Abstract

Background: Cognitive reserve (CR) has been associated with better cognitive function in older people. In contrast, mood disorders are associated with poorer cognitive function but with varying results across studies, suggesting that other factors may moderate the association. The aim of this study was to investigate whether a comprehensive indicator of CR acts as a moderator of this association in CFAS II, a large cohort study, representative of community-dwelling older people in England.

Method: Six thousand six hundred and seventy-five dementia-free people aged 65+ had complete data on the measures of CR, mood, and cognition. The sample was divided into those with low, medium, and high levels of CR and into those with no, a subthreshold, or a clinical mood disorder.

Results: Those with low levels of CR had significantly poorer cognitive performance than those with medium or high levels of CR, while those with no mood disorder performed significantly better than those with a subthreshold or clinical mood disorder. CR did moderate the negative association between mood and cognitive function; the negative effect of a clinical mood disorder on cognitive performance was 2.5 times greater in the low than the high CR group.

Conclusion: These results demonstrate that CR, when considered in terms of multiple proxy measures, can mitigate the negative association between lowered mood and cognition, emphasising the importance of continuing to build CR across the lifespan in order to maintain cognitive health.

6.2 Introduction

Cognitive impairment in later life is associated with increased disability and mortality and less chance of recovery from disability (Langa et al., 2008; Pérès, Verret, Alioum, & Barberger-Gateau, 2005; St John, Tyas, & Montgomery, 2015; Tinetti et al., 2011). The negative outcomes of cognitive impairment make the study of modifiable factors associated with maintaining cognitive function in later life an important area of research.

There is significant variability in cognitive function in later life, even among those older people who are deemed relatively healthy and who reside within the community (Singh-Manoux et al., 2011). There are a number of factors that are thought to influence this variability in cognitive function. Engagement in cognitive activity, such as education, complex occupations and cognitively-stimulating leisure activities, across the lifespan is thought to help build cognitive reserve (CR). Several reviews indicate that CR is associated with better cognitive performance in healthy older people and a reduced risk of cognitive decline and dementia (Fratiglioni & Wang, 2007; Harrison et al., 2015; Meng & D'Arcy, 2012; Opdebeeck al., 2015b, this is the published version of Chapter 2 of this thesis; Valenzuela & Sachdev, 2006a; 2006b). The activities that contribute to CR, and that are considered proxy measures of this construct, have also been associated with lower levels of depression in older people (e.g. Adams et al., 2011; Glass et al., 2006; Jenkins, 2011; Lorant et al., 2003; Narushima et al., 2013). In contrast, lowered mood, especially current experience of depression, has been associated with poorer cognitive performance and an increased risk of cognitive decline, mild cognitive impairment (MCI), and dementia (e.g. Diniz et al., 2013; Reppermund et al., 2011; Steffens et al., 2014; Yates et al., 2013).

Depression and anxiety are the two mood disorders most frequently studied in later life in association with cognition. There is evidence to suggest that both are associated with poorer cognitive performance and a greater risk of cognitive decline and dementia (Beaudreau & O'Hara, 2008; 2009; Diniz et al., 2013; Pietrzak et al., 2012; Steffens et al., 2014). However, the evidence is mixed, with some studies finding no association between depression or anxiety and the risk of dementia or cognitive decline (Becker et al., 2009; de Bruijn et al., 2014). The conflicting evidence suggests that there may be additional factors that mediate the association between mood and cognitive function. As CR has previously been associated with better cognitive function and reduced risk of cognitive decline, it may

moderate the association between mood and cognitive function in later life, accounting for the observed variations.

At present, research into whether CR moderates the association between mood and cognitive function has produced conflicting results. Several studies have noted that clinical depression is associated with poorer cognitive function in those with lower levels of education but not in those with higher educational level (Pálsson et al., 1999; Pálsson et al., 2001). Conversely, other researchers have reported that cognitive performance decreased as depressive symptoms increased in those with higher education but not lower education (Geerlings et al., 2000; O'Shea et al., 2015; Santos et al., 2014). A number of studies have found no role for proxy measures of CR in the association between mood and cognitive function (Bhalla et al., 2005; Wilson et al., 2004). Other studies have yielded mixed results, reporting interaction effects between proxy measures of CR and mood on some but not all of the memory and executive function tests employed (Avila et al., 2009; Potvin et al., 2013).

These variations could be explained in that all of these studies assessed CR with one single measure, for example, educational level, rather than using a combined measure taking account of a range of experiences. Only one study to date has investigated whether CR moderates the association between depression and anxiety, using a proxy measure of CR combining educational attainment, occupational complexity, and engagement in cognitively-stimulating leisure activities (Opdebeeck et al, 2015a, this is the published version of Chapter 5 of this thesis). With this more comprehensive indicator of CR, it was found that higher levels of depressive symptoms and anxiety were associated with poorer cognitive function in those with low levels of CR but not in those with high levels of CR. However, the levels of depressive symptoms and anxiety in this study were low leaving it unclear whether a comprehensive indicator of CR may moderate the association between clinical levels of depression or anxiety and cognitive function.

These conflicting results suggest that the question of whether CR moderates the association between mood and cognitive function in later life warrants further investigation. This study aimed to investigate the associations between a comprehensive proxy measure of CR, mood, and cognitive function in a large cohort of community-dwelling older people utilising data from wave 1 of the second enumeration of the Cognitive Function and Aging Study (CFAS II). The specific aims of this study were:

1. To confirm that there was an association between CR, as assessed by a combination of education, occupation, and current cognitive and social activities, and cognitive function in this community-dwelling population.

2. To assess whether the presence of a mood disorder was associated with cognitive function in this community-dwelling population.

3. To assess whether having higher levels of CR moderated the associations between mood and cognitive function.

6.3 Method

6.3.1 Participants

Participants were drawn from the first wave of the second enumeration of the Medical Research Council Cognitive Function and Aging Study (CFAS II; http://www.cfas.ac.uk/). A total of 7,762 people over 65 completed the study between 13 November 2008 and 25 October 2011 in three geographical areas of England, Cambridgeshire, Newcastle, and Nottingham, and included respondents from both rural and urban populations. For the purposes of the current study, those with a diagnosis of dementia or organicity score of 3 or higher based on Automated Geriatric Examination Assisted Taxonomy (AGECAT) diagnostic algorithms (n = 559) or those without a diagnosis of dementia or organicity score of 3 or higher but who resided in a residential home (n = 86) were removed from the sample. This resulted in a sample of 7,117 community-dwelling older people without dementia.

6.3.2 Procedures

CFAS II drew on the registers of primary care practices in each geographical region. Letters inviting participation (Appendix H) were sent to a randomly selected age stratified population (65-74 years and ≥ 75 years) and followed by a visit from a named researcher. Each geographical area of the study was required to provide 2,500 participants divided equally across the age stratifications.

Interviewers received training in administering the computerised questionnaire battery and visited participants up to three times to complete the assessments. The assessments included questions regarding demographics, health, activities of daily living, social contact, cognitive activities, cognitive function and assessment on the Geriatric Mental State (GMS) examination. A subset of these measures were considered in the current study.

6.3.3 Measures

6.3.3.1 Cognitive reserve assessment

A total cognitive lifestyle score (CLS) was calculated based on participants' educational level, primary occupation, and social and cognitive activities in later life. The calculation of this score was based on the CLS created in CFAS I (Valenzuela et al., 2011) with the addition of responses to questions about cognitive activities, which included the frequency with which participants listen to the radio, read newspapers, magazines, or books, play games such as cards or chess, and do puzzles and/or crosswords. These questions were added in CFAS II, making it possible to examine associations between cognitive activity and cognitive function.

Educational level was expressed as years of education completed, occupation was assessed in line with the procedure of Valenzuela and colleagues (2011) in that the participants' main occupation was coded in terms of social class grouping (from I to V) and socioeconomic grouping (11 to 150). These two groupings were then exploded and ranked to create an occupational complexity score with a possible range of 1-14, that was more fine-grained than either grouping alone. An additional ranking of 15 was given to housewives as these individuals do not receive a formal code in the UK social class ranking system. These ratings were then reversed to be in the same direction as education and social and cognitive engagement, with lower scores indicating a less active cognitive lifestyle. For the later life activity score, current social engagement was recoded from a 3 to a 5-point scale to match the 5-point scale for current participation in cognitive activities, with three questions relating to social engagement and seven questions relating to cognitive activity. The questions used to create the CLS score are presented in Appendix N.

To enable each of the three sub-scores to contribute equally to determining whether a person's cognitive lifestyle reflected low, medium or high levels of activity, the scores were weighted to provide equal distribution across the sub scores, using the following formula:

CLS = (3.4 x education) + (2.4 x occupational complexity) + (1 x social and cognitive engagement).

The CLS was then divided at the tertile level to allow for comparisons between those with low, medium, and high cognitive lifestyle scores, which can be considered a proxy measure for their levels of CR.

6.3.3.2 Mood assessment

Depression and anxiety were assessed using the Geriatric Mental State Automated Geriatric Examination Assisted Taxonomy (GMS AGECAT). The GMS is a semi-structured interview designed to assess organic and psychiatric disorders in older people. The AGECAT programme uses an algorithm to assign diagnoses to provide consistency across time and location. The AGECAT assigns scores ranging from 0 to 5 for depression and anxiety based on clusters of symptoms. These scores were coded into groups of those with no mood disorder (GMS AGECAT for anxiety and depression = 0), a sub-threshold mood disorder (GMS AGECAT for anxiety and/or depression = 1-2), or a clinically relevant mood disorder (GMS AGECAT for anxiety and/or depression = 3+). Absence or presence of a subthreshold or clinical level mood disorder was considered, rather than depression or anxiety individually, due to the strong association between depression and anxiety. Additionally, the GMS AGECAT uses a hierarchical system to determine a main diagnosis, which may give precedence to a diagnosis of depression over a diagnosis of anxiety when overlapping symptoms are reported. The GMS AGECAT has demonstrated good concordance with diagnoses by trained psychiatrists (Cohen's Kappa = 0.84, Copeland, Dewey, & Griffiths-Jones, 1986) and eliminates the variability that has been observed with clinical diagnosis (Copeland et al., 2002).

6.3.3.3 Cognitive assessment

Cognition was assessed using the Cambridge Cognitive Assessment (CAMCOG). The CAMCOG provides an overall score for cognitive function from eight subscales - orientation, language, memory, attention, praxis, calculation, abstract thinking, and perception. Total scores range from 0 to 107. The CAMCOG has good inter-rater reliability (r = .97) with 92% sensitivity and 96% specificity in detecting cognitive impairment, and avoids the ceiling effects seeing in other brief neuropsychological assessments (Roth et al., 1986).

6.3.4 Data analysis

Data was analysed in Stata release 13 and inverse probability weighting was used to adjust for sampling design and non-response. This weighting was calculated by birth cohort, sex, care setting, and deprivation status of postcode, all of which were known for the complete population including those that did not participate in the study. T-tests and Pearson's Chi Square tests were used to compare those with and without missing data.

Regression analyses were used to assess the unique contributions of CR, as indicated by the CLS, and mood to cognitive function. A multiple regression analysis was used to assess whether adding the CR proxy measure to the model containing mood altered the association between mood and cognition. Finally, cognitive function was regressed on mood for low, medium and high CR groups to assess whether these relationships differed by CR level. To adjust for potential age and sex differences, these variables were first entered into the models for all analyses. Residual normality plots indicated that the cognitive function residuals distribution approached normality, satisfying the criteria for regression analysis.

6.4 Results

There were 3,285 males and 3,832 females in this community-dwelling sample of CFAS II participants. All participants were aged over 65 with half the sample aged <75 and half aged >75. Data was missing for 22 participants on education, 117 on occupation, and 20 on current social and cognitive activities, resulting in missing data on the total CLS for 154 participants, 104 females and 50 males, 138 of whom had scores for cognitive performance. Three hundred and four participants had missing scores for the CAMCOG. Differences between those with and without missing data by sex, age, education, presence or absence of anxiety, depression or a general mood disorder, and cognitive performance are presented in Table 6.1. The final sample for analysis comprised 6,675 participants with an average of 10.76 (*95% CI* = 10.70-10.82) years of education and a mean CAMCOG score of 88.91 (*95% CI* = 88.71-89.11) after adjustment for sampling design and non-response.

In relation to the first aim, regression analyses indicated that those with low levels of CR performed significantly poorer on the CAMCOG (*m* = 84.95, *95% CI* = 84.55-85.34) than those with medium levels of CR (*m* = 89.43, *95% CI* = 89.13-89.71) or high levels of CR (*m* = 92.70, *95% CI* = 92.44-92.95), as can be seen from Model 1 in Table 6.2. In relation to the second aim of this study, shown in Model 2 in Table 6.2, those with no mood disorder had significantly better cognitive performance (*m* = 89.49, *95% CI* = 89.24-89.74) than those with a subthreshold mood disorder (*m* = 88.36, *95% CI* = 88.01-88.72), or clinical levels of a mood disorder (*m* = 85.85, *95% CI* = 84.95-86.75).

Table 6.1: Sex, age, education and level of depressive disorder for those included in the analysis and those with missing data

	Sample for analysis (N = 6,675)	With missing data (N = 442)	Test statistic
Male (N)	3,110 (46.59%)	175 (39.59%)	$X^2 = 8.17$*
Age (mean)	74.86 (SD = 6.80)	77.77 (SD = 7.87)	t = -8.62**
Education (mean)	10.86 (SD = 2.48)	10.27 (SD = 2.55)	t = 4.76**
No Depression	5,210 (78.05%)	308 (69.68%)	
Subthreshold Depression	1,039 (15.57%)	90 (20.36%)	$X^2 = 17.77$**
Depression Case	426 (6.38%)	44 (9.95%)	
No Anxiety	4,526 (67.81%)	283 (64.03%)	
Subthreshold Anxiety	2,001 (29.98%)	143 (32.35%)	$X^2 = 5.19$
Anxiety Case	148 (2.22%)	16 (3.6%)	
No Mood Disorder	3,995 (59.85%)	241 (54.52%)	
Subthreshold Mood Disorder	2,174 (32.57%)	150 (34.94%)	$X^2 = 10.51$*
Mood Disorder Case	506 (7.58%)	51 (11.54%)	
CAMCOG (n = 138 missing CLS)	89.36 (SD = 7.71)	86.27 (SD = 11.05)	t = 4.62**

*p < .01 **p < .001

Table 6.2: Regression models for cognitive performance regressed on cognitive reserve (CLS) and level of mood disorder

	Model 1 R^2 = .25, F = 413.80		Model 2 R^2 = .14, F = 195.20		Model 3 R^2 = .26, F = 283.57	
	CI	t	CI	t	CI	t
Sex (Male reference)	-1.57, -0.87	-6.79**	-1.08, -0.33	-3.67**	-1.38, -0.68	-5.75**
Age	-0.35, -0.30	-22.39**	-0.42, -0.37	-26.20**	-0.36, -0.30	-22.71**
CR Low	Reference				Reference	
CR Medium	3.50, 4.43	16.75**			3.37, 4.29	16.30**
CR High	6.43, 7.32	30.27**			6.27, 7.15	29.75**
No Mood Disorder			Reference		Reference	
Subthreshold Disorder			-1.41, -0.59	-4.78**	-0.93, -0.18	-2.88*
Mood disorder			-4.48. -2.72	-8.15**	-3.60, -1.96	-6.65**
Cons	108.35, 112.62	101.33**	117.43, 121.78	107.62**	109.05-113.31	102.12**

*p < .01 **p < .001

Note: CI, confidence interval (lower, upper); CR, cognitive reserve indicated by the CLS; Cons, constant.

Aim 3 of the study sought to determine whether CR mitigates the association between mood and cognition. In the first step, both mood and the CLS, serving as a proxy measure of CR, were entered into the model simultaneously (Model 3, Table 6.2). While the differences in cognitive performance between those with no mood disorder, a subthreshold disorder, or a clinical mood disorder remained significant when CR was included in the model, the regression coefficients decreased. The addition of CR resulted in a decrease of almost 1 point in the coefficient representing the differences in cognitive performance between those with and without a clinical mood disorder, from -3.67 (*SE* = 0.45) to -2.77 (*SE* = 0.42). Post-regression contrasts indicated a small but significant interaction between CR and mood, *F* (4, 6,664) = 2.65, *p* = .032. To further explore how the associations between mood and cognition may differ according to individuals' level of CR a series of regressions were conducted by CLS level (Table 6.3).

The regression coefficients indicate that presence of a mood disorder and membership of the low CR group (*m* = 81.75, *95% CI* = 80.30-83.21) resulted in a 4 point decrease in the regression coefficient for cognitive performance in comparison to those in the low CR group with no mood disorder (*m* = 85.71, *95% CI* = 85.21-86.21). In the medium CR group, the presence of a mood disorder (*m* = 87.67, *95% CI* = 86.31-89.03) resulted in a 2 point decrease in the coefficient for cognitive performance in comparison to those with no mood disorder (*m* = 89.74, *95% CI* = 89.38-90.12). For those in the high CR group presence of a mood disorder resulted in a 1.5 point decrease in the coefficient for cognitive performance (*m* = 91.29, *95% CI* = 90.12-92.46) in comparison to no mood disorder (*m* = 92.89, *95% CI* = 92.58-93.21). In addition, the difference in cognitive performance between those with no mood disorder and those with a subthreshold mood disorder was only significant in the group with lower CR. These differences are illustrated in Figure 6.1, which shows that while cognitive performance decreased with the presence versus absence of a mood disorder across CR groups, this decrease was steeper in the low CR group than in the high CR group. In terms of the mean score differences, there was a difference in mean cognitive performance of 7.19 points between those with low and high CR and no mood disorder and this mean score difference increased to 9.54 points between those with low and high CR and a mood disorder.

Table 6.3: Regression analyses for cognitive performance regressed on level of mood disorder by cognitive reserve level

	Low CR R^2 = .11, F = 54.73		Mid CR R^2 = .13, F = 55.90		High CR R^2 = .14, F = 58.67	
	CI	t	CI	t	CI	t
Sex (Male Reference)	-2.51, -1.05	-4.75**	-1.45, -0.33	-3.13*	-0.83, 0.12	-1.45
Age	-0.39, -0.29	-12.85**	-0.37, -0.27	-12.56**	-0.36, -0.27	-14.56**
No Mood Disorder	Reference		Reference		Reference	
Subthreshold Disorder	-1.77, -0.19	-2.44*	-1.05, 0.12	-1.55	-0.77, 0.26	-0.97
Mood Disorder	-5.51, -2.58	-5.41**	-3.36, -0.73	-3.04*	-2.71, -0.33	-2.51*
Cons	108.85, 116.75	56.30**	110.71, 117.85	64.11**	113.43, 119.58	72.82**

*p < .05 **p < .001

Note: CI, confidence interval (lower, upper); CR, cognitive reserve indicated by the CLS; Cons, constant.

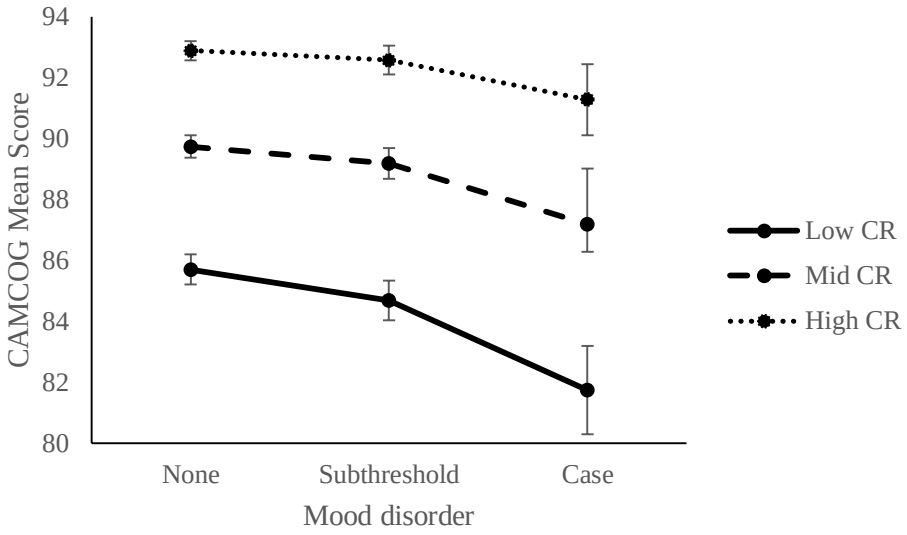


Figure 6.1. Mean cognitive performance by cognitive reserve group (CLS) and level of mood disorder. Error bars represent 95% Confidence Intervals of the means.

To examine whether these associations were apparent only when multiple indicators of CR were combined, additional analyses were conducted to assess the differences in the associations between mood and cognition by educational level, occupation, and engagement in cognitive and social activities. Figures 6.2-4 demonstrate that a similar trend was noted across the three common individual proxy measures of CR, albeit with a much smaller difference between the three occupation groups.

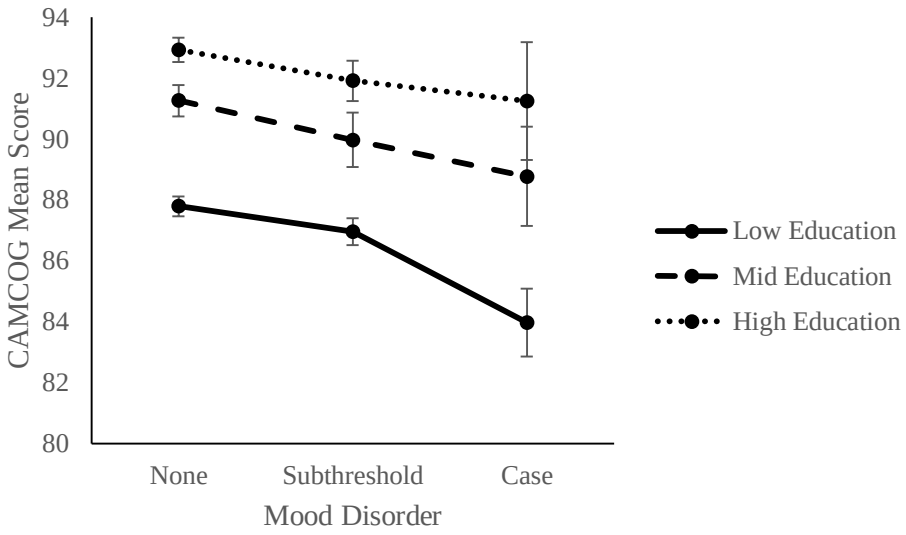


Figure 6.2. Mean cognitive performance by education group and level of mood disorder. Error bars represent 95% Confidence Intervals of the means.

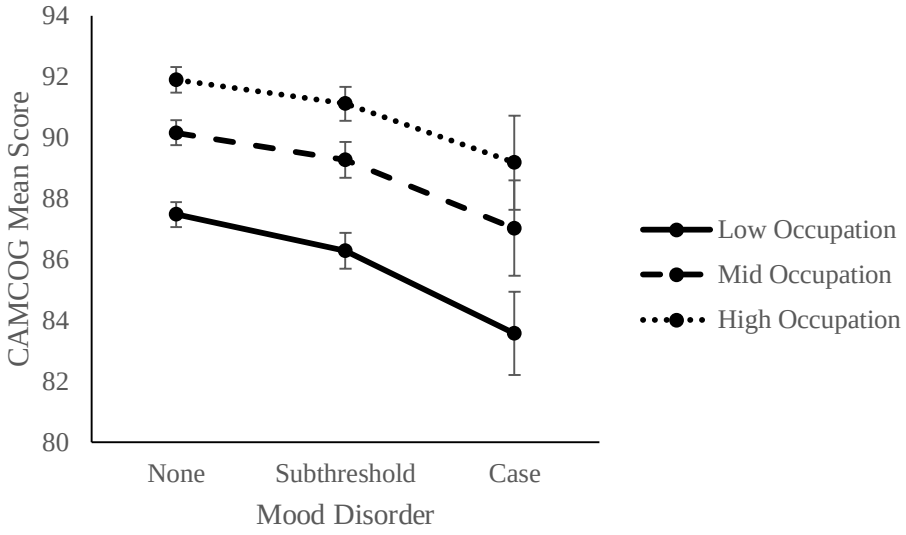


Figure 6.3: Mean cognitive performance by occupation group and level of mood disorder. Error bars represent 95% Confidence Intervals of the means.

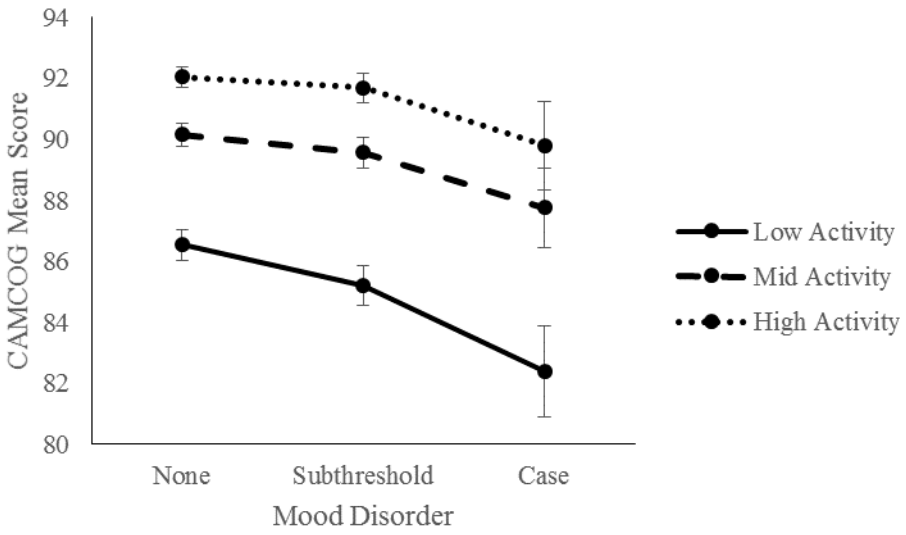


Figure 6.4: Mean cognitive performance by cognitive and social activity group and level of mood disorder. Error bars represent 95% Confidence Intervals of the means.

The figures also demonstrate the large amount of variance seen in cognitive performance in those with a mood disorder in comparison to those without a mood disorder or with a subthreshold mood disorder, regardless of CR level. Additionally, the regression analyses by CR level show that the detrimental effect on cognitive performance of being female was non-significant in the high CR group and had less than a fifth of the effect on performance than was the case in the low CR group (Table 6.3).

6.5 Discussion

In relation to the first aim of this study, those with low levels of CR had significantly poorer cognitive performance than those with medium or high levels of CR. In relation to the second aim of this study, those with no mood disorder had significantly better cognitive performance than those with a sub-threshold or clinical level mood disorder. The third aim of this study was to assess whether CR mitigated the association between mood and cognitive function. The results suggest that CR does mitigate the association between mood and cognition. While there was significantly poorer average cognitive performance in those with a mood disorder versus those without across the CR groups, the difference between those with and without a mood disorder in the low CR group was almost two-fold the difference observed in the medium CR group and two and a half times greater than in the high CR group. However,

there was a large amount of variance in the cognitive function scores for those with a mood disorder across the CR groups, suggesting that while the presence of a mood disorder results in lower cognitive performance on average, this may not be the case for all people with a mood disorder. Interestingly, the association between being female and poorer cognitive performance became negligible in those with high CR, suggesting that CR may also moderate the effect that sex has on cognitive function.

These results support our previous study, reported in Chapter 5, which considered these associations with a comprehensive indicator of CR, and indicated that depressive symptoms and anxiety are negatively associated with cognitive function in those with low CR but not in those with high CR (Opdebeeck et al., 2015a). The current study expands upon these previous findings in that when depression and anxiety are considered at clinical levels, which may require intervention, similar mitigating effects of CR on the association between mood and cognition are found as when self-reported symptoms, which do not reach clinical levels, are considered. In contrast, the observed effect was the opposite of that reported by O'Shea and colleagues (2015) and Geerlings and colleagues (2000) who reported that higher levels of depression were associated with poorer cognitive performance and greater decline in those with high education but not in those with low education. The results also contrasted with several studies that have reported no significant interaction effect between proxy measures of CR and mood on cognition (Bhalla et al., 2005; Wilson et al., 2004).

One possible explanation for these differences is that the current study used a combination of life experiences to indicate levels of CR while the contrasting studies consider only individual proxy measures of CR, most commonly education. However, the above analyses were run considering only education, occupation, or later life cognitive and social activities and similar trends were found, although the strength of the differences in the association between mood and cognitive performance by CR level were not as pronounced, with small differences between mood groups for those with low versus high occupation. Another possible explanation for the differences between the results of the current study and those of other studies is that they could be due to the measure of cognition employed. Several studies, which reported opposing results or no effect of CR on the association between mood and cognition, considered several individual domains of cognition rather than overall cognitive performance (Avila et al, 2009; Bhalla et al., 2005; O'Shea et al., 2015). Two studies that reported that those with current depression performed significantly more poorly

than those without depression in the low education group but not the high education group used the MMSE, a general cognitive performance screening measure (Pálsson et al., 1999; 2001).

The current study is the largest epidemiological study of community-dwelling older people to date to consider whether a comprehensive proxy measure of CR mitigates the association between mood and cognition in community-dwelling older people. It also considers the differences between those with no mood disorder, a subthreshold disorder, and those with a clinically significant mood disorder rather than low levels of depressive symptoms as was the case in several previous studies (Avila et al., 2009; Opdebeeck et al., 2015a; O'Shea et al., 2015). It also considered three levels of a comprehensive indicator of CR rather than dichotomising individual or combined proxy measures of CR as several previous studies have done (e.g. Avila et al., 2009; Bhalla et al., 2005; Opdebeeck et al., 2015a). Nevertheless, there are several limitations to this study. As this was a cross-sectional study, it is not possible to reveal causation in the effects of CR on the association between mood and cognitive function. Future research should consider examining whether a comprehensive proxy measure of CR mitigates the longitudinal association between mood and incidence of cognitive decline and dementia. Additionally, the measure of global cognition employed in this study is more commonly used to differentiate between those with and without cognitive impairment. Employing a more comprehensive neuropsychological assessment may give a better insight into these associations, especially if combined with a longitudinal design.

The prevalence of cognitive impairment and dementia appears to be decreasing (Jagger et al., 2009; Matthews et al., 2013). However, the numbers of people with cognitive impairment or dementia have continued to grow due to increased longevity. This makes the study of factors that may help maintain cognitive functioning in later life an important area of research. CR has previously been described as a fluid construct and it has been suggested that it is possible to continue to build on existing reserve throughout a person's lifespan (e.g. Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Whalley et al., 2006). Interventions in mid- and later life aimed at increasing CR, such as incentives to engage in life-long learning programs or cognitively-complex activities, could aid in further reducing the prevalence of cognitive decline and dementia in the older population.

This large epidemiological study, representative of people aged over 65 dwelling within the community in England, suggests that having a more active cognitive lifestyle and hence higher levels of CR, as indicted by higher educational level, occupation, and engaging in social and cognitive activities in later life, is associated with better cognitive function. Additionally, while the presence of a mood disorder is associated with poorer cognitive performance, having higher levels of CR may help mitigate this association. The results of this study indicate that it is important to encourage engagement in cognitive activities across the lifespan alongside other healthy lifestyle habits, such as maintaining a healthy diet, in the hope of continuing to reduce the incidence of, or delay the onset of, cognitive impairment in older people.

Chapter 7

Discussion

7.1 Introduction

Older people form an increasing proportion of the population, and maintaining cognitive and psychological well-being is of great significance to policy makers and older people themselves (Alzheimer's Society, 2014; Anderson, Day, Beard, Reed, & Wu; 2009; Deary et al., 2009; Kessler, Bowen, Baer, Froelich, & Wahl, 2012; Laditka et al., 2011). It is important to consider a lifespan perspective when investigating what may help to maintain cognitive function and psychological well-being. Such an approach can help inform the timing of preventive interventions which could help maintain cognitive function and reduce levels of depression and anxiety in older people, or at least moderate the negative associations of depression and anxiety with cognitive function in our growing older population. This is especially relevant given the negative impact of cognitive impairment and lowered mood on quality of life, independence, and mortality (Agüero-Torres et al., 2002; Comas-Herrera et al., 2011; Covinsky et al., 2010; Di Carlo et al., 2000; Mezuk et al., 2012). Therefore, in this thesis, I aimed to clarify the associations between cognitive reserve (CR), mood, and cognitive function in later life. I also aimed to explore whether CR, when considered in terms of a combination of the key proxy measures from across the lifespan, moderates the association between mood and cognitive function in community-dwelling older people without dementia. Previous research has only examined whether individual proxy measures of CR moderate the association between mood and cognitive function. In contrast, in this thesis I introduced a new approach to assessing the role of CR in this association by combining multiple proxy measures of CR in two studies. The study reported in Chapter 6 has the additional benefits of assessing these associations in a large cohort that is representative of the English population aged over 65.

