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The Relationship Between Mild Cognitive Impairment and Mood in Older People

Jennifer Ann Yates

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Summary

Mild cognitive impairment (MCI) has received increasing attention since the early 1990s. However, considerable controversy exists over exactly how the concept of MCI is defined and measured, and the implications of assigning or receiving a diagnosis of MCI. There is evidence of a link between MCI and mood, but empirical work remains conflicted and inconclusive. The first chapter provides an overview of the MCI concept and highlights some of the issues surrounding its definition. Chapter 2 provides a detailed description of the methodology and background to the empirical work presented in Chapters 4-6. A systematic review of the literature forms the third chapter of this thesis and establishes the need for further study into the relationship between MCI and mood.

Chapter 4 makes use of data from the first Cognitive Function and Ageing Study (MRC-CFAS I) to investigate the role of subjective memory complaints (SMC) in the relationship between MCI and mood over a two year period. The results indicated that SMC may be related more strongly to mood than to objective cognitive performance, which raises questions about whether SMC should be included as a criterion in the MCI definition. Chapter 5 clarifies these findings using data from a contemporary cohort in the Cognitive Function and Ageing Study Wales (CFAS Wales).

Chapter 6 investigates the role of health in the relationship between MCI and mood, again using data from CFAS Wales. The findings suggest that health problems constitute a risk factor for developing depression and anxiety, which may in turn affect cognitive functioning. This presents a useful opportunity for intervention to improve the quality of life for older people by improving their physical health, or improving the management of long-term conditions.

Social networks were investigated as an influential factor in the relationship between MCI and mood, using data from CFAS Wales. Whilst increases in social network size were

associated with fewer mood problems and increased cognitive functioning, they did not moderate the relationship between the two. However, this finding still showed that having more social contacts is beneficial and important to the quality of life of older people.

The last chapter presents a discussion of the findings in relation to each of the research questions outlined in Chapter 1. The chapter also includes a commentary on the methodological considerations that were faced when developing this thesis, the implications of the findings and directions for future research.

Chapter 1: Introduction

Introduction

Mild cognitive impairment (MCI) in older people is an area that has garnered great interest and research, particularly in the last 25 years, as researchers seek to understand where normal ageing ends and pathological ageing begins. Early clinical diagnosis of cognitive decline and dementia has received considerable attention in order to identify signs that may serve as reliable predictors for disease development (Petersen et al., 2014), so that prevention strategies and interventions could be planned and utilised.

However, the concept of MCI is not simple and there is controversy over the exact definition, how to operationalize criteria and the possible outcomes of receiving a classification of MCI. An issue of importance is the relationship between MCI and mood, as people with mood problems are frequently excluded from research into MCI and cognitive decline, yet both mood and cognitive problems are frequent among older people. This thesis aims to highlight the need for research into this association and explore it in the context of other related factors.

The population in the UK is ageing, shown by increases in the number and proportion of older people in the population and an increase in the average age of the population (Office for National Statistics, 2012). There are currently 10.8 million people aged over 65 years in the UK, a figure that will rise by almost 50% in the next 20 years to over 16 million. The number of people aged over 85 years currently stands at over 1.4 million and this is expected to double in the next 20 years. Current life expectancy at birth is 82.9 years for women and 79.1 years for men (Age UK, 2013). Approximately 65% of the Department for Work and Pensions benefit expenditure goes to those over working age, which accounts for approximately one seventh of public expenditure in the UK (Cracknall, 2013).

There are many changes that people experience as they age, and one of these is changes to cognitive functioning. Changes to cognitive functioning are experienced by many older people and in some cases may progress to dementia. Dementia affects approximately 800,000 people in the UK with one in three people over 65 years likely to develop it (Alzheimer's Society, 2013). Dementia is a major cause of disability in the older population and is estimated to cost the UK approximately £23 billion per year (Age UK, 2013; Alzheimer's Society, 2013). The prevalence of dementia for England in 2011 was estimated to be at 6.5% of the population (Age UK, 2013; Matthews et al., 2013). Older people may also experience changes to their health through the development of chronic diseases or conditions that may become more serious through the ageing process (Brayne, Matthews, McGee, & Jagger, 2001). Changes in health status can result in functional limitations (Stuck et al., 1999), and thus impact on older peoples' quality of life and ability to live independently. Older people also face changes to their social environments, through reduction in social network size or social engagement opportunities (Wenger, 1997), which may again impact on quality of life.

Research into ageing is important given the increasing proportion of older people in the population, and the area of cognitive health is especially important as evidence shows that one of the major risk factors for cognitive decline is age (Tilvis et al., 2010). It is necessary to understand whether other factors exist that may have an effect on cognitive decline as people age, and how such relationships operate, in order to maximise quality of life for people in their later years and plan social policy accordingly. Research in this area can benefit older people who experience cognitive decline themselves, and also their families and friends who may act as informal carers and may experience a decrease in quality of life themselves (Schulz & Martire, 2004). There may also be wider benefits to society through such research, as understanding factors associated with cognitive decline may allow for more timely

diagnoses and interventions that may save health care and service providers money and increase efficiency in these areas.

Currently, research into ageing and associated factors is increasing but there are still many gaps in our knowledge. One area in need of further understanding is the transition between normal ageing and pathological ageing, and is a particular area for controversy as currently this element of cognitive change is difficult to define and measure. There have been many terms used to describe this stage of cognitive decline, beginning with Kral's (1962) definition of benign senescent forgetfulness which distinguished between abnormal memory loss in older people relative to age-matched controls. Other terms that have been used include age-associated memory impairment (National Institute of Mental Health, 1986), age-associated cognitive decline (International Psychogeriatric Association) and cognitive impairment no dementia (Canadian Study of Health and Aging). Mild cognitive impairment (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999) is a term that has become widely accepted to describe cognitive decline beyond that of normal ageing, but still disagreement exists as to the exact definition and criteria, and its relationship with other factors important to the ageing process.

How can mild cognitive impairment be defined?

Mild cognitive impairment (MCI) is a concept developed to describe a transitional state that may exist between normal ageing and pathological ageing, and may represent the beginning of cognitive decline. Individuals classed as having MCI were found to be more likely to progress to dementia, at a rate of 10-15% per year, compared to individuals with normal cognitive function, who convert at a rate of 1-2% per year (Petersen, 2001). There is variation in the progression rates, as shown by a recent meta-analysis, which found that overall 6.7% of people with MCI progressed to any kind of dementia per year. However, this

rose to 10% per annum when stricter criteria for MCI were considered (Mitchell & Shiri-Feshki, 2009). Typical criteria for MCI include the presence of a subjective memory complaint, an objective memory complaint, intact general cognitive function, intact activities of daily living and the absence of a dementia diagnosis.

Currently, several versions of criteria used to define MCI have been published, and differ in the extent to which they endorse each criterion listed above (Stephan, Brayne, McKeith, Bond, & Matthews, 2008). In one study, sixteen different versions of the criteria were retrospectively applied to a large sample of community dwelling older people and resulted in the same individuals being concurrently classed as having MCI according to certain definitions and healthy according to other definitions, highlighting the need for agreement on which definition to use (Matthews, Stephan, McKeith, Bond, & Brayne, 2008). Current definitions include the requirement for subjective cognitive complaints corroborated by objective deficits in cognitive performance, preserved functional independence and an absence of dementia (Petersen et al., 2014). The studies in this thesis have used this definition unless otherwise stated.

Prevalence and types of MCI

The prevalence of MCI ranges from 0.1% to 42% depending on the definition used (Stephan, Matthews, McKeith, Bond, & Brayne, 2007), although it is likely that the prevalence is 3% (Fisk, Merry, & Rockwood, 2003) when applying commonly used criteria. There are two main subtypes of MCI: single-domain and multiple-domain MCI, which can further be divided into amnestic and non-amnestic variants. A classification of single-domain MCI is made when only one aspect of cognitive functioning is impaired and this could involve memory, to fulfil criteria for the amnestic variant, or another cognitive process such as language, to fulfil criteria for non-amnestic MCI. A classification of multiple-domain MCI

is made when more than one aspect of cognitive functioning is impaired. Again, this can involve memory or non-memory domains.

Impact of MCI on society

It is difficult to estimate the financial burden of MCI on society due to the variability in prevalence and progression rates. However, attendance at General Practitioner surgeries and memory clinics does carry a financial cost, and whilst older people classified as having MCI may still retain considerable functional independence, some social care help may be required (Perneczky, Pohl, Sorg, Hatmann, et al., 2006). In addition to formal social care, informal care provided by spouses, adult children or other relatives is likely to be highly utilised by people with MCI, as people with MCI are more likely to live in the community and in their own homes than in residential care. Information is not available to estimate financial costs saved by informal carers but it is likely to be considerable.

The increased risk of progression to dementia for people classified as having MCI may represent a future problem for health and social services, as this group of people are potentially more likely than cognitively normal older people to make use of health and social services in the future. Currently the NHS spends over £1.2 billion, and social services spend approximately £9 billion each year on dementia care.

The health and well-being of relatives and friends of people with MCI is also likely to be affected, as it can be difficult to adapt to increasing needs or cognitive changes. People who provide informal care to those with MCI may be at increased risk of physical and mental illness themselves (Jones & Peters, 1992). It is estimated that 10% and 62% of carers for people with dementia and a comorbid mood disorder meet criteria for major and minor

depression respectively (Schulz & Martire, 2004). Due to the higher likelihood of progression to dementia from MCI (Petersen et al., 1999), this has important implications for those caring for people with MCI, and interventions to provide assistance to people with MCI may in turn benefit people who care for them.

Controversy surrounding MCI as a concept

If MCI were considered as a prodromal form of dementia, as is sometimes suggested, it would be expected that all people classed as having MCI would progress to dementia in the future. However, the progression of cognitive decline in people classed as having MCI is unstable, as some people may remain categorised as having MCI and some will revert to normal cognitive function. In one study, over the course of three years, 12% of participants improved to a normal level of cognitive function and 53% remained classed as having MCI (Wahlund, Pihlstrand, & Jonhagen, 2003). Further research has shown that after 2.7 years, 19.5% of participants had improved to a level of normal cognitive function and 61% of participants continued to meet criteria for MCI but did not progress to dementia (Wolf et al., 1998). Research has suggested that 25% of people with MCI will not progress to having Alzheimer's disease, even ten years after the onset of memory problems (Chertkow, 2002). This suggests that whilst a classification of MCI may pose a risk factor for progression to dementia, further cognitive decline is not inevitable and other lifestyle or health factors may be important.

A measure of objective cognitive performance is required to ascertain whether impairment in a cognitive domain exists, which is necessary for applying most versions of the MCI criteria. This can be problematic because a one-off assessment of an individual only captures a snapshot of performance at one particular time, which may not be able to detect change or decline in cognitive function and may be affected by intra-individual variability.

Furthermore, the use of specific tests or cut-off points to measure objective cognitive performance when making a classification of MCI has not been agreed upon, and consequently a range of different measures exist (Dubois & Albert, 2004; Werner & Korczyn, 2008). Criteria such as performance less than one standard deviation below the mean are likely to include individuals whose life-long scores were at this level and have not changed at all. This may affect the identification of MCI, which would have implications for both research studies and in clinical settings.

A variety of changes in the brain are associated with the development of MCI, including vascular problems, Alzheimer's pathology and brain atrophy, leading to a heterogeneous list of potential causes which may prevent specific diagnostic criteria being developed (Dubois & Albert, 2004). Post mortem studies of individuals classified as having MCI showed pathology similar to vascular disease or Alzheimer's disease, or mixed pathology, while some showed no pathology (Stephan, Matthews, Hunter, Savva, & Bond, 2012), suggesting that MCI may not be a prodromal form of Alzheimer's disease as if it were it would be expected that all cases would display Alzheimer's pathology. Furthermore, a significant proportion of people classified as having MCI improve over time (Mitchell & Shiri-Feshki, 2009), which casts further doubt on the relationship between brain changes and the MCI concept.

As described earlier, the MCI definition encompasses several subtypes. The relationship between the subtypes is unclear, with research suggesting that the multiple domain subtype represents a more severe form of single domain MCI (Brambati et al., 2009) and potentially a further step on the continuum between single domain MCI and dementia. On the other hand, the subtypes of MCI may not be related and may potentially reflect different aetiologies or different outcomes. Klekociuk and Summers (2014) theorise that

multiple-domain amnestic MCI is readily differentiated from other subtypes of MCI and is likely to represent a discreet clinical diagnostic entity.

Many definitions of MCI require the individual to have a subjective memory complaint but controversy exists as to the usefulness of this criterion. Previous research recommends that the subjective memory complaint should not be a diagnostic criterion because it lacks accuracy (Lenehan, Klekociuk, & Summers, 2012) and may be affected by the presence of mood problems. Depression is positively associated with subjective memory complaints (Minett, Da Silva, Ortiz, & Bertolucci, 2008) and may inflate perceptions of memory problems by enhancing negative attributions (Roberts, Clare, & Woods, 2009). Increases in anxiety were associated with an increase in subjective memory complaints in one study, despite a lack of objective cognitive decline (Dux et al., 2008), suggesting that subjective memory complaints may be more strongly related to mood than objective cognitive performance (Minett et al., 2008). Including subjective memory complaints as a criterion in the MCI definition was not found to increase predictive ability (Baars, van Boxtel, Dijkstra, Visser, & van den Akker, 2009), suggesting that this may be unnecessary and may contribute both false positives and false negatives when classifying individuals with MCI (Lenehan et al., 2012).

Most MCI definitions specify that individuals classified as having MCI should have intact activities of daily living. This is sometimes viewed as the main criterion that separates the MCI concept and the diagnosis of dementia (Bruscoli & Lovestone, 2004). However, some researchers have suggested that specific domains of instrumental activities of daily living (IADLs) may be impaired in MCI (Winblad et al., 2004). Impairments in IADLs may be linked to progression to dementia, suggesting that the MCI population may be at risk of losing functional independence, particularly in activities that are cognitively demanding (Reppermund et al., 2011). However, it is difficult to distinguish whether functional

impairment is due solely to cognitive decline in a population where physical and medical comorbidities are common, and currently a standardised tool to distinguish between such causes is not available.