The empirical study in Chapter 3 was the first to consider the associations of a comprehensive indicator of CR, comprising multiple proxy measures, with depressive thoughts and symptoms. In addition, this Chapter also examined the role of the individual proxy measures to assess the direct and indirect associations between the individual proxy measures from different points during the individual's lifetime and depressive thoughts and symptoms in later life. The empirical studies in Chapters 5 and 6 were the first to assess whether a comprehensive indicator of CR moderates the association of depressive symptoms, anxiety, or clinical level mood disorders and cognitive function in community-dwelling older people. Across the three empirical studies, participants were community-dwelling and free

from dementia. In all three studies, CR was indexed by measures that combined educational level, occupational complexity, and engagement in cognitively-stimulating leisure activities. In addition, all three studies included assessments of mood and cognitive function.

In the following sections each of the research questions will be addressed in turn, with the relevant results of the meta-analysis, systematic review, and empirical studies briefly summarised and discussed in relation to existing evidence and wider research. Methodological considerations are then addressed, before theoretical and practical implications are considered.

7.2 Research question 1

Do the three key proxy measures of cognitive reserve, educational level, occupational complexity/status, and engagement in cognitively-stimulating leisure activities, and indices which combine these three measures, differ in their association with cognitive function in healthy older people?

In Chapter 2 the existing literature on the association of the three key components of CR, individually and in combination, with cognitive function across multiple domains was systematically searched and data from 135 studies were entered into a series of meta-analyses. A substantial amount of research has examined the associations between educational level, occupational status or complexity, or engagement in cognitively-stimulating leisure activities and cognitive function with varying findings; while fewer studies have considered the associations between measures that combine multiple proxy measures and cognitive function. In the meta-analyses presented in Chapter 2, a small to moderate positive association was found of all three proxy measures of CR, individually and in combination, with cognitive function across the domains assessed. In Chapters 3, 5, and 6 the associations between CR, as indicted by a combination of educational level, occupational complexity, and engagement in cognitive activities, and cognitive function were assessed in addition to answering the specific research questions addressed in these Chapters. In all three empirical studies, CR was associated with better cognitive function. These results are in line with previous reviews of the associations between the proxy measures of CR and cognitive decline and dementia (Fratiglioni & Wang, 2007; Harrison et al., 2015; Meng & D'Arcy,

2012; Valenzuela & Sachdev, 2006a; 2006b); indicating a beneficial effect of CR on cognitive function.

Previous reviews of this area have considered the association between CR and cognitive decline and dementia whereas the meta-analysis in Chapter 2 introduced a new element, assessing whether the association of CR with cognitive function differed by cognitive domain in community-dwelling older people with no known diagnosis of cognitive impairment or decline. The most consistent associations were noted between educational level and indices that combined multiple proxy measures of CR and function in the different cognitive domains. Greater variation was noted across cognitive domains in the associations with occupational indices and engagement in cognitively-stimulating leisure activities. These results are interesting as they suggest that not all of the most commonly-used proxy measures are associated with each cognitive domain in the same manner. However, the number of studies included in some of these analyses were small meaning that these results will remain tentative until more studies assess the associations between proxy measures of CR, other than education, and different domains of cognitive function. Nevertheless, the variations in the associations across cognitive domains and between the different proxy measures support the argument that there are differential associations between the individual CR proxy measures and cognitive function (Andel et al., 2015; Jefferson et al., 2011; Lachman et al., 2010; R.S. Wilson et al., 2003a; Tucker & Stern, 2011). This adds weight to the argument that CR should be considered in terms of a lifetime of experiences rather than individual experiences or activities at a single time point. Despite this growing argument, the literature search revealed that few studies to date have considered CR in terms of a lifetime of cognitive activity, with measures encompassing multiple proxy measures. The few studies that considered combinations of proxy measures and the evidence from the empirical studies included in this thesis, suggest that such indices of CR have a consistent association with cognitive function, with less variability than has been observed in the relationships between individual proxy measures and cognitive function. Further studies utilising comprehensive indicators of CR are needed in order to identify whether this finding is consistent.

Generally, all the individual proxy measures of CR and measures that combined the proxy measures showed the strongest associations with the screening and general cognitive function measures rather than with the individual cognitive domains. This could provide an argument that the effects observed in Chapter 2 are due to ascertainment bias rather than CR

being directly associated with better cognitive function. Ascertainment bias in this context suggests that those with a higher educational level perform at an initially higher level than people with lower educational level, due to superior test taking ability and a better baseline cognitive function, rather than CR directly helping them to maintain cognitive function into later life (Tukko, Garrett, McDowell, Silverberg, & Kristjansson, 2003). The meta-analysis reported in Chapter 2 cannot clarify whether this is the case due its cross-sectional nature; however, a review of CR in ageing suggested that the effects are not due to ascertainment bias but rather CR is associated with less cognitive decline in individuals with varying baseline abilities (Tucker & Stern, 2011). As memory and executive function are the domains most commonly affected by cognitive decline, function in these domains may show a stronger association with CR longitudinally. A review of longitudinal studies of the association between CR and cognitive decline in different domains is needed to assess whether this is the case or whether CR is most consistently associated with changes in overall cognitive function.

In summary, the findings from the meta-analysis and the empirical Chapters indicate that education and indices that combine the three key proxy measures of CR are consistently moderately associated with cognitive function in community-dwelling older people. Occupational complexity and engagement in cognitively-stimulating activities had less consistent associations with cognitive function. This variation across the proxy measures adds to research that has suggested that the accumulation of experiences that contribute to CR provides additional benefits that help maintain cognitive function in later life, over and above the effect of an individual proxy measure (Valenzuela et al., 2011). While there are limitations to these Chapters, most notably that they only assess the cross-sectional associations, these findings emphasise the importance of building CR in order to help maintain cognitive function into later life.

7.3 Research question 2

Are the three key proxy measures of cognitive reserve, individually or in combination, associated with depressive symptoms and related thoughts in later life?

In Chapter 3, I assessed whether CR was associated not just with cognitive function in later life but also with levels of depressive thoughts and symptoms. The Lifetime of Experiences Questionnaire, which combines the three key proxy measures, had a small negative association with depressive thoughts and a moderate negative association with depressive symptoms, suggesting that higher levels of CR are associated with fewer depressive thoughts and symptoms. Further analysis, to assess the contribution of the individual components of CR, indicated that earlier life experiences, including education and cognitive activities, contribute to mid-life activities, which in turn contribute to late-life activities, which are themselves directly associated with depressive thoughts and symptoms. This was contrary to several previous studies that have indicated that educational level has a direct effect on depression in later life (Bjelland et al., 2008; Ladin, 2008; Ross & Mirowsky, 2006). This difference may have arisen because Chapter 3 assessed additional cognitive activities from across the lifespan that were not considered in these previous studies. There was a small negative association between education and depressive symptoms in the correlational analysis; however, education was not an individually significant predictor of variance in depressive symptoms when considered alongside the other cognitive activities that contribute to CR.

In Chapter 5, CR was not significantly associated with anxiety or depressive symptoms in either those with lower or higher CR. However, when the sample was considered as a whole and correlational analysis conducted, CR had a significant, albeit small, negative association with both anxiety and depressive symptoms, conversely, CR was not associated with rumination (see Appendix O). This supports the results of Chapter 3 that indicated that higher levels of CR are associated with less depressive symptoms, but does not support the association between mood related thought processes and CR.

These findings suggest that the associations of CR, when considered from a lifespan perspective, with depressive thoughts and symptoms and rumination differ from those with cognitive function in older people. Whereas, earlier life experiences have a direct effect on

cognitive function they have a more indirect effect on mood. As there is some overlap between the neuropathology underlying depression and cognitive impairment, we could reasonably have expected a similar direct effect of the earlier life stage on depressive symptoms, as has been observed with cognitive function. In addition, in previous research educational level was directly associated with levels of depressive symptoms in older people (Bjelland et al., 2008; Ladin, 2008; Ross & Mirowsky, 2006). This difference in the findings reported in Chapter 3 to previous research and our assumptions regarding the strength of the associations may be because the participants in this study generally exhibited low levels of depressive symptoms. Mild depressive symptoms could be related to current life events rather than to underlying pathology, which has been argued to be the case for clinical depression in later life. Further longitudinal research with participants with clinical levels of depression is needed to identify whether CR is associated with a lower risk of clinical depression in older people.

The differences in the associations of CR with depressive thoughts and rumination versus with depressive symptoms also needs to be addressed. The LEQ, which provides an indicator of the individual's CR from across the lifespan, accounted for over twice the amount of variance in depressive symptoms than depressive thoughts. The theory underlying the associations between depressive thoughts and symptoms argues that the thought processes are more consistent trait variables that tend to fluctuate less than depressive symptoms (Beck, 2002; Evans et al., 2005; Nolen-Hoeksema et al., 2008; Zauszniewski, 1997; Zauszniewski & Rong, 1999). Depressive thoughts and rumination are amenable to change through treatment, such as cognitive behavioural therapy (e.g. Beck, Rush, Shaw, & Emery, 1979; Kahl, Winter, & Schweiger, 2012; Watkins et al., 2011), however, their very nature as more trait than state variables could explain why levels of depressive thoughts and rumination have a smaller association with CR than depressive symptoms or anxiety. The thought processes considered in this thesis increase the risk of experiencing depression (e.g. Abramson et al., 2002; Beck, 2002; Nolen-Hoeksema et al., 2008) while the individual components of CR reduce the risk of depression (e.g. Adams et al., 2011; Jenkins, 2011; Narushima et al., 2013; Ross & Mirowsky, 2006; 2010). Perhaps an interesting avenue for future research could be to investigate whether CR moderates the association of depressive thoughts and rumination with lowered mood in later life, to assess if CR provides protection to those at an increased risk of experiencing depression and/or anxiety. If this were the case, it would provide further

evidence that could help explain the mechanisms underlying the associations between proxy measures of CR and mood.

The differences in the associations of CR with mood and the related thought processes versus with cognitive function suggest that CR may be more important in maintaining cognitive rather than psychological health in later life. Indeed, this led to the question of whether CR may be more important in mitigating the negative associations between mood and cognitive function than in protecting against lowered mood in of itself.

7.4 Research question 3

Research question 3 – Does cognitive reserve, as indicated by individual proxy measures of cognitive reserve or measures that combine the three key proxy measures, moderate the association between mood and cognitive function in older people?

In Chapter 4, existing research on whether proxy measures of CR moderate the association of depression and anxiety with cognitive function in later life was systematically searched and the results collated to address this question. The studies included were disparate in both their methodology and results but allowed for a tentative conclusion that CR moderates the association between depression and cognitive function in later life; cognitive function in people with lower levels of CR was more negatively affected by depression and depressive symptoms than in people with higher levels of CR. However, the previously published research available for this review, other than the published version of Chapter 5 of this thesis, focused on single proxy measures of CR rather than indices that combine multiple proxy measures. In addition, it was not possible to clearly address the question of whether CR moderates the association between anxiety and cognitive function due to the lack of existing research investigating this association.

Chapters 5 and 6 built upon the previous literature and results of this systematic review, assessing whether comprehensive indicators of CR moderate the association of depressive symptoms, rumination, anxiety, and mood disorders at clinical levels with cognitive function. In Chapter 5, there was a negative association of depressive symptoms and anxiety with cognitive function in those with low levels of CR but there were no significant associations between mood and cognitive function in those with high levels of CR.

However, rumination was not associated with cognitive function in either the high or low CR groups in the correlation analysis. In contrast, rumination has been associated with poorer cognition in several previous studies (Davis & Nolen-Hoeksema, 2000; Lyubomirsky et al., 2003); although, rumination was an independently significant predictor of variation in verbal fluency in the low CR group in the regression analysis, but in the opposite direction than was to be expected. This is an interesting finding because it suggests that when depressive symptoms, anxiety, and rumination were entered into the model simultaneously, higher levels of depressive symptoms and anxiety were associated with poorer cognitive function while higher levels of rumination were associated with better verbal fluency in those with low CR. This would indicate that while rumination is a negative thought process associated with a greater risk of developing depression and maintenance of depression once it has arisen, it might have a differential association with cognitive function than depressive symptoms themselves. Indeed, depressive thoughts were associated with depressive symptoms but were not associated with cognitive function in Chapter 3. Perhaps depressive thoughts and rumination are associated with a vulnerability toward developing depression, as outlined in cognitive theories of depression (Abramson et al., 2002; Beck, 1967; 2002) but depressive symptoms or anxiety need to develop before there is a negative effect on cognitive function.

In Chapter 6, the difference in cognitive performance between those with and those without a mood disorder was almost two and a half times greater in the low CR group than the high CR group. This indicates that the presence of a mood disorder has a greater negative effect on cognitive performance in those with low levels of CR than in those with high levels of CR. This adds greatly to current evidence, as the study in Chapter 6 was the first large, representative cohort study to consider this question utilising a comprehensive indicator of CR. These findings support several previous studies that have noted an association between depression and cognitive function in those with higher CR but not in those with lower CR (e.g. Pálsson et al., 1999; 2001). Nevertheless, they contradict reports by other research teams that noted an opposing effect (e.g. Geerlings et al., 2000; O'Shea et al., 2015). However, none of these previous studies considered an index of CR that combined multiple proxy measures of CR from a lifespan perspective, which may provide a greater protective effect than one experience, such as educational level, alone.

One of the issues that arose in addressing this research question was whether the moderating effect of CR found was due to the associations between mood and CR. In the

studies presented in Chapters 3 and 5, higher levels of CR were associated with fewer depressive symptoms, and in Chapter 6 the prevalence of clinical mood disorders was lower in those with higher CR than in those with lower CR. These results raise the question of whether this mismatch in the levels of symptoms results in the different associations between mood and cognitive function in those with lower and higher levels of CR. This possibility was addressed in Chapter 5 through the creation of depression-matched groups. The analyses of these matched groups indicated that there were indeed variations in the association between mood and cognitive function by CR level when both groups had equal levels of depressive symptoms. The evidence which suggests that there is a pathological overlap between cognitive decline and depression provides a potential explanation as to why higher CR is associated with fewer depressive symptoms and why it moderates the association between mood and cognitive function. Those with more neuropathology may be more likely to experience depression and cognitive decline but those with higher CR may be able to maintain their cognitive functioning despite the neuropathology.

The findings of this thesis suggest that depressive symptoms, anxiety, and clinically relevant mood disorders have greater negative associations with cognitive function in those with lower levels than higher levels of CR. This highlights the importance of CR in maintaining cognitive ability both directly through preserved ability and indirectly through its mitigating effects on the negative association of subclinical mood disorder symptoms and clinical level mood disorders with cognitive function.

7.5 Methodological considerations

Researching CR, mood, and cognitive function is associated with a number of challenges that may have affected the presented studies, and these potential limitations should be considered when interpreting the results presented in this thesis.

There is considerable debate as to how CR is best assessed. The majority of evidence to date has considered CR in terms of single proxy measures with fewer studies employing indices that combine multiple proxy measures, as can be seen from the meta-analysis and systematic review in Chapters 2 and 4. However, as outlined in the introduction, there is a growing argument that CR is a fluid construct that is not fixed at one age or by one experience (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez

Rodríguez et al., 2011; Stern, 2009; Tucker & Stern, 2011; Whalley et al., 2006). As such, it was decided that for the purposes of this thesis, and to extend upon the available evidence, that CR should be assessed by measures which combine multiple proxy measures of CR. When considering activities which represent an individual's CR, the most commonly-used are educational level, occupational complexity, and engagement in cognitively-stimulating activities, hence the utilisation of the Lifetime of Experiences Questionnaire and Cognitive Lifestyle Score in this thesis.

Educational level has acted as the most commonly used proxy measure of CR across all areas of the research that supports the existence of this concept. However, there is considerable argument that educational level simply reflects IQ rather than experiences acquired through education (Stern, 2009) and IQ tends to be highly correlated with cognitive performance (Deary, Whitman, Starr, Whalley & Fox, 2004). However, a recent study examining genetic factors in the association between intelligence and mortality utilising data from three large cohorts, from the US, Sweden, and Denmark, found that IQ was largely inherited (Arden et al., 2015). As such, it is probable that IQ represents brain reserve rather than CR, which is built by engaging in cognitively-stimulating activities. Indeed, in Nucci and colleagues (2011) IQ was only moderately correlated with CR, which was assessed through educational level, occupation, and engagement in cognitively-stimulating leisure activities. This observation led Nucci and colleagues to suggest that there is a distinction between the two constructs of IQ and CR. Additionally, educational level, occupational complexity, and cognitively-stimulating leisure activities impart a protective effect over and above that provided by innate intelligence (Stern, 2009). As such, the focus of this thesis on cognitive activities across the lifespan should go at least some way to overcoming the potential confound of IQ. However, it should be noted that we cannot fully discount the possibility that the level of education an individual obtains and his/her subsequent occupation is at least partially dependent upon IQ, in the same way that nature and nurture effects cannot be fully disentangled. In this thesis, IQ was not considered as a proxy measure of CR due to the above arguments that it is a separate construct and because it is not amenable to modification as are the activities which are thought to contribute to CR, and which have been included here.

Whalley, Deary, Appleton, and Starr (2004) question whether the observed effect of CR on cognitive function is due to the influence of education and occupation on lifestyle

choices and health. For instance, they suggest that having a higher educational attainment and a more complex occupation leads to better personal management of stressful experiences, safer working environments, more choice of and/or greater participation in cognitively-stimulating leisure activities, better use of health services, and better translation of health education into healthier lifestyles. It is difficult to discount this argument based on the findings presented in this thesis. However, the evidence that CR moderates the association between brain pathology and the observable signs and symptoms of cognitive decline and dementia suggests that CR imparts a direct effect (e.g. Brickman et al, 2011; Dufouil et al., 2003; Mortamais et al., 2014; Saczynski et al., 2008).

Jones and colleagues (2010) argued that it is important to consider measures of neuropathology when assessing the association between CR and cognitive and functional impairment. While the majority of studies assessing CR focus on the observation that the activities thought to contribute to CR are associated with better cognitive function and a reduced risk of cognitive decline and dementia, studies in which levels of neuropathology are also assessed add additional weight to the evidence. Unfortunately, assessing the neurological structural and functional correlates of cognitive function and the impact of CR on these associations was beyond the scope of this thesis. However, evidence from previous research supports the argument that the proxy measures used in this thesis influence the association of the neurological pathology underlying cognitive decline and dementia with cognitive performance (e.g. Bartrés-Faz & Arenaza-Urquijo, 2011; Bartrés-Faz et al., 2009; Christensen et al., 2008; Solé-Padullés et al., 2009). The assessment of the theoretical construct of CR is not without its issues; however, utilising measures that combine multiple proxy measures, all of which have neurobiological evidence underpinning their association with cognitive function, may go at least some way toward giving as accurate an estimation of an individual's CR as is possible without the inclusion of neuropathological investigations.

The measures of lifetime cognitive activity and mood in Chapters 3 and 5 were self-report measures that relied on participants to accurately recall their activities from a long time ago and to self-report their experience of depressive thoughts, rumination, depressive symptoms and anxiety. Self-reports may be limited by memory distortion and can be influenced by the participant's current mood (Stone & Shiffman, 2002). The Lifetime of Experiences Questionnaire was administered to the participants, rather than self-completed, in an attempt to elicit information that was as accurate as possible. However, without

longitudinal studies using observational methods it is not possible to avoid at least some bias in recall. The self-report measures of depressive symptoms and anxiety used in Chapters 3 and 5 allow for the assessment of levels of symptoms but do not give sufficient information to consider clinical diagnoses of either depression or anxiety. This issue was overcome in Chapter 6 with the use of the GMS-AGECAT, which includes a structured interview technique that draws from respondents' answers and the interviewer's observations, and uses a well-established diagnostic algorithm that enables the assignation of diagnostic categories for both anxiety and depression ranging from none to clinical levels of a mood disorder. However, in all three empirical studies reported in this thesis, the levels of depressive symptoms, anxiety, and clinically relevant mood disorders were relatively low in comparison to previous reports (Copeland et al., 2004; McDougall et al., 2007; Zhang et al., 2015). This may be because all of the samples were self-selecting and those with a lower current mood, or who are currently experiencing a depressive episode may be unwilling to participate in a study. The study reported in Chapter 6 utilised population-representative sampling rather than convenience sampling as was used in the other empirical studies; as such, this study might have been less subject to the self-selecting bias. Nevertheless, despite the weightings utilised in the analyses to ensure the included sample is demographically representative of the population, it is not possible to tell how many of those contacted regarding participation chose not to take part due to lowered mood. This is a criticism which could be levelled at most studies of community-dwelling older people and cannot be rectified as people can always exercise their rights not to participate or to withdraw from the study. Some inpatient studies are able to overcome the issue of self-selection but are then limited to those clinical samples, with results that cannot be generalised to the community-dwelling population.

There are also several difficulties in assessing cognitive function; for instance, the inherent differences in assessing overall cognitive function versus individual domains. Researchers have argued that an overall decline in cognition in older people is preceded by domain-specific changes (Clark et al., 2012; Deary et al., 2009; Wilson et al., 2002a). In this thesis I utilised not only general assessments of cognitive function, including the Addenbrooke's Cognitive Examination-III, the Montreal Cognitive Assessment, and the Cambridge Cognitive Assessment, but also measures designed to assess memory and executive function, which are two of the domains most commonly affected by age-related cognitive decline (Lindeboom & Weinsteing, 2004; Schönknecht, Pantel, Kruse, Schröder, 2005). However, as we wanted to limit the burden of the testing session on the participants,

we were unable to employ a comprehensive assessment of cognitive function that might have provided a more thorough understanding of the associations between CR, mood, and cognitive function. To build on the results of this thesis it would be beneficial for a future study to utilise a measure that combines multiple indicators of CR, such as those used in this thesis, alongside a comprehensive neuropsychological assessment.

It should also be considered that there may be a number of confounds that can account for the associations found in this thesis. As mentioned above, Whalley and colleagues (2004) argued that the associations between higher cognitive reserve and better cognitive functioning in later life might be accounted for through better use of health resources. Indeed, it is possible that those with higher cognitive reserve have better cognitive function and lower levels of mood disorders in later life as they generally have higher incomes, better health seeking behaviours, and better planning or problem solving skills. Future research could consider controlling for these potential confounds in order to further elucidate whether cognitive reserve, as measured by cognitive activity across the lifespan, is directly associated with better cognitive function and lower levels of mood disorders or whether these potential confounds are accounting for the observed associations.

7.6 Directions for future research

The studies presented in this thesis have contributed to our understanding of the complicated inter-relationships between CR, mood, and cognitive function in later life. The findings also raise some further questions and suggest directions for future research.

Chapters 4, 5, and 6 all support the supposition that CR moderates the association between mood and cognitive function, but the question as to whether CR moderates the association between mood and the increased risk of cognitive decline or dementia remains unclear. It would be beneficial for future research to utilise longitudinal designs to assess this question and to attempt to delineate the direction of any associations. The evidence presented in this thesis and previous arguments that CR is a fluid construct, which is built upon across the lifespan (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern, 2011; Whalley et al., 2006), indicate that future research assessing the impact of CR should utilise comprehensive indicators that consider multiple experiences. If CR does moderate the association between mood and the

risk of developing cognitive decline and dementia, it would provide additional support to the importance of continuing to build on CR throughout the lifespan.

In addition to assessing whether CR moderates the association between depression and the risk of dementia, future research could examine whether it moderates the association between mood and cognitive function in other neurodegenerative conditions. This could be important in a range of conditions, particularly as mood disorders are more common in people with several neurodegenerative diseases, such as Parkinson's disease and multiple sclerosis, than in neurologically intact community-dwelling older people (Dissanayaka et al., 2011; Leddy, Fowler, Giovanonni, & Robson, 2014; Reijnders, Ehrt, Weber, Aarsland, & Leentjens, 2008). I will take Parkinson's disease to provide an example of the associations in such conditions. Depression has been associated with poorer cognitive performance and a greater risk of dementia in people with Parkinson's disease (e.g. Marder, Tang, Cote, Stern, & Mayeaux, 1995; Uekermann, Daum, Peters, Wiebel, Przuntek, & Müller, 2003). In contrast, CR has been associated with better cognitive function in Parkinson's disease (Hindle et al., 2015; Hindle et al., 2014; Muslimovic, Schmand, Speelman, & de Haan, 2007). To date, only one study has specifically considered whether education moderates the association between mood and cognitive function in people with Parkinson's disease (Kummer et al., 2009). In this study, depression was associated with impaired executive function in the less well educated but not in the more highly educated group. No previous study has assessed whether other proxy measures of CR, or indices that combine multiple proxy measures, moderate the association between mood and cognition in people with Parkinson's disease. This is an important line of research as depression and cognitive decline are commonly cited as the most bothersome and care-eliciting non-motor problems of Parkinson's disease (Uebelacker, Epstein-Lubow, Lewis, Broughton, & Friedman, 2014). Future research could aim to build upon the evidence presented in this thesis, that CR moderates the association between mood and cognitive function, by extending the research to include clinical populations, such as those with Parkinson's disease, as demonstrated above. This line of research could enable the development of preventive interventions at the early stage of disease, which may help maintain cognitive function and alleviate the negative affect that the lowered mood associated with neurodegenerative diseases can have on cognitive function.

CR may have a similar effect in protecting against the experience of depression, although it is possible that it also works through increasing people's well-being through their use of health services and better management of stressful-situations, as Whalley and colleagues (2004) suggested. Future research could utilise imaging methods when considering whether CR moderates the association between mood and cognitive function to assess the role played by different types and levels of pathology. In addition, considering measures of health-service utilisation, social networks, stress management, and other lifestyle factors would enable researchers to assess whether the association between CR and mood is actually dependent upon these factors or whether these factors are stronger moderators of the association between mood and cognitive function than CR. Extending the findings of this thesis in such a manner could offer further explanation of the associations observed.

7.7 Implications of the findings

The findings of this thesis have indicated that CR is associated with better cognitive performance and lower levels of depressive thoughts and symptoms, and that it mitigates the negative association between mood disorders, at sub-clinical and clinical levels, and cognitive function. This research provides evidence of what may be helpful in maintaining cognitive and psychological health in later life. Such evidence has previously been used to inform preventive interventions aimed at both directly maintaining cognitive and psychological health and increasing the activities associated with better function in later life.

Several primary preventive interventions have sought to increase the activities associated with CR. Two such examples are the Senior Odyssey study (Stine-Morrow, Parisi, Morrow, & Park, 2008) and the Agewell pilot trial (Clare et al., 2015). The Senior Odyssey programme focused on promoting social and intellectual engagement through participation in a team-based competition in ill-defined problem solving with participants showing benefits in speed of processing, inductive reasoning, and divergent thinking (Stine-Morrow et al., 2008). The Agewell pilot trial was a behaviour change intervention aimed at increasing cognitive and physical activity in a sustainable manner (Clare et al., 2015). This trial succeeded in increasing physical and cognitive activity in the groups that participated in the goal-setting intervention over the group that received information regarding a healthier lifestyle, and the goal setting groups showed several secondary benefits in both cognitive function and health,

although not in all domains (Clare et al., 2015). While both of these primary interventions demonstrate the potential benefits of increasing activity that can be obtained in a cost-effective manner, both studies had some limitations. In Senior Odyssey, there was greater drop-out from those participating in the programme than from the wait-list control group, while in Agewell there was a difficulty in encouraging men to participate in the activities offered at the centre. These limitations suggest that while increasing engagement in the activities associated with CR has potential benefits, the uptake of such programmes may be limited to those who are already interested in increasing their activity levels.

The majority of interventions designed with the intent of reducing the incidence of depression and/or anxiety in later life have concentrated on secondary prevention, focused on those at high risk of developing depression (Hindi, Dew, Albert, Lotrich, & Reynolds, 2011). Several trials, which targeted older people with subsyndromal symptoms of depression and/or anxiety, have shown success with stepped care, administered by nurses, and problem-solving therapy for primary care, delivered by lay health counsellors (e.g. Reynolds et al., 2014; van't Veer-Tazelaar et al., 2009). Hindi and colleagues (2011) argued that, in relation to depression and anxiety, the most efficient use of resources is to target interventions toward those at high risk of developing a mood disorder. However, these types of preventive interventions rely on the identification of older people with elevated depressive symptoms. Primary interventions have predominantly focused on increasing literacy about depression in later life, social activity, or exercise in community and nursing home populations. A review of the evidence suggests that these methods have some success in decreasing the incidence of depression (Forsman, Nordmyr, & Wahlbeck, 2011). To date, it is still unclear as to what approach would be the most successful in reducing the incidence of depression and anxiety in older people. Future research could help address this question by following participants over a longer time period as the current evidence is generally limited to less than two years of follow-up.

While evidence such as that presented in this thesis could help inform future preventive interventions aimed at maintaining both cognitive and psychological health in later life, there are inherent difficulties in designing these interventions. Consideration must be paid to the cost-effectiveness of designs in relation to their efficacy. In theory, as CR is associated with both better cognitive function and fewer depressive thoughts and symptoms, interventions designed to increase an individual's CR should be beneficial. Previous evidence

and the results of this thesis indicate that CR is built across the lifespan therefore increasing cognitive activity in mid-life may also benefit later-life cognitive function. Further longitudinal studies are required to assess what benefits helping people increase their CR earlier in life may have on later life cognitive function. A particular emphasis could be placed upon interventions aimed at encouraging increased engagement in cognitive activity in people with lower levels of education and less complex occupations as it has been previously shown that cognitively-stimulating leisure activities can compensate for lower levels of these experiences (Andel et al., 2015; Lachman et al., 2010). Additionally, Chapter 3 demonstrated the associations of cognitively-stimulating leisure activities in young adulthood and mid-life with cognitive function in later life, supporting the importance of engaging in such activities. However, people need to be willing to participate in such interventions and engage in the relevant activities, and investigations on how to encourage engagement are needed.

There is certainly growing emphasis on the importance of engaging in a healthy lifestyle and keeping your brain active, with frequent reference in the media to what people can do to help reduce the risk of dementia. The growing popularity of such ideas can be seen in the booming business of computerised brain training. Such brain training has shown some benefit to the targeted cognitive domains in older people but it does not appear to translate to other cognitive domains (Kueider, Parisi, Gross, & Rebok; 2012; Lampit, Hallock, & Valenzuela, 2014; Owen et al., 2010). It is probable that the decrease in the prevalence of dementia and cognitive impairment observed in several western countries, including the UK, is at least partially due to greater awareness of the benefits of a healthier lifestyle and implementation of such a lifestyle in those now approaching older age (Jagger et al., 2009; Matthews et al., 2013; Wu et al, 2015). However, this reduction in prevalence rates is limited to a few western countries and the percentages of the older population with cognitive decline and dementia are continuing to increase in low and middle-income countries (Alzheimer's Disease International, 2015). The reduced prevalence of cognitive impairment and dementia in the UK would suggest that policies already in place, such as those that have increased the compulsory requirements for education and encouraged healthier lifestyles, may be starting to show benefits in the current cohort of older people. However, as the older population continues to grow, further emphasis on encouraging people to engage in education and cognitively-stimulating leisure activities, before a person reaches old age, is required to continue to reduce the prevalence of cognitive decline and dementia.

7.8 Conclusions

Cognitive ageing is a growing concern for both society and for older people themselves. The results of this thesis contribute to the growing body of evidence that cognitive activities across the lifespan help to maintain cognitive function in later life. This thesis has implications for future research relating to CR in that it emphasises the importance of considering multiple cognitive activities from across the lifespan, rather than considering CR in terms of a single proxy measure. In addition, this thesis provided evidence that CR, when assessed with consideration to the three key proxy measures, mitigates the negative association of depression and anxiety with cognitive function, both at the subclinical symptom level and at clinical mood disorder levels. The evidence provided here also suggests that higher levels of CR are associated with fewer depressive thoughts and symptoms in community-dwelling older people. Overall, the findings of this thesis have increased our understanding of the complex inter-relationships between CR, mood, and cognitive function, providing further evidence that a focus on increasing CR throughout the lifespan could help people to maintain cognitive and psychological health in later life.

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*, 153-62. doi: 10.1093/geronb/57.2.P153

Abramson, L. Y., Alloy, L. B., Hogan, M. E., Whitehouse, W. G., Donovan, P., Rose, D. T., . . . Raniere, D. (2002). *Cognitive vulnerability to depression: Theory and evidence*. In R. L. Leahy, & E. T. Dowd (Eds.), *Clinical advances in cognitive psychotherapy: Theory and Application* (pp. 75-92). New York: Springer.