The concept of MCI requires further investigation in order to allow researchers and clinicians to create a set of diagnostically useful criteria that could identify people at risk of progression to further cognitive decline and dementia. Criteria should take into consideration the close relationship between MCI and mood, and factors that may moderate or mediate this relationship, including health problems, subjective memory complaints and social networks.

Defining and measuring mood

Psychological problems in later life can include depression and anxiety at symptom and disorder levels. Sub-clinical symptoms of anxiety and depression are common in older people and may cause significant disruption to daily living (Vink, Aartsen, & Schoevers, 2008) although they can be difficult to detect (Kvaal, McDougall, Brayne, Matthews, & Dewey, 2008). There is evidence for frequent occurrence of less severe depressive disorders and clinically relevant depressive symptoms (Buchtemann, Luppa, Bramesfeld, & Riedel-Heller, 2012) suggesting that depression in older people is a major public health problem that may often go unrecognised (Nordhus, 2008).

The criteria for depression can vary depending on the measurement tool used, but typically involve depressed or irritable mood, loss of interest or pleasure, changes in appetite or weight, disturbed sleep, fatigue or loss of energy, feelings of worthlessness, suicidal feelings or attempts, and problems with thinking or concentrating (Nordhus, 2008). Criteria for anxiety vary due to the existence of several subtypes such as generalised anxiety disorder, panic disorder, social phobia and post-traumatic stress disorder. The most common subtype is generalised anxiety disorder, and criteria for diagnosis typically include excessive anxiety

and worry about a number of events or activities for more than six months, worry that is difficult to control and the presence of at least three of the following: restlessness, fatigue, concentration difficulties, irritability, muscle tension and sleep disturbances (Nordhus, 2008).

There is debate regarding the nature of anxiety in older people as it is not clear if it is different from or the same as anxiety in younger adults, as older people may experience symptoms differently, such as increased somatic complaints (Bryant, Jackson, & Ames, 2008). The incidence of depression in older people appears to be similar to that of younger age groups (Buchtemann et al., 2012).

There is little consensus as to the prevalence rates of depression in older people with the European Collaborative on Depression (EURODEP) estimating that the combined prevalence for men and women is 12.3%. Other estimates of the prevalence of depression vary from 8.7% (F. A. McDougall et al., 2007) to 36% (Buchtemann et al., 2012). Prevalence rates also vary according to how depression is defined, with recent research finding that the prevalence of major depression is 2.8%, minor depression is 3.8% and depressive symptoms are thought to have a prevalence rate of 28.7% (Glaesmer, Riedel-Heller, Braehler, Spangenberg, & Luppa, 2011). The prevalence of depression is therefore increased when using broader definitions, with potentially over a quarter of older people experiencing mood problems. The wide variations in prevalence are also likely to be due to the variety of diagnostic tools used in assessing depression in older people (Kvaal et al., 2008).

Variation exists in the prevalence of anxiety in older people, again likely due to differences in how anxiety is defined and measured. Under-reporting could be considerable as current diagnostic criteria may not adequately capture anxiety in older people (Bryant et al., 2008). Up to 65% of older people presenting to medical settings may experience anxiety

whilst the prevalence in the community is thought to be between 2.4% and 15% (Bryant et al., 2008; Gale et al., 2011; Kvaal et al., 2008).

There are several measures used to assess symptoms of anxiety and depression in older people, which can be broadly divided into categorical and dimensional tools. Categorical tools consist of classification systems such as Diagnostic and Statistic Manual of Mental Disorders (DSM) criteria, International Classification of Diseases (ICD) criteria or the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) (Copeland, Dewey, & Griffiths-Jones, 1986) where the presence of symptoms fulfils a certain set of criteria and a diagnosis is made. Dimensional tools consist of symptom rating scales such as the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977), the Geriatric Depression Scale (GDS) (Yesavage et al., 1983) or the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Lushene, 1970) where a questionnaire or inventory is used to assess the presence and/or severity of symptoms (Buchtemann et al., 2012). Cut-off scores are used to determine the presence of clinically significant symptoms. Some measures, such as the GMS-AGECAT and the GDS, are designed specifically for use with an older population.

Several studies have attempted to ascertain factors that may pose a risk for the development or presence of depressive symptoms in later life. Recent systematic reviews have identified many risk factors including female gender, somatic illness, cognitive impairment, functional impairment, lack of social support, history of depression, increased age, lower household income, increased medical conditions, neuroticism and vascular factors (Gale et al., 2011; Glaesmer et al., 2011; F. A. McDougall et al., 2007; Vink et al., 2008). Rick factors for anxiety in older people have also been identified through systematic review, including lower social class (currently or in the past), cognitive decline, functional decline, increased disability, decline in physical health, increased neuroticism, vision or hearing loss,

high blood pressure, psychopathology and being childless (Gale et al., 2011; Vink et al., 2008).

Anxiety and depression frequently co-occur (Bryant et al., 2008; Byers, Yaffe, Covinsky, Friedman, & Bruce, 2010; Nordhus, 2008) at both the diagnostic and sub-threshold level (Kvaal et al., 2008) and research suggests that 66% of people categorised as having depression also have anxiety (Gale et al., 2011). There is evidence for a model whereby anxiety and depression share a common distress factor referred to as negative affect (Vink et al., 2008). It may be beneficial to conceptualise anxiety and depression together as common mental disorders (CMD) as pure anxiety or depression are relatively rare (Kvaal et al., 2008). Comorbidity is likely to result in greater severity and poorer treatment response than either disorder alone (Lenze, Mulsant, et al., 2001). Higher severity of both disorders was found to be associated with higher co-occurrence of the comorbid condition, which suggests that both anxiety and depression have common ground (Schoevers, Beekman, Deeg, Jonker, & van Tilburg, 2003).

Relationship between mood and cognition

Anxiety and depression are linked to cognitive functioning in older people and may pose a risk factor for the development of cognitive decline. MCI is frequent in depressed older people, especially those where depression has occurred later in life (Adler, Chwalek, & Jajcevic, 2004), and reports of low mood three years before MCI detection substantially increased the risk of the development of MCI (Caracciolo, Backman, Monastero, Winblad, & Fratiglioni, 2011). The presence of depressive symptoms was found to be associated with an almost 70% decrease in the odds of being cognitively normal five years after assessment (Spira, Rebok, Stone, Kramer, & Yaffe, 2011).

The relationship between cognitive functioning and mood may also work in the opposite direction whereby cognitive changes may increase the likelihood of experiencing symptoms of anxiety or depression. Anxiety was found to be the most common neuropsychiatric symptom experienced in a group of people classified as having MCI, with over half reporting symptoms (Gallagher et al., 2011). Depression was reported by 61% of participants in a further study and increased as cognitive function worsened (Van der Linde, Stephan, Matthews, Brayne, & Savva, 2010). Other research has also shown that symptoms of both depression and anxiety increased as memory performance decreased (G. J. McDougall, Becker, & Arheart, 2006).

Mood problems may also be related to the progression of cognitive decline. Research has shown that both the presence of symptoms of depression (Gabryelewicz et al., 2007) and the persistence of depressive symptoms (Houde, Bergman, Whitehead, & Chertkow, 2008) are related to increased risk of progression from MCI to dementia. However, a protective effect of depression on progression to dementia was also found (Vicini Chilovi et al., 2009). Anxiety may also increase risk of progression to dementia (Palmer et al., 2007), but has also been associated with a lower risk of progression to Alzheimer's disease (Gallagher et al., 2011). Consequently, findings regarding the association between mood and progression from MCI to dementia remain inconclusive and this highlights the need for further investigation.

Motivations to explore the relationship between MCI and mood

At present there are several gaps in our understanding surrounding cognitive decline, particularly in the area of MCI. The lack of a single, clear definition makes it difficult to work with and usefully apply to cognitive changes in older people. Investigating how the concept is related to mood may help to clarify aspects of it in order to make cognitive decline easier to distinguish and interventions easier to plan. Furthermore, whilst there is plenty of

research regarding depression in older people, research regarding anxiety is lacking, especially in relating anxiety to cognitive changes. Lastly, although there is a growing consensus that MCI and mood are related, it is not well understood how other factors contribute to and influence this relationship, and the present research will explore other aspects that affect older people in order to gain a more holistic picture of the association.

Factors that may influence the relationship between MCI and mood

The relationship between MCI and mood can be viewed through the lens of social cognitive theory, with particular focus on three areas of subjective memory complaints (SMC), health problems, and social networks. Social cognitive theory describes how individuals make sense of social situations and places an emphasis on the role of self-efficacy, or feelings of personal control (Conner & Norman, 2005). People with higher levels of self-efficacy are likely to feel more capable in enacting certain behaviours, such as undertaking exercise, and they may feel more positively about their ability to perform in social situations. High levels of self-efficacy may also influence how people appraise their abilities, such as their cognitive functioning and memory. Viewing the relationship between MCI and mood in the context of social cognitive theory is useful as the theory has links to both cognitive functioning and mood problems. A strong sense of self-efficacy and competence facilitates cognitive processes and performance, whilst self-efficacy is related to feelings of anxiety, depression and helplessness (Luszczynska & Schwarzer, 2005). People rely partly on somatic and emotional states when judging their sense of capability (Bandura, 1998), which suggests that feelings of depression or anxiety may negatively affect self-efficacy, and in turn cognitive processes.

The area of subjective memory complaints potentially overlaps with social cognitive theory and may involve similar cognitive processes. SMC are common in older people and

reflect processes of metacognition. Metacognition and meta-memory are concerned with people's knowledge about their own memory and cognitive processes (Zanardo, De Beni, & Moe, 2006). Self-reports of memory may provide insights into how people perceive their own cognitive functioning, but are often only weakly associated with objective cognitive test performance (Frerichs & Tuokko, 2006; Johansson, 2008). The self-reporting of cognitive problems or change may be associated with the ability to monitor and control cognitive activities, and the decrease in such reporting with age may indicate changes in the ability to monitor cognitive processes (Mecacci & Righi, 2006). However, subjective complaints may also uncover the impact of depression or negative affect on cognitive performance (Johansson, 2008) or the appraisal of cognitive performance (Dux et al., 2008). Stress reactions, such as experiencing anxiety, may be perceived as inefficacy, and so anxious people may regard their memory more negatively than those who do not experience feelings of anxiety, and feel less capable of remembering things. Positive mood enhances feelings of efficacy and therefore is likely to increase a sense of capability in remembering things (Bandura, 1998).

Social cognitive theory often features in theories of health behaviour and health promotion activities as social cognition is involved in the regulation of health-related behaviours through feelings of self-efficacy (Luszczynska & Schwarzer, 2005). People who report feelings of self-efficacy are more likely to engage in healthy behaviours such as taking part in exercise, or adhering to medication plans (Conner & Norman, 2005). Half of older people living in England and Wales reported very good or good health in the 2011 Census, with 35% of older adults reporting fair general health and the remaining 15% reporting bad or very bad general health (Office for National Statistics, 2013). Approximately 40% of people over 65 have a limiting longstanding illness (Age UK, 2013). Poor health was found to be linked to problems with mood (Williamson & Schulz, 1992b) and with cognitive decline due

to vascular issues (Elwood, Pickering, Bayer, & Gallacher, 2002). From a social cognitive perspective it could be considered that the feelings of self-efficacy required for adequate regulation of health behaviours may be disrupted by cognitive decline or mood problems. This may lead to health problems, increased use of health and social services, and poorer perceived health.

Social networks are the third area explored when looking at the relationship between MCI and mood, and may also be considered within the context of social cognitive theory. Creating and maintaining social networks requires feelings of self-efficacy (Bandura, 1998), which may be reduced by anxiety and depression, leading to smaller social networks. The 2011 census reports that 31% of people over 65 years live alone (Office for National Statistics, 2013) and 7% of older people report that they often or always feel lonely (Age UK, 2013). Older people's social networks may change with age (Wenger, 1997) due to lack of opportunities to be sociable or a desire to be more selective about social contacts (Carstensen, Fung, & Charles, 2003). Research suggests that greater levels of social interaction are related to better mental health outcomes (Seeman, Lusignolo, Albert, & Berkman, 2001) and decreased psychological distress (Wenger, 1997), and may prevent depression (Berkman, Glass, Brissette, & Seeman, 2000). A rich social network was shown to be protective against the development of dementia (Wang, Karp, Winblad, & Fratiglioni, 2002) and it is also thought that people with a high degree of loneliness are twice as likely to develop Alzheimer's disease as people who report a low degree of loneliness (Age UK, 2013).

Social cognitive theory can also link the three areas of SMC, health problems and social networks together and suggest how they may impact on one another. Health behaviours are often promoted and reinforced by members of our social networks (Bandura, 2004), suggesting that feeling capable of building and maintaining social networks in later life can enhance health through associating with other older people engaging in positive health

behaviours. Social relationships can also provide cognitive stimulation, and by maintaining a social network an older person may have increased opportunities to demonstrate mental capabilities. This may reinforce a positive view of metacognitive processes and decrease reporting of subjective memory complaints. Anxiety and depression can reduce feelings of capability, which can impact directly on subjective memory complaints, health and social networks, and indirectly on subjective memory complaints and health though social networks.

The aim of the thesis is to explore the relationship between MCI and mood by investigating subjective memory complaints, health problems and social networks. Data collected from a large, representative sample using standardised methodology will be used to examine the relationship between MCI and mood. The thesis includes a systematic review and meta-analysis in order to identify the existing literature and draw together estimates of the risk of development of MCI and the risk of progression from MCI to dementia in relation to mood. Assessment of the existing literature has identified gaps in current knowledge and areas for further investigation. In this thesis, I aim to discuss the relationship between MCI and mood in terms of the MCI concept and definition and its applicability in both clinical and community settings. This thesis will build on previous research by adding to the literature regarding anxiety and depression in older people, introduce a new perspective on how MCI may be defined and investigate how the factors of subjective memory complaints, health and social networks may be involved in the relationship between MCI and mood.

Research questions

The following research questions are addressed in this thesis:

1. Are MCI and mood problems related?
2. Do subjective memory complaints modify the relationship between MCI and anxiety or depression?
3. Is the relationship between MCI and anxiety or depression mediated by perceived health or health state?
4. What is the nature of the three-way relationship between MCI, mood and social networks?
5. What impact do the findings of this thesis have on the concept of MCI for the future?