Abramson, L. Y., Metalsky, G. I., & Alloy, L. B. (1989). Hopelessness depression: a theory-based subtype of depression. *Psychological Review, 96*, 358-372. doi: 10.1037/0033-295X.96.2.358

Acevedo, A., Loewenstein, D. A., Agrón, J., & Duara, R. (2007). Influence of sociodemographic variables on neuropsychological test performance in Spanish-speaking older adults. *Journal of Clinical and Experimental Neuropsychology, 29*, 530-544. doi: 10.1080/13803390600814740

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 & Society, 31*, 683-712. doi: 10.1017/S0144686X10001091

Age UK. (2014). *Care in crisis 2014*. Retreived from: http://www.ageuk.org.uk/professional-resources-home/research/social-research/home--care/

Agüero-Torres, H., Thomas, V. S., Winblad, B., & Fratiglioni, L. (2002). The impact of somatic and cognitive disorders on the functional status of the elderly. *Journal of Clinical Epidemiology, 55*, 1007-1012. doi: 10.1016/S0895-4356(02)00461-4

Aiken Morgan, A. T., Sims, R. C., & Whitfield, K. E. (2010). Cardiovascular health and education as sources of individual variability in cognitive aging among African Americans. *Journal of Aging and Health, 22*, 477-503. doi: 10.1177/0898264310361627

Al Hazzouri, A. Z., Haan, M. N., Galea, S., & Aiello, A. E. (2011). Life-course exposure to early socioeconomic environment, education in relation to late-life cognitive function among older Mexicans and Mexican Americans. *Journal of Aging and Health, 23*, 1027-1049. doi: 10.1177/0898264311421524

Albert, S. M. & Teresi, J. A. (1999). Reading ability, education, and cognitive status assessment among older adults in Harlem, New York City. *American Journal of Public Health, 89*, 95-97. doi: 10.2105/AJPH.89.1.95

Alden, D., Austin, C., & Sturgeon, R. (1989). A correlation between the Geriatric Depression Scale long and short forms. *Journal of Gerontology, 44*, 124-125. doi: 10.1093/geronj/44.4.P124

Alexopoulos, G. S. (2005). Depression in the elderly. *The Lancet, 365*, 1961-1970. doi: 10.1016/S0140-6736(05)66665-2

Alvarado, B. E., Zunzunegui, M. V., Del Ser, T., & Beland, F. (2002). Cognitive decline is related to education and occupation in a Spanish elderly cohort. *Aging Clinical and Experimental Research, 14*, 132-142. doi: 10.1007/bf03324426

Alvarado, B. E., Zunzunegui, M. V., Béland, F., Sicotte, M., & Tellechea, L. (2007). Social and gender inequalities in depressive symptoms among urban older adults of Latin America and the Caribbean. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 62*, S226-S236. doi: 10.1093/geronb/62.4.s226

Alzheimer's Disease International (2015). *World Alzheimer's Report 2015. The Global Impact of Dementia: An analysis of prevalence, incidence, cost and trends*. Retrieved from http://www.alz.co.uk/research/world-report-2015

Alzheimer's Society. (2014). *Public health, prevention and dementia*. Retrieved from: http://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=2766

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Arlington, VA: American Psychiatric Association.

Andel, R., Kåreholt, I., Parker, M. G., Thorslund, M., & Gatz, M. (2007). Complexity of primary lifetime occupation and cognition in advanced old age. *Journal of Aging and Health, 19*, 397-415. doi: 10.1177/0898264307300171

Andel, R., Silverstein, M., & Kåreholt, I. (2015). The role of midlife occupational complexity and leisure activity in late-life cognition. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 70*, 314-321. doi: 10.1093/geronb/gbu110

Anderson, L. A., Day, K. L., Beard, R. L., Reed, P. S., & Wu, B. (2009). The public's perceptions about cognitive health and Alzheimer's disease among the U.S. population: a national review. *The Gerontologist, 49*, S3-S11. doi: 10.1093/geront/gnp088

Angel, L., Fay, S., Bouazzaoui, B., Baudouin, A., & Isingrini, M. (2010). Protective role of educational level on episodic memory aging: an event-related potential study. *Brain and Cognition, 74*, 312-323. doi: 10.1016/j.bandc.2010.08.012

Anstey, K. & Christensen, H. (2000). Education, activity, health, blood pressure and apolipoprotein E as predictors of cognitive change in old age: a review. *Gerontology, 46*, 163-177. doi: 10.1159/000022153

Anstey, K. J., Hofer, S. M., & Luszcz, M. A. (2003). A latent growth curve analysis of late-life sensory and cognitive function over 8 years: evidence for specific and common factors underlying change. *Psychology and Aging, 18*, 714-726. doi: 10.1037/0882-7974.18.4.714

Arbuckle, T. Y., Gold, D., & Andres, D. (1986). Cognitive functioning of older people in relation to social and personality variables. *Psychology and Aging, 1*, 55-62. doi: 10.1037/0882-7974.1.1.55

Arden, R., Luciano, M., Deary, I. J., Reynolds, C. A., Pedersen, N. L., Plassman, B. L., . . . Visscher, P. M. (2015). The association between intelligence and lifespan is mostly genetic. *International Journal of Epidemiology*. (Advance online publication). doi: 10.1093/ije/dyv112

Ardila, A., Ostrosky-Solis, F., Rosselli, M., & Gómez, C. (2000). Age-related cognitive decline during normal aging: the complex effect of education. *Archives of Clinical Neuropsychology, 15*, 495-513. doi: 10.1016/S0887-6177(99)00040-2

Ashley, J. G. (2009). *The relation between different forms of activity and cognition in older adults.* (Doctoral dissertation) Southern Illinois University Carbondale. Retrieved from http://search.proquest.com/docview/21069568?accountid=14874

Avila, R., Moscoso, M. A. A., Ribeiz, S., Arrais, J., Jaluul, O., & Bottino, C. M. C. (2009). Influence of education and depressive symptoms on cognitive function in the elderly. *International Psychogeriatrics, 21*, 560-567. doi: 10.1017/S1041610209008928

Baddeley, A., Emslie, H., & Nimmo-Smith, I. (1993). The spot-the-word test: a robust estimate of verbal intelligence based on lexical decision. *British Journal of Clinical Psychology, 32*, 55-65. doi: 10.1111/j.2044-8260.1993.tb01027.x

Ballmaier, M., Toga, A. W., Blanton, R. E., Sowell, E. R., Lavretsky, H., Peterson, J., . . . Kumar, A. (2004). Anterior cingulate, gyrus rectus, and orbitofrontal abnormalities in elderly depressed patients: an MRI-based parcellation of the prefrontal cortex. *American Journal of Psychiatry, 161*, 99-108. doi: 10.1176/appi.ajp.161.1.99

Barnes, D. E., Tager, I. B., Satariano, W. A., & Yaffe, K. (2004). The relationship between literacy and cognition in well-educated elders. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 59*, 390-395. doi: 10.1093/gerona/59.4.M390

Barnes, L. L., Wilson, R. S., de Leon, C. F., & Bennett, D. A. (2006). The relation of lifetime cognitive activity and lifetime access to resources to late-life cognitive function in older African Americans. *Aging, Neuropsychology and Cognition, 13,* 516-528. doi: K8005180774554M6

Barnes, L. L., Wilson, R. S., Hebert, L. E., Scherr, P. A., Evans, D. A., & Mendes de Leon, C. F. (2011). Racial differences in the association of education with physical and cognitive function in older blacks and whites. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 66,* 354-363. doi: 10.1093/geronb/gbr016

Bartres-Faz, D. & Arenaza-Urquijo, E. M. (2011). Structural and functional imaging correlates of cognitive and brain reserve hypotheses in healthy and pathological aging. *Brain Topography, 24,* 340-357. doi: 10.1007/s10548-011-0195-9

Bartrés-Faz, D., Solé-Padullés, C., Junqué, C., Rami, L., Bosch, B., Bargalló, N., . . . Molinuevo, J. L. (2009). Interactions of cognitive reserve with regional brain anatomy and brain function during a working memory task in healthy elders. *Biological Psychology, 80,* 256-259. doi: 10.1016/j.biopsycho.2008.10.005

Beard, J. R. & Bloom, D. E. (2015). Towards a comprehensive public health response to population ageing. *The Lancet, 385,* 658-661. doi: 10.1016/S0140-6736(14)61461-6

Beatty, W. W., Mold, J. W., & Gontkovsky, S. T. (2003). RBANS performance: Influences of sex and education. *Journal of Clinical and Experimental Neuropsychology, 25,* 1065-1069. doi: 10.1076/jcen.25.8.1065.16732

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. doi: 10.1037/a0016035

Beaudreau, S. A. & O'Hara, R. (2008). Late-life anxiety and cognitive impairment: a review. *The American Journal of Geriatric Psychiatry, 16,* 790-803. doi: 10.1097/JGP.0b013e31817945c3

Beck, A. T. (2002). Cognitive models of depression. In R. L. Leahy E. T. Dowd (Ed.), *Clinical Advances in Cognitive Psychotherapy: Theory and Application* (pp. 29-61). New York, NY: Springer Publishing Co.

Beck, A. T. (1967). *Depression: Clinical, experimental, and theoretical aspects*. New York: Harper & Row.

Beck, A. T., Rush, A. J., Shaw, B. F., & Emery, G. (1979). *Cognitive therapy of depression*. New York, NY: The Guilford Press.

Becker, J. T., Chang, Y., Lopez, O. L., Dew, M. A., Sweet, R. A., Barnes, D., . . . Reynolds III, C. F. (2009). Depressed mood is not a risk factor for incident dementia in a community-based cohort. *The American Journal of Geriatric Psychiatry, 17*, 653-663. doi: 10.1097/JGP.0b013e3181aad1fe

Beekman, A. T., de Beurs, E., van Balkom, A. J., Deeg, D. J., van Dyck, R., & van Tilburg, W. (2000). Anxiety and depression in later life: co-occurrence and communality of risk factors. *American Journal of Psychiatry, 157*, 89-95. doi: 10.1176/ajp.157.1.89

Beekman, A. T. F., Bremmer, M. A., Deeg, D. J. H., van Balkom, Anton J. L. M., Snut, J. H., de Beurs, E., . . . van Tilburg, W. (1998). Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. *International Journal of Geriatric Psychiatry, 13*, 717-726. doi:10.1002/(SICI)1099-1166(1998100)13:10<717::AID-GPS857>3.0.CO;2-M

Beekman, A. T. F., Copeland, J. R. M., & Prince, M. J. (1999). Review of community prevalence of depression in later life. *The British Journal of Psychiatry, 174*, 307-311. doi: 10.1192/bjp.174.4.307

Benedict, R. H. B., Morrow, S. A., Weinstock Guttman, B., Cookfair, D., & Schretlen, D. J. (2010). Cognitive reserve moderates decline in information processing speed in multiple sclerosis patients. *Journal of the International Neuropsychological Society, 16*, 829-835. doi: 10.1017/S1355617710000688

Bhalla, R. K., Butters, M. A., Zmuda, M. D., Seligman, K., Mulsant, B. H., Pollock, B. G., & Reynolds, C. F.,3rd. (2005). Does education moderate neuropsychological impairment in late-life depression? *International Journal of Geriatric Psychiatry, 20*, 413-417. doi: 10.1002/gps.1296

Bielak, A. A. M. (2010). How can we not 'lose it' if we still don't understand how to 'use it'? Unanswered questions about the influence of activity participation on cognitive performance in older age—A mini-review. *Gerontology, 56*, 507-519. doi: 10.1159/000264918

Bierman, E. J. M., Comijs, H. C., Jonker, C., & Beekman, A. T. F. (2005). Effects of anxiety versus depression on cognition in later life. *The American Journal of Geriatric Psychiatry, 13*, 686-693. doi: 10.1097/00019442-200508000-00007

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale: an updated literature review. *Journal of Psychosomatic Research, 52*, 69-77. doi: 10.1016/S0022-3999(01)00296-3

Bjelland, I., Krokstad, S., Mykletun, A., Dahl, A. A., Tell, G. S., & Tambs, K. (2008). Does a higher educational level protect against anxiety and depression? The HUNT study. *Social Science & Medicine, 66*, 1334-1345. doi: 10.1016/j.socscimed.2007.12.019

Blake, H., Mo, P., Malik, S., & Thomas, S. (2009). How effective are physical activity interventions for alleviating depressive symptoms in older people? A systematic review. *Clinical Rehabilitation, 23*, 873-887. doi: 10.1177/0269215509337449

Blane, D., Webb, E., Wahrendorf, M., & Netuveli, G. (2012). Life course influences on quality of life at age 50 years: evidence from the national child development study (1958 British birth cohort study). *Longitudinal and Life Course Studies, 3*, 346-358. doi: 10.14301/llcs.v3i3.178

Blazer, D. G. (2003). Depression in late life: review and commentary. *Focus, 7*, 118-136. doi: 10.1176/foc.7.1.foc118

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

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2009). *Introduction to meta-analysis*. Chichester: John Wiley & Sons, Ltd.

Boyles, A. L., Harris, S. F., Rooney, A. A., & Thayer, K. A. (2011). Forest plot viewer: a new graphing tool. *Epidemiology and Community Health, 22*, 746-747. doi: 10.1097/EDE.0b013e318225ba48

Braam, A. W., Copeland, J. R. M., Delespaul, P. A. E. G., Beekman, A. T. F., Como, A., Dewey, M., . . . Skoog, I. (2014). Depression, subthreshold depression and comorbid anxiety symptoms in older Europeans: results from the EURODEP concerted action. *Journal of Affective Disorders, 155*, 266-272. doi: 10.1016/j.jad.2013.11.011

Brand, H. L. S. (Oct 2002). *The relationship between social-cognitive factors and physical health on memory function in older adults.* (Doctoral dissertation) Saint Louis University. Retrieved from http://search.proquest.com/docview/619951287?accountid=14874

Brewster, P. W., Melrose, R. J., Marquine, M. J., Johnson, J. K., Napoles, A., MacKay-Brandt, A., . . . Mungas, D. (2014). Life experience and demographic influences on cognitive function in older adults. *Neuropsychology, 28*, 846-858. doi: 10.1037/neu0000098

Brickman, A. M., Siedlecki, K. L., Muraskin, J., Manly, J. J., Luchsinger, J. A., Yeung, L., . . . Stern, Y. (2011). White matter hyperintensities and cognition: testing the reserve

hypothesis. *Neurobiology of Aging, 32*, 1588-1598. doi: 10.1016/j.neurobiolaging.2009.10.013

Bruce, M. L. (2002). Psychosocial risk factors for depressive disorders in late life. *Biological Psychiatry, 52*, 175-184. doi: 10.1016/S0006-3223(02)01410-5

Byers, A. L. & Yaffe, K. (2011). Depression and risk of developing dementia. *Nature Reviews Neurology, 7*, 323-331. doi: 10.1038/nrneurol.2011.60

Capitani, E., Barbarotto, R., & Laiacona, M. (1996). Does education influence the age-related cognitive decline? A further inquiry. *Developmental Neuropsychology, 12*, 231-240. doi: 10.1080/87565649609540648

Carmelli, D., Swan, G. E., & Cardon, L. R. (1995). Genetic mediation in the relationship of education to cognitive function in older people. *Psychology and Aging, 10*, 48-53. doi: 10.1037/0882-7974.10.1.48

Carson, K. P., Schriesheim, C. A., & Kinicki, A. J. (1990). The usefulness of the "fail-safe" statistic in meta-analysis. *Educational and Psychological Measurement, 50*, 233-243. doi: 10.1177/0013164490502001

Chen, J., Lin, K., & Chen, Y. (2009). Risk factors for dementia. *Journal of the Formosan Medical Association, 108*, 754-764. doi: 10.1016/S0929-6646(09)60402-2

Chiang, K. S., Green, K. E., & Cox, E. O. (2009). Rasch analysis of the geriatric depression Scale–Short form. *The Gerontologist, 49*, 262-275. doi: 10.1093/geront/gnp018

Christensen, H., Korten, A., Jorm, A. F., Henderson, A. S., Scott, R., & Mackinnon, A. J. (1996). Activity levels and cognitive functioning in an elderly community sample. *Age and Ageing, 25*, 72-80.

Christensen, H., Anstey, K. J., Leach, L. S., & Mackinnon, A. J. (2008). Intelligence, education, and the brain reserve hypothesis. In F. I. M. Craik, & T. A. Salthouse (Eds.), *The Handbook of Aging and Cognition* (3rd ed., pp. 133-188). New York, NY: Psychology Press.

Christensen, H., Batterham, P. J., Mackinnon, A. J., Anstey, K. J., Wen, W., & Sachdev, P. S. (2009). Education, atrophy, and cognitive change in an epidemiological sample in early old age. *The American Journal of Geriatric Psychiatry, 17*, 218-226. doi: 10.1097/JGP.0b013e3181961a84

Christofoletti, G., Oliani, M. M., Stella, F., Gobbi, S., & Bucken Gobbi, L. T. (2007). The influence of schooling on cognitive screening test in the elderly. *Dementia & Neuropsychologia, 1*, 46-51.

Clare, L., Nelis, S. M., Jones, I. R., Hindle, J. V., Thom, J. M., Nixon, J. A., . . . Whitaker, C. J. (2015). The Agewell trial: a pilot randomised controlled trial of a behaviour change intervention to promote healthy ageing and reduce risk of dementia in later life. *BMC Psychiatry, 15,* 25-43. doi: 10.1186/s12888-015-0402-4

Clark, L. R., Schiehser, D. M., Weissberger, G. H., Salmon, D. P., Delis, D. C., & Bondi, M. W. (2012). Specific measures of executive function predict cognitive decline in older adults. *Journal of the International Neuropsychological Society, 18,* 118-127. doi: 10.1017/S1355617711001524

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112,* 155-159. doi: 10.1037/0033-2909.112.1.155

Cole, M. G. & Dendukuri, N. (2003). Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *American Journal of Psychiatry, 160,* 1147-1156. doi: 10.1176/appi.ajp.160.6.1147

Coleman, P. G. & O'Hanlon, A. (2008). Ageing and Adpation. In B. Woods, & L. Clare (Eds.), *Handbook of the Clinical Psychology of Ageing* (Second ed., pp. 17-32). Chicester: John Wiley & Sons.

Comas-Herrera, A., Wittenberg, R., Pickard, L., & Knapp, M. (2007). Cognitive impairment in older people: future demand for long-term care services and the associated costs. *International Journal of Geriatric Psychiatry, 22,* 1037-1045. doi: 10.1002/gps.1830

Comas-Herrera, A., Northey, S., Wittenberg, R., Knapp, M., Bhattacharyya, S., & Burns, A. (2011). Future costs of dementia-related long-term care: exploring future scenarios. *International Psychogeriatrics, 23,* 20-30. doi: 10.1017/S1041610210000025

Constantinidou, F., Christodoulou, M., & Prokopiou, J. (2012). The effects of age and education on executive functioning and oral naming performance in Greek Cypriot adults: the neurocognitive study for the aging. *Folia Phoniatrica Et Logopaedica, 64,* 187-198. doi: 10.1159/000340015

Copeland, J. R., Beekman, A. T. F., Braam, A. W., Dewey, M. E., Delespaul, P., Fuhrer, R., . . . Wilson, K. C. (2004). Depression among older people in Europe: the EURODEP studies. *World Psychiatry, 3,* 45-49.

Copeland, J. R., 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. doi: 10.1017/S0033291700057779

Copeland, J. R., 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. doi: 10.1002/gps.667

Correa Ribeiro, P. C., Lopes, C. S., & Lourenço, R. A. (2013). Complexity of lifetime occupation and cognitive performance in old age. *Occupational Medicine, 63*, 556-562. doi: 10.1093/occmed/kqt115

Corsentino, E. A., Collins, N., Sachs-Ericsson, N., & Blazer, D. G. (2009). Religious attendance reduces cognitive decline among older women with high levels of depressive symptoms. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 64A*, 1283-1289. doi: 10.1093/gerona/glp116

Covinsky, K. E., Yaffe, K., Lindquist, K., Cherkasova, E., Yelin, E., & Blazer, D. G. (2010). Depressive symptoms in middle age and the development of later-life functional limitations: the long-term effect of depressive symptoms. *Journal of the American Geriatrics Society, 58*, 551-556. doi: 10.1111/j.1532-5415.2010.02723.x

Crawford, J. R., Henry, J. D., Crombie, C., & Taylor, E. P. (2001). Normative data for the HADS from a large non-clinical sample. *British Journal of Clinical Psychology, 40*, 429-434. doi: 10.1348/014466501163904

Davey, A., Dai, T., Woodard, J. L., Miller, L. S., Gondo, Y., Johnson, M. A., . . . Georgia Centenarian. (2013). Profiles of cognitive functioning in a population-based sample of centenarians using factor mixture analysis. *Experimental Aging Research, 39*, 125-144. doi: 10.1080/0361073X.2013.761869

Davis, R. N. & Nolen-Hoeksema, S. (2000). Cognitive inflexibility among ruminators and nonruminators. *Cognitive Therapy & Research, 24*, 699-711. doi: 10.1023/A:1005591412406

de Araújo Carvalho, S., Barreto, S. M., Guerra, H. L., & Gama, A. C. C. (2009). Oral language comprehension assessment among elderly: a population based study in Brazil. *Preventive Medicine, 49*, 541-545. doi: 10.1016/j.ypmed.2009.09.017

de Bruijn, R. F. A., Direk, N., Mirza, S. S., Hofman, A., Koudstaal, P. J., Tiemeier, H., & Ikram, M. A. (2014). Anxiety is not associated with the risk of dementia or cognitive decline: the Rotterdam study. *The American Journal of Geriatric Psychiatry, 22*, 1382-1390. doi: 10.1016/j.jagp.2014.03.001

de Oliveira Wachholz, T. B. & Yassuda, M. S. (2011). The interpretation of proverbs by elderly with high, medium and low educational level: abstract reasoning as an aspect of executive functions. *Dementia & Neuropsychologia, 5*, 31-37.

de Souza-Talarico, J. N., Caramelli, P., Nitrini, R., & Chaves, E. C. (2007). The influence of schooling on working memory performance in elderly individuals without cognitive decline. *Dementia & Neuropsychologia, 1,* 276-281.

Deary, I. J., Corley, J., Gow, A. J., Harris, S. E., Houlihan, L. M., Marioni, R. E., . . . Starr, J. M. (2009). Age-associated cognitive decline. *British Medical Bulletin, 92,* 135-152. doi: 10.1093/bmb/ldp033

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. doi: 10.1037/0022-3514.86.1.130

Debette, S. & Markus, H. S. (2010). The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: systematic review and meta-analysis. *British Medical Journal, 341,* 1-9. doi: 10.1136/bmj.c3666

Denney, N. W. & Thissen, D. M. (1983). Determinants of cognitive abilities in the elderly. *The International Journal of Aging & Human Development, 16,* 29-41. doi: 10.2190/KBVP-A13Q-433A-T8VY

Dennis, R. E., Boddington, S. J. A., & Funnel, N. J. (2007). Self-report measures of anxiety: are they suitable for older adults? *Aging and Mental Health, 11,* 668-677. doi: 10.1080/13607860701529916

DerSimonian, R. & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials, 7,* 177-188. doi: 10.1016/0197-2456(86)90046-2

Di Carlo, A., Baldereschi, M., Amaducci, L., Maggi, S., Grigoletto, F., Scarlato, G., . . . for the Italian Longitudinal Study on Aging Working Group. (2000). Cognitive impairment without dementia in older people: prevalence, vascular risk factors, impact on disability. The Italian longitudinal study on aging. *Journal of the American Geriatrics Society, 48,* 775-782. doi: 10.1111/j.1532-5415.2000.tb04752.x

Diehl, M., Willis, S. L., & Schaie, K. W. (1995). Everyday problem solving in older adults: Observational assessment and cognitive correlates. *Psychology and Aging, 10,* 478-491. doi: 10.1037/0882-7974.10.3.478

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, 20,* 329-335. doi: 10.1192/bjp.bp.112.118307

Dissanayaka, N. N. W., Sellbach, A., Silburn, P. A., O'Sullivan, J. D., Marsh, R., & Mellick, G. D. (2011). Factors associated with depression in Parkinson's disease. *Journal of Affective Disorders, 132*, 82-88. doi: 10.1016/j.jad.2011.01.021

Dorbath, L., Hasselhorn, M., & Titz, C. (2013). Effects of education on executive functioning and its trainability. *Educational Gerontology, 39*, 314-325. doi: 10.1080/03601277.2012.700820

Dotson, V. M., Beydoun, M. A., & Zonderman, A. B. (2010). Recurrent depressive symptoms and the incidence of dementia and mild cognitive impairment. *Neurology, 75*, 27-34. doi: 10.1212/WNL.0b013e3181e62124

Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: changes in grey matter induced by training. *Nature, 427*, 311-312. doi: 10.1038/427311a

Draganski, B., Gaser, C., Kempermann, G., Kuhn, H. G., Winkler, J., Büchel, C., & May, A. (2006). Temporal and spatial dynamics of brain structure changes during extensive learning. *The Journal of Neuroscience, 26*, 6314-6317. doi: 10.1523/JNEUROSCI.4628-05.2006

Duff, K., Shprecher, D., Litvan, I., Gerstenecker, A., Mast, B., & ENGENE investigators. (2013). Correcting for demographic variables on the modified Telephone Interview for Cognitive Status. *The American Journal of Geriatric Psychiatry, 22*, 1438-1443. doi: S1064-7481(13)00338-2

Dufouil, C., Alpérovitch, A., & Tzourio, C. (2003). Influence of education on the relationship between white matter lesions and cognition. *Neurology, 60*, 831-836. doi: 10.1212/01.wnl.0000049456.33231.96

Elbejjani, M., Fuhrer, R., Abrahamowicz, M., Mazoyer, B., Crivello, F., Tzourio, C., & Dufouil, C. (2015). Depression, depressive symptoms, and rate of hippocampal atrophy in a longitudinal cohort of older men and women. *Psychological Medicine, 15*, 1931-1944. doi: 10.1017/S0033291714003055

Elias, M. F., Elias, P. K., D'Agostino, R. B., Silbershatz, H., & Wolf, P. A. (1997). Role of age, education, and gender on cognitive performance in the Framingham heart study: community-based norms. *Experimental Aging Research, 23*, 201-235. doi: 10.1080/03610739708254281

Enzinger, C., Fazekas, F., Matthews, P. M., Ropele, S., Schmidt, H., Smith, S., & Schmidt, R. (2005). Risk factors for progression of brain atrophy in aging: six-year follow-up of

normal subjects. *Neurology, 64*, 1704-1711. doi: 10.1212/01.WNL.0000161871.83614.BB

Erickson, K. I., Colcombe, S. J., Wadhwa, R., Bherer, L., Peterson, M. S., Scalf, P. E., . . . Kramer, A. F. (2007). Training-induced functional activation changes in dual-task processing: an fMRI study. *Cerebral Cortex, 17*, 192-204. doi: 10.1093/cercor/bhj137

Eskes, G. A., Longman, S., Brown, A. D., McMorris, C. A., Langdon, K. D., Hogan, D. B., & Poulin, M. (2010). Contribution of physical fitness, cerebrovascular reserve and cognitive stimulation to cognitive function in post-menopausal women. *Frontiers in Aging Neuroscience, 2*. doi: 10.3389/fnagi.2010.00137

Evans, J., Heron, J., Lewis, G., Araya, R., & Wolke, D. (2005). Negative self-schemas and the onset of depression in women: longitudinal study. *The British Journal of Psychiatry, 186*, 302-307. doi: 10.1192/bjp.186.4.302

Eysenck, M. W. (1992). *Anxiety: The cognitive perspective*. Hillsdale: Lawrence Erlbaum Associates.

Fan, Z. J., Bonauto, D. K., Foley, M. P., Anderson, N. J., Yragui, N. L., & Silverstein, B. A. (2012). Occupation and the prevalence of current depression and frequent mental distress, WA BRFSS 2006 and 2008. *American Journal of Industrial Medicine, 55*, 893-903. doi: 10.1002/ajim.22094

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. doi: 10.1002/gps.4155

Fillenbaum, G. G., Hughes, D. C., Heyman, A., George, L. K., & Blazer, D. G. (1988). Relationship of health and demographic characteristics to mini-mental state examination score among community residents. *Psychological Medicine, 18*, 719-726. doi: 10.1017/S0033291700008412

Finkel, D., Andel, R., Gatz, M., & Pedersen, N. L. (2009). The role of occupational complexity in trajectories of cognitive aging before and after retirement. *Psychology and Aging, 24*, 563-573. doi: 10.1037/a0015511

Fisk, J. D., Rockwood, K., Hondas, B., Tripp, D. A., Stadnyk, K., & Doble, S. E. (1995). Cognitive screening in a population-based sample of community-living elderly: effects of age and education on the construct of cognitive status. *International Journal of Geriatric Psychiatry, 10*, 687-694. doi: 10.1002/gps.930100809

Foley, J. M., Ettenhofer, M. L., Kim, M. S., Behdin, N., Castellon, S. A., & Hinkin, C. H. (2012). Cognitive reserve as a protective factor in older HIV-positive patients at risk for cognitive decline. *Applied Neuropsychology: Adult, 19*, 16-25. doi: 10.1080/09084282.2011.595601

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. doi: 10.1016/0022-3956(75)90026-6

Forsman, A. K., Nordmyr, J., & Wahlbeck, K. (2011). Psychosocial interventions for the promotion of mental health and the prevention of depression among older adults. *Health Promotion International, 26*, i85-i107. doi: 10.1093/heapro/dar074

Forstmeier, S., & Maercker, A. (2008). Motivational reserve: Lifetime motivational abilities contribute to cognitive and emotional health in old age. *Psychology and Aging, 23*, 886-899. doi: 10.1037/a0013602

Foubert-Samier, A., Catheline, G., Amieva, H., Dilharreguy, B., Helmer, C., Allard, M., & Dartigues, J. (2012). Education, occupation, leisure activities, and brain reserve: a population-based study. *Neurobiology of Aging, 33*, 423.e15-423.e25. doi: 10.1016/j.neurobiolaging.2010.09.023

Fournet, N., Roulin, J. L., Vallet, F., Beaudoin, M., Agrigoroaei, S., Paignon, A., . . . Desrichard, O. (2012). Evaluating short-term and working memory in older adults: French normative data. *Aging & Mental Health, 16*, 922-930. doi: 10.1080/13607863.2012.674487

Fox, N. C. & Schott, J. M. (2004). Imaging cerebral atrophy: Normal ageing to Alzheimer's disease. *The Lancet, 363*, 392-394. doi: 10.1016/S0140-6736(04)15441-X

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. doi: 10.1016/S1474-4422(04)00767-7

Fratiglioni, L. & Wang, H. X. (2007). Brain reserve hypothesis in dementia. *Journal of Alzheimer's Disease, 12*, 11-22.