Structure of thesis

The chapters of this thesis are based on journal articles that have already been published, submitted for publication, or will be published in the future. The chapters included in the thesis may include additional information to the articles, or have information omitted to reduce repetition. Chapters 5 to 7 present results from the same group of participants and there is some overlap of methodology.

Chapter 2 presents an overview of the methodology used in both the Medical Research Council Cognitive Function and Ageing Study (MRC-CFAS I) and the Cognitive Function and Ageing Study Wales (CFAS Wales).

Chapter 3 provides a systematic review and meta-analyses of the relationship between anxiety, depression and MCI, and the risks of both the development of MCI and the progression from MCI to dementia. The review includes 60 studies consisting of both cross-

sectional and longitudinal design and taking place in both clinical and community settings. The review highlights the increased risk of developing mood problems in people classified as having MCI and the increased risk of developing MCI in older people with anxiety or depression. The effect of mood problems on the progression to dementia was less clear and this was identified as an area for further research. This review was published in *Reviews in Clinical Gerontology* (Yates, Clare, & Woods, 2013).

Chapter 4 presents a follow-up study using data from MRC-CFAS I collected in the 1990s. The study looks at the role of subjective memory complaints within the MCI definition and the relationship with anxiety and depression. The findings indicate that subjective memory complaints, which are a requirement for a classification of MCI, may actually be related to mood problems rather than objective cognitive performance. This highlights the need for greater understanding of metacognitive processes in older people and suggests that many older people who do not report subjective memory complaints may not be accessing valuable assistance for cognitive or mood-related problems. This chapter was presented at an OPAN Symposium (Swansea University; February 2014).

Chapter 5 presents the first study based on data from CFAS Wales and looks at the role of subjective memory complaints in relation to mood problems using a cross-sectional design. This study builds on the previous chapter by using a current data set and again highlights the finding that subjective memory complaints are related to mood problems rather than objective cognitive performance, suggesting that a revision of the MCI criteria may be appropriate. This chapter was presented at the British Society of Gerontology 43rd Annual Conference (Southampton University; September 2014).

Chapter 6 is an empirical investigation into the relationship between MCI, mood and health using data from CFAS Wales. This investigation considers subjective ratings of health,

objective measures of health and other lifestyle factors such as health service use and level of physical activity, to give an overall picture of health in later life and how it is related to both mood problems and MCI. The findings of this chapter suggest that health problems have an impact on mood, which may in turn affect cognitive functioning, and provides evidence for the usefulness of interventions involving older people with physical health problems.

Chapter 7 explores the relationship between mood problems, MCI and social networks using data from CFAS Wales to investigate whether social networks moderate this relationship. Social networks were not found to moderate the relationship, but maintaining social networks appeared to have beneficial on both cognitive function and mood.

Chapter 8 concludes the thesis by summarising the previous work and drawing the findings together. The chapter discusses and evaluates the relationship between mood and MCI and considers how other factors complicate this relationship. The chapter highlights limitations and areas for future research, and presents recommendations for changes to the MCI concept based on the outcomes of the investigations presented in this thesis.

Dissemination of research

All findings of this thesis are being submitted for publication in peer-reviewed academic journals and findings will also be presented at conferences where relevant. To date, the following chapters have been published or presented:

- Chapter 3 is published in Reviews in Clinical Gerontology: Yates, J. A., Clare, L. & Woods, R. T. (2013). Mild cognitive impairment and mood: A systematic review. *Reviews in Clinical Gerontology,* 23, (4), 317-356. DOI: 10.1017/S0959259813000129.

Chapter 3 was presented as a poster at the British Society of Gerontology 42nd Annual Conference, Oxford, September 2013.

- Chapter 4 was presented as talk at an OPAN symposium, Swansea University, February 2014.
- Chapter 5 was presented as an oral presentation for the British Society of Gerontology 43rd Annual Conference, Southampton, September 2014.

Conclusion

Mild cognitive impairment poses an increased risk for the development of dementia and consequently it is important to understand what factors may influence the development of, or progression from, MCI. This thesis aims to develop a greater understanding of the relationship between MCI and mood, and address gaps in the current understanding of how this complex relationship may operate, through considering factors that may influence the relationship using a large community sample.

Chapter 2: Methodology

Summary

This chapter provides an overview of the history and background to the Medical Research Council Cognitive Function and Ageing Study I (MRC-CFAS I) and explains how the Cognitive Function and Ageing Study II (CFAS II) and the Cognitive Function and Ageing Study Wales (CFAS Wales) were developed from, and are related to it. The chapter includes detailed information regarding the design of the studies and data collection procedures, and provides a comprehensive overview of how the data were accessed, managed and prepared for analysis in order to answer the research questions outlined in Chapter 1 and further questions included in each of the empirical chapters (Chapters 4-7).

Introduction

This chapter presents an overview of the methodology employed in the empirical chapters of this thesis (Chapters 4-7). The studies in Chapters 4-7 draw upon data from the Medical Research Council Cognitive Function and Ageing Study I (MRC-CFAS I), the Cognitive Function and Ageing Study II (CFAS II) and the Cognitive Function and Ageing Study Wales (CFAS Wales), and background information about these studies, their development and their relationship to each other will be outlined. Included is a detailed description of the data collection procedure used in MRC-CFAS I, as data from this study were used in Chapter 4 to answer the research question of how subjective memory complaints (SMC) mediate the relationship between MCI and mood, and of the data collection procedure used in CFAS Wales, as data from this study were used in Chapters 5-7 to answer the research questions of how the relationship between MCI and mood is affected by SMC, health and social networks. Information about the topic areas covered in the interviews and the interview procedure for MRC-CFAS I, CFAS II and CFAS Wales is described in the following sections. An explanation of how data were accessed, managed and prepared for analysis, and how key variables were created, and a brief overview of the statistical techniques used in Chapters 4-7 is also included in this chapter.

The data used in Chapters 4-7 were collected as part of the Cognitive Function and Ageing studies (CFAS), a series of population-based investigations involving people over the age of 65 years and living in the community. The main aim of CFAS is to investigate dementia and cognitive decline, and over time the research themes have been broadened to also include depression, disability and healthy living, and health policy and health.

CFAS began with the Medical Research Council multicentre study of cognitive function and ageing (MRC-CFAS I) and was able to join up with an earlier, similar MRC

study in Liverpool, which had started in 1989 and used a slightly different design. MRC-CFAS I data were collected through the use of standardised interviews with older people and informants at several time points shown in Figure 2.1. Additionally, blood and saliva samples were collected, and participants were asked if they wished to donate their brains.

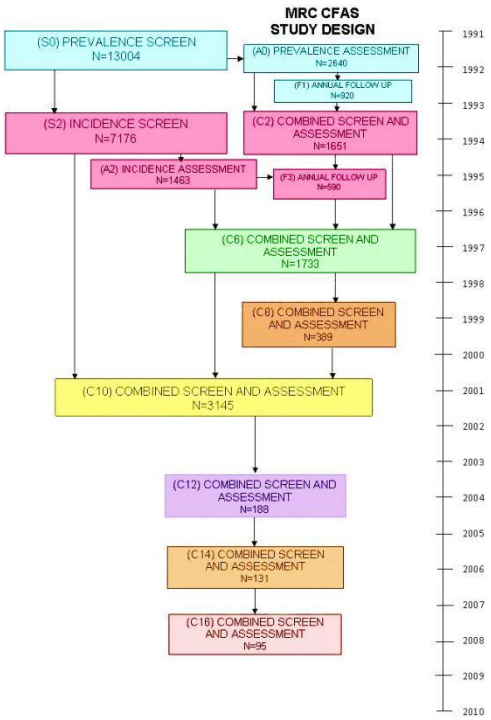

*Figure 2.1:*Design of MRC-CFAS I (http://www.cfas.ac.uk/pages/bcfasidi/index.html)

Over time, the data collected for CFAS can be used as a resource to answer questions regarding generational changes in dementia, cognition and life expectancy which led to the development of further phases of the initial study. CFAS II is considered to be the daughter study to MRC-CFAS I and began in three areas of England in 2008. CFAS II used a similar design to MRC-CFAS I differing in that the two-stage screen and assessment process was combined into a single stage.

CFAS Wales can be considered a sister project to CFAS II, taking place in two areas of Wales from 2011 and using the same design as CFAS II, while also including additional measures from a social perspective. As the Gwynedd area of CFAS Wales was previously

investigated during the MRC-CFAS I study, the impact of policy changes regarding older people, which have arisen due to devolution from England can be studied. The addition of a new urban area in South Wales allows for comparisons between urban and rural populations. The key research themes for CFAS Wales include resilience, protective effects of lifestyle factors, social networks, nutritional status and bilingualism. Detailed information about CFAS Wales and CFAS II can be found below.

I contributed to the CFAS Wales data collection by conducting 141 respondent interviews and 11 informant interviews in Gwynedd and Ynys Môn between February 2012 and September 2013 using the procedure outlined in this chapter.

The following two sections of this chapter describe the design, participants and procedure for the MRC-CFAS I study and the CFAS II/CFAS Wales studies in depth to provide a detailed overview of the origins of the data used in Chapters 4-7.

Medical Research Council Cognitive Function and Ageing Study (MRC-CFAS I)

Design

The MRC-CFAS I study is a multicentre population study primarily examining cognitive function in individuals aged over 65 years at two time points separated by two years. MRC-CFAS I used a two-stage procedure consisting of an initial screening interview mainly concerning cognitive functioning (Stage 1) and an assessment interview which provided a more complete psychiatric assessment (Stage 2). Approximately one month after the screening interview, a 20% subsample, which was biased towards cognitively frail individuals, completed the assessment interview and this subsample was followed up at least every two years for twelve years. Data were collected from six centres in Cambridge, Gwynedd, Liverpool, Newcastle, Nottingham and Oxford.

Participants

MRC-CFAS I aimed to achieve a total sample size of 2500 participants from each geographical area, except Liverpool where 6000 participants were recruited. Participants were aged 65 years or over and were chosen from Family Health Service Authority (FHSA) lists within the geographical area. General practitioners were asked to check the lists to resolve problems arising from inaccuracy or due to patients having died or moved away from the study area. The sample was stratified into two age groups of 65-74 years and 75+ years.

Geographical areas

The study covered both urban and rural areas. The rural areas consisted of Cambridgeshire, comprising Ely and its surrounding villages, and Gwynedd, comprising the areas of Ynys Môn and Dwyfor. The urban areas were Liverpool, which included a sample drawn from the city based on the postal districts of L1-L19, L24 and L25-27; Newcastle, sampled from all postcodes north of the river Tyne and within the city boundary; Nottingham, sampled from the entire city apart from four wards; and Oxford, sampled using postcodes 1-4 in the city.

Interviewers

Screening interviews were conducted by lay interviewers who had been recruited specifically for the study. The interviewers had received training from both local and the national co-ordinator, and reliability checks were made during the study. A separate set of interviewers, again recruited and trained specifically for the study, conducted the assessment and annual interviews, and were not aware of the outcome of the first screening interview.

Approach

All potential participants were sent an introductory letter organised by the study centre and signed by the relevant general practitioner. In some centres, a letter from the centre was also sent to explain the study and provide contact details. In other centres, the interviewers visited potential respondents personally after the letters had been received to explain the study and arrange a date for the interview. Approaches were abandoned after four unsuccessful attempts to contact potential respondents.

Interviews

The screening interview was conducted with all respondents who consented, in their place of residence, using a laptop computer and software specially designed to present the questionnaire. Screening interviews lasted between 30 and 45 minutes, but could be shortened and placed into a quicker 'priority mode' if the respondent was unable to answer all the questions. The assessment and annual interviews were also conducted using laptop computers and lasted between 45 and 90 minutes. Again, a 'priority mode' could be invoked either automatically or manually if the interview became too much for a respondent.

Assessment instruments

The screening interview used items from the organicity scale of the Geriatric Mental State (GMS; a semi-structured standardised psychiatric interview designed for use with older people), the Mini-Mental State Examination plus additional cognitive items and questions regarding essential activities of daily living (ADL), socio-demographic variables and risk factors for dementia identified by EURODEM and can be found here: http://www.cfas.ac.uk/pages/bquestionnaires/prev_screen_interview.htm.

The assessment interview used the GMS version B3, the Cambridge Mental Disorders Examination (CAMDEX) (Roth et al., 1986) and the History and Aetiology Scale (HAS; a tool used to collect information regarding psychiatric illness and putative aetiological factors) and can be found here: http://www.cfas.ac.uk/pages/bquestionnaires/CSA.htm.

The HAS was modified in order to calculate the Blessed Dementia Rating Scale and Hachinski Index. The Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) (Copeland et al., 1986) score is derived from the GMS and HAS using an algorithm and is used to categorise individuals according to diagnosis and level of severity, ranging from zero to either four or five. A score of zero or one represents no or few symptoms and is not a case. A score of three or above is considered clinically significant and constitutes a case, whereas a score of two is considered borderline symptoms and is known as a subcase.

Cognitive Function and Ageing Study Wales (CFAS II/CFAS Wales)

Design

The Cognitive Function and Ageing Study II (CFAS II) and its sister study, the Cognitive Function and Ageing Study Wales (CFAS Wales) are large multicentre population-based studies in the UK that focuses on cognition, activities of daily living, health, medication and mortality. Data were collected at two time points, two years apart, from five centres in Cambridge, Nottingham, Newcastle, Bangor and Swansea. Interviews and follow-up interviews were to be undertaken over two two-year periods.

Participants

The study aimed to achieve a sample of 2500 people born prior to 1942 from each geographical area. The methods used to sample participants were the same as in the original

MRC-CFAS I study. General practice records were used as the sampling frame and individuals who resided in the locations selected by each centre were drawn from these lists. General practitioners were asked to update lists to account for potential participants having died or moved out of the study area and oversampling was used to account for the expectation that 15% of individuals may be ineligible or incorrectly registered, and an 80% response rate. The sample was stratified into two equal sized age groups of 65-74 years and 75+ years.

Geographical areas

The areas included in CFAS II include three of the original MRC-CFAS I areas: Cambridgeshire (consisting of the rural area of East Cambridgeshire and the Fenland centred on the city of Ely and its surrounding villages), and the cities of Newcastle and Nottingham. CFAS Wales includes one of the original MRC-CFAS I areas: the rural areas of Dwyfor in Gwynedd and Ynys Môn. Neath/Port Talbot was added for CFAS Wales and was administered from Swansea University.

Interviewers

The interviews were conducted by research assistants who had undergone training provided by staff from the co-ordinating centre in Cambridge. Further training was conducted at each centre and regular meetings ensured that training was kept up to date.

Approach

The method of approaching potential participants was the same as in the original MRC-CFAS I study. Individuals selected from General Practice lists were approved by the General Practitioner and sent an invitation letter which included further detailed information about the study. Interviewers then personally visited the houses of potential participants,

usually within one week of the individual receiving the letter, to discuss queries and make an appointment to conduct the interview.

Interviews

The interview was usually conducted in participants' homes. It consisted of the combined screen and assessment interview used in the MRC-CFAS I study with some additional questions. This allows for the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT)(Copeland et al., 1986) algorithm to be calculated and draws from respondent and interviewer observations. The interview typically took two hours to complete and comprised the following sections:

- Demographic characteristics – marital status, education, social class, social economic group, residential status and intellectual activity (Adapted from the European Prospective Investigation into Cancer & Nutrition protocol; EPIC, 1992)

- Lifestyle variables – smoking and alcohol history, brief measure of physical activity (Adapted from the European Prospective Investigation into Cancer & Nutrition protocol; EPIC, 1992)

- Health status including self-perceived health, self-reported chronic diseases (including heart disease, angina, diabetes, stroke, Parkinson's disease, epilepsy and meningitis) and medication history (Chen, Dewey, & Avery, 2001; Rose, 1962).

- Functional limitations, disability and extended activities of daily living and objective assessments of physical function (Bond & Carstairs, 1982) (Adapted from the English Longitudinal Study of Ageing protocol; ELSA, 2002)

- Cognitive function: MMSE (Folstein, Folstein, & McHugh, 1975) and extended items (verbal fluency, executive function; MRC, 1993); depression, dementia and anxiety

from the Geriatric Mental State Automated Geriatric Examination Assisted Taxonomy (GMS AGECAT) (Copeland et al., 1986); CAMCOG (Huppert, Brayne, Gill, Paykel, & Beardsall, 1995; Roth et al., 1986)

- Social support, social capital, care needs and social networks, including receipt of informal care (Lubben, 1988; Wenger, 1989)
- Measures of hearing and visual impairment (as at baseline), plus a further hearing test by HearCheck Screener to estimate hearing loss.
- Sputum specimen for DNA acquisition.
- Individuals were asked for permission to flag for death notification and embarkations at the Office of National statistics and access to health and social care records (as at baseline)
- Receipt of health services, social services, special housing and disability benefits – questions relevant to policy would be included based on retrospective questions on use of services to respondents and informants (Adapted from CFAS Resource Implication Study; RIS, 1992-1994)

The following sections were asked only in CFAS Wales:

- Personality and resilience (Windle, Markland, & Woods, 2008)
- Well-being (using the Satisfaction with Life Scale) (Diener, Emmons, Larsen, & Griffin, 1985)
- Language history and preference (Added by the CFAS Wales team with advice from Dr Enlli Thomas)

- Measures of activity level, social or civic participation and loneliness (de Jong-Gierveld & Kamphuis, 1985)

The CFAS II Questionnaires can be found here: http://www.cfas.ac.uk/pages/cfasIIquestionnaires/index.html.

The CFAS Wales Questionnaire can be found here:

http://cfaswales.bangor.ac.uk/research-information.php.en?menu=1&catid=8832&subid=0

Informant interview

An informant interview was conducted for a 20% sample of all respondents, weighted toward cognitive and functional impairment. The informant interview consists of the GMS and History and Aetiology Schedule that is used by AGECAT and enables the DSM IV and ICD10 classification of organic and mood disorders (as at baseline). The informant interview can be found here: http://www.cfas.ac.uk/pages/cfasIIquestionnaires/index.html (CFAS II) and here http://cfaswales.bangor.ac.uk/research-information.php.en?menu=1&catid=8832&subid=0 (CFAS Wales).

CFAS Wales data collection

This section gives a detailed description of how the data for CFAS Wales was collected. I contributed to the data collection for CFAS Wales and data from CFAS Wales is used in Chapters 5-7 of this thesis.

Before the interview

Each CFAS Wales interviewer was allocated a batch of potential respondents by the co-ordinating centre at Cambridge, typically including 20 names and addresses and grouped into one geographical area. Each batch included all paperwork required for the interview

(invitation letter from the GP, information sheets, four consent forms, drawing sheets for use during the cognitive tasks in the interview, information sheets for relatives/carers, consent forms for relatives/carers in the event of an informant interview being conducted, thank you letters and unable to contact letters; see Appendices D-K), saliva collection kits and storage bags, cardboard inserts for use with the HearCheck Scanner, an Iron Key flash drive containing the interview data to be loaded on to the laptop, contact details for all participants, envelopes, address labels and stamps.

On receipt of the batch, the interviewer loaded the interview data from the Iron Key flash drive on to the laptop used to conduct the interviews. The interviewer then prepared the letters to be sent to the potential respondents, which included a letter from the GP and an information sheet, in both English and Welsh. Approximately one week after the potential respondents received their letters, the interviewer visited them at their home addresses to discuss any further queries and make an appointment to conduct the interview or make a note of a refusal and the reasons for this. In circumstances where respondents were unable to take part in the interview, but were happy for a relative or carer to be interviewed on his/her behalf, contact details for an informant were obtained and the informant was contacted to arrange an interview.

In situations where a potential respondent could not be located, a letter was sent asking the person to contact the interviewer or the centre by telephone and provide directions to his/her house should s/he wish to take part. If an interviewer discovered that a potential respondent was no longer living at the address listed, the potential respondent's details were re-checked with the GP surgery lists and reallocated with the correct information. The centre and co-ordinating centres were informed of any potential respondents who had died. Respondents who wished to take part but were unable to at that time were reallocated to the interviewer at a later date.

The interview

Interviews typically took place in the respondent's home at a time convenient to them. On arrival the interviewer explained the research again briefly and invited any further questions before beginning the consent process. The respondent was given as much time as needed to complete the consent forms and ask any questions during this process, before beginning the interview. The interviews were conducted using laptop computers and a standardised interview program which presented the questions in the correct order and allowed for a break in the middle. At the end of the interview, the interviewer collected contact information for two relatives or friends who would know the respondent's whereabouts in case s/he changed addresses between the baseline and follow-up interviews. If an informant interview was required, the interviewer collected contact details to arrange an interview with an informant. After the interview, the interviewer gave the respondent a thank you letter.

After the interview

The interviewer scored the drawing sheets used during the cognitive tasks in the interview and prepared a short vignette that provided information on the respondent's mental, physical and social well-being in order to aid in making diagnoses if necessary. The saliva samples were logged at each centre. A Residential Environmental Assessment Tool was completed for each address where an interview was completed, and was returned to the centre. Once all respondents in the batch had been contacted, the batch was returned to the co-ordinating centre at the University of Cambridge.

Cognitive status groups

Participants were categorised according to their cognitive status, using the cognitive status algorithm which is outlined in the data management section below and shown in Figure 2.2. This section defines each cognitive status group and provides an explanation of the characteristics. Table 2.1 shows a summary of the criteria used to categorise participants in each cognitive status group.

Not cognitively impaired (NCI)

Not cognitively impaired (NCI) is a variable created from the cognitive status algorithm (Figure 2.2) to categorise participants who do not meet criteria for cognitive impairment. It is used in Chapters 4-7 in looking at the relationship between MCI and mood, to compare risks of anxiety and depression between people without cognitive impairment and those with MCI. In order to be categorised as NCI, participants fulfilled the following criteria: MMSE score of equal to or greater than 22, no impairment on any scales of the CAMCOG according to the age-adjusted cut-offs (a score falling more than one standard deviation below the age norm for each scale) and no diagnosis of dementia according to the AGECAT algorithm. For both MRC-CFAS I and CFAS Wales data participants categorised as NCI could have subjective memory complaints (SMC) and impaired activities of daily living (ADLs).

Mild cognitive impairment (MCI)

The relationships between MCI, mood and SMC were investigated in Chapters 4 and 5, between MCI, mood and health in Chapter 6 and between MCI, mood and social networks in Chapter 7. An appropriate classification of participants who met criteria for MCI was

required in order to investigate these relationships. This was completed using the cognitive status algorithm (Figure 2.2).

In Chapters 4-7 participants were categorised as MCI when they reported SMC, displayed impairment on either the memory or non-memory subscales, or both memory and non-memory subscales of the CAMCOG according to age-adjusted cut-off scores (a score falling more than one standard deviation below the age norm for each scale), had an MMSE score equal to or greater than 22, had intact ADLs and were not categorised as having dementia according to the AGECAT algorithm. In Chapters 4-7 participants with MCI that specifically included SMC were directly compared to participants categorised as mild cognitive impairment-without SMC (MCIW; see below) to investigate what effect of the presence of subjective memory complaints had on the odds of experiencing symptoms of anxiety and depression.

Mild cognitive impairment-without (MCIW)

Chapters 4 and 5 investigate the role of SMC in the relationship between MCI and mood. Typical definitions of MCI include SMC as a criterion, but there is controversy over whether this is necessary. In Chapters 4 and 5 a comparison is made between participants who have MCI that includes SMC and participants who would otherwise meet established criteria for MCI (objective cognitive complaint, intact general cognition, intact ADLs and absence of dementia) but do not report SMC. The second group is therefore categorised as MCI-without SMC (MCIW) and the category was created using the cognitive states algorithm (Figure 2.2). The MCIW category was also used whilst investigating the relationships between MCI, mood and health in Chapter 6, and between MCI, mood and social networks in Chapter 7 to explore the role of SMC.

Other cognitive impairment no dementia (OCIND)

Chapters 4-7 investigate the relationship between MCI and mood in the MRC-CFAS I data (Chapter 4) and the CFAS Wales data (Chapters 5-7). It was necessary to distinguish between participants who met criteria for MCI and those that had a greater level of cognitive impairment to maintain the accuracy of the MCI definition. The other cognitive impairment no dementia (OCIND) variable was created using the cognitive status algorithm (Figure 2.2) to categorise participants who did not have intact general cognition (shown by an MMSE score of less than 22) but did not meet criteria for dementia or have impaired ADLs. In Chapter 4, data from two time points of MRC-CFAS I were analysed to investigate the role of SMC in the relationship between MCI and mood. Participants categorised as OCIND were excluded from baseline analyses, but the category of OCIND was used at follow-up to show that participants could progress from one cognitive state to another. Chapters 5-7 include data from one time point of CFAS Wales and participants categorised as OCIND were excluded from analyses due to not meeting criteria for MCI.

Impaired activities of daily living (ADL)

A further cognitive classification that represented a level of impairment beyond that expected for participants with MCI was the ADL category. The ADL variable was created using the cognitive status algorithm (Figure 2.2) and included participants who did not meet criteria for dementia, but displayed general cognitive impairment (shown by an MMSE score of less than 22) and impaired ADLs. Impaired ADLs were reported with an answer of "no, needs help" to any of the following questions asked during the MRC-CFAS I and CFAS Wales interviews: "are you able to wash all over and bathe?", "can you prepare and cook a hot meal?", "are you able to put on your shoes and stockings?", or if the interviewer rated the participant's mobility as non-ambulant. The ADL variable was used to exclude participants from analyses in Chapters 5-7 as only cognitive impairment meeting criteria for MCI was investigated. Participants categorised as ADL were excluded from baseline analyses of MRC-

CFAS I data in Chapter 4 but the category was used at the follow-up time point in this Chapter because participants could change cognitive categories during the two years between baseline and follow-up.

Dementia

The dementia variable was necessary as this thesis does not investigate participants with dementia. The MCI definition includes the absence of dementia as a criterion and it was crucial to accurately classify participants as having dementia in order to properly apply the MCI definition and also exclude participants categorised as having dementia from analyses. The dementia variable includes all participants with AGECAT scores of O3-O5 and was created from cognitive status algorithm (Figure 2.2). Participants classified as having dementia were excluded from all analyses in Chapters 5-7 as only the relationship between MCI/MCIW and mood is investigated. Participants with dementia were excluded from the baseline analyses in Chapter 4 as only the relationship between MCI/MCIW, mood and subjective memory complaints were investigated that this time point. However, the category of dementia was used at the follow-up time point in Chapter 4 as participants could progress from one cognitive state to another in the two years between the baseline and follow-up time points of MRC-CFAS I.

Table 2.1: Cognitive categories created from the cognitive status algorithm

	Objective cognitive problems	Subjective memory complaint	Impaired ADLs	General cognitive decline	Presence of dementia
NCI	×	✓/×	✓/×	×	×
MCI	✓	✓	×	×	×
MCIW	✓	×	×	×	×
OCIND	✓	✓/×	×	✓	×
ADL	✓	✓	✓	✓	×
Dementia	✓	✓	✓	✓	✓

NCI: Not cognitively impaired; MCI: Mild cognitive impairment; MCIW: Mild cognitive impairment without the presence of subjective memory complaints; OCIND: Other cognitive impairment no dementia; ADL: Activities of daily living impairments without presence of dementia.

Data access procedures

Data were accessed from the University of Cambridge by completion of two request forms, one of which was sent to the University of Cambridge and one to Bangor University. The forms required data users to specify research questions and planned analyses, and the items from the data set that were required for addressing the research questions. Anonymised data were transmitted using encrypted files by the University of Cambridge.

Data management

MRC-CFAS I data had been cleaned and the CAMCOG, MMSE and AGECAT variables generated prior to the beginning of this thesis. Once the data had been requested and approved it was transferred electronically in an encrypted format to me.