Frisoni, G. B., Rozzini, R., Bianchetti, A., & Trabucchi, M. (1993). Principal lifetime occupation and MMSE score in elderly persons. *Journal of Gerontology, 48*, S310-S314. doi: 10.1093/geronj/48.6.S310

Fritsch, T., McClendon, M. J., Smyth, K. A., Lerner, A. J., Friedland, R. P., & Larsen, J. D. (2007). Cognitive functioning in healthy aging: the role of reserve and lifestyle factors early in life. *The Gerontologist, 47*, 307-322. doi: 10.1093/geront/47.3.307

Fuhrer, R., Antonucci, T. C., & Dartigues, J. (1992). The co-occurrence of depressive symptoms and cognitive impairment in a French community: are there gender differences? *European Archives of Psychiatry and Clinical Neuroscience, 242,* 161-171. doi: 10.1007/BF02191564

Fyffe, D. C., Mukherjee, S., Barnes, L. L., Manly, J. J., Bennett, D. A., & Crane, P. K. (2011). Explaining differences in episodic memory performance among older African Americans and whites: the roles of factors related to cognitive reserve and test bias. *Journal of the International Neuropsychological Society, 17*, 625-638. doi: 10.1017/S1355617711000476

Gale, C. R., Allerhand, M., & Deary, I. J. (2012). Is there a bidirectional relationship between depressive symptoms and cognitive ability in older people? A prospective study using the English longitudinal study of ageing. *Psychological Medicine, 42*, 2057-2069. doi: 10.1017/S0033291712000402

Gallacher, J., Bayer, A., Fish, M., Pickering, J., Pedro, S., Dunstan, F., . . . Ben-Shlomo, Y. (2009). Does anxiety affect the risk of dementia? Findings from the Caerphilly prospective study. *Psychosomatic Medicine, 71,* 659-666. doi: 10.1097/PSY.0b013e3181a6177c

Gallucci, M., Antuono, P., Ongaro, F., Forloni, P. L., Albani, D., Amici, G. P., & Regini, C. (2009). Physical activity, socialization and reading in the elderly over the age of seventy: what is the relation with cognitive decline? Evidence from "the Treviso Longeva (TRELONG) study". *Archives of Gerontology and Geriatrics, 48,* 284-286. doi: 10.1016/j.archger.2008.02.006

Ganguli, M., Snitz, B. E., Lee, C., Vanderbilt, J., Saxton, J. A., & Chang, C. H. (2010). Age and education effects and norms on a cognitive test battery from a population-based cohort: the Monongahela–Youghiogheny healthy aging team. *Aging & Mental Health, 14*, 100-107. doi: 10.1080/13607860903071014

Garnefski, N. & Kraaij, V. (2006). Relationships between cognitive emotion regulation strategies and depressive symptoms: a comparative study of five specific samples. *Personality and Individual Differences, 40*, 1659-1669. doi: 10.1016/j.paid.2005.12.009

Gaugler, J. E., Duval, S., Anderson, K. A., & Kane, R. L. (2007). Predicting nursing home admission in the U.S: a meta-analysis. *BMC Geriatrics, 7*, 13-26. doi: 10.1186/1471-2318-7-13

Geerlings, M. I., Schoevers, R. A., Beekman, A. T., Jonker, C., Deeg, D. J., Schmand, B., . . . Van Tilburg, W. (2000). Depression and risk of cognitive decline and Alzheimer's

disease. Results of two prospective community-based studies in the Netherlands. *The British Journal of Psychiatry, 176,* 568-575. doi: 10.1192/bjp.176.6.568

Giannakouris, K. (2010). Regional population projections EUROPOP2008: most EU regions face older population profile in 2030. *Population and Social Conditions, Eurostat Statistics in Focus, 1.*

Gilhooly, K. J., Gilhooly, M. L., Phillips, L. H., Harvey, D., Murray, A., & Hanlon, P. (2007). Cognitive aging: activity patterns and maintenance intentions. *The International Journal of Aging & Human Development, 65,* 259-280. doi: 10.2190/AG.65.3.d

Giogkaraki, E., Michaelides, M. P., & Constantinidou, F. (2013). The role of cognitive reserve in cognitive aging: results from the neurocognitive study on aging. *Journal of Clinical and Experimental Neuropsychology, 35,* 1024-1035. doi: 10.1080/13803395.2013.847906

Giordano, N., Tikhonoff, V., Palatini, P., Bascelli, A., Boschetti, G., De Lazzari, F., . . . Casiglia, E. (2012). Cognitive functions and cognitive reserve in relation to blood pressure components in a population-based cohort aged 53 to 94 years. *International Journal of Hypertension, 2012,* 274851. doi: 10.1155/2012/274851

Glass, T. A., De Leon, C. F. M., Bassuk, S. S., & Berkman, L. F. (2006). Social engagement and depressive symptoms in late life: longitudinal findings. *Journal of Aging and Health, 18,* 604-628. doi: 10.1177/0898264306291017

Glymour, M. M., Weuve, J., Berkman, L. F., Kawachi, I., & Robins, J. M. (2005). When is baseline adjustment useful in analyses of change? An example with education and cognitive change. *American Journal of Epidemiology, 162,* 267-278. doi: 10.1093/aje/kwi187

Gonzales, C. (2013). *The psychometric properties of the lifetime experience questionnaire (LEQ) in older American adults.* (Doctoral dissertation) University of North Carolina, Greensboro. Retrieved from http://libres.uncg.edu/ir/uncg/listing.aspx?id=8629

Gonzalez, H. M., Tarraf, W., Bowen, M. E., Johnson-Jennings, M. D., & Fisher, G. G. (2013). What do parents have to do with my cognitive reserve? Life course perspectives on twelve-year cognitive decline. *Neuroepidemiology, 41,* 101-109. doi: 10.1159/000350723

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. doi: 10.1111/j.1532-5415.2010.03233.x

Gow, A. J., Avlund, K., & Mortensen, E. L. (2014). Leisure activity associated with cognitive ability level, but not cognitive change. *Frontiers in Psychology, 5*, 1176. doi: 10.3389/fpsyg.2014.01176

Gow, A. J., Avlund, K., & Mortensen, E. L. (2012). Occupational characteristics and cognitive aging in the Glostrup 1914 cohort. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 69*, 228-236. doi: 10.1093/geronb/gbs115

Gow, A. J., Corley, J., Starr, J. M., & Deary, I. J. (2012). Reverse causation in activity-cognitive ability associations: the Lothian birth cohort 1936. *Psychology and Aging, 27*, 250-255. doi: 10.1037/a0024144

Gunning-Dixon, F. & Raz, N. (2000). The cognitive correlates of white matter abnormalities in normal aging: a quantitative review. *Neuropsychology, 14*, 224-232. doi: 10.1037/0894-4105.14.2.224

Harrison, S. L., Sajjad, A., Bramer, W. M., Ikram, M. A., Tiemeier, H., & Stephan, B. C. M. (2015). Exploring strategies to operationalize cognitive reserve: a systematic review of reviews. *Journal of Clinical and Experimental Neuropsychology, 37*, 253-264. doi: 10.1080/13803395.2014.1002759

Hashimoto, R., Meguro, K., Lee, E., Kasai, M., Ishii, H., & Yamaguchi, S. (2006). Effect of age and education on the trail making test and determination of normative data for Japanese elderly people: the Tajiri project. *Psychiatry and Clinical Neurosciences, 60*, 422-428. doi: 10.1111/j.1440-1819.2006.01526.x

Hassing, L., Wahlin, Å., & Bäckman, L. (1998). Minimal influence of age, education, and gender on episodic memory functioning in very old age: a population-based study of nonagenarians. *Archives of Gerontology and Geriatrics, 27*, 75-57. doi: 10.1016/S0167-4943(98)00101-0

Helmer, C., Letenneur, L., Rouch, I., Richard-Harston, S., Barberger-Gateau, P., Fabrigoule, C., . . . Dartigues, J. F. (2001). Occupation during life and risk of dementia in French elderly community residents. *Journal of Neurology, Neurosurgery & Psychiatry, 71*, 303-309. doi: 10.1136/jnnp.71.3.303

Hertzog, C., Kramer, A. F., Wilson, R. S., & Lindenberger, U. (2008). Enrichment effects on adult cognitive development: can the functional capacity of older adults be preserved and enhanced? *Psychological Science in the Public Interest, 9*, 1-65. doi: 10.1111/j.1539-6053.2009.01034.x

Higgins, J. P. T., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *British Medical Journal, 327*, 557-560. doi: 10.1136/bmj.327.7414.557

Hill, R. D., Wahlin, Å., Winblad, B., & Bäckman, L. (1995). The role of demographic and life style variables in utilizing cognitive support for episodic remembering among very old adults. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 50B*, 219-227. doi: 10.1093/geronb/50B.4.P219

Hindi, F., Dew, M. A., Albert, S. M., Lotrich, F. E., & Reynolds III, C. F. (2011). Preventing depression in later life: state of the art and science circa 2011. *Psychiatric Clinics of North America, 34*, 67-78. doi: 10.1016/j.psc.2010.11.008

Hindle, J. V., Hurt, C. S., Burn, D. J., Brown, R. G., Samuel, M., Wilson, K. C., & Clare, L. (2015). The effects of cognitive reserve and lifestyle on cognition and dementia in Parkinson's disease? A longitudinal cohort study. International Journal of Geriatric Psychiatry. (Advance online publication). doi: 10.1002/gps.4284

Hindle, J. V., Martyr, A., & Clare, L. (2014). Cognitive reserve in Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism & Related Disorders, 20*, 1-7. doi: 10.1016/j.parkreldis.2013.08.010

Ho, Y., & Chan, A. S. (2005). Comparing the effects of mahjong playing and reading on cognitive reserve of the elderly. *Journal of Psychology in Chinese Societies, 6*, 5-26.

Hong, S., Hasche, L., & Bowland, S. (2009). Structural relationships between social activities and longitudinal trajectories of depression among older adults. *The Gerontologist, 49*, 1-11. doi: 10.1093/geront/gnp006

Hsieh, S., Schubert, S., Hoon, C., Mioshi, E., & Hodges, J. R. (2013). Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders, 49*, 1-11. doi: 10.1159/000351671

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*, 1-11. doi: 10.1093/geronj/48.1.P1

Inouye, S. K., Albert, M. S., Mohs, R., Sun, K., & Berkman, L. F. (1993). Cognitive performance in a high-functioning community-dwelling elderly population. *Journal of Gerontology, 48*, 146-151. doi: 10.1093/geronj/48.4.M146

Inzelberg, R., Schechtman, E., Abuful, A., Masarwa, M., Mazarib, A., Strugatsky, R., . . . Friedland, R. P. (2007). Education effects on cognitive function in a healthy aged Arab

population. *International Psychogeriatrics, 19*, 593-603. doi: 10.1017/S1041610206004327

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. doi: 10.1093/ageing/afp016

Jefferson, A. L., Gibbons, L. E., Rentz, D. M., Carvalho, J. O., Manly, J., Bennett, D. A., & Jones, R. N. (2011). A life course model of cognitive activities, socioeconomic status, education, reading ability, and cognition. *Journal of the American Geriatrics Society, 59*, 1403-1411. doi: 10.1111/j.1532-5415.2011.03499.x

Jenkins, A. (2011). Participation in learning and wellbeing among older adults. *International Journal of Lifelong Education, 30*, 403-420. doi: 10.1080/02601370.2011.570876

Jones, R. N., Fong, T. G., Metzger, E., Tulebaev, S., Yang, F. M., Alsop, D. C., . . . Inouye, S. K. (2010). Aging, brain disease, and reserve: implications for delirium. *The American Journal of Geriatric Psychiatry, 18*, 117-127. doi: 10.1097/JGP.0b013e3181b972e8

Jorm, A. F. (2001). History of depression as a risk factor for dementia: an updated review. *Australian and New Zealand Journal of Psychiatry, 35*, 776-781. doi: 10.1046/j.1440-1614.2001.00967.x

Kahl, K. G., Winter, L., & Schweiger, U. (2012). The third wave of cognitive behavioural therapies: what is new and what is effective? *Current Opinion in Psychiatry, 25*, 522-528. doi: 10.1097/YCO.0b013e328358e531

Kaplan, R. F., Cohen, R. A., Moscufo, N., Guttmann, C., Chasman, J., Buttaro, M., . . . Wolfson, L. (2009). Demographic and biological influences on cognitive reserve. *Journal of Clinical and Experimental Neuropsychology, 31*, 868-876. doi: 10.1080/13803390802635174

Karp, A., Andel, R., Parker, M. G., Wang, H., Winblad, B., & Fratiglioni, L. (2009). Mentally stimulating activities at work during midlife and dementia risk after age 75: follow-up study from the Kungsholmen project. *The American Journal of Geriatric Psychiatry, 17*, 227-236. doi: 10.1097/JGP.0b013e318190b691

Kasckow, J. W., Karp, J. F., Whyte, E., Butters, M., Brown, C., Begley, A., . . . Reynolds III, C. F. (2013). Subsyndromal depression and anxiety in older adults: health related, functional, cognitive and diagnostic implications. *Journal of Psychiatric Research, 47*, 599-603. doi: 10.1016/j.jpsychires.2013.01.017

Katzman, R., Terry, R., DeTeresa, R., Brown, T., Davies, P., Fuld, P., . . . 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. doi: 10.1002/ana.410230206

Kempler, D., Teng, E. L., Dick, M., Taussig, I. M., & Davis, D. S. (1998). The effects of age, education, and ethnicity on verbal fluency. *Journal of the International Neuropsychological Society, 4*, 531-538.

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. doi: 10.1207/S15324826AN1003_04

Kesse-Guyot, E., Andreeva, V. A., Lassale, C., Ferry, M., Jeandel, C., Hercberg, S., . . . SU.VI.MAX 2 Research Group. (2013). Mediterranean diet and cognitive function: a French study. *The American Journal of Clinical Nutrition, 97*, 369-376. doi: 10.3945/ajcn.112.047993

Kessler, E. M., Bowen, C. E., Baer, M., Froelich, L., & Wahl, H. W. (2012). Dementia worry: a psychological examination of an unexplored phenomenon. *European Journal of Ageing, 9*, 275-284. doi: 10.1007/s10433-012-0242-8

Kilander, L., Nyman, H., Boberg, M., & Lithell, H. (1997). Cognitive function, vascular risk factors and education. a cross-sectional study based on a cohort of 70-year-old men. *Journal of Internal Medicine, 242*, 313-321.

Kim, H. C., Lee, K. S., Cheong, H. K., Lee, Y. H., Lim, K. Y., Chung, Y. K., . . . Hong, C. H. (2011). Application of health concern and activity model on cognition in the elderly. *Archives of Gerontology and Geriatrics, 53*, 187-191. doi: 10.1016/j.archger.2010.09.001

Kindermann, S. S. & Brown, G. G. (1997). Depression and memory in the elderly: a meta-analysis. *Journal of Clinical and Experimental Neuropsychology, 19*, 625-642. doi: 10.1080/01688639708403749

Kirkegaard Thomsen, D. (2006). The association between rumination and negative affect: a review. *Cognition and Emotion, 20*, 1216-1235. doi: 10.1080/02699930500473533

Kizilbash, A. H., Vanderploeg, R. D., & Curtiss, G. (2002). The effects of depression and anxiety on memory performance. *Archives of Clinical Neuropsychology, 17*, 57-67. doi: 10.1016/S0887-6177(00)00101-3

Korczyn, A. D. & Halperin, I. (2009). Depression and dementia. *Journal of the Neurological Sciences, 283,* 139-142. doi: 10.1016/j.jns.2009.02.346

Kraaij, V., Pruymboom, E., & Garnefski, N. (2002). Cognitive coping and depressive symptoms in the elderly: a longitudinal study. *Aging and Mental Health, 6,* 275-281. doi: 10.1080/13607860220142387

Kueider, A. M., Parisi, J. M., Gross, A. L., & Rebok, G. W. (2012). Computerized cognitive training with older adults: a systematic review. *PloS One, 7,* e40588. doi: 10.1371/journal.pone.0040588

Kummer, A., Harsanyi, E., Dias, F. M., Cardoso, F., Caramelli, P., & Teixeira, A. L. (2009). Depression impairs executive functioning in Parkinson disease patients with low educational level. *Cognitive and Behavioral Neurology, 22,* 167-172. doi: 10.1097/WNN.0b013e3181b278f9

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. doi: 10.1002/gps.1867

La Rue, A. (2010). Healthy brain aging: role of cognitive reserve, cognitive stimulation, and cognitive exercises. *Clinics in Geriatric Medicine, 26*, 99-111. doi: 10.1016/j.cger.2009.11.003

Lachman, M. E., Agrigoroaei, S., Murphy, C., & Tun, P. A. (2010). Frequent cognitive activity compensates for education differences in episodic memory. *The American Journal of Geriatric Psychiatry, 18,* 4-10. doi: 10.1097/JGP.0b013e3181ab8b62

Ladin, K. (2008). Risk of late-life depression across 10 European Union countries: deconstructing the education effect. *Journal of Aging and Health, 20*, 653-670. doi: 10.1177/0898264308321002

Laditka, J. N., Laditka, S. B., Liu, R., Price, A. E., Wu, B., Friedman, D. B., . . . Logsdon, R. G. (2011). Older adults' concerns about cognitive health: commonalities and differences among six United States ethnic groups. *Ageing & Society, 31,* 1202-1228. doi: 10.1017/S0144686X10001273

Lampe, I. K., Pol, H. E. H., Janssen, J., Schnack, H. G., Kahn, R. S., & Heeren, T. J. (2003). Association of depression duration with reduction of global cerebral gray matter volume in female patients with recurrent major depressive disorder. *The American Journal of Psychiatry, 160,* 2052-2054. doi: 10.1176/appi.ajp.160.11.2052

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized cognitive training in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. *PLoS Med, 11* doi: 10.1371/journal.pmed.1001756

Lang, I. A., Llewellyn, D. J., Langa, K. M., Wallace, R. B., Huppert, F. A., & Melzer, D. (2008). Neighborhood deprivation, individual socioeconomic status, and cognitive function in older people: analyses from the English longitudinal study of ageing. *Journal of the American Geriatrics Society, 56,* 191-198. doi: 10.1111/j.1532-5415.2007.01557.x

Langa, K. M., Larson, E. B., Karlawish, J. H., Cutler, D. M., Kabeto, M. U., Kim, S. Y., & Rosen, A. B. (2008). Trends in the prevalence and mortality of cognitive impairment in the United States: is there evidence of a compression of cognitive morbidity? *Alzheimer's & Dementia, 4*, 134-144. doi: 10.1016/j.jalz.2008.01.001

Le Carret, N., Lafont, S., Letenneur, L., Dartigues, J., Mayo, W., & Fabrigoule, C. (2003). The effect of education on cognitive performances and its implication for the constitution of the cognitive reserve. *Developmental Neuropsychology, 23*, 317-337. doi: 10.1207/S15326942DN2303_1

Leddy, S., Fowler, A. J., Giovanonni, G., & Dobson, R. (2014). Depression in MS: a systematic review and meta-analysis. *Journal of Neurology, Neurosurgery & Psychiatry, 85,* e4-e4. doi:10.1136/jnnp-2014-309236.134

Lee, Y. S., Lee, C. L., & Yang, H. T. (2012). Effects of aging and education on false memory. *International Journal of Aging & Human Development, 74*, 287-298.

Leggett, A., Zarit, S. H., Hoang, C. N., & Nguyen, H. T. (2013). Correlates of cognitive impairment in older Vietnamese. *Aging & Mental Health, 17*, 915-923. doi: 10.1080/13607863.2013.799116

Leibovici, D., Ritchie, K., Ledésert, B., & Touchon, J. (1996). Does education level determine the course of cognitive decline? *Age and Ageing, 25*, 392-397. doi: 10.1093/ageing/25.5.392

Lenze, E. J., Rogers, J. C., Martire, L. M., Mulsant, B. H., Rollman, B. L., Dew, M. A., . . . Reynolds III, C. F. (2001). The association of late-life depression and anxiety with physical disability: a review of the literature and prospectus for future research. *The American Journal of Geriatric Psychiatry, 9*, 113-135. doi: 10.1097/00019442-200105000-00004

Leonard, B. E. (2007). Inflammation, depression and dementia: are they connected? *Neurochemical Research, 32*, 1749-1756. doi: 10.1007/s11064-007-9385-y

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. (2010). Examining the association between participation in late-life leisure activities and cognitive function in community-dwelling elderly Chinese in Hong Kong. *International Psychogeriatrics, 22*(1), 2-13. doi: 10.1017/S1041610209991025

Lezak, M. D. (1995). *Neuropsychological Assessment (3rd Ed.).* Oxford: Oxford University Press.

Li, C. Y., Wu, S. C., & Sung, F. C. (2002). Lifetime principal occupation and risk of cognitive impairment among the elderly. *Industrial Health, 40,* 7-13. doi: 10.2486/indhealth.40.7

Li, X., Wang, K., Wang, F., Tao, Q., Xie, Y., & Cheng, Q. (2013). Aging of theory of mind: the influence of educational level and cognitive processing. *International Journal of Psychology, 48*, 715-727. doi: 10.1080/00207594.2012.673724

Lin, F., Friedman, E., Quinn, J., Chen, D, & Mapstone, M. (2012). Effect of leisure activities on inflammation and cognitive function in an aging sample. *Archives of Gerontology and Geriatrics, 54*, 398-404. doi: 10.1016/j.archger.2012.02.002

Lin, H., Chan, R. C. K., Zheng, L., Yang, T., & Wang, Y. (2007). Executive functioning in healthy elderly Chinese people. *Archives of Clinical Neuropsychology, 22*, 501-511. doi: 10.1016/j.acn.2007.01.028

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. doi: 10.1016/j.ejphar.2004.02.046

Linderberger, U. & Baltes, P. B. (1997). Intellectual functioning in old and very old age: cross-sectional results from the Berlin aging study. *Psychology and Aging, 12*, 410-432. doi: 10.1037/0882-7974.12.3.410

Lindesay, J., Briggs, K., & Murphy, E. (1989). The guy's/Age concern survey. Prevalence rates of cognitive impairment, depression and anxiety in an urban elderly community. *The British Journal of Psychiatry, 155*, 317-329. doi: 10.1192/bjp.155.3.317

Lloyd-Sherlock, P. (2000). Population ageing in developed and developing regions: implications for health policy. *Social Science & Medicine, 51,* 887-895. doi: 10.1016/S0277-9536(00)00068-X

Lorant, V., Deliège, D., Eaton, W., Robert, A., Philippot, P., & Ansseau, M. (2003). Socioeconomic inequalities in depression: a meta-analysis. *American Journal of Epidemiology, 157,* 98-112. doi: 10.1093/aje/kwf182

Luppa, M., Sikorski, C., Luck, T., Ehreke, L., Konnopka, A., Wiese, B., ... & Riedel-Heller, S. G. (2012). Age-and gender-specific prevalence of depression in latest-life–systematic review and meta-analysis. *Journal of Affective Disorders, 136,* 212-221. doi: 10.1016/j.jad.2010.11.033

Luszcz, M. A. (1992). Predictors of memory in young-old and old-old adults. *International Journal of Behavioral Development, 15*, 147-166. doi: 10.1177/016502549201500108

Lyman, G. H. & Kuderer, N. M. (2005). The strengths and limitations of meta-analyses based on aggregate data. *BMC Medical Research Methodology, 5,* 14. doi: 10.1186/1471-2288-5-14

Lyubomirsky, S., Kasri, F., & Zehm, K. (2003). Dysphoric rumination impairs concentration on academic tasks. *Cognitive Therapy and Research, 27*, 309-330. doi: 10.1023/A:1023918517378

Mangione, C. M., Seddon, J. M., Cook, E. F., Krug, J. H., Sahagian, C. R., Campion, E. W., & Glynn, R. J. (1993). Correlates of cognitive function scores in elderly outpatients. *Journal of the American Geriatrics Society, 41,* 491-497.

Manly, J. J., Jacobs, D. M., Touradji, P., Small, S. A., & Stern, Y. (2002). Reading level attenuates differences in neuropsychological test performance between African American and white elders. Journal of the International Neuropsychological Society, 8, 341-348. doi: 10.1017/S1355617702813157

Manly, J. J., Schupf, N., Tang, M. X., & Stern, Y. (2005). Cognitive decline and literacy among ethnically diverse elders. Journal of Geriatric Psychiatry and Neurology, 18, 213-217. doi: 10.1177/0891988705281868

Manly, J. J., Touradji, P., Tang, M., & Stern, Y. (2003). Literacy and memory decline among ethnically diverse elders. *Journal of Clinical and Experimental Neuropsychology, 5*, 680-690. doi: 10.1076/jcen.25.5.680.14579

Marder, K., Tang, M. X., Cote, L., Stern, Y., & Mayeux, R. (1995). The frequency and associated risk factors for dementia in patients with Parkinson's disease. *Archives of Neurology, 52*, 695-701. doi: 10.1001/archneur.1995.00540310069018

Marioni, R. E., van den Hout, A., Valenzuela, M. J., Brayne, C., Matthews, F. E., & MRC Cognitive Function and Ageing Study. (2012). Active cognitive lifestyle associates with cognitive recovery and a reduced risk of cognitive decline. *Journal of Alzheimer's Disease, 28,* 223-230. doi: 10.3233/JAD-2011-110377

Martin, L. L. & Tesser, A. (1996). Some ruminative thoughts. In R. S. Wyer (Ed.), *Ruminative Thoughts. Advances in Social Cognition* (Vol. 9, pp. 1-47). Hillsdale, England: Lawrence Erlbaum Associates.

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. doi: 10.1159/000338233

Mathuranath, P. S., Cherian, J. P., Mathew, R., George, A., Alexander, A., & Sarma, S. P. (2007). Mini Mental State Examination and the Addenbrooke's Cognitive Examination: effect of education and norms for a multicultural population. *Neurology India, 55,* 106-110. doi: 10.4103/0028-3886.32779

Matioli, M. N. P. S., Caramelli, P., Marques, B. D., da Rocha, F. D., de Castro, M. C. C., Yamashita, S. R., & de M. Soares, A. (2008). EXIT25—Executive interview applied to a cognitively healthy elderly population with heterogeneous educational background. *Dementia & Neuropsychologia, 2,* 305-309.

Matthews, F. E., Arthur, A., Barnes, L. E., Bond, J., Jagger, C., Robinson, L., & Brayne, C. (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. doi: 10.1016/S0140-6736(13)61570-6

Matthews, F. E., Stephan, B. C. M., McKeith, I. G., Bond, J., Brayne, C., & the 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. doi: 10.1111/j.1532-5415.2008.01820.x

Maurer, J. (2011). Education and male-female differences in later-life cognition: International evidence from Latin America and the Caribbean. *Demography, 48,* 915-930. doi: 10.1007/s13524-011-0048-x

McCarty, S. M., Siegler, I. C., & Logue, P. E. (1982). Cross-sectional and longitudinal patterns of three Wechsler memory scale subtests. *Journal of Gerontology, 37,* 169-175. doi: 10.1093/geronj/37.2.169

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 CFA study. *Psychological Medicine, 37,* 1787-1795. doi: 10.1017/S0033291707000372

Mejia, S., Pineda, D., Alvarez, L. M., & Ardila, A. (1998). Individual differences in memory and executive function abilities during normal aging. *International Journal of Neuroscience, 95*, 271-284. doi: 10.3109/00207459809003345

Meng, X. & D'Arcy, C. (2012). Education and dementia in the context of the cognitive reserve hypothesis: a systematic review with meta-analyses and qualitative analyses. *Plos One, 7*, e38268. doi: 10.1371/journal.pone.0038268

Mezuk, B., Edwards, L., Lohman, M., Choi, M., & Lapane, K. (2012). Depression and frailty in later life: a synthetic review. *International Journal of Geriatric Psychiatry, 27*, 879-892. doi: 10.1002/gps.2807

Milan, G., Iavarone, A., Vargas, N. F., Vargas, N. M., Fiorillo, F., Galeone, F., . . . Postiglione, A. (2004). Effects of demographic and environmental variables on cognitive performance in a rural community sample of elderly people living in Southern Italy. *Aging Clinical and Experimental Research, 16*, 398-402.

Mitrushina, M., Patel, P. G., Satz, P., D'Elia, L., & McConnell, M. J. (1989). Changes in semantic memory processing in normal and at-risk aging adults. *Developmental Neuropsychology, 5*, 321-333. doi: 10.1080/87565648909540442

Mohlman, J., Price, R. B., Eldreth, D. A., Chazin, D., Glover, D. M., & Kates, W. R. (2009). The relation of worry to prefrontal cortex volume in older adults with and without generalized anxiety disorder. *Psychiatry Research: Neuroimaging, 173*, 121-127. doi: 10.1016/j.pscychresns.2008.09.010

Moraes, C., Pinto, J. A., Jr., Lopes, M. A., Litvoc, J., & Bottino, C. M. C. (2010). Impact of sociodemographic and health variables on mini-mental state examination in a community-based sample of older people. *European Archives of Psychiatry and Clinical Neuroscience, 260*, 535-542. doi: 10.1007/s00406-010-0104-3

Morgan, A. A., Marsiske, M., & Whitfield, K. E. (2007). Characterizing and explaining differences in cognitive test performance between African American and European American older adults. *Experimental Aging Research, 34*, 80-100. doi: 10.1080/03610730701776427

Mortamais, M., Portet, F., Brickman, A. M., Provenzano, F. A., Muraskin, J., Akbaraly, T. N., . . . Artero, S. (2014). Education modulates the impact of white matter lesions on the risk of mild cognitive impairment and dementia. *The American Journal of Geriatric Psychiatry, 22,* 1336-1345. doi: 10.1016/j.jagp.2013.06.002

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. doi: 10.1076/jcen.25.5.671.14584

Mousavi-Nasab, S., Kormi-Nouri, R., & Nilsson, L. (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. doi: 10.1111/bjop.12044

Mueller, A. E., Raymond, N., & Yochim, B. P. (2013). Cognitive activity engagement predicts future memory and executive functioning in older adults. *Activities, Adaptation & Aging, 37*, 251-264. doi: 10.1080/01924788.2013.816833

Mulgrew, C. L., Morgenstern, N., Shetterly, S. M., Baxter, J., Barón, A. E., & Hamman, R. F. (1999). Cognitive functioning and impairment among rural elderly Hispanic and non Hispanic whites as assessed by the mini-mental state examination. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 54B*, 223-230. doi: 10.1093/geronb/54B.4.P223

Mungas, D., Reed, B. R., Haan, M. N., & González, H. (2005). Spanish and English neuropsychological assessment scales: relationship to demographics, language, cognition, and independent function. *Neuropsychology, 19*, 466-475. doi: 10.1037/0894-4105.19.4.466

Murayama, N., Iseki, E., Tagaya, H., Ota, K., Kasanuki, K., Fujishiro, H., . . . Sato, K. (2013). Intelligence or years of education: which is better correlated with memory function in normal elderly Japanese subjects? *Psychogeriatrics, 13*, 9-16. doi : 10.1111/j.1479-8301.2012.00408.x

Murden, R. A., McRae, T. D., Kaner, S., & Bucknam, M. E. (1991). Mini-Mental State Exam scores vary with education in blacks and whites. *Journal of the American Geriatrics Society, 39*, 149-155. doi: 10.1111/j.1532-5415.1991.tb01617.x

Murphy, M. & O'Leary, E. (2010). Depression, cognitive reserve and memory performance in older adults. *International Journal of Geriatric Psychiatry, 25*, 665-671. doi: 10.1002/gps.2404

Murrell, S. A., Salsman, N. L., & Meeks, S. (2003). Educational attainment, positive psychological mediators, and resources for health and vitality in older adults. *Journal of Aging and Health, 15*, 591-615. doi: 10.1177/0898264303256198

Muslimovic, D., Schmand, B., Speelman, J. D., & De Haan, R. J. (2007). Course of cognitive decline in Parkinson's disease: a meta-analysis. *Journal of the International Neuropsychological Society, 13*, 920-932. doi: 10.1017/S1355617707071160

Nakagawa, S. (2004). A farewell to bonferroni: the problems of low statistical power and publication bias. *Behavioral Ecology, 15,* 1044-1045. doi: 10.1093/beheco/arh107

Narushima, M., Liu, J., & Diestelkamp, N. (2013). The association between lifelong learning and psychological well-being among older adults: implications for interdisciplinary health promotion in an aging society. *Activities, Adaptation & Aging, 37*, 239-250. doi: 10.1080/01924788.2013.816834

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 53*, 695-699. doi: 10.1111/j.1532-5415.2005.53221.x

Nebes, R. D., Vora, I. J., Meltzer, C. C., Fukui, M. B., Williams, R. L., Kamboh, M. I., . . . Reynolds, C. F. (2001). Relationship of deep white matter hyperintensities and apolipoprotein E genotype to depressive symptoms in older adults without clinical depression. *American Journal of Psychiatry, 158*, 878-884. doi: 10.1176/appi.ajp.158.6.878

Nelson, H. E. (1982) *National adult reading test*. Windsor: NFER-Nelson.

Newson, R. S. & Kemps, E. B. (2005). General lifestyle activities as a predictor of current cognition and cognitive change in older adults: a cross-sectional and longitudinal examination. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 60,* 113-120. doi: 10.1093/geronb/60.3.P113

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology, 100,* 569-582. doi: 10.1037/0021-843X.100.4.569

Nolen-Hoeksema, S. (2000). The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *Journal of Abnormal Psychology, 109*, 504-511. doi: 10.1037/0021-843x.109.3.504

Nolen-Hoeksema, S. (2004). The response style theory. In C. Papageorgiou, & A. Wells (Eds.), *Depressive rumination: Nature, theory and treatment* (pp. 107-124) Chichester: Wiley.

Nolen-Hoeksema, S. & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta earthquake. *Journal of Personality and Social Psychology, 61,* 115-121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400-424. doi: 10.1111/j.1745-6924.2008.00088.x

Nordhus, I. H. (2008). Manifestations of depression and anxiety in older adults. In B. Woods, & L. Clare (Eds.). *The Handbook of the Clinical Psychology of Ageing* (Second ed., pp. 97-110). Chichester: John Wiley & Sons.