CFAS Wales data were returned to the coordinating centre at University of Cambridge by the interviewers using Iron Key flash drives and were loaded on to the central database by the administration team. The data management team checked the variables for any entry errors which were cross-checked with interviewer notes and vignettes. The data manager completed calculations of the AGECAT and MMSE variables. Professor Carol Brayne (University of Cambridge) viewed the data responses and made diagnoses for participants for whom only informant interviews were conducted and for participants whose AGECAT score could not be calculated. Upon completion of these processes the CFAS Wales dataset was released and transferred electronically in an encrypted format to me. All items relevant to the analysis conducted in this thesis were examined individually to ensure adequacy of responses and check for missing values.

An algorithm was used to categorise participants into cognitive status groups (Table 1) and is shown in Figure 2.2. The algorithm was initially provided by Dr Blossom Stephan (Newcastle University) and used as a basis for creating the algorithm shown below. Originally, informant reports of memory problems were also used to categorise participants as having MCI even when the participants themselves did not report SMC, and I removed this from the algorithm so that SMC could only be reported by the participant. In addition, participants with impairments in activities of daily living (ADL) were excluded from the no cognitive impairment (NCI) category in the original algorithm, and I modified this so that they could be included if they did not have any cognitive impairments that would render them categorised as having MCI/MCIW, OCIND, or ADL. The original algorithm did not include the category of MCIW and I modified it to create this category. Initially, participants who met the criteria for MCIW were categorised as OCIND and I created the MCIW category to classify these participants as meeting the same criteria for MCI, excluding the requirement for SMC. The original algorithm and subsequent changes that I made to it were written using STATA software. Creation of cognitive categories for analysis in Chapter 4 was completed in STATA before the dataset was saved as an SPSS file for further analyses to be completed. I translated the algorithm from STATA to SPSS for use in Chapters 5-7 and changed terms included in the algorithm to reflect variable names included in the CFAS Wales dataset that differed to those in the MRC-CFAS I dataset.

The cognitive status groups of dementia, OCIND and ADL were excluded at baseline in all analyses but are included at the follow-up analyses in Chapter 4 as participants were able to progress to these categories over time. The MCIW category was created for analysis in Chapters 4 and 5, but was found to be an interesting concept and I decided to include it in analyses in Chapters 6 and 7. The algorithm used the CAMCOG score after adjustment for age as a measure of objective cognitive problems, presence of impaired activities of daily

living (ADLs), impaired general cognition measured by the total MMSE score, the presence of subjective memory complaints and the presence of dementia. Dementia diagnoses were provided by the AGECAT algorithm which was a complete variable in the dataset.

The distributions of the variables that had been created (total IADL score, health index score, total physical activity score, total service use score and social network score) were checked for normality. Appropriate levels of skewness and kurtosis were deemed to be +/- 2 on the basis of accepted statistical techniques. All variables displayed levels of skewness and kurtosis between -1 and +1, except for total service use score, which was transformed using a square root transformation to make the values less than 1.

During the interview responses to questions were entered using numerical codes. For questions that were unanswered, interviewers could enter 7 (“don’t know”), 8 (“no answer”) or 9 (“not asked”). On receipt of the dataset, all responses of 7, 8 or 9 for questions used to calculate the CAMCOG and MMSE were changed to 0 (incorrect) in accordance with the guidelines for scoring these measures. For questions other than these, all responses of 7, 8 or 9 were recoded as system missing to represent missing data.

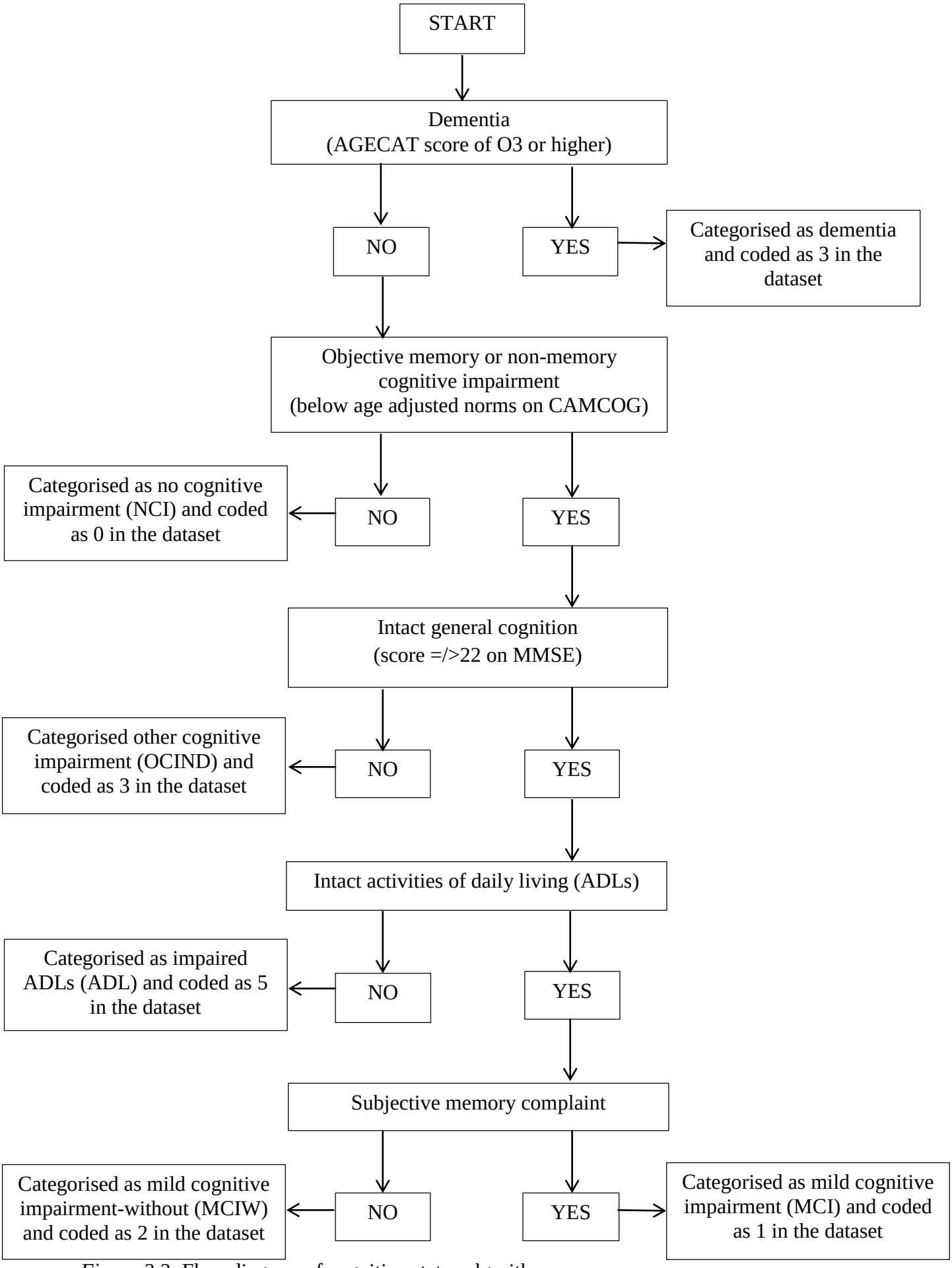

Figure 2.2: Flow diagram of cognitive status algorithm

Key variables used in the thesis

There are a number of variables used in this thesis that require further explanation of their development and meaning. The following section gives a detailed description of the key variables that were used and how they were created.

AGECAT

The AGECAT algorithm (Copeland et al., 1986) was described previously in this chapter and was used to provide a measure of anxiety and depression for Chapters 4-7, which investigate the relationship between MCI and mood in both MRC-CFAS I and CFAS Wales data. The AGECAT classification also provides a diagnosis of dementia. This was required in Chapters 4-7 to exclude participants from baseline analyses as participants with cognitive decline that is more severe than MCI were not investigated in this thesis. The dementia diagnosis was also used in Chapter 4 at the follow up time point as participants were able to progress from one cognitive state to another between baseline and follow-up. The AGECAT classification was provided in full by the coordinating centre at the University of Cambridge as part of the dataset. AGECAT scores that were of interest in investigating the relationship between MCI and mood were those representing depression (D0-2, DN3-4, DP3-5), anxiety (AN0-5) and dementia (O0-5). On receipt of the dataset I recoded the AGECAT scores into new variables to create dichotomous categories of depression and anxiety called DEP and ANX, with scores of level two and above considered as depression or anxiety in order to account for borderline symptoms. Scores of O3 and above were recoded into a new variable called dementia to indicate the presence of dementia.

MMSE

The Mini-Mental State Exam (Folstein et al., 1975) is used extensively in assessing the cognition of older people, and forms part of the cognitive section in the respondent interview. The MMSE has a total score of 30 and was used in the cognitive states algorithm (Figure 2.2) to determine whether participants have intact general cognition, indicated by a score of equal to or greater than 22. The MMSE variable was created during the interview, but was subsequently cleaned by the coordinating centre at the University of Cambridge to remove missing values and check the accuracy of the scores. In particular, responses to the serial sevens question[1] had to be checked to ensure that the responses had been entered correctly during the interview, as responses to this question were entered in alphanumeric format instead of using a numerical code. The cleaned version of the MMSE variable was included in the MRC-CFAS I and CFAS Wales datasets provided by the University of Cambridge.

CAMCOG

The Cambridge Cognitive Examination (CAMCOG) (Huppert et al., 1995; Roth et al., 1986) is a measure of cognitive function comprised of ten subscales that assess orientation, language, memory, attention, praxis, abstract thinking and perception. The CAMCOG is used in the cognitive status algorithm (Figure 2.2) to determine objective memory and non-memory impairment that are beyond age-specified norms. The questions included in each scale were asked during the interview and scored according to the guidelines specified by the authors of the measure (Roth et al., 1986). The subscales were calculated by the coordinating centre at the University of Cambridge in the MRC-CFAS I data set. Questions regarding the

[1] The serial sevens question requires participants to subtract 7 from 100, and then subtract 7 from the answer they gave a further four times. The correct answers are 93, 86, 79, 72, 65.

tactile recognition of coins and calculating their sum, and the recognition of two people in the room were removed from CAMCOG during MRC-CFAS I and therefore the total possible CAMCOG score within MRC-CFAS I is 103 rather than 107.

I calculated the total scores for the CAMCOG subscales in the CFAS Wales data set by creating a sum of the responses for the CAMCOG questions. I then calculated the total CAMCOG score by creating a sum of the subscale scores. The total possible score on the CAMCOG for CFAS Wales was 106, as the questions regarding the tactile recognition of coins and calculating their sum were included; however the question regarding the recognition of two people in the room was not asked, and so the original total score of 107 could not be achieved.

CAMCOG median split

The CAMCOG median split variable was used in mediation analyses with CFAS Wales data in assessing whether subjective memory complaints mediate the relationship between cognition and mood (Chapter 5). The variable was created from the total CAMCOG score in the CFAS Wales dataset. A median value for each age group of 65-69, 70-74, 75-79, 80-84, 85-89 and 90+, further separated by gender and educational level (nine years or less and ten years or more) was calculated (see Appendix P). Participants in each age/gender/education category were coded 0 (lower) or 1 (higher) in the CAMCOG median split variable depending on whether their CAMCOG score was lower or higher than the median value for their category.

Cognitive impairment as a continuous variable

Cognitive impairment was used as a continuous variable in the sensitivity analyses included in Chapter 5 and was created by me by reversing the scores of the CAMCOG for

each participant. This was done by subtracting each score from the highest obtained score on the CAMCOG plus one, and was checked to make sure that the distributions and standard deviations remained the same using Z transformations.

Centre

Centre is a dichotomous variable that refers to the geographical area in CFAS Wales and distinguishes between data collected in the urban area of Swansea and the rural area of Gwynedd/Ynys Môn.

Social network scale

I created the social network variable for use in Chapter 7 which investigates the nature of the three-way relationship between MCI, mood and social networks using data from CFAS Wales. The variable was created from the Lubben Social Network Scale Six Item version (Lubben et al., 2006) (LSNS-6; Appendix O) as these questions were asked during the CFAS Wales interview. The LSNS-6 is comprised of six questions about the number of friends and relatives that the participant has contact with and has a maximum score of 30. The LSNS-6 has good internal consistency (α=0.83) and discriminant validity, of the whole measure and for both subscales (Lubben et al., 2006), and showed good internal consistency when used in this study (α=0.73).

Comorbidity index

Chapter 6 addresses the research question of whether the relationship between MCI and mood is mediated by perceived health or health state. To answer this question I created the comorbidity index variable (Appendix N) to provide an objective measure of health state from questions that were asked in the CFAS Wales interviews based on the Charlson Co-Morbidity Index (Charlson, Pompei, Ales, & MacKenzie, 1987). Conditions included were

angina, intermittent claudication, high/low blood pressure, sugar diabetes, Parkinson's disease, stroke, heart attack, fits/epilepsy, serious head injury, chronic bronchitis, asthma (excluding childhood asthma), arthritis, peptic ulcers, pernicious anaemia, transient ischemic attack (TIA), thyroid problems, meningitis, shingles, cancer (and whether this was a current problem). Each positively answered question was given a score of one, except for cancer which scored two, with an additional point for current problems. The scores were summed to create an overall co-morbidity score ranging from zero to 21.

Perceived health

The perceived health variable was created by me to investigate the extent to which perceived health mediates the relationship between MCI and mood, which is explored in Chapter 6. The variable is comprised of responses to the question "Would you say that for someone of your age, your own health in general is: Excellent/good/fair/poor/don't know?" asked in the CFAS Wales interview. A collapsed, dichotomous version of the variable was also created; this grouped the responses of excellent and good together, and fair and poor together.

Physical activity score

The physical activity score variable (Appendix N) was created by me to address the research question regarding the role of health in the relationship between MCI and mood which is investigated in Chapter 6. The CFAS Wales interview included several questions regarding the frequency of recreational physical activity of mild, moderate and vigorous intensity undertaken by the participants, which had been adapted from the protocol used in the English Longitudinal Study of Ageing (ELSA, 2002). During the interview, participants were firstly asked if they took part in vigorous activities, and could respond with yes or no. If the participant responded with no the interview programme automatically coded all vigorous

activities with 9999 and skipped those questions. Participants were then asked if they took part in moderate and mild activities using the same process. The responses to each activity question were entered using numerical codes of 0 (no), 1 (more than once a week), 2 (once a week), 3 (one to three times a month) and 4 (hardly ever, or never) or with 9999 to represent that the question had been not asked. On receipt of the dataset I changed scores of 9999 to zero to indicate that this activity was not undertaken. I reversed the scores so that a higher frequency of activities resulted in a higher total score. A total overall summary score for physical activity was created by summing the score for each physical activity together and possible scores ranged from zero to 72.

Total IADL score

I created the Total IADL score variable for use in Chapter 6, which investigates the impact of health on the relationship between MCI and mood, as it could be considered the ability to perform instrumental activities of daily living (IADLs) may serve as a proxy measure for health. I decided to consider IADLs only, and not ADLs, as the MCI definition states that individuals should have intact ADLs. During the interview, participants were asked about their ability to perform particular IADLs. Responses were coded by the interviewer as 0 for needing help, 1 if the participant had some difficulty performing the task and 2 if the participant was able to perform the activity without difficulty. I reversed the scores so that greater capability resulted in a higher score and totalled the scores from each question to create an overall summary score.

Total service use score

The total service use score variable (Appendix N) was created by me to address the research question of the impact of health on the relationship between MCI and mood, explored in Chapter 6, as it was considered that service use could act as a proxy marker for

health. The variable was created from questions asked in the CFAS Wales interview regarding the use of health or social services. One point was scored for each service used, except for three questions as a positive response to these prompted the interview program to present further questions regarding how frequently they were used. A positive response to "During the last year have you been in hospital for treatment as a day patient", led to the question "How many separate stays in hospital have you had as a day patient?", "During the last year have you been in hospital as an inpatient, overnight or longer?" led to the question "How many separate stays have you had as an inpatient" and "How many nights altogether were you in hospital on each occasion?", and "During the last 3 complete calendar months, did you attend the casualty or outpatients department of a hospital?" led to the question "Which months was this?" and "How many times did you attend the casualty or outpatient department during that month?". A negative response to the first set of questions would not prompt further questions and the interview program would automatically code these as 9999. I changed the scores of 9999 to zero to denote that these services had not been used. If the services had been used, they scored one multiplied by the number of times they had been used, so that a higher score represented an increased frequency of use. The scores from each question were then summed to create an overall score of service use. The total service use score could range from zero upwards, as there was no limit on the frequency of hospital use.

SMC

The subjective memory complaints (SMC) variable was used in Chapters 4-7 as the presence of SMC formed a step in the cognitive states algorithm (Figure 2.2) used to determine which participants had MCI, as this was necessary to investigate the relationship between MCI and mood. The SMC variable was also used to address the research question investigating the mediating role of SMC on the relationship between MCI and mood using the MRC-CFAS I dataset (Chapter 4), and using the CFAS Wales dataset (Chapter 5), by

comparing participants with and without SMC. In Chapter 4 the SMC variable was created from two questions asked in the screening interview and one in the assessment interview: "Have you ever had difficulty with your memory?" and "Have you tended to forget things recently?", and "Have you had any difficulty with your memory?" where a positive answer to any of these questions resulted in a score of one on the SMC variable, and a negative answer to all three of these questions resulted in a score of zero. In Chapter 5 the variable was created from two questions asked in the CFAS Wales interview: "Have you ever had any difficulty with your memory?" and "Have you tended to forget things recently?" A positive response to either question resulted in a score of one on the SMC variable, whereas a negative response resulted in a score of zero.

MRC-CFAS I, CFAS II and CFAS Wales include questions regarding informant rating of memory problems in the informant interviews, which were completed for approximately 20% of the sample. Previous CFAS studies have included informant ratings of memory problems; however, they were not included in the empirical work presented in this thesis as informant ratings were not felt to reflect participants' own metacognitive processes. In addition, the informant ratings are only available for a small proportion of participants and it was felt pragmatic to use only participants' ratings to ensure the robustness of analyses.

Statistical techniques

Statistical techniques are explained in detail in each chapter, but briefly I have used quantitative methods including multivariate statistics, logistic regression, and structural equation modelling to assess the relationship between MCI and mood. The sample size required for adequate statistical power was estimated using G*Power software (Faul, Erdfelder, Buchner, & Lang, 2009) for all regression analyses and it was found that a sample of 300 should be sufficient to avoid Type I and II errors at the $\alpha = 0.05$ and $\beta = 0.95$ levels.

Our sample greatly exceeds this and as such any inferences made from regression analyses should be considered robust. For structural equation modelling a small effect (r=0.1) at the $\alpha = 0.05$ and $\beta = 0.95$ levels should be detected with a sample size of at least 330, with smaller samples required for stronger effects. Our sample is greater than this and as such the results of the structural equation models can be considered reliable.

Ethical approval

Ethical approval was sought from the relevant NHS ethics committee. Applications and relevant correspondence can be found in Appendix A.

Conclusion

This chapter provided an overview of the development of the MRC-CFAS I, CFAS II and CFAS Wales studies, and a description of how the data were collected. This chapter covered the management of the data, and how data from MRC-CFAS I and CFAS Wales were prepared for analysis in order to investigate the relationship between MCI and mood through SMC, health and social networks. A systematic review forms the next chapter of this thesis (Chapter 3), which describes the evidence base and existing literature in the field of MCI and mood at the commencement of this thesis. The findings from the systematic review form the basis for the development of the empirical research questions addressed in this thesis.

Chapter 3: Mild cognitive impairment and mood: A systematic review

Summary

This chapter provides a solid foundation to the empirical studies included in chapters 4-7 by presenting a systematic review of the evidence base surrounding this relationship.

This systematic review, with meta-analyses conducted where data were available, aimed to investigate the prevalence of symptoms of depression and anxiety in MCI and to establish how symptoms of depression and anxiety relate to the progression from no cognitive impairment to MCI, and from MCI to dementia. Sixty studies were included in the review. Meta-analyses indicated that symptoms of depression and anxiety were more prevalent in people with MCI than in people with normal cognitive functioning, and increased the risk of progression from no cognitive impairment to MCI. There were mixed results regarding the effect of symptoms of anxiety and depression on the progression from MCI to dementia. The findings of this chapter highlight the need for more research in this area which could be used to inform interventions to slow or halt the progression of cognitive impairment in later life, with resulting benefits for quality of life. The findings of this chapter were also used to inform other research questions addressed during the thesis.

Introduction

Mild cognitive impairment (MCI) is a concept that was developed in an attempt to describe a proposed transitional state which may exist between age appropriate levels of cognitive functioning and pathological cognitive decline (Matthews et al., 2008). In general, core elements of the MCI classification are a subjective memory complaint, an objective memory impairment, typically demonstrated by performance on a battery of neuropsychological tests, intact general cognitive function and intact activities of daily living (ADLs). MCI is a broad term encompassing several subtypes. A primary distinction is made between single-domain MCI, where only one aspect of cognitive functioning is impaired, and multiple-domain MCI, which involves impairment in more than one aspect of cognitive functioning. A secondary division can then be made into amnestic MCI, where memory is impaired, or non-amnestic MCI, in which only aspects of cognitive functioning other than memory, such as executive function, are impaired. Thus for example, individuals classified as having multiple domain amnestic subtype MCI experience impairments in both memory and other cognitive functions.

However, controversy surrounds the concept of MCI. At least sixteen variations on the criteria used to classify MCI have been identified and these differ in the extent to which they include each of the elements described above (Stephan et al., 2008). It is also unclear whether the subtypes identified under the broad umbrella term of MCI are truly distinct categories and how they work together. Furthermore, although MCI is often seen as a transitional state between normal ageing and pathological decline, or even as a prodrome of dementia, not everyone diagnosed with MCI will convert to having dementia. Indeed, in one study, 12% of participants classified as having MCI improved and 53% remained stable over three years (Wahlund et al., 2003). A separate study found after 2.7 years 19.5% of participants had improved to a normal level of cognitive functioning and 61% of participants

remained at a stable level of cognitive functioning (Wolf et al., 1998). The concept is also controversial due to the heterogeneity of aetiologies that may underlie the cognitive changes experienced in MCI, such as vascular changes or Alzheimer's pathology. This heterogeneity prevents the development of a set of specific diagnostic criteria (Dubois & Albert, 2004) such as those used in making a dementia diagnosis. A small post mortem study revealed that there was no single type of pathology across all cases of MCI, suggesting that it would be unwise to conceptualise MCI simply as a prodromal form of Alzheimer's disease (Stephan et al., 2012).

Nevertheless, the concept of MCI is useful for identifying individuals who may be at increased risk of progression to a diagnosis of dementia. People classified as having MCI are more likely than individuals without cognitive impairment to progress to a diagnosis of dementia, at a rate of 10-15% compared to 1-2% per year (Petersen et al., 2001). Individuals at an early stage of cognitive decline may benefit from implementing strategies to cope with cognitive change which could help to increase independence and quality of life. Given the increased risk of progressing to dementia from MCI, it is important to understand any associated factors that may contribute to the development of MCI.

One important factor associated with MCI is mood, in particular low mood or high levels of anxiety (D. E. Barnes, Alexopoulos, Lopez, Williamson, & Yaffe, 2006; Bhalla et al., 2009; Geda et al., 2006). Possible explanations for this association include the suggestions that worries may compete for cognitive resources, leaving less capacity for cognitive functioning, (Butters et al., 2011) or that symptoms of anxiety may lead individuals to be more vigilant towards their cognitive functioning and more aware of subtle changes in their cognitive function. Depression is related to cognitive disturbances in older people who are ageing normally (Palmer et al., 2007) although it is unclear in which direction the relationship operates. On the one hand, depression might lead to reduced cognitive

functioning, but on the other hand, individuals classified as having MCI may be at risk of developing symptoms of depression or anxiety (Chan, Kasper, Black, & Rabins, 2003). It is possible that both explanations could occur concurrently, indicating a circular relationship between mood and MCI. On discovering a cognitive impairment an individual may become anxious with regards to how his or her cognitive functioning may change in the future and what implications any changes might have. It is important to examine the nature of the association between MCI and mood, and a systematic review is an appropriate way to synthesise existing literature in this area.

This review aims to answer the following questions:

1. Are people with MCI more likely to show low mood or increased anxiety than people with normal cognitive function, and does this vary by MCI subtype?

2. What is the temporal relationship between mood problems and the development of MCI?

3. Does the presence of low mood or increased anxiety in people with MCI increase the risk of progression to dementia?

Methods

A search of the electronic databases PsychInfo, PubMed, Science Direct and Web of Knowledge was conducted on 17th November 2012 using the terms 'mild cognitive impairment', 'MCI' and 'cognitive impairment' combined with 'depress*', 'anxi*', 'neuropsychiatric symptoms', 'NPS' and 'mood'. The terms 'depress*' and 'anxi*' were used as these are the aspects of mood that this review is addressing. The term neuropsychiatric symptoms was included as it is frequently used in a way that encompasses the concepts of anxiety and depression, especially in studies that have used the

Neuropsychiatric Inventory (NPI) to assess mood. Other terms used to describe cognitive impairment, such as 'cognitive impairment no dementia' (CIND) were not included as the aim was to achieve a consistent population of individuals with MCI. Studies were included if they considered symptoms or diagnoses of depression or anxiety in older people who, according to the study authors, met criteria for MCI. The search process is shown in Figure 3.1. All titles and abstracts identified in the initial database search were assessed. Full articles were retrieved if the title and abstract suggested that the study both considered symptoms of anxiety or depression and classified participants as having MCI. Further studies were identified through the reference sections of selected studies. There was no restriction on the definition of MCI. As the term MCI was not widely used before 1991 there was no limit set on the year of publication as it was thought that there would not be papers published before this date (Roberts et al., 2009). Only quantitative studies published in English were included. Conceptual studies and review articles were excluded.

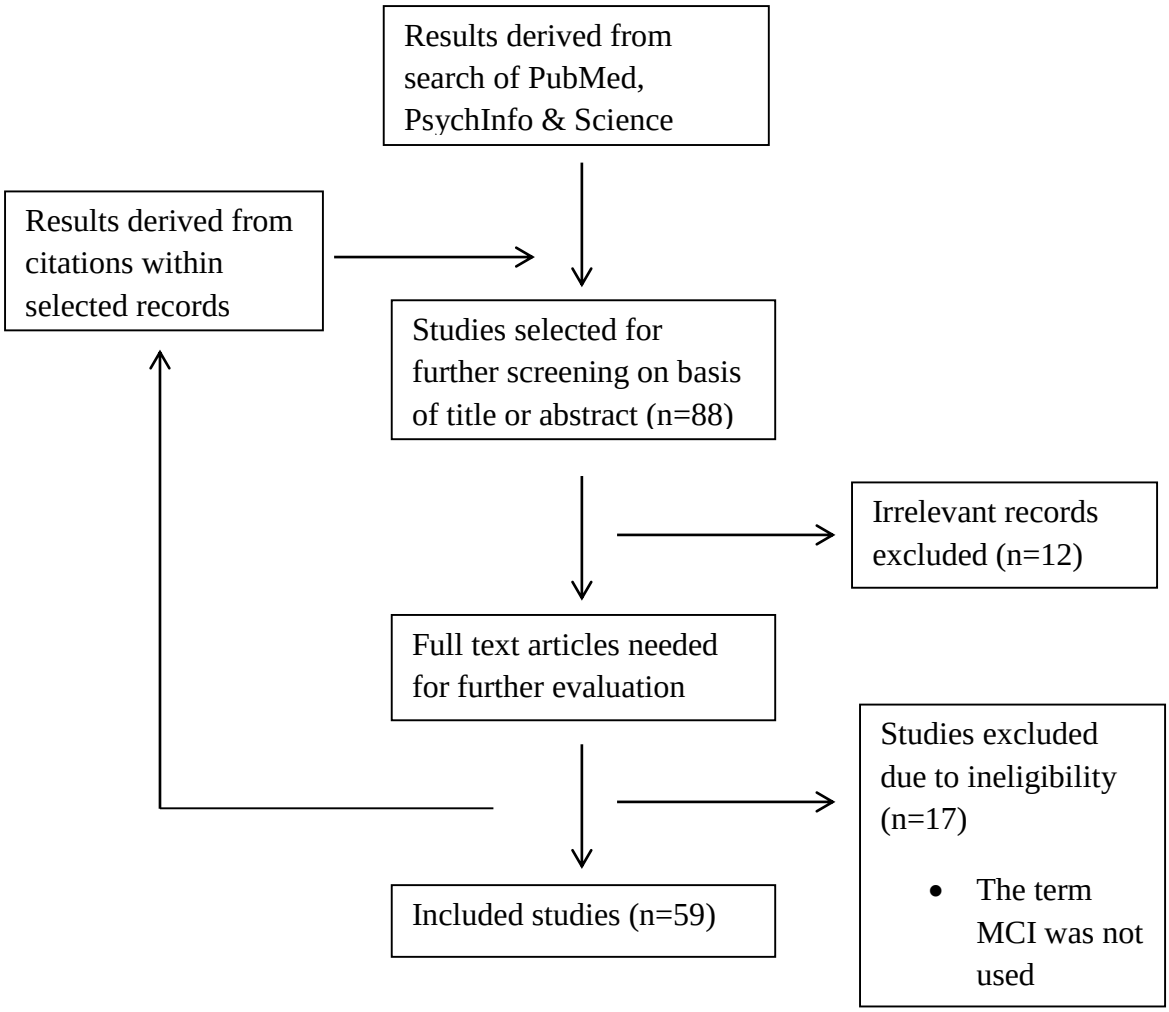

Figure 3.1: The process used for selecting studies to be included in the review.