Nucci, M., Mapelli, D., & Mondini, S. (2011). The cognitive reserve questionnaire (CRIq): a new instrument for measuring the cognitive reserve. *Aging Clinical and Experimental Research, 23*, 218-226. doi: 10.3275/7800

O'Brien, J. T., Lloyd, A., McKeith, I., Gholkar, A., & Ferrier, N. (2004). A longitudinal study of hippocampal volume, cortisol levels, and cognition in older depressed subjects. *American Journal of Psychiatry, 161*, 2081-2090. doi: 10.1176/appi.ajp.161.11.2081

O'Connor, D. W., Pollitt, P. A., Treasure, F. P., Brook, C. P. B., & Reiss, B. B. (1989). The influence of education, social class and sex on mini-mental state scores. *Psychological Medicine, 19*, 771-776. doi: 10.1017/S0033291700024375

O'Shea, D. M., Fieo, R. A., Hamilton, J. L., Zahodne, L. B., Manly, J. J., & Stern, Y. (2015). Examining the association between late-life depressive symptoms, cognitive function, and brain volumes in the context of cognitive reserve. International Journal of Geriatric Psychiatry, 30, 614-622. doi: 10.1002/gps.4192

Office for National Statistics. (2010). *Standard occupational classification 2010. Volume 3. The National Statistics Socio-economic Classification (NS-SEC rebased on the SOC2010).* Retrieved from http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec–rebased-on-soc2010–user-manual/index.html

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (2015a). How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life? *Aging & Mental Health, 19*, 705-712. doi: 10.1080/13607863.2014.962005

Opdebeeck, C., Martyr, A., & Clare, L. (2015b). Cognitive reserve and cognitive function in healthy older people: a meta-analysis. *Aging, Neuropsychology, and Cognition.* Advance online publication. doi: 10.1080/13825585.2015.1041450

Owen, A. M., Hampshire, A., Grahn, J. A., Stenton, R., Dajani, S., Burns, A. S., . . . Ballard, C. G. (2010). Putting brain training to the test. *Nature, 465*, 775-778. doi: 10.1038/nature09042

Pálsson, S., Aevarsson, O., & Skoog, I. (1999). Depression, cerebral atrophy, cognitive performance and incidence of dementia. Population study of 85-year-olds. *The British Journal of Psychiatry, 174*, 249-253. doi: 10.1192/bjp.174.3.249

Pálsson, S., Larsson, L., Tengelin, E., Waern, M., Samuelsson, S., Hallstro, T., & Skoog, I. (2001). The prevalence of depression in relation to cerebral atrophy and cognitive performance in 70- and 74-year-old women in Gothenburg. The Women's Health Study. *Psychological Medicine, 31*, 39-49. doi: 10.1017/s0033291799003050

Parisi, J. M., Stine-Morrow, E. A. L., Noh, S. R., & Morrow, D. G. (2009). Predispositional engagement, activity engagement, and cognition among older adults. *Aging, Neuropsychology, and Cognition, 16*, 485-504. doi: 10.1080/13825580902866653

Parmentier, H., García-Campayo, J., & Prieto, R. (2013). Comprehensive review of generalized anxiety disorder in primary care in Europe. *Current Medical Research and Opinion, 29*, 355-367. doi: 10.1185/03007995.2013.770731

Parslow, R. A., Jorm, A. F., Christensen, H., & Mackinnon, A. (2006). An instrument to measure engagement in life: factor analysis and associations with sociodemographic, health and cognition measures. *Gerontology, 52*, 188-198. doi: 10.1159/000091829

Paterniti, S., Verdier-Taillefer, M. H., Dufouil, C., & Alpérovitch, A. (2002). Depressive symptoms and cognitive decline in elderly people longitudinal study. *The British Journal of Psychiatry, 181*, 406-410. doi: 10.1192/bjp.181.5.406

Paula, J. J., Costa Dde, S., Bertola, L., Miranda, D., & Malloy-Diniz, L. F. (2013). Verbal fluency in older adults with low educational level: what is the role of executive functions and processing speed? *Revista Brasileira De Psiquiatria, 35*, 440-442. doi: 10.1590/1516-4446-2013-1118

Paulson, D., Bowen, M. E., & Lichtenberg, P. A. (2014). Does brain reserve protect older women from vascular depression? *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 69*, 157-167. doi: 10.1093/geronb/gbt007

Pedersen, N. L., Reynolds, C. A., & Gatz, M. (1996). Sources of covariation among mini-mental state examination scores, education, and cognitive abilities. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 51B*, 55-63. doi: 10.1093/geronb/51B.2.P55

Pérès, K., Verret, C., Alioum, A., & Barberger-Gateau, P. (2005). The disablement process: factors associated with progression of disability and recovery in French elderly people. *Disability and Rehabilitation, 27*, 263-276. doi: 10.1080/09638280400006515

Petersen, R. C., Smith, G., Kokmen, E., Ivnik, R. J., & Tangalos, E. G. (1992). Memory function in normal aging. *Neurology, 42*, 396-401. doi: 10.1212/WNL.42.2.396

Peterson, R. A. & Brown, S. P. (2005). On the use of beta coefficients in meta-analysis. *Journal of Applied Psychology, 90*, 175-181. doi:10.1037/0021-9010.90.1.175

Pietrzak, R. H., Maruff, P., Woodward, M., Fredrickson, J., Fredrickson, A., Krystal, J. H., . . . 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. doi: 10.1097/JGP.0b013e3182107e24

Plassman, B. L., Welsh, K. A., Helms, M., Brandt, J., Page, W. F., & Breitner, J. C. (1995). Intelligence and education as predictors of cognitive state in late life: a 50-year follow-up. Neurology, 45, 1446-1450. doi: 10.1212/WNL.45.8.1446

Plassman, B. L. Williams, Jr., 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. doi: 10.7326/0003-4819-153-3-201008030-00258

Platts, L. G., Webb, E., Zins, M., Goldberg, M., & Netuveli, G. (2015). Mid-life occupational grade and quality of life following retirement: a 16-year follow-up of the French GAZEL study. *Aging & Mental Health, 19,* 634-646. doi: 10.1080/13607863.2014.955458

Plumet, J., Gil, R., & Gaonac'h, D. (2005). Neuropsychological assessment of executive functions in women: effects of age and education. *Neuropsychology, 19*, 566-577. doi: 10.1037/0894-4105.19.5.566

Poletti, M., Emre, M., & Bonuccelli, U. (2011). Mild cognitive impairment and cognitive reserve in Parkinson's disease. *Parkinsonism & Related Disorders, 17*, 579-586. doi: 10.1016/j.parkreldis.2011.03.013

Porter, V., Buxton, W. G., Fairbanks, L. A., Strickland, T., O'Connor, S. M., Rosenberg-Thompson, S., & Cummings, J. L. (2003). Frequency and characteristics of anxiety amongst patients with Alzheimer's disease and related dementias. *The Journal of Neuropsychiatry and Clinical Neurosciences, 15*, 180-186. doi: 10.1176/appi.neuropsych.15.2.180

Portin, R., Saarijärvi, S., Joukamaa, M., & Salokangas, R. K. R. (1995). Education, gender and cognitive performance in a 62-year-old normal population: results from the Turva project. *Psychological Medicine, 25*, 1295-1298. doi: 10.1017/S0033291700033262

Potter, G. G., Helms, M. J., & Plassman, B. L. (2008). Associations of job demands and intelligence with cognitive performance among men in late life. *Neurology, 70*, 1803-1808. doi: 10.1212/01.wnl.0000295506.58497.7e

Potter, G. G., Plassman, B. L., Helms, M. J., Foster, S. M., & Edwards, N. W. (2006). Occupational characteristics and cognitive performance among elderly male twins. *Neurology, 67*, 1377-1382. doi: 10.1212/01.wnl.0000240061.51215.ed

Potvin, O., Bergua, V., Meillon, C., Le Goff, M., Bouisson, J., Dartigues, J., & Amieva, H. (2013). State anxiety and cognitive functioning in older adults. *The American Journal of Geriatric Psychiatry, 21*, 915-924. doi: 10.1016/j.jagp.2013.01.029

Prince, M., Bryce, R., Albanese, E., Wimo, A., Ribeiro, W., & Ferri, C. P. (2013). The global prevalence of dementia: a systematic review and meta-analysis. *Alzheimer's & Dementia, 9*, 63-75. doi: 10.1016/j.jalz.2012.11.007

Puccioni, O. & Vallesi, A. (2012a). High cognitive reserve is associated with a reduced age-related deficit in spatial conflict resolution. *Frontiers in Human Neuroscience, 6*, 327. doi: 10.3389/fnhum.2012.00327

Puccioni, O. & Vallesi, A. (2012b). Conflict resolution and adaptation in normal aging: the role of verbal intelligence and cognitive reserve. *Psychology and Aging, 27*, 1018-1026. doi: 10.1037/a0029106

Raftery, A. E., Li, N., Ševcíková, H., Gerland, P., & Heilig, G. K. (2012). Bayesian probabilistic population projections for all countries. *Proceedings of the National Academy of Sciences, 109*, 13915-13921. doi: 10.1073/pnas.1211452109

Raven, J. C. (1960) *Guide to the Standard Progressive Matrices*. London: H. K. Lewis.

Raz, N., Gunning-Dixon, F., Head, D., Rodrigue, K. M., Williamson, A., & Acker, J. D. (2004). Aging, sexual dimorphism, and hemispheric asymmetry of the cerebral cortex: replicability of regional differences in volume. *Neurobiology of Aging, 25*, 377-396. doi: 10.1016/S0197-4580(03)00118-0

Reijnders, J. S. A. M., Ehrt, U., Weber, W. E. J., Aarsland, D., & Leentjens, A. F. G. (2008). A systematic review of prevalence studies of depression in Parkinson's disease. *Movement Disorders, 23*, 183-189. doi: 10.1002/mds.21803

Reppermund, S., Brodaty, H., Crawford, J. D., Kochan, N. A., Slavin, M. J., Trollor, J. N., . . . Sachdev, P. S. (2011). The relationship of current depressive symptoms and past depression with cognitive impairment and instrumental activities of daily living in an elderly population: the Sydney memory and ageing study. *Journal of Psychiatric Research, 45*, 1600-1607. doi: 10.1016/j.jpsychires.2011.08.001

Rexroth, D. F., Tennstedt, S. L., Jones, R. N., Guey, L. T., Rebok, G. W., Marsiske, M. M., . . . Unverzagt, F. W. (2014). Relationship of demographic and health factors to cognition in older adults in the ACTIVE study. *Journal of Aging and Health, 25*, 128S-146S. doi: 10.1177/0898264313498415

Reyes-Ortiz, C. A., Berges, I. M., Raji, M. A., Koenig, H. G., Kuo, Y., & Markides, K. S. (2008). Church attendance mediates the association between depressive symptoms and cognitive functioning among older Mexican Americans. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 63*, 480-486.

Reynolds, C. F., Thomas, S. B., Morse, J. Q., Anderson, S. J., Albert, S., Dew, M. A., . . . Quinn, S. C. (2014). Early intervention to preempt major depression among older black and white adults. *Psychiatric Services, 65*, 765-773. doi: 10.1176/appi.ps.201300216

Reynolds, S. L., Haley, W. E., & Kozlenko, N. (2008). The impact of depressive symptoms and chronic diseases on active life expectancy in older Americans. *The American Journal of Geriatric Psychiatry, 16*, 425-432. doi: 10.1097/JGP.0b013e31816ff32e

Richard, E., Reitz, C., Honig, L. S., Schupf, N., Tang, M. X., Manly, J. J., . . . Luchsinger, J. A. (2013). Late life depression, mild cognitive impairment and dementia. *JAMA Neurology, 70*, 374-382. doi: 10.1001/jamaneurol.2013.603

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. doi: 10.1002/ana.20637

Richards, M. & Sacker, A. (2003). Lifetime antecedents of cognitive reserve. *Journal of Clinical and Experimental Neuropsychology, 25*, 614-624. doi: 10.1076/jcen.25.5.614.14581

Ritchie, S. J., Bates, T. C., Der, G., Starr, J. M., & Deary, I. J. (2013). Education is associated with higher later life IQ scores, but not with faster cognitive processing speed. *Psychology and Aging, 28*, 515-521. doi: 10.1037/a0030820

Robinson, C. & Schumacker, R. E. (2009). Interaction effects: centering, variance inflation factor, and interpretation issues. *Multiple Linear Regression Viewpoints, 35*, 6-11.

Rosenberg, P. B., Mielke, M. M., Xue, Q. L., & Carlson, M. C. (2010). Depressive symptoms predict incident cognitive impairment in cognitive healthy older women. *The American Journal of Geriatric Psychiatry, 18*, 204-211. doi: 10.1097/JGP.0b013e3181c53487

Ross, C. E. & Mirowsky, J. (2006). Sex differences in the effect of education on depression: resource multiplication or resource substitution? *Social Science & Medicine, 63*, 1400-1413. doi: 10.1016/j.socscimed.2006.03.013

Ross, C. E. & Mirowsky, J. (2010). Gender and the health benefits of education. *Sociological Quarterly, 51,* 1-19. doi: 10.1111/j.1533-8525.2009.01164.x

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. doi: 10.1192/bjp.149.6.698

Rutter, M. (1985). Family and school influences on cognitive development. *Journal of Child Psychology and Psychiatry, 26,* 683-704. doi: 10.1111/j.1469-7610.1985.tb00584.x

Saczynski, J. S., Jonsdottir, M. K., Sigurdsson, S., Eiriksdottir, G., Jonsson, P. V., Garcia, M. E., . . . Launer, L. J. (2008). White matter lesions and cognitive performance: the role of cognitively complex leisure activity. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 63A,* 848-854. doi: 10.1093/gerona/63.8.848

Salthouse, T. A. (2006). Mental exercise and mental aging evaluating the validity of the "use it or lose it" hypothesis. *Perspectives on Psychological Science, 2,* 68-87. doi: 10.1111/j.1745-6916.2006.00005.x

Salthouse, T. A. (2009). When does age-related cognitive decline begin? *Neurobiology of Aging, 30,* 507-514. doi: 10.1016/j.neurobiolaging.2008.09.023

Sánchez Rodríguez, J. L., 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. doi: 10.1177/15333175114288150

Sandu, A., Staff, R. T., McNeil, C. J., Mustafa, N., Ahearn, T., Whalley, L. J., & Murray, A. D. (2014). Structural brain complexity and cognitive decline in late life — A longitudinal study in the Aberdeen 1936 birth cohort. *Neuroimage, 100,* 558-563. doi: 10.1016/j.neuroimage.2014.06.054

Santos, N. C., Costa, P. S., Cunha, P., Portugal-Nunes, C., Amorim, L., Cotter, J., . . . Sousa, N. (2014). Clinical, physical and lifestyle variables and relationship with cognition and mood in aging: a cross-sectional analysis of distinct educational groups. *Frontiers in Aging Neuroscience, 6.* doi: 10.3389/fnagi.2014.00021

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. doi: 10.1037/0894-4105.7.3.273

Scarmeas, N. & Stern, Y. (2003). Cognitive reserve and lifestyle. *Journal of Clinical and Experimental Neuropsychology, 25,* 625-633. doi: 10.1076/jcen.25.5.625.14576

Schaie, K. W. (1996). Intellectual development in adulthood. In Birren, J.E. & Schaie, K.W. (Eds.), *Handbook of the psychology of aging* (4th ed., pp. 266-286). San Diego, CA.: Academic Press.

Scherr, P. A., Albert, M. S., Funkenstein, H. H., Cook, N. R., Hennekens, C. H., Branch, L. G., . . . Evans, D. A. (1988). Correlates of cognitive function in an elderly community population. *American Journal of Epidemiology, 128*, 1084-1101.

Schmand, B., Smit, J., Lindeboom, J., Smits, C., Hooijer, C., Jonker, C., & Deelman, B. (1997). Low education is a genuine risk factor for accelerated memory decline and dementia. *Journal of Clinical Epidemiology, 50*, 1025-1033. doi: S0895-4356(97)00121-2

Schoevers, R. A., Smit, F., Deeg, D. J. H., Cuijpers, P., Dekker, J., van Tilburg, W., & Beekman, A. T. F. (2006). Prevention of late-life depression in primary care: do we know where to begin? *American Journal of Psychiatry, 163*, 1611-1621. doi: 10.1176/ajp.2006.163.9.1611

Schönknecht, P., Pantel, J., Kruse, A., & Schröder, J. (2005). Prevalence and natural course of aging-associated cognitive decline in a population-based sample of young-old subjects. *American Journal of Psychiatry, 162*, 2071-2077. doi: 10.1176/appi.ajp.162.11.2071

Senanarong, V., Poungvarin, N., Sukhatunga, K., Prayoonwiwat, N., Chaisewikul, R., Petchurai, R., . . . Viriyavejakul, A. (2001). Cognitive status in the community dwelling Thai elderly. *Journal of the Medical Association of Thailand, 84*, 408-416.

Sheres, D. K. (Apr 2002). *The relationship of lifestyle variables to cognitive functioning and aging.* (Doctoral dissertation) California School of Professional Psychology, San Diego. Retrieved from http://search.proquest.com/docview/619966231?accountid=14874

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. doi: 10.1017/S1355617709090857

Singh-Manoux, A., Marmot, M. G., Glymour, M., Sabia, S., Kivimaki, M., & Dugravot, A. (2011). Does cognitive reserve shape cognitive decline? *Annals of Neurology, 70*, 296-304. doi: 10.1002/ana.22391

Smart, E. L., Gow, A. J., & Deary, I. J. (2014). Occupational complexity and lifetime cognitive abilities. *Neurology, 83*, 2285-2291. doi: 10.1212/WNL.0000000000001075

Smits, C. H. M., van Rijsselt, R. J. T., Jonker, C., & Deeg, D. J. H. (1995). Social participation and cognitive functioning in older adults. *International Journal of Geriatric Psychiatry, 10*, 325-331. doi: 10.1002/gps.930100409

Snaith, R. P. & Zigmond, A. S. (1994). *HADS: Hospital anxiety and depression scale*. Windsor: NFER-Nelson.

Snitz, B. E., Unverzagt, F. W., Chang, C. H., Bilt, J. V., Gao, S., Saxton, J., . . . Ganguli, M. (2009). Effects of age, gender, education and race on two tests of language ability in community-based older adults. *International Psychogeriatrics, 21*, 1051-1062. doi: 10.1017/S1041610209990214

Snowdon, D. A. (2003). Healthy ageing and dementia: findings from the nun study. *Annals of Internal Medicine, 139*, 450-454.

Snowdon, D. A. (1997). Aging and Alzheimer's disease: lessons from the nun study. *The Gerontologist, 37*, 150-156. doi: 10.1093/geront/37.2.150

Solé-Padullés, C., Bartrés-Faz, D., Junqué, C., Vendrell, P., Rami, L., Clemente, I. C., . . . Molinuevo, J. L. (2009). Brain structure and function related to cognitive reserve variables in normal aging, mild cognitive impairment and Alzheimer's disease. *Neurobiology of Aging, 30*, 1114-1124. doi: 10.1016/j.neurobiolaging.2007.10.008

Spinhoven, P. H., Ormel, J., Sloekers, P. P. A., & Kempen, G. I. J. M. (1997). A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological Medicine, 27*, 363-370. doi: 10.1017/S0033291796004382

Spreen, O. & Strauss, E. (1991). *A compendium of neuropsychological tests: Administration, norms, and commentary*. New York, NY: Oxford University Press.

St. John, P. D., Tyas, S. L., & Montgomery, P. R. (2015). Cognition, even in the normal range, predicts disability: cross-sectional and prospective analyses of a population-based sample. *International Journal of Geriatric Psychiatry, 30*, 1008-1016. doi: 10.1002/gps.4254

Staff, R. T., Murray, A. D., Deary, I. J., & Whalley, L. J. (2004). What provides cerebral reserve? *Brain, 127*, 1191-1199. doi: 10.1093/brain/awh144

Steffens, D. C., R McQuoid, D., & Potter, G. G. (2014). Amnestic mild cognitive impairment and incident dementia and Alzheimer's disease in geriatric depression. *International Psychogeriatrics, 26*, 2029-2036. doi: 10.1017/S1041610214001446

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society, 8,* 448. doi: 10.1017/S1355617702813248

Stern, Y. (2006). Cognitive reserve and Alzheimer's disease. Alzheimer's Disease & Associated Disorders, 20, 112-117. doi: 10.1097/01.wad.0000213815.20177.19

Stern, Y. (2009). Cognitive reserve. Neuropsychologia, 47, 2028. doi: 10.1016/j.neuropsychologia.2009.03.004

Stern, Y. (2011). Elaborating a hypothetical concept: comments on the special series on cognitive reserve. *Journal of the International Neuropsychological Society, 17*, 639-642. doi: 10.1017/S1355617711000579

Stewart, R. (2004). Depressive symptoms and cognitive decline—disentangling the effect of affect. *Journal of Neurology, Neurosurgery & Psychiatry, 75*, 5-5. doi: 10.1136/jnnp.2003.028399

Stine-Morrow, E., Parisi, J. M., Morrow, D. G., & Park, D. C. (2008). The effects of an engaged lifestyle on cognitive vitality: a field experiment. *Psychology and Aging, 23*, 778-786. doi: 10.1037/a0014341

Stone, A. A. & Shiffman, S. (2002). Capturing momentary, self-report data: a proposal for reporting guidelines. *Annals of Behavioral Medicine, 24*, 236-243. doi: 10.1207/S15324796ABM2403_09

Takeuchi, H., Sekiguchi, A. F., Taki, Y. F., Yokoyama, S. F., Yomogida, Y. F., Komuro, N. F., . . . Kawashima, R. (2010). Training of working memory impacts structural connectivity. *The Journal of Neuroscience, 30,* 3297-3303. doi: 10.1523/JNEUROSCI.4611-09.2010

Then, F. S., Luck, T., Luppa, M., Thinschmidt, M., Deckert, S., Nieuwenhuijsen, K., . . . Riedel-Heller, S. G. (2014a). Systematic review of the effect of the psychosocial working environment on cognition and dementia. *Occupational and Environmental Medicine, 71*, 358-365. doi: 10.1136/oemed-2013-101760

Then, F. S., Luck, T., Luppa, M., Arelin, K., Schroeter, M. L., Engel, C., . . . Riedel-Heller, S. G. (2014b). Association between mental demands at work and cognitive functioning in the general population - results of the health study of the Leipzig research center for civilization diseases (LIFE). *Journal of Occupational Medicine and Toxicology, 9.* doi:10.1186/1745-6673-9-23

Thomsen, D. K. (2006). The association between rumination and negative affect: a review. *Cognition and Emotion, 20*, 1216-1235. doi: 10.1080/02699930500473533

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. doi: 10.1111/j.1532-5415.2011.03573.x

Tombaugh, T. N., Kozak, J., & Rees, L. (1999). Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Archives of Clinical Neuropsychology, 14*, 167-177. doi: 10.1093/arclin/14.2.167

Tucker, A. M. & Stern, Y. (2011). Cognitive reserve in aging. *Current Alzheimer Research, 8*, 354-360. doi: 10.2174/156720511795745320

Tuokko, H., Garrett, D. D., McDowell, I., Silverberg, N., & Kristjansson, B. (2003). Cognitive decline in high-functioning older adults: reserve or ascertainment bias? *Aging & Mental Health, 7*, 259-270. doi: 10.1080/1360786031000120750

Uebelacker, L. A., Epstein-Lubow, G., Lewis, T., Broughton, M. K., & Friedman, J. H. (2014). A survey of Parkinson's disease patients: most bothersome symptoms and coping preferences. . *Journal of Parkinson's Disease, 4*, 717-723. doi: 10.3233/JPD-140446

Uekermann, J., Daum, I., Peters, S., Wiebel, B., Przuntek, H., & Müller, T. (2003). Depressed mood and executive dysfunction in early Parkinson's disease. *Acta Neurologica Scandinavica, 107*, 341-348. doi: 10.1034/j.1600-0404.2003.02155.x

United Nations. (2013). World population aging report 2013. Retrieved from http://www.un.org/en/development/desa/population/publications/ageing/WorldPopulationAgeingReport2013.shtml

Unverzagt, F. W., Hall, K. S., Torke, A. M., Rediger, J. D., Mercado, N., Gureje, O., . . . Hendrie, H. C. (1996). Effects of age, education, and gender on CERAD neuropsychological test performance in an African American sample. *The Clinical Neuropsychologist, 10*, 180-190. doi: 10.1080/13854049608406679

Valenzuela, M. J., Brayne, C., Sachdev, P., Wilcock, G., Matthews, F. E., & Medical Research Council Cognitive Function and Ageing Study. (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. doi: 10.1093/aje/kwq476

Valenzuela, M. J., Leon, I., Suo, C., Martinez-Piamba, D., Kochan, N., Brodaty, H., & Sachdev, P. (2013). Cognitive lifestyle in older persons: the population-based Sydney Memory and Ageing Study. *Journal of Alzheimer's Disease, 36*, 87-97. doi: 10.3233/JAD-130143

Valenzuela, M. J., & Sachdev, P. (2006a). Brain reserve and cognitive decline: a non-parametric systematic review. Psychological Medicine, 36, 1065. doi: 10.1017/S0033291706007744

Valenzuela, M. J. & Sachdev, P. (2006b). Brain reserve and dementia: a systematic review. Psychological Medicine, 36, 441-454. doi: 10.1017/S003329170500626

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. doi: 10.1017/S003329170600938X

van der Flier, W. M., Middelkoop, H. A., Weverling-Rijnsburger, A. W., Admiraal-Behloul, F., Bollen, E. L., Westendorp, R. G., & van Buchem, M. A. (2005). Neuropsychological correlates of MRI measures in the continuum of cognitive decline at old age. *Dementia and Geriatric Cognitive Disorders, 20*, 82-88. doi: 10.1159/000086072

Van der Linden, M., Philippot, P., & Heinen, P. (1997). Effect of age, education and verbal efficiency on memory performance and memory self-assessment. *Archives De Psychologie, 65*, 171-185.

van Exel, E., Gussekloo, J., de Craen, A. J. M., Bootsma-van der Wiel, A., Houx, P., Knook, D. L., & Westendorp, R. G. J. (2001). Cognitive function in the oldest old: women perform better than men. *Journal of Neurology, Neurosurgery & Psychiatry, 71*, 29-32. doi: 10.1136/jnnp.71.1.29

van Hooren, S. A., Valentijn, S. A., Bosma, H., Ponds, R. W., van Boxtel, M. P., & Jolles, J. (2005). Relation between health status and cognitive functioning: a 6-year follow-up of the Maastricht aging study. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 60*, 57-60. doi: 10.1093/geronb/60.1.P57

van Hooren, S. A., Valentijn, A. M., Bosma, H., Ponds, R. W. , van Boxtel, M. P. J., & Jolles, J. (2007). Cognitive functioning in healthy older adults aged 64-81: a cohort study into the effects of age, sex, and education. *Aging, Neuropsychology, and Cognition, 14*, 40-54. doi: 10.1080/138255890969483

van't Veer-Tazelaar, P. J., van Marwijk, Harm W. J., van Oppen, P., van Hout, Hein P. J., van, d. H., Cuijpers, P., . . . Beekman, A. T. F. (2009). Stepped-care prevention of anxiety and depression in late life: a randomized controlled trial. *Archives of General Psychiatry, 66*, 297-304. doi: 10.1001/archgenpsychiatry.2008.555

Vaughan, L., Erickson, K. I., Espeland, M. A., Smith, J. C., Tindle, H. A., & Rapp, S. R. (2014). Concurrent and longitudinal relationships between cognitive activity, cognitive performance, and brain volume in older adult women. *The Journals of Gerontology.*

Series B, Psychological Sciences and Social Sciences, 69, 826-836. doi: 10.1093/geronb/gbu109

Vemuri, P., Lesnick, T. G., Przybelski, S. A., Machulda, M., Knopman, D. S., Mielke, M. M., . . . Jack, C. R.,Jr. (2014). Association of lifetime intellectual enrichment with cognitive decline in the older population. *JAMA Neurology, 71*, 1017-1024. doi: 10.1001/jamaneurol.2014.963

Verghese, J., Lipton, R. B., Katz, M. J., Hall, C. B., Derby, C. A., Kuslansky, G., . . . Buschke, H. (2003). Leisure activities and the risk of dementia in the elderly. *New England Journal of Medicine, 348*, 2508-2516. doi: 10.1056/NEJMoa022252

Vinkers, D. J., Gussekloo, J., Stek, M. L., Westendorp, R. G. J., & van der Mast, R. C. (2004). Temporal relation between depression and cognitive impairment in old age: prospective population based study. *British Medical Journal, 329*, 881-884. doi: 10.1136/bmj.38216.604664.DE

von Hippel, W., Vasey, M. W., Gonda, T., & Stern, T. (2008). Executive function deficits, rumination and late-onset depressive symptoms in older adults. *Cognitive Therapy Research, 32*, 474-487. doi: 10.1007/s10608-006-9034-9

Watkins, E. R. (2008). Constructive and unconstructive repetitive thought. *Psychological Bulletin, 134*, 163-206. doi: 10.1037/0033-2909.134.2.163

Watkins, E. R., Mullan, E., Wingrove, J., Rimes, K., Steiner, H., Bathurst, N., . . . Scott, J. (2011). Rumination-focused cognitive-behavioural therapy for residual depression: Phase II randomised controlled trial. *The British Journal of Psychiatry, 199*, 317-322. doi: 10.1192/bjp.bp.110.090282

Weisenbach, S. L. & Kumar, A. (2014). Current understanding of the neurobiology and longitudinal course of geriatric depression. *Current Psychiatry Reports, 16*, 463-472. doi: 10.1007/s11920-014-0463-y

Welsh, K. A., Breitner, J. C., & Magruder-Habib, K. M. (1993). Detection of dementia in the elderly using telephone screening of cognitive status. *Cognitive and Behavioral Neurology, 6*, 103-110.

Welsh-Bohmer, K. A., Østbye, T., Sanders, L., Pieper, C. F., Hayden, K. M., Tschanz, J. T., & Norton, M. C. (2009). Neuropsychological performance in advanced age: influences of demographic factors and apolipoprotein E: findings from the Cache County Memory Study. *The Clinical Neuropsychologist, 23*, 77-99. doi: 10.1080/13854040801894730

Whalley, L. J., Deary, I. J., Appleton, C. L., & Starr, J. M. (2004). Cognitive reserve and the neurobiology of cognitive aging. *Ageing Research Reviews, 3,* 369-382. doi: 10.1016/j.arr.2004.05.001

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. doi: 10.1016/S1474-4422(05)70286-6

Wiederholt, W. C., Cahn, D., Butters, N. M., Salmon, D. P., Kritz-Silverstein, D., & Barrett-Connor, E. (1993). Effects of age, gender and education on selected neuropsychological tests in an elderly community cohort. *Journal of the American Geriatrics Society, 41*, 639-647.

Wight, R. G., Aneshensel, C. S., & Seeman, T. E. (2002). Educational attainment, continued learning experience, and cognitive function among older men. *Journal of Aging and Health, 14*, 211-236. doi: 10.1177/089826430201400203

Wilson, B. A., Cockburn, J., & Baddeley, A. D. (2003). *Rivermead Behavioural Memory Test* (Second ed.). Bury St Edmunds, Suffolk: Thames Valley Test Company.

Wilson, R. S., Barnes, L. L., & Bennett, D. A. (2003a). Assessment of lifetime participation in cognitively stimulating activities. *Journal of Clinical and Experimental Neuropsychology, 25*, 634-642. doi: 10.1076/jcen.25.5.634.14572

Wilson, R. S., Barnes, L. L., Krueger, K. R., Hoganson, G., Bienias, J. L., & Bennett, D. A. (2005). Early and late life cognitive activity and cognitive systems in old age. Journal of the International Neuropsychological Society, 11, 400-407. doi: 10.1017/S1355617705050459

Wilson, R. S., Barnes, L. L., Mendes, d. L., Aggarwal, N. T., Schneider, J. S., Bach, J., . . . Bennett, D. A. (2002b). Depressive symptoms, cognitive decline, and risk of AD in older persons. *Neurology, 59*, 364-370. doi: 10.1212/WNL.59.3.364

Wilson, R. S., Beckett, L. A., Barnes, L. L., Schneider, J. A., Bach, J., Evans, D. A., & Bennett, D. A. (2002a). Individual differences in rates of change in cognitive abilities of older persons. *Psychology and Aging, 17,* 179-193. doi: 10.1037/0882-7974.17.2.179

Wilson, R. S., Bennett, D. A., Beckett, L. A., Morris, M. C., Gilley, D. W., Bienias, J. L., . . . Evans, D. A. (1999). Cognitive activity in older persons from a geographically defined population. The Journals of Gerontology: Series B: Psychological Sciences and Social Sciences, 54B, 155-160. doi: 10.1093/geronb/54B.3.P155

Wilson, R. S., Bennett, D. A., Bienias, J. L., de Leon, C. F. Mendes, Morris, M. C., & Evans, D. A. (2003b). Cognitive activity and cognitive decline in a biracial community population. *Neurology, 61*, 812-816. doi: 10.1212/01.WNL.0000083989.44027.05

Wilson, R. S., de Leon, C. F. M., Bennett, D. A., Bienias, J. L., & Evans, D. A. (2004). Depressive symptoms and cognitive decline in a community population of older persons. *Journal of Neurology, Neurosurgery & Psychiatry, 75*, 126-129.

Wilson, R. S., Scherr, P. A., Schneider, J. A., Tang, Y., & Bennett, D. A. (2007). Relation of cognitive activity to risk of developing Alzheimer disease. Neurology, 69, 1911-1920. doi: 10.1212/01.wnl.0000271087.67782.cb

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. doi: 10.1016/j.neurobiolaging.2014.02.015

Wu, Y., Fratiglioni, L., Matthews, F. E., Lobo, A., Breteler, M. M. B., Skoog, I., & Brayne, C. (2015). Dementia in Western Europe: epidemiological evidence and implications for policy making. *The Lancet Neurology*. Advance online publication. doi: 10.1016/S1474-4422(15)00092-7

Yao, S., Zeng, H., & Sun, S. (2009). Investigation on status and influential factors of cognitive function of the community-dwelling elderly in Changsha city. *Archives of Gerontology and Geriatrics, 49*, 329-334. doi: 10.1016/j.archger.2008.11.007

Yates, J. A., Clare, L., & Woods, R. T. (2013). Mild cognitive impairment and mood: a systematic review. *Reviews in Clinical Gerontology, 23*, 217-356. doi: 10.1017/S0959259813000129

Yates, J. A., Clare, L., & Woods, R. T. (2015). Subjective memory complaints, mood and MCI: a follow-up study. *Aging & Mental Health.* Advance online publication. doi: 10.1080/13607863.2015.1081150

Yen, Y. C., Rebok, G. W., Gallo, J. J., Jones, R. N., & Tennstedt, S. L. (2011). Depressive symptoms impair everyday problem-solving ability through cognitive abilities in late life. *American Journal of Geriatric Psychiatry, 19*, 142-150. doi: 10.1097/JGP.0b013e3181e89894

Yesavage, J. A. & Sheikh, J. I. (1986). Geriatric depression scale (GDS), recent evidence and development of a shorter version. *Clinical Gerontologist, 5*, 165-173. doi: 10.1300/J018v05n01_09

Zahodne, L. B., Glymour, M. M., Sparks, C., Bontempo, D., Dixon, R. A., MacDonald, S. W., & Manly, J. J. (2011). Education does not slow cognitive decline with aging: 12-year evidence from the Victoria longitudinal study. *Journal of the International Neuropsychological Society, 17*, 1039-1046. doi: 10.1017/S1355617711001044

Zahodne, L. B., Nowinski, C. J., Gershon, R. C., & Manly, J. J. (2014). Which psychosocial factors best predict cognitive performance in older adults? *Journal of the International Neuropsychological Society, 20*, 487-495. doi: 10.1017/S1355617714000186

Zauszniewski, J. A. (1995). Development and testing of a measure of depressive cognitions in older adults. *Journal of Nursing Measurement, 3*, 31-41.