Methodological quality was assessed using a checklist adapted from the QUADAS tool [Quality Assessment of Diagnostic Accuracy Studies (Whiting, Rutjes, Reitsma, Bossuyt, & Kleijnen, 2003)]. The QUADAS tool was developed for use in systematic reviews and was adapted by the present authors to allow for studies of varied methodologies through the omission of several items. The original tool has 14 items, seven of which were not applicable to this review, and were omitted. The primary reviewer identified the studies, extracted the relevant data and conducted the quality assessment. Ten per cent of the studies were randomly selected for review for quality assessment by a secondary reviewer.

Statistical analysis

Random effects meta-analyses were conducted where possible to synthesise results of similar studies, which reported usable data, using MIX 2.0 Pro software. Heterogeneity ranged from moderate to high for the analyses. Odds ratios were examined to address research question (RQ) 1. Odds ratios were either taken directly from the study reports or calculated from frequencies presented in the results sections of study reports. Hazard ratios were examined to address RQ2 and these were either taken directly from study reports or calculated from data given in the results sections. Relative risk ratios were examined to address RQ3 and were either obtained directly from study reports or calculated from available data.

Results

Sixty studies were included in this review. Studies focusing on cognitive changes in people with mood problems are summarised in Table 3.1. Studies investigating changes in mood in participants classified as having MCI are summarised in Table 3.2. Forty-four studies found a significant positive association between MCI and depression or anxiety, with one study finding a negative association between depression and MCI (Vicini Chilovi et al., 2009).

Table 3.1: Studies investigating the occurrence of MCI in participants with mood problems

Name and year	Participants, n, and mean age	Design	Definition of MCI used	MMSE	Symptoms assessed	Measures used in assessment	Results
Adler et al., (2004)	34 with depression including 18 with MCI Age: 73.4 (6.5)	Cross-sectional study	A cut off score of less than 46 on the Structured Interview for the Diagnosis of Dementia of the Alzheimer Type, multi-infarct dementia, and dementias of other etiology according to DSM-III-R and ICD-10 (SIDAM)	Not used	Depression	Hamilton Depression Scale (HMD; Hamilton, 1967)	MCI is frequent in depressed older adults, particularly those with late onset of depression. However, depression and the severity of affective symptoms had no relevant impact on cognitive performance and its course. MCI had no negative impact on recovery from depression
Barnes et al., (2006)	2220 Mean age: 74	Prospective, population based longitudinal study, part of the Cardiovascular Health Study	Individuals not meeting dementia criteria who exhibited poor cognitive function that reflected a decline from a prior level	Modified Mini-Mental State Examination (3MS) was used and the average score across participants was 95.2 (2.9)	Depression	Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977)	41% of participants were described as having low levels of depressive symptoms and 20% were described as having moderate/high levels of depressive symptoms. 13% of participants developed MCI. More depressive symptoms increased the risk of MCI
Bhalla et al., (2009)	109 non-MCI meeting criteria for depression Age: 74.7 (5.6) 65 non-MCI, never depressed	Cross-sectional study	Petersen criteria (Petersen, 2004)	Depressed: 28.2 (1.9) Non-depressed: (28.9 (1.2)	Instrumental activities of daily living Depression	Hamilton Depression Scale (HMD; Hamilton, 1967)	Significantly more depressed patients had a cognitive diagnosis than non-depressed patients

	Age: 74.0 (5.6)						
Brodaty et al., (2012)	799 including 319 MCI Age: 79.01 (4.7) 480 NCI Age: 78.41 (4.72)	Longitudinal	Petersen et al., (1997; 2004)	MCI: 27.61 (1.6) NCI: 28.45 (1.22)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	NPS were significantly associated with the amnestic-multiple-domain MCI subtype. There were no significant relationships between level of NPS at baseline and progression from MCI to dementia.
Caracciolo et al., (2012)	764 Age: 75+	Longitudinal	Petersen et al., (1999; 2005)	Not specified	Depression	Self-report of perceived sadness	53% of incident cases of MCI occurred in those with low mood over 6 years. Incidence of MCI in baseline low mood was 2.5 times higher than in people without low mood. 50 people with MCI progressed to dementia and 70% of these had baseline low mood.
Cherbuin et al., (2009)	18 MCI	Longitudinal	Petersen et al., (1999) criteria	29.11 (0.83)	Anxiety Depression	Goldberg Anxiety and Depression Scales (GAS; Goldberg & Hillier, 1979)	Taking anxiety and anti-depression medication was significantly predictive of progression to MCI from NCI over four years. 71% of those with MCI at wave one reverted to NCI by wave two. A self-report of anxiety or depression was only mildly predictive of MCI.
Dotson et al., (2010)	1239 aged 55.5 (18.8)	Longitudinal study as part of the Baltimore Longitudinal Study of Aging	Petersen criteria (Petersen, 2004) where MCI was diagnosed by impairment on a single domain or multiple domains	Not used	Depression	Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977)	88 participants were found to have MCI. MCI was not related to the recurrence of elevated depressive symptoms

			without significant functional loss				
Geda et al., (2006)	840 normal older people Age: 78.0	Longitudinal	Petersen criteria (Petersen, 2004)	28.0	Depression	15-item Geriatric Depression Scale (GDS-15; Yesavage et al., 1982)	17% of participants developed depression, of which 13.3% developed MCI, compared to 4.9% of participants without depression. The risk of MCI was greater for newly developed depression than a life history of depression. The incidence of MCI did not increase with increasing severity of depression.
Goveas et al., (2011)	6,376 aged 65-79	Prospective cohort study	Petersen criteria (Petersen et al., 1992), poor performance on at least one CERAD test, some decline in IADLs, intact ADLs, absence of other conditions that may explain decline in cognitive function and no dementia	Modified Mini-Mental State Examination (3MS) was used. Depressive Disorder: 95.0 (4.7) No Depressive Disorder: 96.0 (3.9)	Depressive disorders	Burnam screening algorithm (Using six items from the Center for Epidemiologic Studies Depression Scale [CES-D; Radloff, 1977] and two items from the National Institute of Mental Health's Diagnostic Interview Schedule [DIS])	Depressive disorder was associated with a greater risk of incident MCI
Kumar et al., (2006)	29 MCI Age: 62.65 (1.36) 520 Controls Age: 62.55 (1.46)	Cross-sectional study derived from the PATH Through Life Project	Consensus clinical judgement using Petersen (1999) criteria used to define MCI	Not used	Depression Physical disability	Goldberg Depression Scale (Goldberg et al., 1988) PRIME-MD Patient Health Questionnaire (PHQ) depression section (Spitzer et al., 1999).	Participants with MCI are more likely to have a lack of energy, feel slowed up, and feel worse in the mornings. A higher depression score and a DSM-IV diagnosis for minor depression were significant predictors for MCI
Lee et al., (2006)	129 meeting DSM-IV	Longitudinal	Performance 1.5 SD below mean	27.7 (2.1)	Depression	Duke Depression Evaluation Schedule	55.2% of participants had MCI at baseline and 44.8%

	criteria for major depression aged 68.0 (6.4)		levels on one or more of eight memory measures.			(Landerman et al., 1989). Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979)	had MCI at year one. 59.4% remained stable MCI and 26.7% progressed from NCI to MCI. Having MCI at baseline increased risk of having MCI at year one by four times even when no longer depressed.
Panza et al., (2008)	139 MCI 2824 Controls Age: 73.4 (5.69)	Longitudinal	Petersen et al., (1999) criteria but without requirement for subjective memory complaints	26.5 (2.2)	Depression	Geriatric Depression Scale (GDS-30; Yesavage et al., 1982)	Over 3.5 years there were 113 new cases of MCI but there were no significant associations found between depressive symptoms and the rate of incident MCI.
Shahnawaz et al., (2012)	767 Total participants Age: 78.53 (4.68) including 299 MCI	Cross sectional of community dwellers	Winblad et al., (2004) criteria	MMSE was not used	Depression Psychological distress (which primarily focuses on depression and anxiety)	15-item Geriatric Depression Scale (GDS-15; Yesavage et al., 1982) Kessler Psychological Distress Scale (K10; Kessler et al., 1994).	A significantly greater proportion of participants with clinically relevant depressive symptoms (GDS>6) met criteria for MCI than non-depressed participants (57.4% compared to 37.8%). Depressive symptoms were significantly associated with the amnestic MCI subtype (aMCI).
Spira et al., (2012)	302 Age: 86.9 (2.1)	Longitudinal population based	Petersen et al., (1999) criteria	Not specified	Depression	Geriatric Depression Scale 15 item version (GDS-15; Yesavage et al., 1982)	41.5% or participants were found to have MCI. 70% of those with elevated depressive symptoms had MCI.
Steenland et al., (2012)	3010 MCI 5845 Control Age: 73.0 (10.0)	Longitudinal	National Alzheimer's Coordinating Center Codebook (2006)	28.3 (2.0)	Depression	Clinician Interview GDS-5 (GDS-5; Yesavage et al., 1982) NPI-Q (NPI; Cummings et al., 1994)	Depression throughout the study was associated with progression from not cognitively impaired to having MCI, with 15% progressing. 38% of those with MCI progressed to

							having AD over 2.6 years. Past depression was not related to an increased risk of MCI.
Wilson et al., (2007)	1256 not cognitively impaired at baseline Age: 76.8 (7.7)	Longitudinal	Bennett et al., (2002) criteria.	28.7 (1.5)	Chronic distress Depression	Distress was assessed using six items from the Neuroticism scale of the NEO Five-Factor (Costa & McRae, 1992) Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977)	482 participants developed MCI over 12 years. The risk of MCI increased by approximately 2% for each point increase on the distress score. The risk of MCI increased by approximately 6% for each depression symptom on the CES-D. The association between depression and MCI did not remain significant when distress was controlled for.

Table 3.2: Studies investigating symptoms of mood in participants with MCI

Name and year	Participants, n, and mean age	Design	Definition of MCI used	MMSE	Symptoms assessed	Measures used in assessment	Results
Artero et al., (2008)	6892 including 2882 MCI Age: 74.2 (5.6)	Longitudinal study	Winblad et al., (2004) criteria	MMSE was not used	Depressive symptoms	Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) Mini International Neuropsychological Interview (MINI)	6.6% progressed to dementia, 56.5% remained stable with MCI and 37% reverted to normal cognitive functioning. Depressive symptoms were present in participants with MCI and subclinical depressive symptoms increased the risk of progression from MCI to dementia in female participants.
Baiyewu et al., (2012)	53 MCI Age: 80.9 (5.6)	Longitudinal study	Informant or clinician detected impairment in cognition, cognitive test scores 1.5 SD below a normative reference and normal ADLs	17.3 (3.0)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	90.6% of participants with MCI had any NPI symptom in the past four weeks. The most frequent symptom measured by the NPI was depression (45.3%). Anxiety was less common (18.9%).
Chan et al., (2003)	333 Dementia Age: 81.8 (7.1) 121 MCI Age: 78.4 (6.3)	Prospective observational cohort study	1.5 SD below the mean on any one test or 1 SD below the mean on two tests or more. No requirement for a subjective memory complaint, and the diagnosis was not limited to an objective memory	Dementia: 16.9 (7.2) MCI: 24.1 (3.2)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994) The Behavior Symptom Rating Scale (BSRS; Rabins, 1994)	47% of patients with MCI had at least one behavioural/psychiatric symptom. Symptoms experienced by patients with MCI were associated with IADL and ADL difficulties

			complaint, but instead an objective impairment on cognitive function was used				
Clement et al., (2009)	30 MCI Age: 65.97 (10.43) 27 control Age: 68.19 (8.37)	Cross sectional	Petersen et al., (2001) criteria	MMSE was not used	Psychiatric symptoms	Indices de Detresse Psychologique (French translation of Psychiatric Symptom Index; Illfield et al., 1976) Geriatric Depression Scale (Yesavage et al., 1982)	A main group effect for depression and anxiety was found for participants with MCI compared to healthy controls. Participants with MCI showed more mood disturbances.
Collie et al., (2002)	23 MCI Age: 65.9 (5.4) 23 control Age: 67.8 (7.8)	Cross sectional study as part of an on-going longitudinal study	Impaired cognitive function on three consecutive behavioural assessments.	MCI: 28.8 (1.1) Control: 28.1 (1.4)	Anxiety Depression	Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) The State-Trait Anxiety Inventory (STAI)	Participants with MCI experienced higher levels of state anxiety than control participants. Few subjects remained consistently impaired across all three assessments (13%).
Devier et al., (2009)	148 MCI Age: 67. 1 (9.9) 63 Control Age: 65.7 (9.3)	Longitudinal study	Subjective memory complaint and impaired performance on measures of delayed recall and preferably an informant's confirmation of memory decline	MCI: 27.5 (2.2) Control: 29.4 (0.8)	Anxiety Depression	The State-Trait Anxiety Inventory (STAI) Hamilton Depression Scale (HMD; Hamilton, 1967)	Mean anxiety and depression scores were higher for participants with MCI than for control participants. 26.4% of participants converted from MCI to AD. Depression was not a significant predictor for conversion. Higher trait anxiety was significantly associated with a lower risk of developing AD.
Di Iulio et al., (2010)	119 AD Age: 74.4 (7.0) 68 md-MCI	Cross sectional study	Petersen criteria (Petersen, 2004)	AD: 22.6 (3.2)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI;	Participants with md-MCI had similar levels of depressive symptoms to