Zauszniewski, J. A. (1997). The depressive cognition scale: further psychometric evaluation. *Journal of Nursing Measurement, 5*, 191-200. doi:10.1177/0193945910396731

Zauszniewski, J. A. & Bekhet, A. K. (2011). Measuring use of resourcefulness skills: psychometric testing of a new scale. *ISRN Nursing*, doi:10.5402/2011/787363

Zauszniewski, J. A. & Bekhet, A. K. (2012). Screening measure for early detection of depressive symptoms: The depressive cognition scale. *Western Journal of Nursing Research, 34*, 230-244. doi: 10.1177/0193945910396731

Zauszniewski, J. A. & Rong, J. (1999). Depressive cognitions and psychosocial functioning: a test of beck's cognitive theory. *Archives of Psychiatric Nursing, 13*, 286-293. doi: 10.1016/S0883-9417(99)80060-0

Zhang, X., Norton, J., Carrière, I., Ritchie, K., Chaudieu, I., & Ancelin, M. (2015). Generalized anxiety in community-dwelling elderly: prevalence and clinical characteristics. *Journal of Affective Disorders, 172*, 24-29. doi: 10.1016/j.jad.2014.09.036

Zhou, S., Zhu, J., Zhang, N., Wang, B., Li, T., Lv, X., . . . Wang, H. (2014). The influence of education on Chinese version of Montreal Cognitive Assessment in detecting amnesic mild cognitive impairment among older people in a Beijing rural community. *The Scientific World Journal, 2014*, 689456. doi: 10.1155/2014/689456

Zimmerman, F. J., Christakis, D. A., & Vander Stoep, A. (2004). Tinker, tailor, soldier, patient: work attributes and depression disparities among young adults. *Social Science & Medicine, 58*, 1889-1901. doi: 10.1016/S0277-9536(03)00410-6

Zimmerman, M. E., Bigal, M. E., Katz, M. J., Brickman, A. M., & Lipton, R. B. (2012). Sleep onset/maintenance difficulties and cognitive function in nondemented older adults: the role of cognitive reserve. *Journal of the International Neuropsychological Society, 18*, 461-470. doi: 10.1017/S1355617711001901

Appendices

Appendix A. Ethical approval from Bangor University for the two new empirical studies

Dear Carol Anne,

2013-11524 Cognitive reserve, cognitive function, and well-being in later life

Your research proposal number 2013-11524 has been reviewed by the School of Psychology Ethics and Research Committee and the committee are now able to confirm ethical and governance approval for the above research on the basis described in the application form, protocol and supporting documentation. This approval lasts for a maximum of three years from this date.

Ethical approval is granted for the study as it was explicitly described in the application

If you wish to make any non-trivial modifications to the research project, please submit an amendment form to the committee, and copies of any of the original documents reviewed which have been altered as a result of the amendment. Please also inform the committee immediately if participants experience any unanticipated harm as a result of taking part in your research, or if any adverse reactions are reported in subsequent literature using the same technique elsewhere.

Governance approval is granted for the study as it was explicitly described in the application and we are happy to confirm that this study is now covered by the University's indemnity policy.

If any new researchers join the study, or any changes are made to the way the study is funded, or changes that alter the risks associated with the study, then please submit an amendment form to the committee.

Yours sincerely

Everil McQuarrie

--
Rhif Elusen Gofrestredig / Registered Charity No. 1141565

Appendix A. Ethical approval from Bangor University for the two new empirical studies

Dear Carol Anne,

2012-5442 Psychological factors contributing to cognitive reserve in later life

Your research proposal number 2012-5442 has been reviewed by the School of Psychology Ethics and Research Committee and the committee are now able to confirm ethical and governance approval for the above research on the basis described in the application form, protocol and supporting documentation. This approval lasts for a maximum of three years from this date.

Ethical approval is granted for the study as it was explicitly described in the application

If you wish to make any non-trivial modifications to the research project, please submit an amendment form to the committee, and copies of any of the original documents reviewed which have been altered as a result of the amendment. Please also inform the committee immediately if participants experience any unanticipated harm as a result of taking part in your research, or if any adverse reactions are reported in subsequent literature using the same technique elsewhere.

Governance approval is granted for the study as it was explicitly described in the application and we are happy to confirm that this study is now covered by the University's indemnity policy.

If any new researchers join the study, or any changes are made to the way the study is funded, or changes that alter the risks associated with the study, then please submit an amendment form to the committee.

Yours sincerely

Everil McQuarrie

--
Rhif Elusen Gofrestredig / Registered Charity No. 1141565

Appendix B. List of ethics approvals granted for CFAS II

Ethical approvals for CFAS II

MRC Cognitive Function and Ageing Study (CFAS) was approved locally at all sites from 1991, approvals obtained for CFAS II are detailed below

Date	Study Title:	Ethical Committee	REC No	Notes
2007	Is Ageing Changing? Health, healthy life and cognition across generations	Cambridgeshire 4 Research Ethics Committee	07/MRE05/48	
10/08/2008	Newcastle LREC	Newcastle PCT Research and Development Dept	2007EC001	
01/12/2009	Newcastle LREC	NHS North of Tyne	2002PCMH003	Amendment 2/3
03/07/2007	Nottingham LREC	Nottingham Research Ethics Committee 1	07/H0403/105	
07/05/2008	Nottingham LREC	Nottinghamshire County teaching PCT	Amendment 2/3	
20/11/2007	Cambridgeshire LREC	Cambridgeshire NHS PCT	L00808	
08/09/2014	Cambridgeshire LREC	Cambridgeshire Community Services NHS Trust		RMG Oversight doc – CSP studies 2014

For CFAS office use

Project No. ……..

The Cognitive Function and Ageing Studies
Data Application Form

Section A: Information regarding the investigator of the proposed Ancillary Study

1. Principal investigator of the ancillary study details:

Title: Ms Name: Carol Opdebeeck

Institution: Bangor University

Address: School of Psychology, Bangor University, Bangor, Gwynedd, LL572DG

Telephone No: 01248 382938 Fax Number……...

Email: pspe5e@bangor.ac.uk

2. List of all investigators expected to participate in the ancillary study with affiliations

Professor Linda Clare, School of Psychology, Bangor University

Professor Bob Woods, School of Psychology, Bangor University

Dr Fiona Matthews, MRC Biostatistics Unit, Cambridge

Section B: Description of the proposed Ancillary study (2-4 pages)

Title of study: **Effects of mood, loneliness, and worry on cognitive reserve and cognitive function**

Expected duration of the project: from 01/04/2014 to 31/12/2014

CFAS Sponsor:

……

Has this proposal been peer-reviewed: NO *(Please delete as appropriate)*

If yes please provide any comments with proposal

……
……

If no, are there plans for review?

No but it has been reviewed by the lead investigator's PhD committee and discussed at the CFAS Wales management meeting

Study Description – Max 500 words

Background:

With an aging population it is important to investigate the relationships between potentially modifiable psychosocial variables and cognitive function in later life. These modifiable variables could include depression, anxiety, worry, loneliness, and levels of activity in later life a contributor to cognitive reserve.

Cognitive reserve is the concept that has been proposed to account for at least a proportion of the variance seen in cognitive function in later life. Greater cognitive reserve, as indicated by higher education, cognitively demanding occupation and/or participation in cognitive leisure activities has been related to better cognitive function and less cognitive decline (Nucci et al., 2011; Valenzuela & Sachdev, 2006).

Previous research has shown that depression, anxiety and loneliness are negatively associated with cognitive function in later life (Kohler et al., 2010; Luanaigh & Lawlor, 2008; Reppermund et al., 2011). Wisocki (1988) suggested that older people seem particularly susceptible to worry and there is evidence that worry is associated with depression and anxiety (Muris et. al. 2005).

With a role established for cognitive reserve and mood in cognitive ability in older people, it is of interest to assess whether these psychological variables moderate the relationship between cognitive reserve and cognitive function.

Aims:

1. To confirm that there is a relationship between cognitive reserve and cognitive function in this sample.
2. To assess the relationship between depression, anxiety, worry, and loneliness and cognitive function.
3. To investigate whether depression, anxiety, worry, and loneliness play a role in the relationship between cognitive reserve and cognitive function.

Design

The current proposed study will comprise an analysis of variables taken from Wave 1 of the Cognitive Function and Ageing Studies-II (CFAS II) and Wave 1 of CFAS Wales. Participants will be excluded if they meet criteria for dementia or report a prior history of Parkinson's disease, stroke, or head injury.

Measures

Cognitive function

Scores from the Cambridge Cognitive Examination (CAMCOG) neuropsychological screening battery will be used to assess cognitive function.

Mood

Depression, anxiety, and worry will be assessed using questions from the Geriatric Mental State Examination (GMS).

Loneliness

Loneliness will be assessed with 10 questions which include the 6-item de Jong Gierveld Loneliness scale for Emotional and Social Loneliness.

Cognitive reserve

Cognitive reserve will be assessed using the Cognitive Lifestyle Score (CLS). Valenzuela, Brayne, Sachdev, Wilcock, and Mathews (2011) created the CLS from CFAS I data and this will be replicated here. CLS comprises scores for educational level, occupational complexity, and current levels of social engagement.

Proposed Analyses

Initial analyses will utilise descriptive statistics to give an indication of average levels and ranges of the predictor variables of depression, anxiety, loneliness, worry, cognitive reserve, and the outcome variable of cognitive function.

To address aims 1 and 2 of this study a series of regression analyses will be carried out. To evaluate the third aim, whether mood and related psychosocial variables play a role in the relationship between cognitive reserve and cognitive function, a path analysis will be carried out.

2. Please provide a Lay Summary (max 500 words)

As people age, memory and thinking problems become more common; however not everyone will experience these problems. There are a number of factors that may help explain why some older people show poorer performance in memory, thinking and planning than others. These can include the types of activities the individual participates in currently, his/her life experiences, and current mood.

It has been proposed that the higher a person's education level, the more challenging his/her occupation, and the more stimulating activities he/she participates in the better prepared his/her brain is to cope with the changes seen in normal ageing. This concept has been called cognitive reserve. Cognitive reserve is not fixed but can be added to throughout the lifespan. Individuals can continue to build upon it through continuing education, work, or engaging in stimulating activities, such as completing Sudoku puzzles or crosswords, reading, and socialising. Having higher cognitive reserve helps people to perform better on memory and thinking assessments in later life and may help to delay cognitive decline and dementia.

Depression, anxiety, worry, and loneliness have all been related to increased memory and thinking problems, whereas greater cognitive reserve is associated with fewer problems. While times of lower mood and loneliness are experienced by many people, and may have a negative impact on memory and thinking, it is possible to address these issues. This means that, like cognitive reserve, mood can be modified, which may in turn affect memory and thinking. This makes the study of how cognitive reserve and mood interact with memory and thinking in later life an important area of research.

This study would investigate whether depression, anxiety, worry, and loneliness influence the relationship between cognitive reserve and cognitive function. In other words, does cognitive reserve become less important to memory and thinking performance when you consider an individual's mood? To do this we would analyse anonymous information from a large number of participants in the CFAS studies to find out more about these relationships.

Section C: Additional Information

Requirements of the proposed study

- For CFAS Questionnaire data complete items a,b,e,f,g
- For existing biological CFAS data complete items c,e,f,g
- For new biological CFAS data complete items d,e,f,g

A. What interview data will be collected from (please circle)

CFAS II: 3 centres: Cambridge, Newcastle, Nottingham

Currently Limited availability (for further information please contact a member of the Senior Investigator team).

W1 Baseline questionnaire (S_w1)

W1 Informant interview HAS (h_w1), EHAS (e_w1)

W2 – Currently unavailable

B. Which questions do you need to address your research questions?

Please be very specific and consistent with your proposal

(For more information visit www.cfas.ac.uk/pages/bquestionnaire/index.html)

1. Prior history of Parkinson's disease, stroke, or head injury (Qs 412, 418,429; exclusion criteria)
2. Cambridge Cognitive Examination (CAMCOG, Qs 266-372 and extra CAMCOG variables)
3. Depression and anxiety (Qs 82-135 and AGECAT algorithm)
4. Loneliness (Qs 82-91)
5. Years of education (Qs 40)
6. Occupation (Qs 45-50)
7. Social contact (Qs 67-68)
8. Cognitive activities (Qs 69-76)

C. What biological data do you need? *Please be very specific and consistent with your proposal*

(For more information visit: www.cfas.ac.uk/pages/bneurof/index.html)

None

D. What type of data do you intend to collect? Please provide sample type, volumes needed and number of samples. Please justify this and provide the name and address of the laboratory that will analyse the specimens.

None

Section D: Analyses

Note that in case of studies where neuropathological data are linked to clinical data, the analysis will either be conducted by our BSU/CAMS statisticians or the researcher will perform the analysis at BSU/CAMS. Funds for the statistician or overhead costs should be specified in a financial contract agreement. Individuals requiring central statistical support must discuss their needs with the CFAS core group.

A. Are you intending to carry out the analysis yourself?

YES *(Please delete as appropriate)*

If yes where? *Please note that approval is for this place only*

Bangor University

B. Are you intending to carry out the analyses at BSU/CAMS

NO

C. Are you intending to use one of our statisticians

NO

All data will be given on CD, please indicate the format required: *(Please delete as appropriate)*

- SPSS
- Version of software: 20
- System: PC

D. Does this study involve the support or collaboration of a for-profit entity

NO

If yes, provide the names and details of this or these for-profit entities

……
…….

E. Could the proposed study result in a patent?

NO

Applicant:

Signed: …  …….

Name (Block Capitals): ……Carol Opdebeeck……..

Date: 13/05/2014

Head of Dept approval by Institute or Sponsor of the proposed study

Signed……
….

Name: (Block Capitals):……Dr John Parkinson ……

Position:……Acting Head of School of Psychology……..

Date: 14/05/2014

The Cognitive Function and Ageing Studies
Data Transfer Agreement

All use of CFAS data should be in agreement with the conditions below:

1. Purpose: To use CFAS data only for non-commercial research or non-commercial teaching. In the case of any other proposed use, the principal investigator should seek further approval of the CFAS CMC.

2. Report of results: Any publication, conference presentation or report containing CFAS data should be submitted for CFAS CMC approval prior to submission for publication or for conference. CFAS CMC will not accept or approve any publication, conference presentation or report containing findings which were not previously proposed in the data application. In case of any findings which are not within the limits of the objectives purposed in the data application, the principal investigator should seek approval of new objectives to the CFAS CMC prior to the manuscript submission to the CFAS CMC for review.

3. Confidentiality: At all times confidentiality of individuals and institutions data should be preserved.

4. Report of progress: For projects taking longer than one year, a short progress report should be written to the CFAS CMC, counted from the day of data application acknowledgement approval.

5. Acknowledgement: Any publication, conference presentation or report, whether printed, electronic or broadcast, based wholly or in part of CFAS data, should acknowledge the Cognitive Function and Ageing Study. Also, in cases when the analyses were not performed by the CFAS team statisticians, a declaration that CFAS holds no responsibility for analysis and interpretation of the collaborative study should be included in the manuscript.

6. Publications: Any publication, conference presentation or report must conform to the CFAS Publications Policy (see Clause 15 Agreed form of Authorship), quoting the dataset version number. Two copies of any published work, conference presentation or report must be deposited with the CFAS Study Administrator.

7. Copyright: Not to distribute copies of the data to others, nor to make copies of them except as necessary to carry out the purpose specified (see Clause 1).

8. 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 CMC for the specified purpose.

9. Derived dataset deposit: To deposit in the CFAS data archive, BSU, Cambridge, prior to manuscript submission to CFAS-CMC, 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.

10. Errors: To notify CFAS of any errors discovered in the materials.

11. Charges: To meet agreed charges for the supply of materials.

12. Liability: To accept that CFAS CMC bears no legal responsibility for the accuracy or comprehensiveness of the materials.

13. Completion: To inform CFAS CMC of the completion of the project specified in this application.

14. Destruction of data: After the data has been deposited and verified by the CFAS data archive (see Clause 9), except where an application has been received to use the data for a further project, all complete, partial or derived copies of the data which have been made available for this application on completion of the specified project must be destroyed / erased irrecoverably, and the CFAS CMC must be informed that this has been done with signing and completion of the data destruction form.

15. Agreed form of Authorship: For publication, conference presentation or report results using CFAS data you will agree to abide by the CFAS Authorship and Publications Policy which can be found on the CFAS Website: www.cfas.ac.uk

16. Publicity: The study must be mentioned in the abstract and where possible the title. MRC CFAS is our preferred title therefore ALL PAPERS regardless of the appropriate authorship would include one of the three following phrases within the abstract:

- The paper reports on analysis of the MRC Cognitive Function and Ageing study (MRC CFAS) data version x.x.
- Study participants for this paper were originally part of the MRC Cognitive Function and Ageing study (MRC CFAS).
- The methodology developed within this paper was validated using the MRC Cognitive Function and Ageing study (MRC CFAS).

17. Acknowledgements: The paper must acknowledge the funders of the study: MRC and Department of Health for papers using CFAS I data/tissues Grant No: [G9901400] and the MRC for papers using CFAS II data Grant No: [G0601022] and the respondents applicable to the paper, alongside any author specific acknowledgements of other funding. Neuropathology papers should acknowledge the specific funding available to support brain retrieval and banking and the CFAS neuropathology resource, full details can be found in the CFAS Authorship and Publications Policy.

18. When the collaborative study involves collection of new data, the data listed in the Data Transfer Agreement will be transmitted to the principal Investigator of the collaborative study once the Coordinating Centre has received the new data collected. These data will be integrated into the main database.

Signed: 

Name (Block Capitals): Carol Opdebeeck

Date: 2/09/2014

Ysgol Seicoleg
Coleg y Gwyddorau Iechyd a Ymddygiad
Prifysgol Bangor
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Ffacs: (01248) 382599

e-bost: pspe5e@bangor.ac.uk
Ffon: (01248) 382938

PRIFYSGOL BANGOR UNIVERSITY

School of Psychology
College of Health and Behavioural Sciences
Bangor University
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Fax: (01248) 382599

e-mail: pspe5e@bangor.ac.uk
Tel: (01248) 382938

PARTICIPANT INFORMATION SHEET

What helps to maintain cognitive health and well-being in later life?

We would like to invite you to take part in our research project. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. You can ask the researchers to explain anything that is not clear or if you would like more information. Please take your time to decide whether or not you wish to take part in our project.

Who are the researchers?

We are five Masters students and one PhD student from Bangor University, working under the supervision of Professor Linda Clare.

What is the purpose of the study?

The aim of our research is to investigate different psychological factors that may affect health and well-being. The information we gain from this project will give us a greater understanding of what helps to maintain cognitive health, how people feel about getting older and their well-being and may be used to inform strategies to promote healthy aging.

Who we are looking for:

We would like to invite individuals over the age of 65 living independently in the community to take part in the project.

What the study involves:

The study involves meeting with a researcher for up to 2 hours. You will be asked to complete some questionnaires, which ask about how you feel about getting older, your general well-being, and your life experiences. You will also be asked to complete a few simple tasks involving memory, thinking, and planning skills. If you take part in the study, you can meet the researchers at the University, or if you prefer, the researchers will come to see you at your home.

What are the benefits and risks?
We do not think that taking part in the study will involve any disadvantages or any specific risks to you. Although you will not directly benefit from participating in this study, the findings of this study will help us to look at different factors that affect well-being and health, which may help produce strategies to promote health and well-being in later life. You may withdraw from the study at any time, without giving a reason, and this will not affect your legal rights in any way.

What will happen to your information?
All of the information we obtain from you will be kept confidentially, and you will not be identifiable in any report, thesis or publication that arises from this study. The anonymised data from this study will be stored securely for 5 years after the project is completed. If you choose to withdraw from the study then you have the right to request that your data is not used. If you would like to know the findings of the study then you can request to be contacted by the research team at the end of the study. Any audio recordings will be kept securely and you will not be identifiable. Audio recordings will be deleted once the information has been written down. You can keep up-to-date with the Bangor University Research in Ageing and Cognitive Health (REACH) group's research activities by visiting our website: http://reach.bangor.ac.uk/.

If you are interested in taking part in our study:
If you would like to find out more about the study please e-mail one of us below or contact Carol Opdebeeck (PhD student) Tel: 01248 382938 or e-mail pspe5e@bangor.ac.uk

Contact details of researchers:

Alison Windsor	psp26a@bangor.ac.uk
Amy Maynard	psp237@bangor.ac.uk
Emily Keen	psud43@bangor.ac.uk
Heledd Tomos	psp2b0@bangor.ac.uk
Kellie Lovett	psp24e@bangor.ac.uk

Lead Researchers:
Professor Linda Clare, Carol Opdebeeck, Dr Anthony Martyr, and Dr Catherine Lawrence.

If you have any concerns about this study:
If you have any complaints about the conduct of this study you can contact:
Mr. Hefin Francis, School Manager, School of Psychology, Bangor University, Bangor, Gwynedd, LL57 2AS.
Tel: 01248 388339, Email: h.francis@bangor.ac.uk

Thank you for reading this information sheet.

Appendix D. Information sheet and consent form for empirical study 1 (Chapter 3)

Ysgol Seicoleg
Coleg y Gwyddorau Iechyd a Ymddygiad
Prifysgol Bangor
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Ffacs: (01248) 382599

e-bost: pspe5e@bangor.ac.uk
Ffon: (01248) 382938

PRIFYSGOL BANGOR UNIVERSITY

School of Psychology
College of Health and Behavioural Sciences
Bangor University
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Fax: (01248) 382599

e-mail: pspe5e@bangor.ac.uk
Tel: (01248) 382938

ID: _____

CONSENT FORM

What helps people to maintain well-being in later life?

Lead Researchers: Professor Linda Clare, Carol Opdebeeck, Dr Anthony Martyr, and Dr Catherine Lawrence

Researchers: Alison Windsor, Amy Maynard, Emily Keen, Heledd Tomos and Kellie Lovett

Please initial box

1. I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my legal rights being affected. ☐
3. I agree to take part in the above study. ☐

Optional:

4. I agree for my contact details to be kept securely by the lead investigator for future studies conducted by the research team. I understand that my contact details will not be passed on to other researchers without my explicit consent. I understand that if I agree to my contact details being kept that I am free to decline to take part in any future studies. ☐
5. I consent to be audio recorded on some tasks to ensure accurate scoring of the information I provide. I understand these recordings will be anonymous and kept securely by the research team. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

Ysgol Seicoleg
Coleg y Gwyddorau Iechyd a Ymddygiad
Prifysgol Bangor
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Ffacs: (01248) 382599

e-bost: psychology@bangor.ac.uk
www.bangor.ac.uk/psychology/

PRIFYSGOL BANGOR UNIVERSITY

School of Psychology
College of Health and Behavioural Sciences
Bangor University
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Fax: (01248) 382599

e-mail: psychology@bangor.ac.uk
www.bangor.ac.uk/psychology/

PARTICIPANT INFORMATION SHEET

What helps people to maintain well-being in later life?

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. Ask the researchers if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part.

Who we are:

We are eight Masters students and one PhD student from Bangor University, working under the supervision of Professor Linda Clare.

What is the purpose of the study?

Our research is investigating different psychological factors that may affect health and well-being. The information we gain from this project will give us a greater understanding of how people feel about their well-being and memory, and may be used to inform strategies to promote healthy aging.

Who we are looking for:

Individuals over the age of 65 living independently in the community.

What the study involves:

The study involves meeting with a researcher for approximately 90 minutes. You will be asked to complete some questionnaires, which ask about your general well-being, quality of life, social activities and your life experiences. You will also be asked to complete a few simple tasks involving memory and thinking skills. If you take part in the study, you can meet the researchers at the University, or if you prefer, the researchers will come to see you at your home.

What are the benefits and risks?
We do not think that participation will involve any disadvantages or any specific risks to you. Although you will not directly benefit from participating in this study, the findings of this study will help us look at different factors that affect well-being and health, which may help produce strategies to promote health and well-being in later life. You may withdraw from the study at any time without giving a reason and this will not affect your legal rights in any way.

What will happen to my information?
All data collected will be confidential, and you will not be identifiable in any report, thesis or publication which arises from this study. The data from this study will be stored securely for 5 years after the project is completed. If you choose to withdraw from the study and your data is identifiable to the research team, then you have the right to request that your data is not used. You may also request to be contacted concerning the results of the study once it has been completed, if you wish to know what was found. You may also find periodic updates about this research and other research conducted by the Bangor University Research in Aging and Cognitive Health (REACH) group by going to http://reach.bangor.ac.uk/.

If you are interested in taking part in our study:
If you do decide to take part in the study, you can arrange a suitable time to meet with one of us in person, email one of us below or return the reply slip provided and we will contact you. If you have any questions about the study, please feel free to contact one of the researchers.

Contact details of researchers:
Emma Bashford: psp098@bangor.ac.uk
Anvita Janardhanan: psp04e@bangor.ac.uk
Emma McCormack: psp02e@bangor.ac.uk
Sarah Morris: psub01@bangor.ac.uk
Catherine Mulholland: psp047@bangor.ac.uk
Adele Simpson: psp060@bangor.ac.uk
Lucinda Willington: psua32@bangor.ac.uk
Rachael Young: psuab6@bangor.ac.uk

Professor Linda Clare, School of Psychology, Bangor University, Bangor, Gwynedd, LL57 2AS, Tel: 01248 388178, Email: l.clare@bangor.ac.uk
Carol Opdebeeck, School of Psychology, Bangor University, Bangor, Gwynedd, LL57 2AS, Tel: 01248 382938, Email: pspe5e@bangor.ac.uk

If you have any concerns about this study:
If you have any complaints about the conduct of this study you can contact: Mr. Hefin Francis, School Manager, School of Psychology, Bangor University, Bangor, Gwynedd, LL57 2AS. Tel: 01248 388339, Email: h.francis@bangor.ac.uk

Thank you for reading this information sheet.

Ysgol Seicoleg
Coleg y Gwyddorau Iechyd a Ymddygiad
Prifysgol Bangor
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Ffacs: (01248) 382599

e-bost: psychology@bangor.ac.uk
www.bangor.ac.uk/psychology/

PRIFYSGOL BANGOR UNIVERSITY

School of Psychology
College of Health and Behavioural Sciences
Bangor University
Bangor, Gwynedd LL57 2AS
http://www.bangor.ac.uk/psychology/
Fax: (01248) 382599

e-mail: psychology@bangor.ac.uk
www.bangor.ac.uk/psychology/

ID: _____

CONSENT FORM

What helps people to maintain well-being in later life?
Lead Researchers: Professor Linda Clare and Carol Opdebeeck
Researchers: Emma Bashford, Anvita Janardhanan, Emma McCormack, Sarah Morris, Catherine Mulholland, Adele Simpson, Lucinda Willington, Rachael Young

Please initial box

1. I confirm that I have read and understood the information sheet for the above study, dated 15/12/2011, and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my legal rights being affected. ☐

3. I agree to take part in the above study. ☐

Optional:

4. I agree for my contact details to be kept securely by the lead investigator for future studies conducted by the lab. I understand that my details will not be passed on to other researchers without my explicit consent. I understand that if I agree to my details being kept that I am free to decline to take part in any future studies. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

1 for participant; 1 for researcher

MRC CFAS II

Dept of Public Health & Primary Care
Institute of Public Health
University of Cambridge
Forvie Site
Robinson Way
Cambridge CB2 0SR

Tel: 01223 330312
Fax: 01223 330330

CAMBRIDGESHIRE PROJECT FOR LATER LIFE
STUDY II
PARTICIPANT INFORMATION SHEET

(letter head amended for each centre)

We would like to invite you to take part in a research study. Before you decide whether to take part is it important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully.

The purpose of the study

Ageing is now recognized as one of the major challenges facing the world's populations. It presents challenges to national and local policy makers and service providers in planning and providing for the needs of the older population.

This study is based on the original MRC Cognitive Function and Ageing Study (CFAS) which looked at ageing and health in six centres in the UK; Newcastle, Nottingham, Liverpool, Gwynedd, Cambridgeshire and Oxford. The study began in 1991 with 18,000 participants, and it still continues today.

Since the start of the original CFAS study there has been an increase in life expectancy and improved screening, diagnosis and treatment of many chronic disorders. The aim of this study is to find out how health and well-being change as people grow older. Some people experience difficulties as they get older while others remain fit and active. We are interested in the full range of experiences so that we can get a true picture of ageing in the population.

We now wish to see whether health patterns change between different generations and we can only do this by inviting a new generation of people of 65 years and above to take part. In this new study we plan to approach **12,500** people at **four** of the original six CFAS centres, Newcastle, Nottingham, **Gwynedd**, and Cambridgeshire (based on Ely and surrounding villages); **and also a new centre at Neath, West Glamorgan.**

Why have I been chosen?

You have been randomly selected from National Health Service records. The only information provided to MRC CFAS is your name, address, sex, and date of birth, all of this information has been processed by us in accordance with the Data Protection Act 1998. We do not know anything else about you, and have not seen your medical records and would ask for your written consent to look at them.

Do I have to take part?

No, there is no obligation to take part and you can withdraw at any stage, without giving any reason. The study is for medical research only and will not affect your medical care or legal rights.

What will happen if I decide to take part?

If you should decide to take part, a research interviewer will visit you at your home. If the time is not convenient they will return at a more convenient time for you. They will go through the information sheet with you and answer any questions you may have about the study. You will then be asked to sign a consent form to say you have read the information sheet, have had the opportunity to ask questions, and would like to take part in the study.

Following this you will be asked questions on your background, health, contact with friends and family and day to day activities, there will also be a section on memory and concentration. The interview will take approximately 1½-2 hours.

We will invite you to take part in a short hearing test which would involve placing a small device next to your ear and sending a short pulse of sound into your ear which will establish if there is any hearing loss. The results will be available immediately, and with your permission we will inform your GP of the results, if measurements lie outside normal values and you do not already have a hearing aid.

During the interview you will also be asked if you would consent to supply a saliva sample by depositing a small amount of saliva into a small container which will be stored for research purposes investigating ageing which will include genetic (DNA) tests.

The study includes a follow up and, with your permission; we would hope to ask you to see us again in two years time.

Subject to future funding some participants may be asked to supply a blood sample which would also be stored for research purposes which would include genetic (DNA) tests, the blood would be taken by a trained phlebotomist. The results of these investigations are unlikely to have any implications for participants personally. Consent will be sought from respondents to inform their GP of the results, if measurements lie outside normal values.

Some people in the original CFAS study have made a further contribution to the study by agreeing to possible future examination of the brain after death. This gift, so generously given, has helped us to improve understanding of brain changes in ageing, some of which cause dementia, such as Alzheimer's disease. We may in the future be able to continue this

work, by asking participants in this new study whether they might consider Declarations of Intentions to donate (DOI). If participants express an interest in this aspect of the study, further information will be given by our Research Team.

Depending on future funding we may invite participants to take part in new areas of research such as brain imaging. Any future new research would require specific ethical approval.

Confidentiality

All the information collected by the study is completely confidential and it is stored without personal details on secure systems in compliance with the Data Protection Act 1998. Occasionally we may ask to tape record an interview, audio tapes are anonymised and used for training and quality control purposes only and will be destroyed when no longer required.

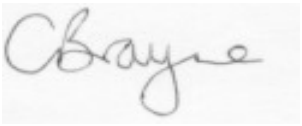
Data collected by the study will only be analysed by approved researchers.

This study has been considered by the Cambridge 4 Research Ethics Committee.

If the addressee is unable to respond, we would be grateful if a relative or carer could discuss with us whether an interview can take place or whether the relative/carer would be willing to be interviewed instead.

If you have any concerns or complaints about anything to do with the study please contact us on 01223 330311 and ask to speak to the Study Coordinator who if unable to help you will direct you to the appropriate person. Indemnity arrangements for the study are provided by the University of Cambridge and the NHS.

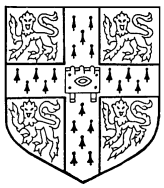
If you would like any further information or have any questions please contact us on 01223 330312 or look at our website www.cfas.ac.uk



Professor Carol Brayne
Local Principal Investigator

Linda Barnes
Study Coordinator MRC CFAS II

CAMBRIDGESHIRE PROJECT FOR LATER LIFE II



Department of Public Health
& Primary Care
Institute of Public Health
University of Cambridge
Forvie Site
Robinson Way
Cambridge CB2 2SR
Telephone: 01223 330312
Fax: 01223 330330

(Letterhead amended for each centre)

CONSENT FORM

Respondent identifier: _____

Please Initial

I confirm that I have read and understood the information sheet **(version 1.6 dated 03/12/2009)** for the above study and have had the opportunity to ask questions. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected ☐

I agree to take part in the above study. ☐

I understand that this interview is to be taped for training and quality control purposes. I agree to this interview being audio recorded. ☐

All the information collected by the study is completely confidential and is stored anonymously, without personal details. Audio tapes are anonymised and used for training and quality control purposes only and will be destroyed when no longer required.

Name of Respondent…….

Signature of Respondent……..

Date……..

Name of Interviewer…….

Signature of Respondent……

Date……..

REACH Research in Ageing and Cognitive Health at Bangor University

PRIFYSGOL BANGOR UNIVERSITY

WOULD YOU BE INTERESTED IN TAKING PART IN A RESEARCH STUDY?

Well-being in later life

What is the purpose of the study?

This study aims to understand different psychological factors that may affect health and well-being. The information we gain from this project will give us a greater understanding of how people feel about getting older, their well-being, and memory and may be used to inform strategies to promote healthy aging.

Who can take part?

The researchers are looking for people over 65 who can spare up to 2 hours.

What is involved?

If you take part in the study, a researcher will meet you at Bangor University, or if you prefer, researchers will visit you at your home. The researchers will:

1. Ask you to complete some questionnaires, which ask about your general well-being, your life experiences, and how you feel about getting older.
2. Ask you to complete a few simple tasks involving memory, thinking, and planning skills.

How can I take part?

If you are interested in taking part or if you would like find out more about the study please contact:

Ms Carol Opdebeeck,
School of Psychology, Bangor University, Bangor, Gwynedd LL57 2AS
Tel: 01248 382938
Email: pspe5e@bangor.ac.uk

Contact details of researchers:

Alison Windsor psp26a@bangor.ac.uk Amy Maynard psp237@bangor.ac.uk
Emily Keen psud43@bangor.ac.uk Heledd Tomos psp2b0@bangor.ac.uk
Kellie Lovett psp24e@bangor.ac.uk

WOULD YOU BE INTERESTED IN TAKING PART IN A RESEARCH STUDY?

Well-being in later life

What is the purpose of the study?

This study aims to understand different psychological factors that may affect health and well-being. The information we gain from this project will give us a greater understanding of how people feel about their well-being and memory, and may be used to inform strategies to promote healthy aging.

Who can take part?

The researchers are looking for people over 65 who can spare approximately 90 minutes to help out.

What is involved?

If you take part in the study, a researcher will meet you at Bangor University, or if you prefer, researchers will come to see you at your home. The researchers will:

1. Ask you to complete some questionnaires, which ask about your general well-being, quality of life, social activities and your life experiences.
2. Ask you to complete a few simple tasks involving memory and thinking skills.

How can I take part?

If you are interested in taking part or if you would like find out more about the study you can contact:

Ms Carol Opdebeeck,
School of Psychology, Bangor University, Bangor, Gwynedd LL57 2AS
Tel: 01248 382938
Email: pspe5e@bangor.ac.uk

Contact details of researchers:

Emma Bashford: psp098@bangor.ac.uk
Anvita Janardhanan: psp04e@bangor.ac.uk
Emma McCormack: psp02e@bangor.ac.uk
Sarah Morris: psub01@bangor.ac.uk
Catherine Mulholland: psp047@bangor.ac.uk
Adele Simpson: psp060@bangor.ac.uk
Lucinda Willington: psua32@bangor.ac.uk
Rachael Young: psuab6@bangor.ac.uk

Appendix H. CFAS II Introductory letter

GP Address:

Dept of Public Health & Primary Care
Institute of Public Health
University of Cambridge
Forvie Site
Robinson Way
Cambridge CB2 0SR

Tel: 01223 330312
Fax: 01223 330330

CAMBRIDGESHIRE PROJECT FOR LATER LIFE II

Dear

This surgery is taking part in a research study conducted by the Department of Public Health and Primary Care at Cambridge University. Ageing is now recognized as one of the major challenges facing the world's populations. The aim of this study is to find out how health and well-being change as people grow older. Some people experience difficulties as they get older while others remain fit and active. We are interested in the full range of experiences so that we can get a true picture of the ageing process and whether these are changing over time.

This research is part of a national study which aims to improve our understanding of changes which occur with ageing and to help policy makers meet the needs of the modern generation of older people.

The interviewers for this study will be calling in the next week or so to ask if you would be able to help. You have been randomly selected from our list and none of your medical details have been passed to the researchers. The research will be most valuable if as many as possible of those of you who are approached are willing to take part.

When the research interviewer calls s/he will produce identification and explain the study in more detail. If s/he calls at an inconvenient time s/he will be happy to call again later. Your cooperation is, of course, voluntary and your decision will not affect your medical care. I have enclosed an information sheet explaining the study in further detail.

If you have any questions, please telephone the research team on 01223 330312 to discuss your queries. We hope you will take up the opportunity to support this research.

Yours Sincerely

Dr

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Authors	**Participants and demographic details**	**Proxy measure of cognitive reserve**	**Cognitive outcomes and correlations**
Educational level			
Aartsen et al. (2002)	3,107 (mean age = 68.7) from the Longitudinal Aging Study Amsterdam (LASA)	Education in years	Screening measure (MMSE, *r* = .30), memory (immediate recall, *r* = .220), executive function (Coding Task – processing speed, *r* = .40), and general cognition (RPM, *r* = .34)
Acevedo et al. (2007)	89 (mean age = 74.56, SD = 4.7)	Education categorised as 3-8 years , 9-12 years, and 13-23 years	Memory (Logical memory and visual reproduction immediate and delayed, *r* = .445), working memory (DS forward, *r* = .330), executive function (Trails B, Similarities, category fluency, phonemic fluency (FAS), *r* = .401), language (BNT), *r* = .33), and visuospatial ability (copying a figure, *r* = .196)
Aiken-Morgan et al. (2010)	449 (mean age = 67.31) from the Baltimore Study of Black Aging	Education in years	Screening measure (MMSE, *r* = .36), memory (CVLT), *r* = .249), working memory (DS Forward, *r* = .24), executive function (DS Backward, *r* = .26), and visuospatial ability which was included in overall cognition only (RPM and Card Rotation Test, *r* = .24)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Al Hazzouri et al. (2011)	7,042 (mean age = 70.6) from the Sacramento Area Latino Study (SALSA) and Mexican Health and Aging Study (MHAS)	Education in years	General cognition (short-term verbal recall, *r* = .09
Albert & Teresi (1999)	161 participants (mean age = 75.4, SD = 7.3)	Education in years	Screening measure (MMSE, *r* = .21)
Alvarado et al. (2002)	557 (aged 65-89) from the Aging in Leganes Study	Education categorised as literate (no formal education), 1-3 years formal education, primary or more	General cognition (time orientation, space orientation, personal information, naming test, immediate & delayed recall (6 objects), and logical memory (short story recall), *r* = .148)
Andel et al. (2015)	810 (mean age = 83) from the Swedish Level of Living Survey and Swedish Panel Study of Living Condition of the Oldest Old (SWEOLD)	Education in years	Screening measure (MMSE, *r* = .08)
Angel et al. (2010)	28 (mean age = 66.5, SD = 6.44)	Education dichotomised into lower (< 10 yrs.) and higher (> 10 yrs.)	Memory (word recall completion, *r* = .531 and accuracy, *r* = .419)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Anstey et al. (2003)	1,823 (mean age = 77.7, SD = 6.56) participants from the Australian Longitudinal Study of Aging (ALSA)	Education in years	Memory (symbol, picture, and word recall, *r* = .226) and executive function (DSST, *r* = .331)
Arbuckle et al. (1986)	285 (median age = 71.6)	Education in years	Memory (index comprising free recall (of 9 words), DS forward, and correct factual and inferential answers (10 multiple choice Qs. based on short story), *r* = .46)
Ardila et al. (2000)	250 aged 66-85	Education categorised as 1-4 years, 5-9 years, and 10+ years	Memory (recall of words and semi-complex figure, cueing, and recognition, *r* = .195), executive function (DS backward, visual detection, 20 minus 3, similarities, calculation, and sequences, and semantic and phonemic fluency, *r* = .331) visuospatial ability (copy of a figure, *r* = .287), and language (naming, repetition, and comprehension, *r* = .121). All subtests of NEUROPSI
Ashley (2008) (PhD thesis)	63 (mean age = 77.3)	Education in years	Executive function (choice reaction time, *r* = .07) and general cognition (word recall, letter series, and DSST, *r* = .28)
Barnes et al. (2004)	664 (mean age = 76) from Sonoma, California	Education in years	Screening measure (MMSE, *r* = .34), memory (CVLT, *r* = .245), and executive function (TMT-B, Stroop, and DSST, *r* = .30-.36)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Barnes et al. (2006)	108 (mean age = 72.6)	Education in years	General cognition (includes MMSE, memory (East Boston Story), perceptual speed (SDMT) and working memory (DS Backward), *r* = .580)
Barnes et al. (2011)	6,158 65+ from the Chicago Health and Aging Project (CHAP)	Education in years	General cognition (includes MMSE, memory (East Boston Story), perceptual speed (SDMT) and working memory (DS Backward), r = .117)
Beatty et al. (2003)	634 aged 64-94 from the Oklahoma Longitudinal Assessment of Health Outcomes of Mature Adults (OAKLAHOMA)	Education categorised as 8^{th} grade or less, some high school, GED, high school graduate, some college, or postgraduate	Memory (immediate and delayed, *r* = .208), executive function (attention, *r* = .293), language (*r* = .206), visuospatial ability (*r* = .205), and general cognition (all the subtests of the RBANS used, *r* = .295)
Capitani et al. (1996)	220 aged 56-85	Education dichotomised into low (mean years = 4.78-5.41) and high education (mean years = 13.07-13.62)	Memory (SRT and Block Tapping Learning, 56-70 year olds, *r* = .21 and 71-85 year olds, *r* = .21), executive function (semantic verbal fluency, 56-70 year olds, *r* = .18 and 71-85 year olds, *r* = .18), and general cognition (RPM, 56-70 year olds, *r* = .18 and 71-85 year olds, *r* = .19)
Carmelli et al. (1995)	522 (mean age = 64)	Education in years	Screening measure (Iowa Screening Battery, *r* = .29 and MMSE, *r* = .30)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Christensen et.al (1996)	703-852 participants aged 70-89 from Canberra and Quanbeyan	Education in years	Screening measure (MMSE, *r* = .35, *n* = 852) and memory (word and address recall, *r* = .21, *n* = 703)
Christensen et al. (2009)	472 aged 60-64 (mean age = 62.6, SD = 1.4) from Personality and Total Health (PATH) Through Life study	Education categorised as 0-12 years, 13 years, 14-15 years, 16+ years	Memory (immediate and delayed recall, *r* = .21) and executive function (SLMT, *r* = .25)
Christofoletti et al. (2007)	116 (mean age = 73.6)	Education categorised as 0, 1-4, 5-8, 9-11, >11	Memory (incidental, immediate and delayed recall, and recognition, *r* = .301), executive function (verbal fluency and clock drawing, *r* = .695-.733), and language (naming, *r* = -.564)
Constantinidou et al. (2012)	359 (mean age = 74.64, SD = 3.97)	Education categorised as 0-4 years, 5-9 years, and >/= to 10 years	Executive function (Trials-B, SDMT, and animal fluency, *r* = .312-.483), visuospatial ability (Trails-A and word finding, *r* = .333), and language (Peabody Picture Vocabulary Test and BNT, *r* = .365)
Correa-Ribeiro et al. (2013)	624 aged 65+	Education categorised as illiterate, 1-4 years, 5-8 years, 9-12 years, and >/=13 years	Screening measure (MMSE, *r* = .264-.402)
Davey et al. (2013)	244 aged 98-108	Education in years	Screening measure (MMSE, *r* = .36), memory (FOME recall and recognition, *r* = .09), and executive function

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			(COWAT, Similarities, and the Behavioural Dyscontrol Test, *r* = .26)
de Araújo Carvalho et al. (2009)	333 (mean age = 68)	Education in years	Language (oral comprehension, *r* = .74)
de Oliveira-Wachholz et al. (2011)	67 aged 60-75	Education categorised as 1-4 years, 5-8 years, and 9 or more years	Screening measure (MMSE, *r* = .37), memory (incidental memory and immediate and delayed recall, *r* = .15), working memory (DS forward, *r* = .05), executive function (clock drawing, DS backward, verbal fluency, *r* = .25-.35), and language (naming, *r* = 0, all at ceiling)
de Souza-Talarico et al. (2007)	40 (mean age = 72)	Education in years	Working memory (DS forward, *r* = .28) and executive function (DS backward, *r* = .41)
Denney & Thissen (1983)	115 men (mean age = 71.16, SD = 7.97)	Education in years	Executive function (Block Design and Twenty Questions Task, *r* = .14), language (vocabulary, *r* = .42), and general cognition (Twenty Questions Task, classification, and vocabulary, *r* = .33)
Diehl et al. (1995)	62 (Mean age = 76.4)	Education in years	Working memory (DS forward, *r* = .05), executive function (processing speed, *r* = -.04), and general cognition (Rey figure type test and recognising synonyms, *r* = .17-.30

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Dorbath et al. (2013)	64 (mean age = 68.05)	Education dichotomised into lower (< 14 years) and higher (> 18 years)	Executive function (focus switching task, cost *r* = .19, accuracy *r* = .31)
Duff et al. (2013)	576 (mean age = 68.1)	Education in years	Screening measure (TICS, *r* = .21)
Elias et al. (1997)	1,002 aged 65-88 from the Framingham Heart Study	Education categorised as 5-8 years, 9-11 years, 12 years, and >12 years	Memory (logical memory and paired associates, *r* = .31), working memory (DS forward, *r* = .27), executive function (DS backward, *r* = .30), and visuospatial ability (reproduction, *r* = .28)
Ferreira et al. (2015)	3,515 aged 65+	Education categorised as none, primary school (to age 11), secondary school, (to age 16) further education: A levels (to age 18 years), technical/vocational, university degree, postgraduate or professional qualification	Memory (Paired Associate Learning, *r* = .02), working memory (DS forward and spatial search task, *r* = .07), and language (grammatical reasoning, *r* = .15)
Fillenbaum et al. (1988)	1,637 aged 60+	Education in years	Screening measure (MMSE, *r* = .45)
Fisk et al. (1995)	361 (mean age = 73.8) From Canadian Sample of Health and Aging (Nova Scotia sample)	Education in years	Screening measure (Halifax Mental Status Scale, *r* = .35)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Foubert-Samier et al. (2012)	331 (mean age = 76.1, SD = 3.9) from the Three Cities Cohort (3C)	Education level categorised as 5 levels from primary school without a diploma to university level	Verbal fluency (IST, *r* = .235)
Fournet et al. (2012)	445 aged 55-85	Education categorised as < 8 years, 8-12 years, and 13 years	Memory (recall of words, locations, and patterns, *r* = .282) and working memory (word and location span, *r* = .337)
Fritsch et al. (2007)	349 (mean age = 74.8, SD = 1)	Education in years	Screening measure (TICS-M, *r* = .23), memory (WMS-R Logical Memory test, *r* = .24) and executive function (timed months of the year backwards and verbal fluency, *r* = .17)
Ganguli et al. (2010)	1413 (mean = 77.6) from the Monongahela-Youghiogheny Healthy Aging Team (MYHAT) study	Education categorised as less than high school, high school graduate, and more than high school	Memory (WMS-R Logical Memory (immediate and delayed recall), WMS-R Visual Reproduction (immediate and delayed recall), and 3-trial FOME with Semantic Interference, *r* = .17), executive function (TMT-B, clock drawing, and phonemic verbal fluency, *r* = .12), language (BNT, verbal fluency categories, and Indiana State Token Test, *r* = .20), and visuospatial ability (*r* = .20)
Giogkaraki et al. (2013)	383 (mean age = 73.33)	Education in years	Memory (HVLT and WMS-R Logical Memory Story A immediate and delayed recall, *r* = .32), executive

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			function (TMT-B, SDMT, category fluency, phonemic fluency, *r* = .36-.56), and visuospatial ability (TMT-A, *r* = .35)
Giordano et al. (2012)	288 (mean age = 73.5)	Education in years	Screening measure (MMSE, *r* = -.01), memory (immediate and delayed prose memory and memory with interference at 10 and 30 seconds, *r* = .33), working memory (DS forward, *r* = .06), executive function (TMT-B and clock drawing, *r* = .21-.28), and visuospatial ability (copying overlapping figure and TMT-A, *r* = .24)
Glymour et al. (2005)	5,726 aged 70+ from the AHEAD study	Education categorised as <12 years, 12 years, or >12 years	General cognition (composite of TICS and delayed recall, *r* = .29)
Gonzalez et al. (2013)	8,833 (mean age = 73.9) from the Health and Retirement Study (HRS)	Education in years	Screening measure (abbreviated TICS, *r* = .44)
Hashimoto et al. (2006)	155 aged 70 +	Education categorised as 6 years, 8 years and >/= 10 years	Executive function (TMT-B, *r* = .23) and visuospatial ability (TMT-A, *r* = .25)
Hassing et al. (1998)	80 aged 90+	Education in years	Screening measure (MMSE, *r* = .32) and memory (word and object recall immediate and delayed, *r* = .21)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Hill, Whalin et al. (1995)	253 (mean age = 84.1, SD = 5.06)	Education in years	Memory (recall, *r* = .25)
Ho & Chan (2005)	204 (mean age = 68.33, SD = 7.41)	Education in years	General cognition (Chinese version of the Mattis Dementia Rating Scale, *r* = .52)
Inouye et al. (1993)	1,182 aged 70-79 from the MacArthur Foundation Research Network on Successful Aging	Education categorised as 0-7 years, 8-12 years, and >12 years	Memory (delayed recall and recognition, *r* = .11), executive function (abstraction, *r* = .55), language (naming, *r* = .34, and visuospatial ability (copying, *r* = .36)
Inzelberg et al. (2007)	260 (mean age = 72.4)	Education categorised as 0-4 years, 5-8 years, and >8 years	Screening measure (MMSE, *r* = .56)
Jefferson et al. (2011)	951 participants aged 54-100	Education scored from 0 (no formal education) to 30 (multiple advanced degrees)	Memory (WMS-R Logical Memory Story A, East Boston Story, word list learning, BNT and verbal fluency, *r* = .15), working memory (WMS-R Digit Span, Digit Ordering, r = .14), executive function (SDMT, number comparison, Stroop Color-Word, r = .08), visuospatial ability which was included in overall cognition only (line orientation and RPM, *r* = .27), and global cognition (z-score average from all domains, *r* = .19)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Kaplan et al. (2009)	95 participants (aged 75-90)	Education in years	Memory (RBANS List Recall, List Learning, and Semantic Fluency, r = .21), executive function (CalCAP sequential RT, RBANS Coding, and Stroop Color-Word, r = .29), and visuospatial skills (RBANS Figure Copy, Line Orientation, Trail Making Test B, Picture Naming, *r* = .31)
Kempler et al. (1998)	317 aged 54 -99	Education dichotomised as 0-8 years and 9+ years	Executive function (Category fluency, *r* = .20)
Kesse-Guyot et al. (2013)	3083 participants (mean age = 65.4, SD = 4.6) from the Supplementation with Vitamins and Mineral Antioxidants (SU.VI.MAX) study	Education categorised as primary, secondary, or university	Global cognition(word recall, verbal fluency, forward and backward digit span, and alternate trail-making test scores were converted into T scores and combined, *r* = .37)
Kilander et al. (1997)	504 men aged 69-74 from Uppsala Health Survey	Education categorised as low (elementary school/6-7 years), medium (secondary school), and high (university studies)	General cognition (mean z score of 13 tests to assess audio–verbal and visuospatial short term memory, learning and retention, processing speed and set-shifting capacity, *r* = .40)
Kim et al. (2011)	3157 (mean age = 72.3) from the Korean	Education in years	Screening measure (Korean MMSE, *r* = .48)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

	Longitudinal Study of Aging (KLoSA)		
Lang et al. (2008)	2,397 aged 70+ from English Longitudinal Study of Ageing (ELSA)	Education categorised as age at which left school (</=14, 15, 16, 17,18, >/=19)	General cognition (mean z score of 6 tests assessing orientation, immediate and delayed memory, prospective memory, verbal fluency, and attention and processing speed, *r* = .27)
Le Carrett et al. (2003)	1,022 (mean age =72.97) from Personnes Agées Quid study (PAQUID)	Education categorised as 0-5 years, 6-9 years, 10-12 years, and 12+ years	Screening measure (MMSE, *r* = .10)
Lee, Lee, & Yang (2012)	50 aged 60+	Education dichotomised as low (mean = 8.52 years) and high (mean = 13.32 years)	Memory (recall and recognition, *r* = .53)and executive function (DS backward, *r* = .17)
Leggett et al. (2013)	489 (mean age = 69)	Education categorised as none, primary school, lower secondary school, upper secondary or vocational, college or higher	Screening measure (MMSE, *r* = .39)
Leung et al. (2010)	512 (mean age = 74.5, SD = 7.1)	Education in years	Screening measure (Chinese MMSE and ADAS-Cog, *r* = .44 and .45), memory (word learning and delayed recall, *r* = .34), working memory (DS forward, *r* = .26,

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			and executive function (DS backward and category fluency, *r* = .23-.47)
Li et al. (2013)	52 aged 60+	Education dichotomised into low (mean = 9.71 years) and high (mean = 15.79 years)	Working memory (DS forward, *r* = .30) and executive function (DSST, Stroop, Plus-Minus Shifting Task, and information updating (memory paradigm), *r* = .34)
Lin et al. (2007)	58 aged 60+	Education in years	Executive function (HSCT Part A, Monotone Counting Test, word fluency, category score and perseveration errors in a modified WCST, Stroop interference, HSCT Part B, raw score, profile score, and number of rule-breaks in a modified version of the Six Elements Test (SET), *r* = .50)
Linderberger & Baltes (1997)	516 (mean age = 84.9, SD = 8.7) from the Berlin Aging Study (BASE)	Education in years	General cognition (perceptual speed (Digit Letter, DSST, and Identical Pictured); reasoning (Figural Analogies, Letter Series, and Practical Problems); memory (Activity Recall, Memory for Text, and Paired Associates); knowledge (Practical Knowledge, Spot-a-Word, and Vocabulary); and verbal fluency (Animals and Letter S), *r* = .39)
Luszcz (1992)	119 (mean age = 71.6)	Education in years	Screening measure (MMSE, *r* = .34), memory (prose recall immediate and delayed, symbol recall, *r* = .21), executive function (DSST completion time and correct

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			at 90 seconds, *r* = .29, and general cognition (RPM, *r* = .14)
Mangione et al. (1993)	472 aged 65+	Education categorised as <8th grade, some high school, high school graduate, some college, college graduate, some postgraduate, and postgraduate degree.	Screening measure (TICS, *r* = .58)
Mathuranath et al. (2007)	488 (mean age = 68.5)	Education categorised as no formal education, 1-4 years, 5-8 years, 9-12 years, and > 12 years	Screening measure (Malayalam ACE and MMSE, *r* = .35)
Matioli et al. (2008)	83 (mean age of 71.4)	Education categorised as 1-4 years, 5-8 years, and > 8 years	Screening measure (MMSE, *r* = .26), memory (delayed recall, *r* = .07), and executive function (clock drawing and animal fluency, *r* = .27-.41)
Maurer (2011)	3,069 aged 60+ from SABE	Education in years	Screening measure (MMSE, *r* = .19 - .50)
McCarty et al. (1982)	172 aged 63-97 from Duke longitudinal study of aging	Education in years	Memory (logical memory immediate and delayed and Associate Learning, *r* = .45) and visuospatial ability (copying, *r* = .50)
Mejia et al. (1998)	60 (mean age = 69.66)	Education in years	Memory (WMS Associative Learning and Logical Memory and AMSET, *r* = .15) and executive function

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			(WCST and phonemic and semantic verbal fluency, *r* = .11-.15)
Milan et al. (2004)	226 (mean age = 70.1)	Education categorised as none, 1-5 years, 6-10 years, >10 years	Screening measure (MMSE, *r* = .47)
Mitrushina et al. (1989)	156 (mean = 70.7 years)	Education in years	Language (Vocabulary scaled score from WAIS, *r* = .29)
Morgan et al. (2007)	162 (mean age = 73.7)	Education in years	Screening measure (MMSE, *r* = .24), memory (Rey AVLT, Hopkins VLT-R, RBMT I short story recall, *r* = .24), executive function (DSST, finding A's, identical pictures, *r* = .24).
Mousavi-Nasab et al. (2014)	794 (mean age = 74.12, SD = 7.1) form baseline of the Betula project	Education in years	Memory (recall and recognition, *r* = .29)
Mueller et al. (2013)	44 (mean age = 75.3)	Education in years	Memory (CVLT, *r* = .35) and executive function (TMT-B and D-KEFS 20 Question Subtest, *r* = .17)
Mulgrew et al. (1999)	1360 aged 60+ from San Luis Valley Health and Aging Study	Education in years	Screening measure (MMSE, *r* = .18)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Mungas et al. (2005) (Al Hazzouri et al. (2011) included for general cognition for the same dataset)	497 (mean age = 70.9, SD = 7.5) from SALSA and Woodland	Education in years	Memory (word list and spatial configuration learning, *r* = .34), working memory (verbal attention span, *r* = .53), executive function (conceptual thinking, *r* = .59), language (object naming, picture association, comprehension, and verbal expression, *r* = .65), and visuospatial ability (pattern recognition and spatial localization, *r* = .50)
Murayama et al. (2013)	118 (mean age = 69)	Education in years	Memory (verbal and visual immediate and delayed recall, *r* = .19)
Murphy & O'Leary (2009)	99 aged 60-83	Education dichotomised into lower (less than 12 yrs.) and higher (greater than 12 yrs.)	Memory (Immediate and delayed recall of the CERAD, *r* = .16 - .27)
Murden et al. (1991)	94 of 358 included aged 70-99	Education dichotomised into high (9^{th} grade or higher) and low (8^{th} grade or lower)	Screening measure (MMSE, *r* = -.15-.43)
O'Connor et al. (1989)	1,822 aged 75+ from Cambridge 75+ study	Education dichotomised into low (left school before 15) and high (left school at 15 or older)	Screening measure (MMSE, *r* = .06)
O'Shea et al. (2014)	3,484 (mean age = 76.07, SD = 6.4) from Washington	Education in years	Memory (SRT and BVRT, *r* = .31), executive function (Similarities from WAIS-R, nonverbal reasoning,

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

	Heights/Hamilton Heights Inwood Columbia Aging Project (WHICAP)		verbal fluency (COWAT), and category fluency, *r* = .40), language (BNT, repetition, and auditory comprehension, *r* = .57), and visuospatial ability (Rosen Drawing Test and multiple choice matching of figures from the BVRT, *r* = .50)
Parisi et al. (2009)	189 (mean age = 72.9, SD = 8.2)	Education in years	Working memory (letter-number sequencing, *r* = .14), executive function (Letter and Pattern Comparison, Finding As, Identical Pictures, Letter Sets, Figure Classification, Everyday Problem Solving, Substitutes Uses, Ornamentation, and Opposites Test, Alternate Uses, Word Associations, and FAS, *r* = .21), and general cognition (composite of tests, *r* = .21)
Paula et al. (2013)	60 (mean age = 74.08, SD = 6.51)	Education in years	Executive function (verbal fluency, *r* = .51)
Pedersen et al. (1996)	580 (mean = 66.3, SD = 7.6) from the Swedish Adoption/Twin Study of Aging (STATSA)	Education categorised as elementary school, secondary school, junior college, and university	Screening measure (MMSE, *r* = .16-.21) and general cognition (Synonyms, Figure Logic, Block Design, and Figure Identification, *r* = .30-.41
Petersen et al. (1992)	161 with mean age = 79.8 (SD = 7.6)	Education in years	Memory (SRT and Rey AVLT immediate and delayed recall and WMS-R, *r* = .188) and executive function (DS backward, *r* = .03)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Plassman et al. (1995)	930 (mean age = 66.63)	Education in years	Screening measure (TICS-M, *r* = .41)
Plumet et al. (2005)	49 aged 60-69, 44 aged 70+	Education dichotomised into 7-11 years and =/>12 years	Executive function (Card Sorting Task and semantic verbal fluency, *r* = .22 - .37)
Portin et al. (1995)	389 aged 62	Education dichotomised into primary schooling or (up to 6 years) less and more than primary schooling	Memory (object memory and Paired Word Associates, *r* = .06-.07), working memory (DS forward, *r* = .29), executive function (Digit Symbol, Block Design, Similarities, and months backward, *r* = .30-.36), and visuospatial ability (TMT-A, *r* = .15-.32)
Puccioni & Vallesi (2012a)	17 (mean age = 73)	Education in years	Executive function (Stroop, *r* = .33)
Puccioni &Vallesi 2 (2012b)	23 (mean age = 71)	Education in years	Executive function (Stroop, *r* = .63)
Rexroth et al. (2014)	2,782 (mean = 73.6, SD = 5.9) from baseline of the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study	Education categorised as <12 years, 12 years, 13-15 years, and >15 years	Memory (RVLT, HVLT, and RBMT short story recall, *r* = .10) and executive function (Letter Sets, Letter Series Sets, Word Series Test, and Useful Field of View Tasks 2-4, *r* = .07)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Ritchie et al. (2013)	1628 aged 70 and 80 from the Lothian 1921 and 1936 Birth Cohorts	Education in years	Executive function (processing speed, *r* = .11 - .17)
Scherr et al. (1988)	3,564 – 3603 (varies by analysis) aged 65+ from the East Boston Study	Education categorised as some elementary, some high school, and some college	Memory (short story immediate recall, *r* = .06) and executive function (DS backward, *r* = .07)
Schmand et al. (1997)	4,051 (mean age = 75.4, SD = 5.7) from the Amsterdam Study of the Elderly (AMSTEL)	Education dichotomised into low (incomplete primary – general intermediate education) and high (intermediate vocational to university education)	Screening measure (MMSE, *r* = .20)
Senanarong et al. (2001)	3,177 aged 60+	Education in years	Screening measure (Thai MMSE, *r* = .47)
Smits et al. (1995)	115 aged 55-89	Education in years	Memory (Twelve Words Test immediate and delayed recall and Everyday Memory Test, *r* = .25), executive function (Coding Task, *r* = .39), and general cognition (RPM, *r* = .36)
Then et al. (2014b)	422 (mean age = 71) from Leipzig Research Centre for Civilization Diseases	Education categorised as high (third level), medium (secondary), and low (primary)	Screening measure (MMSE, *r* = .08)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Unverzagt et al. (1996)	83 (mean age = 74.6, SD = 7.1)	Education in years	Screening measure (MMSE, *r* = .65), memory (word list learning, delayed recall, and recognition, *r* = .53), executive function (Constructional Praxis and category fluency, *r* = .47-.63) , and language (BNT, *r* = .65)
Van der Linden et al. (1997)	48 aged 60 - 80	Education dichotomised as low (maximum 12 years) and high (minimum 12 years)	Memory (free and cued recall, *r* = .51-.59)
van Exel et al. (2001)	446 aged 85+ from the Leiden 85-plus Study	Education dichotomised as low (primary or <6 years) and high (more than primary or >6 years)	Memory (word list immediate and delayed, r = 0) and executive function (Stroop, r = .30)
van Hooren et al. (2007)	576 aged 65-81 from the Maastricht Aging Study (MAAS)	Education categorised as low (elementary and lower vocational), medium (intermediate secondary or vocational), high (higher secondary, vocational, university, and scientific)	Memory (VVLT, *r* = .08) and executive function (Stroop, Concept Shifting Task, and verbal fluency, *r* = .19-.20)
Vaughan et al. (2014)	393 (mean age = 81.21, SD = 4.26) from the Women's Health Initiative Study	Education in years	General cognition (combination of TICS, category verbal fluency, TMT-B, and DS Backward, *r* =.16)
Welsh-Bohmer et al. (2009)	507 age 66+ from the Cache study	Education in years	Memory (word list learning and delayed, WMS Logical Memory and BVRT immediate and delayed, *r*

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			= .09), executive function (TMT-B, category fluency, Constructional Praxis, COWAT, and SDMT, *r* = .18-.29), language (BNT, *r* = .09), and visuospatial ability (TMT-A, *r* = .09)
Wiederholt et al. (1993)	1,692 aged 55-94 from the Rancho Bernardo study	Education dichotomised into less than college or college	Screening measure (MMSE, *r* = .34), memory (Bushke SRT and visual reproduction immediate and delayed, *r* = .22), executive function (TMT-B and category fluency, *r* = .26), visuospatial ability (copying, *r* = .21), and general cognition (2 items from the Blessed Information-Memory-Concentration Test, *r* = .36)
Yao et al. (2009)	1,000 (mean = 71.34 years, SD = 7.10) from Changsha City Study	Education in years	Screening measure (MMSE, *r* = .17)
Zahodne et al. (2011)	1,014 participants aged 54-95 (mean age = 68.8, SD = 6.8)	Education in years	Memory (sentence construction and span test, and immediate recall of 2 word lists and 2 short stories, *r* = .24 - .31), executive function (lexical decision and sentence verification, r = .15 and verbal fluency - 3 written tests from the Kit of Factor Referenced Cognitive Tests – controlled associates, opposites and figures of speech, *r* = .41). All standardised to z scores

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Zahodne et al. (2014)	487 (mean age = 69.6, SD = 8.8) from the National Institute of Health (NIH) Toolbox norming study	Education in years	Memory (Picture Sequence Memory, *r* = .11), working memory (List Sorting, *r* = .33), and executive function (Flanker Inhibitory Control, Dimensional Change Card Sort and speed of Pattern Comparison, *r* = .38)
Zhou et al. (2014)	172 (mean age = 67.17 – 67.66)	Education dichotomised as lower (<6 years) and higher (7-12 years)	Screening measure (MoCA and MMSE, *r* = .51)
Zimmerman et al. (2012)	549 (mean age =79.7, SD = 5.0) from the Einstein Aging Study (EAS)	Education dichotomised as lower (=/>12 years) and higher (=/>13 years)	Memory (SRT, *r* = .04), working memory (DS forward, *r* = .07), executive function (TMT-B, DS backward, and phonemic and category fluency, *r* = .15-.20), and visuospatial ability (TMT-A, *r* = .04)
Occupational Complexity			
Alvarado et al. (2002)	557 aged 65-89 from the Aging in Leganes Study	Main occupation categorised into nine categories from farm workers to white-collar workers	General cognition (time orientation, space orientation, personal information, naming test, immediate and delayed recall (6 objects), and logical memory (short story recall), *r* = .27)
Andel et al. (2015)	810 (mean age = 83) from the Swedish Level of Living Survey and Swedish Panel	Complexity of work with data and people in main occupation as classified by 1970 US census.	Screening measure (MMSE, *r* = .26-.33)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

	Study of Living Condition of the Oldest Old (SWEOLD)		
Correa-Ribeiro et al. (2013)	624 aged 65+	Complexity of work with data and people in main occupation as classified by 1970 US census.	Screening measure (MMSE, *r* = .08)
Finkel et al. (2009)	565 (mean age = 64.3)	Complexity of work with data and people in main occupation as classified by 1970 US census	Memory (DS, Picture Memory, and Names & Faces, *r* = .19-.25), executive function (Symbol Digit and Figure Identification, *r* = .19), and visuospatial ability (Figure Logic, Block Design, and Card Rotation, *r* = .28-.32)
Forstmeier & Maercker (2008)	147 aged 60-94	Main Occupation as classified by O*Net to indicate motivational and cognitive abilities	Global cognition score (comprised of memory (WAIS-III DS Forward and Backward), verbal fluency (animal naming), and executive function (Stroop Color-Word Test and WAIS-III Digit-Symbol Substitution Test), r = .13 - .20)
Foubert-Samier et al. (2012)	331 (mean age = 76.1, SD = 3.9)	Main occupation level as classified into 10 levels according to the International Classification of Occupations (1988)	Verbal fluency (IST of verbal semantic fluency, *r* = .30)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Frisoni et al. (1993)	524 aged over 70	Main occupation classified into 6 categories from white collar workers to housewives	Screening measure (MMSE, *r* = .49)
Fritsch et al. (2007)	349 (mean age = 74.8, SD = 1)	Main occupation mental demands assessed using the US department of Labour's Dictionary of Occupations (DOT)	Screening measure (TICS-M, *r* = .04), memory (WMS-R Logical Memory test, *r* = .09), and executive function (timed months of the year backwards and verbal fluency (animal naming), *r* = .10-.11)
Gow, Avlund & Mortensen (2012)	425 at age 60 from Glostrup 1914 Cohort	Intellectual challenge of current or last held occupation assessed at age 60 based on questionnaire responses.	General cognition (comprising Digit Symbol, Block Design, DS, and Picture Completion from the WAIS, *r* = .33)
Kesse-Guyot et al. (2013)	3083 (mean age = 65.4, SD = 4.6) from the Supplementation with Vitamins and Mineral Antioxidants (SU.VI.MAX) study	Main occupation categorised as homemaker, manual worker, or blue- or white-collar worker	Global cognition(word recall, verbal fluency, forward and backward digit span, and alternate trail-making test scores were converted into T scores and combined, *r* = .33)
Le Carrett et al. (2003)	1,022 (mean age =72.97) from Personnes Agées Quid study (PAQUID)	Main occupation categorised into seven categories from farm/domestic workers to intellectual professions	Screening measure (MMSE, *r* = .06), memory (BVRT and Paired Associates, *r* = .05-.08), executive function (Similarities, DSST, and verbal fluency (IST), *r* = 0-.06)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Leung et al. (2010)	512 (mean age = 74.5, SD = 7.1)	Main Occupation categorised into five categories from unskilled labourer to professional/company director	Screening measure (Chinese MMSE and ADAS-Cog, *r* = .19-.26 and), memory (word learning and delayed recall, *r* = .14), working memory (DS forward, *r* = .11), and executive function (DS backward and category fluency, *r* = .08-.23)
Linderberger & Baltes (1997)	516 (mean age = 84.9, SD = 8.7) from Berlin Aging Study (BASE)	Occupational prestige of last job held based on German occupational prestige rating	General cognition (perceptual speed (Digit Letter, DSST, and Identical Pictured); reasoning (Figural Analogies, Letter Series, and Practical Problems); memory (Activity Recall, Memory for Text, and Paired Associates); knowledge (Practical Knowledge, Spot-a-Word, and Vocabulary); and verbal fluency (Animals and Letter S), *r* = .41)
Mangione et al. (1993)	472 aged 65+	Main occupation categorised as service, skilled, and farm workers to management or professionals	Screening measure (TICS, *r* = .39)
Potter et al. (2006)	3,880 (mean age = 65.83, SD = 2.74) from Duke Twins Study of Aging	Main occupation characterised using factor analysis of DOT work characteristics to assess complexity, their factor of general intellect which included positive loading for complexity with data	Screening measure (TICS-M, *r* = .31)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

		and people, reasoning, language, mathematics aptitude, and greater time spent	
Scherr et al. (1988)	3,564 – 3603 varies by analysis (aged 65+) from East Boston Study	Main occupation rated according to Duncan's socioeconomic index score	Memory (short story immediate recall, *r* = .06-.08) and executive function (DS backward, *r* = .06)
Smart et al. (2014)	1,066 (mean age = 69.6, SD = 0.8) from 1936 Lothian Birth Cohort	Complexity of work with data and people in main occupation as classified by 1970 US census	Memory (WMS-III – Logical Memory (immediate and delayed), Spatial Span (forward and backward), and Verbal Paired Associated (immediate and delayed recall), *r* = .22-.28), executive function (Symbol Search, Digit Symbol, inspection time, and simple and choice reaction time, *r* = .25-.27), and general cognition (WAIS-III – Letter-Number Sequencing, Matrix Reasoning, Block Design, Digit Symbol, DS Backward, & Symbol Search, *r* = .32-.36)
Staff et al. (2004)	99 aged 79	Occupation (highest obtained) as classified by the UK's Office of Population Statistics (1990)	Memory (AVLT, r = .15) and general cognition (RPM, r = .28)
Then et al. (2014b)	1,468 aged 60 -79 from the Leipzig Research Centre for Civilization Diseases	Occupational mental demands before retirement classed as high, medium or low determined using	Screening measure (MMSE, *r* = .21), executive function (TMT-B, verbal fluency, r = .14-.15)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

		O*NET descriptor variables of "Cognitive Activities" at work	
Cognitively-stimulating leisure activities			
Andel et al. (2015)	810 (mean age = 83) from the Swedish Level of Living Survey and Swedish Panel Study of Living Condition of the Oldest Old (SWEOLD)	Cognitive activities in mid-life (e.g. how often they read books or went to the theatre)	Screening measure (MMSE, r = .28)
Arbuckle et al. (1986)	285 (median age = 71.6)	Current cognitive activity (rated for degree of intellectual effort by 10 graduate students)	Memory (index comprising free recall (of 9 words), forward digit span, and correct factual and inferential answers (10 multiple choice Qs. based on short story), r = .49)
Ashley (2008)	63 (mean age = 77.3)	Current cognitive activity assessed by Activity Questionnaire (Hultsch et al., 1999)	Executive function (choice reaction time, r = .25) and general cognition (word recall, letter series, and DSST, r = .28)
Barnes et al. (2006)	108 (mean age = 72.6)	Participation in cognitively demanding activities at age 6 (3 items), age 12 (6 items), 18 (6 items), age 40 (5 items) and	General cognition (includes MMSE, memory (East Boston Story), perceptual speed (SDMT) and working memory (DS Backward), r = .21)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

		currently (5 items) from daily to once a year or less.	
Brand (2003) Dissertation	94 (mean age = 72.17)	Current cognitive activity - Frequency of crossword puzzles, reading frequency, and amount read. Assessed with a mental exercise survey	Memory (CVLT, *r* = .04-.32)
Brewster et al. (2014)	333 aged 60+ from UC Davis Aging Diversity Cohort	Current cognitive activity and at age 40 assessed by the Life Experiences and Activities Form (LEAF)	Memory (word list learning, *r* = .05-.14) and executive function (category and phonemic fluency, DS backward, visual-span backward, and list sorting, *r* = .05-.15)
Eskes et al. (2010)	42 (mean age = 65.1) All female	Current cognitive activity questionnaire calculated total no of activities (diversity) and total time spent in activities (duration)	Memory (Bushke SRT, Medical Complex of Georgia Complex Figures Test, *r* = -.02 - .39), executive function (DSMT and D-KEFS Color-Word Interference Test, Auditory Consonant Trigrams Test, D-KEFS Card Sorting Test, and verbal fluency, *r* = 0 - .46), language (D-KEFS verbal fluency C-Score and WASI vocabulary, *r* = -.01 - .49), visuospatial ability (WASI Matrix Reasoning and Benton Line Orientation, *r* = .05 - .30), , and global

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

			cognition score which comprised all tests (r = .01 - .49).
Ferreira et al. (2015)	3,515 aged 65+	Current cognitive activity – participation in four different activities (e.g. crosswords)	Memory (paired associate learning, r = .05-.11), working memory (DS forward and spatial search task, r = .01-.15), and language (grammatical reasoning, r = .03-.11)
Foubert-Samier et al. (2012)	331 (mean age = 76.1, SD = 3.9)	A self-administered questionnaire to assess participation in leisure activities in mid-life and currently. The measure comprised 30 activities, 17 of which related to cognitively stimulating activities. Only the analyses of these 17 are included here.	Verbal fluency (IST, r = .40)
Fritsch et al. (2007)	349 (mean age = 74.8, SD = 1)	Participation in mental, physical and social activities in high school. Only mental activities included.	Screening measure (TICS-M, r = .18), memory (WMS-R Logical Memory test, r = .13), and executive function (timed months of the year backwards and animal verbal fluency, r = .11-.27)
Gallucci et al. (2009)	668 aged 70+ from the Treviso Longeva Study	Current reading activity (none vs reading newspapers or novels)	Screening measure (MMSE, r = .46)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Gilhooly et al. (2007)	145 (mean = 78.19)	Cognitive activities in the last year, e.g. reading, playing chess or cards	Executive function (DSST, *r* = .26)
Gow, Avlund, & Mortensen (2014)	576 aged 75 from Glostrup 1914 Cohort	Current cognitive activity in 17 activities (e.g. going to theatre, travel, adult education)	Executive function (Digit Symbol and DS backward, *r* = .16-.28)
Gow, Corley et al. (2012)	778 (mean age = 69.5) from the 1936 Lothian Birth Cohort	Current cognitive activity – questionnaire combined both social and leisure (e.g. reading and visits to friends/family)	Memory (Logical Memory immediate and delayed recall, Spatial Span, Verbal Paired Associates immediate and delayed recall, *r* = .21) and executive function (Symbol Search, Digit Symbol, choice reaction time, inspection time, simple reaction time, *r* = .19)
Hill, Whalin et al. (1995)	253 aged 75-96 (mean age = 84.1, SD = 5.06)	Current cognitive activity – frequency of activities (e.g. attending concerts and adult education classes	Memory (immediate, organised, and cued recall, *r* = .21-.33)
Ho & Chan (2005)	204 (mean age = 68.33, SD = 7.41)	Current cognitive activity measured on a 9 point scale from never to everyday (e.g. reading, attending classes)	General cognition (Chinese version of the Mattis Dementia Rating Scale, *r* =.59)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Hultsch et al. (1993)	484 (mean age = 69.2) from Victoria Longitudinal Study	Current cognitive activity with 16 items pertaining to integrative information processing, 25 to novel information processing, and 4 regarding physical activity	Memory (immediate word list and prose recall, *r* = .18-.26), working memory (word span, *r* = .14), executive function (semantic processing speed and verbal fluency, *r* = .22-.27), and language (naming, *r* = .21)
Jefferson et al. (2011)	951 aged 54-100	Cognitive activity - early-, mid-, and late-life cognitive activities were measured using the CAS, a structured questionnaire assessing the frequency of participation in specific cognitive activities (Wilson et al. 2007).	Memory (WMS-R Logical Memory Story A, East Boston Story, word list learning, BNT and verbal fluency, *r* = ..08-.17) working memory (WMS-R Digit Span, Digit Ordering, r = .08-.17), executive function (SDMT, number comparison, Stroop Color-Word, r = .14-.38), visuospatial ability which was included in overall cognition only (line orientation and RPM, *r* = .08-.17), and global cognition (z-score average from all domains, *r* = .11-.27)
Lin et al. (2012)	342 aged 60-84 from MINDUS	Current cognitive activity – frequency of participation in activities (e.g. reading, playing games)	Memory (word list immediate and delayed, *r* = .13) and executive function (DS backward, category fluency, Number Series, and Backward Counting, *r* = .35)
Mueller et al. (2013)	44 (mean age = 75.3)	Current cognitive activity assessed as frequent activity (FA), higher cognitive load activity	Memory (CVLT, *r* = .28-.37) and executive function (D-KEFS 20 Question Subtest, *r* = .22-.31)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

		(HC), and activity maintenance (AM, decrease during the past year)	
Murphy & O'Leary (2009)	99 aged 60-83	Current cognitive activity as measured by the number of hours spent in activities daily.	Memory (immediate and delayed recall from the CERAD, *r* = .01 - .10)
Newson & Kemps (2005)	755 (Mean age at time 1 = 77.4) from the Australian Longitudinal Study of Aging (ALSA)	Current cognitive activity as measured by the Adelaide Activities Profile	Memory (incidental recall, *r* = .24), executive function (WAIS-R DSST and verbal fluency, *r* = .24-.28), and language (picture naming, *r* = .22),
Parisi et al. (2009)	189 (mean age = 72.9, SD = 8.2)	Current cognitive activity assessed as literacy, competitive leisure, travel, and mathematical/ accounting activities	Working memory (Letter-Number Sequencing, *r* = .07-.25), executive function (Letter and Pattern Comparison, Finding As, Identical Pictures, Letter Sets, Figure Classification, Everyday Problem Solving, Substitutes Uses, Ornamentation, and Opposites Test, Alternate Uses, Word Associations, and FAS, *r* = -.09-.33), visuospatial ability (Card Rotation and Hidden Patterns, *r* = -.01-.37), and general cognition (combines tests, *r* = -.11-.33)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Parslow et al. (2006)	2,522 aged 60-64 from the Personality and Total Health (PATH) Through Life study	Cognitive activity undertaken in past 6 months assessed by RIASEC activity questionnaire	Executive function (SDMT, *r* = .19-.26)
Saczynski et al. (2008)	1,787 (mean age = 75.7) from the Age, Gene/Environment Susceptibility Study (AGES-Reykjavik)	Current cognitive activity assessed by participation in 10 activities (e.g. playing games, attending a performance)	Memory (CVLT, *r* = .25) and executive function (DS backward, Cantab Spatial Working Memory Test, and Stroop – Word-Color Interference, *r* = .28-.42)
Sheres (2002) Thesis	77 (mean = 77.8, SD = 4.7)	Current cognitive activity – frequency of activity (e.g. reading, playing bridge or chess)	General cognition (Block Design and Matrix Reasoning from WASI, *r* = .26)
Smits et al. (1995)	115 aged 55-89	Current cognitive activity – frequency of socio-cultural activities (e.g. visiting a museum)	Memory (Twelve Words Test immediate and delayed recall and Everyday Memory Test, *r* = .21-.39), executive function (Coding Task, *r* = .50), and general cognition (RPM, *r* = .44)
Vaughan et al. (2014)	393 (mean age = 81.21, SD = 4.26) from the Women's Health Initiative Study	Cognitive activities over the prior 12 months measured using the CAS, a structured questionnaire assessing the frequency of participation in specific cognitive activities (Wilson et al. 1999).	General cognition (combination of TICS, category verbal fluency, TMT-B, and DS Backward, *r* = .30)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Vemuri et al. (2014)	1,995 (mean age = 78.9) from the Mayo Clinic Study of Aging (MCSA)	Mid- and late life cognitive activity (participation in 10 items)	General cognition (average of z-transformation from 4 domains – executive function (TMT-B, DSST, category fluency), language (BNT), memory (WMS_R Logical Memory-II, Visual Reproduction-II, and AVLT – all delayed recall), *r* = .22)
Wilson et al. (1999)	6,162 participants (mean age = 75, SD = 7.2) from baseline of Chicago Health and Aging Project (CHAP)	Current cognitive activity – frequency of participation in 7 areas, e.g. listening to radio, reading, or playing games, rated for cognitive intensity involved.	Memory (immediate and delayed recall of orally presented story), executive function (SDMT) and global cognition (summary measure using z scores from each of the 4 tests, *r* = .04 - .54)
Wirth et al. (2014)	92 aged 60-90 from the Berkley Aging Cohort (BAC)	Participation in cognitively demanding activities at age 6 (3 items), age 12 (6 items), 18 (6 items), age 40 (5 items) and currently (5 items) from daily to once a year or less	Global cognition (comprises episodic memory – CVLT, Logical Memory recall of story A and B, and Visual Reproduction delayed recall and recognition, and executive function – Stroop Test, COWAT, TMT-B, and Digit Symbol Coding Test, *r* = ..09-.21)
Combined Measures			
Gonzales (2013)	90 participants (mean age = 75.98, SD = 7.05)	Lifetime of Experiences Questionnaire (Valenzuela & Sachdev, 2007)	Screening measure (MMSE, *r* = .19)

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Opdebeeck et al. (2014)	236 (mean age = 70.86, SD = 7.66)	Lifetime of Experiences Questionnaire	Screening measure (MoCA, *r* = .32), memory (RBMT short story recall immediate and delayed, *r* = .33-.36), and executive function (verbal fluency (FAS), *r* = .38)
Puccioni & Vallesi (2012a)	17 (mean age = 73)	Cognitive Reserve Index questionnaire (CRIq)	Executive function (Stroop, *r* = .42)
Puccioni &Vallesi 2 (2012b)	23 (mean age = 71)	Cognitive Reserve Index questionnaire (CRIq)	Executive function (Stroop, *r* = .45)
Then et al. (2014b)	1,438 aged 60 -79 from the Leipzig Research Centre for Civilization Diseases	Education/occupation combined	Screening measure (MMSE, r = .27) and executive function (TMT-B, verbal fluency, r = .21-.23)
Vemuri et al. (2014)	1,995 (mean age = 78.9) from Mayo Clinic Study of Aging (MCSA)	Education/occupation combined	General cognition (average of z-transformation from 4 domains – executive function (TMT-B, DSST, category fluency), language (BNT), memory (WMS-R Logical Memory-II, Visual Reproduction-II, and AVLT – all delayed recall), *r* = .38)

Note: MMSE, Mini Mental State Exam; RPM, Raven's Progressive Matrices; DS, digit span; BNT, Boston Naming Test; CVLT, California Verbal Learning Test; DSST, digit symbol substitution test; TMT, Trail Making Test; SDMT, symbol digit modalities test; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SRT, Selective Reminding Test; SLMT, symbol letter modalities test; FOME, Fuld Object Memory Evaluation; COWAT, Controlled Oral Word Association Test; TICS-M, Telephone Inventory for Cognitive Status - Modified; IST, Isaac's Set Test of verbal fluency; WMS-R, Wechsler Memory Scale - Revised; HVLT, Hopkin's Verbal Learning Test; CalCAP, California Computerised Assessment Battery; ADAS-Cog, Alzheimer's Disease Assessment Scale cognitive subtest; HSCT, Hayling Sentence Completion Test; WCST, Wisconsin Card

Appendix I. Meta-analysis (Chapter 2) supplementary table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Sorting Task; ACE, Addenbrooke's Cognitive Examination; AMSET, Associative Memory with Semantic Enhancement; VVLT, visual verbal learning test; AVLT, auditory verbal learning test; VLT-R, Verbal Learning Test- Revised; RBMT, Rivermead Behavioural Memory Test; CERAD, Consortium to Establish a Registry for Alzheimer's disease Neuropsychological Battery; D-KEFS, Delis-Kaplan Executive Function System; WASI, Wechsler Abbreviated Scale of Intelligence; BVRT, Benton Visual Retention Test

Depressive Cognitions Scale

Please tell me the response that best describes your current opinion or feelings according to the following scale:

Totally disagree	Mostly disagree	Slightly disagree	Slightly agree	Mostly agree	Totally agree
0	1	2	3	4	5

I think my life is pretty full	0	1	2	3	4	5
I can do many things well	0	1	2	3	4	5
I am hopeful about my future	0	1	2	3	4	5
I have many people in my life	0	1	2	3	4	5
I believe that life is worth is living	0	1	2	3	4	5
I am in control of my life	0	1	2	3	4	5
I feel useful and needed	0	1	2	3	4	5
I am a worthwhile human being	0	1	2	3	4	5

Geriatric Depression Scale

Below are a set of questions asking about how you have felt over the past week. Please circle the answer that most represents you. Circle yes if you have felt this way and no if you have not felt this way in the past week.

Are you basically satisfied with your life?	Yes	No
Have you dropped many of your activities and interests?	Yes	No
Do you feel that your life is empty?	Yes	No
Do you often get bored?	Yes	No
Are you in good spirits most of the time?	Yes	No
Are you afraid that something bad is going to happen to	Yes	No
Do you feel happy most of the time?	Yes	No
Do you often feel helpless?	Yes	No
Do you prefer to stay at home, rather than going out and doing ne things?	Yes	No
Do you feel you have more problems with memory than	Yes	No
Do you think it is wonderful to be alive now?	Yes	No
Do you feel pretty worthless the way you are now?	Yes	No
Do you feel full of energy?	Yes	No
Do you feel that your situation is hopeless?	Yes	No
Do you think that most people are better off than you are?	Yes	No

Lifetime of Experiences Questionnaire

Please answer these questions as accurately as possible – choose the option which most closely fits with your experience.

1. Please circle how old you were when started and left school/college/university, if a gap was taken please circle age when continuous education was finished.

4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25

If you went back to education later in life, for how many years?

1 2 3 4 5 6 7 8 9 10

2. How many years of secondary school (i.e. high school) did you complete?

3. What was the highest level of qualification achieved (e.g. O-Level, GCSE, A level Degree etc)?

4. Did you continue with any type of training or study after leaving school?

   Yes No

   If yes, please fill in the table below. If no, go to question 5.

   Please specify what type(s) of training or study you attempted and for how long you were enrolled. Some categories are given below. If your experience is not covered by this list, please fill in the details under 'other'.

Ages (from – to) e.g. 30-54	Course type	Course name	No. of yrs enrolled	F/T or P/T?	Scoring	Score
	Clerical training				4 points	
	Business course				4 points	
	Trade apprenticeship				8 points (if 4 yrs)	
	Other technical course				6 points	
	College diploma				8 points (3 or 4 years)	

Ages (from – to) e.g. 30-54	Course type	Course name	No. of yrs enrolled	F/T or P/T?	Scoring	Score
	University undergraduate				10 points	
	University Masters				8 points	
	University PhD/Doctorate				10 points	
	Other graduate course				4 points (per yr of study)	
	Any other course?				(2 points)	
					Total Score	

5. Please provide a timeline or history of the jobs or occupations that you have been involved in **since the age of 30**. Please indicate the main job or occupation which you were involved with and which of your jobs or occupations required that you were in charge of, directing, or responsible for other people?

Age from/to	Job title	Job description	No of people in charge of	Score
30 -34				
35-39				
40-44				

45-49				
50-54				
55-59				
60-65				
65+				
			Total Score 30-65	

LEQ – Young Adulthood
The following questions apply to the time in your life **between 13 and 30 years of age**.

Never	Less than monthly	Monthly	Every two weeks	Weekly	Daily
0	**1**	**2**	**3**	**4**	**5**

7	How often were you seeing a member of your family or a friend during this time?	0	1	2	3	4	5
8	How often were you practicing or playing a musical instrument?	0	1	2	3	4	5
9	How often would you practice or develop an artistic pastime (e.g. drawing, painting, writing, acting, singing)?	0	1	2	3	4	5
10	How often did you do any kind of physical exercise?	0	1	2	3	4	5
11	How often did you read (material of any sort) for more than five minutes?	0	1	2	3	4	5
12	How often did you practice speaking a second/third language?	0	1	2	3	4	5

LEQ 7-12 Score =

13. Did you travel to any of the following continents between the ages of 13 and 30?

Europe	Latin/Central America
North America	Asia/subcontinent/Australia
Middle East	Other
Africa	**Scoring: 0-5**

Early Life Travel Total = **Score =**

Early Life Non-Specific Total Score =

13. Between the **ages of 13 and 30** did you have any other pastime, hobby or special interest?

_____
_____
_____
_____

Total number of hobbies =

LEQ – Mid life

We are now moving on to experience during your middle age years. This refers to the time **after you were 30 years of age until 65 years old or retirement.**

Never	Less than monthly	Monthly	Every two weeks	Weekly	Daily
0	**1**	**2**	**3**	**4**	**5**

15	How often were you seeing a member of your family or a friend during this time?	0	1	2	3	4	5
16	How often were you practicing or playing a musical instrument?	0	1	2	3	4	5
17	How often would you practice or develop an artistic pastime (e.g. drawing, painting, writing, acting, singing)?	0	1	2	3	4	5
18	How often did you do any kind of physical exercise?	0	1	2	3	4	5
19	How often did you read (material of any sort) for more than five minutes?	0	1	2	3	4	5
20	How often did you practice speaking a second/third language?	0	1	2	3	4	5

LEQ 15-20 Total =

21. Did you travel to any of the following continents between the ages of 30 and 65?

Europe	Latin/Central America
North America	Asia/subcontinent/Australia
Middle East	Other
Africa	**Scoring: 0-5**

Mid Life Travel Total = **Score =**

Mid Life Non-Specific Total =

22. Between the **ages of 30 and 65** did you have any other pastime, hobby, or special interest?

_____
_____
_____
_____

LEQ – Retirement

You will now be asked questions about the present phase of your life, beginning from **when you were retired OR from around 65 years of age** (whichever came first).

23. At what age did you retire (please indicate if not applicable)?
(Check that this matches employment history)

24. Do you currently reside:

Alone with a partner with a friend with family

How many people live with you: _____

25. Are you currently a member of any social clubs or groups?
Yes No

If YES, please indicate how many: [ ]

Scoring: 0-5
Total= Score=

26. Do you do any charity or volunteer work?
Yes No

If YES, please indicate nature of the activity.
And how many? [ ]

Total= Score=

27. How often might you make an outing to see a family member, friend or group of friends?

Never	Less than monthly	Monthly	Every 2 weeks	Weekly	Daily
0	1	2	3	4	5

28. What types of events or entertainment have you undertaken in the past 2 months?
Please enter how many times you have attended each one:

Films/cinema		Dancing	
Plays/drama		Visiting friends	
Pub		Sporting event	
Concert/recital		Other: specify:	

Scoring: 0-5
Total= Score

29. How would you spend a typical day?
Please circle or underline any of the following activities *if you undertake them on a typical day*:

Sleep/Nothing	Reading
Housework	Voluntary work
TV	Paid work
Radio	Strategic games (e.g. chess, bridge, cards)
Listening to music	Helping friends/family
Walking	Pet care
Gardening	Artistry
Crosswords/Sudoku	Prayer/religious activity
Socialising	Playing music
Writing	Learning something new
Studying	Hobby/pastime
Intellectual/professional	Other, please specify

Total activities =
Scoring: Please circle

0-4 = 1	**8-9 = 3**	**12-14 = 5**	**17-18 = 7**	**21-22 = 9**
5-7 = 2	**10-11 = 4**	**15-16 = 6**	**19-20 = 8**	**23+ = 10**

30. How do you acquire information about world and national events? Circle as many as are relevant to you:

Don't seek information	Newspapers
Friends	Magazine
TV	Internet
Radio	Other, please specify:
	Scoring: 0-5

Total= **Score=**

31. What kind of material do you read on a regular basis? Circle as many as are appropriate.

Just what is needed to get by
Newspaper articles
Magazine articles
Fiction
Journals/monographs
Non-fiction books
All of above
Other, please specify:

Scoring: 0-5

Total= Score=

Retirement Specific Total =

The following questions apply to the time in your life **since retirement or after the age of 65**.

Never	Less than monthly	Monthly	Every two weeks	Weekly	Daily
0	**1**	**2**	**3**	**4**	**5**

32	How often were you seeing a member of your family or a friend during this time?	0	1	2	3	4	5
33	How often were you practicing or playing a musical instrument?	0	1	2	3	4	5
34	How often would you practice or develop an artistic pastime (e.g. drawing, painting, writing, acting, singing)?	0	1	2	3	4	5
35	How often did you do any kind of physical exercise?	0	1	2	3	4	5
36	How often did you read (material of any sort) for more than five minutes?	0	1	2	3	4	5
37	How often did you practice speaking a second/third language?	0	1	2	3	4	5

LEQ 32-37 Total =

38. Did you travel to any of the following continents since retiring or the age of 65?

Europe
North America
Middle East
Africa
Latin/Central America
Asia/subcontinent/Australia
Other

Scoring: 0-5

Travel Total= Score=

Retirement Non-Specific Score =

38. Since **retiring OR the age of 65** (whichever came first), have you had any other pastime, hobby or special interest?

    _____
    _____
    _____
    _____

    Total number of hobbies =

Ruminative Response Scale

People think and do many different things when they feel sad, blue or depressed. Please read each of the items below and indicate how often you behave in the way described below when you feel down, sad or depressed. Please indicate what you generally do, not what you think you should do.

Almost never	Sometimes	Often	Almost always
1	2	3	4

	Almost never			Almost always
I think what am I doing to deserve this	1	2	3	4
I analyse recent events to try to understand why I am depressed	1	2	3	4
I think why do I always react like this	1	2	3	4
I go away by myself and think about why I feel like this	1	2	3	4
I write down what I am thinking and analyse it	1	2	3	4
I think about a recent situation, wishing it had gone better	1	2	3	4
I think why do I have problems other people don't have	1	2	3	4
I think why can’t I handle things better	1	2	3	4
I analyse my personality to try and understand why I am depressed	1	2	3	4
I go someplace alone to think about my feelings	1	2	3	4

Cognitive Lifestyle Score (CLS) Questions

Question numbers correspond to full CFAS questionnaire

Education

Q40 How many years did you spend in full time education

Occupation

Q45 What has been your main occupation for most of your working life?

Q46 What type of work was/is this?

Q47 Were/are you self employed?

Q48 Were/are you a foreman, supervisor or manager? (If Yes, what did you do?)

Q49 Foreman/supervisor/Manager: What did/do you do?

Q50 How many employees were/are you responsible for?

These questions were used by the CFAS team to create the social class and social grouping scores which were then used to create the finer detailed occupation score

Cognitive activities

How often do you take part in the following activities

Q69 Listening to the Radio
a. Once a year or less
b. Several times a year
c. Several times a month
d. Several times a week
e. Every day or almost every day

Q70 Read a newspaper
a. Once a year or less
b. Several times a year
c. Several times a month
d. Several times a week
e. Every day or almost every day

Q71 Read a magazine
a. Once a year or less
b. Several times a year
c. Several times a month

d. Several times a week
e. Every day or almost every day

Q72 Read a book
a. Once a year or less
b. Several times a year
c. Several times a month
d. Several times a week
e. Every day or almost every day

Q73 Playing games such as cards, chess
a. Once a year or less
b. Several times a year
c. Several times a month
d. Several times a week
e. Every day or almost every day

Q74 Crosswords
a. Once a year or less
b. Several times a year
c. Several times a month
d. Several times a week
e. Every day or almost every day

Q75 Puzzles
a. Once a year or less
b. Several times a year
c. Several times a month
d. Several times a week
e. Every day or almost every day

Social activities

Q63 How often do you see any of your (children or other) relatives to speak to?
0. Never
1. Daily
2. 2-3 times a week
3. At least weekly
4. At least monthly
5. Less often
8. No answer
9. Not asked

Q67 Do you attend meetings of any community, church/mosque or social groups, such as over 60's clubs, evening classes or anything like that?

0. No

1. Yes, occasionally
2. Yes, regularly
8. No answer
9. Not asked

Q77 How often do you see any of your neighbours to have a chat or do something with?

0. No neighbours/Never
1. Daily
2. 2-3 times a week
3. At least weekly
4. At least monthly
5. Less often
8. No answer
9. Not asked

Appendix O. Additional correlations from Chapter 5

Additional correlations from Chapter 5 between cognitive reserve and mood for the whole sample (N = 236)

	Cognitive reserve (LEQ)	Depressive symptoms	Anxiety	Rumination
Cognitive reserve (LEQ)	--	-.251**	-.187**	-.015
Depressive symptoms		--	.482**	.328**
Anxiety			--	.411**
Rumination				--

** indicates significant at $p < .01$
Note: LEQ, Lifetime of Experiences Questionnaire