	Age: 71.0 (6.5) 58 a-MCI Age: 7.1 (6.5) 107 Control Age: 68.1 (8.2)			md-MCI: 26.6 (2.0) a-MCI: 28.0 (1.8) Control: 28.5 (1.6)		Cummings et al., 1994)	those with AD, with 75% of md-MCI having clinically significant depressive symptoms. However, symptoms were more likely to be less severe in md-MCI than in AD. Apathy symptoms increased as the severity of cognitive symptoms increased.
Edwards et al., (2009)	521 with MCI Aged over 50 years	Longitudinal study	MCI was defined using a neuropsychological battery and included diagnoses or amnestic disorder and cognitive impairment no dementia (CIND) according to DSM III-R and DSM IV	Three or less NPS: 26.4 (2.7) Four or more NPS: 26.0 (2.7)	Functional status Neuropsychiatric symptoms	Clinical evaluation to determine NPS	Participants with high levels of NPS were more likely to have amnestic MCI than those with low levels of NPS. Depression was twice as frequent in patients with amnestic MCI. 75% of participants had at least one NPS
Elfgren et al., (2010)	24 with subjective memory complaint Age: 56.6 (8.3) 22 with MCI Age: 61.3 (6.3) 13 with Dementia Age: 62.4 (9.5) from outpatient memory clinic	Three year cohort study of people presenting with subjective memory complaints	Subjective memory complaint, impaired memory function, preserved general cognitive abilities, normal ADLs, no dementia	SMC: 29.1 (1.1) MCI: 27.9 (1.4) Dementia: 22.2 (2.8)	Depression Anxiety	Montgomery-Asberg depression scale (MADRS; Montgomery & Asberg, 1979) Anxiety measured through self-report and clinical signs	High prevalence of psychosocial stress and anxiety amongst participants with a subjective memory complaint
Fernandez-Martinez et al., (2010)	485 Total participants, including 91 MCI Age: 74.19 50 Control	Longitudinal	Petersen et al., (1999) criteria	MCI: 26.4 Control: 28.6	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	70.3% of people with MCI had at least one symptom on the NPI compared to 42% of control participants. 33% of those with MCI had depression compared to 8%

	Age: 74.55						of control participants and these differences were significant.
Forsell et al., (2003)	89 MCI Age: 83.1 (2.5) 353 Non-MCI Age: 84.3 (3.5)	Population based study (the Kungsholmen Project)	Subjects with MMSE scores 1SD below age/education-specific means	MCI: 22.6 (1.5) Non-MCI: 25.6 (2.7)	Psychiatric symptoms including depression, anxiety and psychotic symptoms	Comprehensive Psychopathological Rating Scale (CPRS) DSM-III-R	Memory complaints, suspiciousness, anxiety syndromes, social withdrawal, worrying over trifles and loss of initiative were more often found in people with MCI than Non-MCI
Gabryelewicz et al., (2006)	105 community dwelling individuals with MCI Age: 69.3 (7.2)	Longitudinal	Criteria similar to those set out by Petersen (1997): memory complaint, normal activities of daily living, objective memory impairment or an impairment in another area of cognitive function, normal global cognitive functioning and no dementia	27.2 (1.8)	Depression	Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979)	The mean MADRS score was significantly higher in participants who progressed to dementia than those who remained stable
Gallagher et al., (2011)	161 MCI Age: 73.7 (7.1)	Cross sectional study	Petersen criteria (Petersen, 2004)	Convertors: 24.7 (2.5) Stable MCI: 26.0 (2.4)	Neuropsychiatric symptoms	Behavioural Pathology in AD Rating Scale (BEHAVE-AD; Reisberg et al., 1996)	76% of participants had at least one NPS with anxiety being the most common at 52%. The total BEHAVE-AD score correlated with clinical severity and cognitive status. The annual rate of conversion was 19%.
Gallassi et al., (2007)	49 MCI aged 71.06 (8.07)	Cross sectional	Petersen et al., (2001) and Winblad et al., (2004) criteria	27.29 (2.31)	Depression Anxiety	Beck Depression Inventory (BDI; Beck et al., 1961)	Significantly more participants with MCI had symptoms of depression according to the NPI than

						Neuropsychiatric Inventory (NPI; Cummings et al., 1994) The State-Trait Anxiety Inventory (STAI; Spielberg et al., 1980)	participants with no cognitive impairment who had subjective cognitive complaints. No differences were found between groups on the BDI and STAI.
Geda et al., (2008)	319 MCI Age: 70-91 1590 Non-MCI Age: 70-91	Cross-sectional case control study comparing MCI with normal cognition	Petersen criteria (Petersen, 2004)	MMSE was not used	Neuropsychiatric symptoms	Neuropsychiatric Inventory Questionnaire (NPI-Q; Cummings et al., 1994)	51% of participants with MCI compared to 27% of participants with normal cognition had at least one neuropsychiatric symptom.
Hidaka et al., (2012)	1888 community dwelling Age: 73 (6.0)	Cross sectional	Cognitive complaints, objective impairment 1.5 SD below norms on at least one of five measures of cognition, preserved ADLs and no dementia	MMSE was not used	Depression	Geriatric Depression Scale, 15 item version (GDS-15; Yesavage et al., 1982)	19.5% of the sample had MCI. 26.3% of those with MCI also had depression compared to 18.0% of those with normal cognition. There was no difference found between the different subtypes of MCI and the prevalence of depression, but the multiple domain subtype was more prevalent in those with depression compared to those without depression.
Huddon et al., (2008)	33 Control Age: 66.2 (9.9) 18 a-MCI/D+ Age: 65.1 (11.1) 26 a-MCI Age: 65.2 (8.0)	Cross sectional	Petersen criteria (Petersen, 2004)	MMSE was not used	Depressive symptoms	Geriatric Depression Scale, five item version (GDS-5; Hoyl et al., 1999)	a-MCI/D+ made more errors on tests of cognitive function and were slower on tests of inhibition than controls or a-MCI
Houde et al., (2008)	60 MCI aged 74.5 (6.5)	Longitudinal	Petersen, et al (2001) criteria	27.1 (1.9)	Depression	Geriatric Depression Scale (Yesavage et al., 1982)	After a mean follow up of 4.3 years 60% progressed to dementia, equivalent to a 14% annual conversion rate.

							53% of those who progressed had depression at baseline. There was no difference between levels of depression at baseline between those who progressed to dementia and those who remained stable MCI.
Hwang et al., (2004)	28 MCI aged 73.4 (6.4)	Cross sectional	Petersen, et al (1999) criteria	28.7 (1.3)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	A significant difference in total NPI score was found between MCI and healthy controls. 25% of those with MCI had symptoms measured by the NPI and frequent symptoms included dysphoria, apthy, irritability and anxiety.
Johnson et al., (2012)	105 with MCI aged 67.0 (14.44)	Longitudinal	Petersen, et al (1999) criteria	MMSE was not used	Depressive symptoms	Geriatric Depression Scale (Yesavage et al., 1982)	33 participants had non-amnestic MCI and 72 participants had amnestic MCI. 51% of those with non-amnestic MCI had depression compared to 33% of those with amnestic MCI.
Kruger et al., (2012)	83 MCI aged 80.0 (7.7)	Longitudinal	Winblad, et al (2004) criteria	MMSE was not used	Depressive symptoms	Geriatric Depression Scale (Yesavage et al., 1982)	Participants with MCI reported more depressive symptoms on the GDS than healthy controls (4.7 vs 3.2). Each point increase on the GDS was associated with a 14% increase in the odds of an MCI diagnosis.
Lopez et al., (2005)	228 MCI Age: 70.1 (9.1) 427 AD Age: 73.2 (8.1)	Cross sectional study	Memory performance 1.5 SD below age/education	MCI: 25.9 (2.1) AD 23.5 (1.9)	Neuropsychiatric symptoms Depression	Semi-structured CERAD Interview	The proportion of MCI participants with major depression and aggression

			means, ADLs may be slightly impaired			Hamilton Depression Rating Scale (HMD; Hamilton, 1967)	was similar to the proportion in early AD.
Luppa et al., (2012)	1006 Age: 81.5 (4.8) Including 198 MCI	Cross sectional	Winblad et al., (2004) criteria	Not specified	Depressive symptoms	Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977)	Participants with MCI showed an increased risk of depressive symptoms but only the multiple domain or non-amnestic subtypes.
Lyketsos et al., (2002)	320 MCI Age: 75 (5.0) 362 Dementia Age: 77 (5.0)	Cross-sectional study derived from the longitudinal Cardiovascular Health Study	Cognitive decline not meeting DSM-IV criteria for dementia that was 1.5 SD below same age and education level means on standardised tests	Modified Mini-Mental State Examination was used but no figures are given	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	Just under half of participants with MCI exhibited neuropsychiatric symptoms
McDougall et al., (2006)	265 from SeniorWISE study Age: 75	A baseline study as part of a larger clinical trial	Criteria used were: having cognitive decline, memory impairment, no dementia, essentially normal activities of daily living, and cognitive complaints not normal for the age of the individual	Participants were required to have a score of >23, although those falling just below the cut-off, but scoring well on other measures were accepted	Health Anxiety Depression Memory complaints Memory performance Instrumental activities of daily living	Health Scale (from the Multilevel Assessment Instrument) The State-Trait Anxiety Inventory (STAI) Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977)	As memory performance decreased, symptoms of anxiety and depression increased. Individuals with poorer memory function performed significantly worse on the DAFS
McIlvane et al., (2008)	46 MCI Age: 77.3 (7.1) 29 Care partners	Cross-sectional study	Performance one to two SD below expectations for estimated premorbid intellect with no dementia	26.3 (3.14)	Psychologic Well-being Perceptions of Illness Coping	Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977)	Relatively low depressive symptoms, high life satisfaction, high mastery and high mental and physical quality of life were found. More emotion and problem focused coping

					Perceptions of Need for Help and Caregiving Service Use and Needs	Life Satisfaction Index-Z (LSI-Z; Wood et al., 1969) Short Form Health Survey (SF-36; Ware & Sherbourne, 1992)	was used in comparison to dysfunctional coping. Participants minimised their risk for AD and endorsed the effectiveness of health promotion activities to prevent AD. Participants reported relatively little stress in relation to memory problems
Muangpaisan et al., (2008)	77 MCI Age: 63.7 (7.3) 30 non-MCI Age: 66.3 (7.9)	Population based study	Petersen's criteria (Petersen et al., 1999), showing impairment on at least one measure of memory, clinician's judgement based on use of the Clinical Dementia Rating Scale (CDR; score of 0.5) and Global Deterioration Scale (GDS; Reisberg et al., 1982) score of 3	Thai version Mini Mental State Examination (TMSE) was used. Patients with scores of <24 were excluded. MCI: 26.5 (1.6) Non-MCI: 28.1 (1.8)	Neuropsychiatric symptoms Financial status	Neuropsychiatric Inventory (NPI; Cummings et al., 1994) Financial status was self-reported on the balance of income and expenditure	Patients with MCI had significantly higher levels of dysphoria, anxiety and night time behaviours, and a tendency to suffer from a higher degree of apathy. Male patients had a higher percentage of dysphoria and anxiety symptoms. Patients who reported a poor financial status had a higher percentage of dysphoria and anxiety symptoms
Palmer et al., (2007)	47 MCI 185 Control Age: 84.0 (5.1)	Longitudinal population based	Subjective memory complaint, no dementia, intact ADLs, objective evidence of cognitive impairment on neuropsychological tests	Not specified	Neuropsychiatric symptoms	Comprehensive Psychopathological Rating Scale (CPRS)	Participants with MCI were four times more likely to have one clinically significant psychiatric symptom compared to NCI participants. The presence of mood-related depressive symptoms did not increase risk of progression from MCI to dementia over three years. For each increase in the number of anxiety symptoms the risk of progression from MCI to dementia almost doubled.

Palmer et al., (2010)	131 MCI Age: 70.8 (6.5)	Longitudinal study	Petersen criteria (Petersen, 2004)	27.2 (2.0)	Depression Apathy Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994) Structured interview	36.6% of participants had depression but this was not found to increase the risk of conversion to AD. 10.7% of participants had apathy, with a 20% increase in risk of conversion to AD with each point increase for apathy on the NPI.
Panza et al., (2008)	1445 including 139 MCI	Longitudinal	Petersen et al., (1999) criteria	Not specified	Depressive symptoms	Geriatric Depression Scale (Yesavage et al., 1982)	15 participants with MCI progressed to dementia over 3.5 years. Of these, 9 had a GDS score >10. A significant association between depressive symptoms and rates of conversion to dementia in MCI was not found.
Ramakers et al., (2009)	263 MCI Age: 66.9 (7.7)	Longitudinal	MCI was broadly defined as a score of 2 or 3 on the Global Deterioration Scale (GDS; Reisberg et al., 1982). The amnestic subtype was further defined as a score 1.5 SD below the reference population on the Auditory Verbal Learning Test.	27.6 (2.1)	Depression	Hamilton Depression Scale (HMD; Hamilton, 1967)	Depression was associated with a lower risk of MCI when MCI was defined according to the broad definition of MCI but not when the amnestic subtype was used.
Ravaglia et al., (2008)	72 MCI Age: 78.1 (8.3) 595 Control Age: 72.3 (5.6)	Longitudinal Population based	Winblad et al., (2004) criteria but without requirement for subjective memory complaints	MCI: 21.4 (2.1) Control: 28.5 (1.3)	Depression	Geriatric Depression Scale (Yesavage et al., 1982)	The prevalence of depression in MCI was 44% which was almost two times that of the control participants.
Robert et al., (2006)	251 a-MCI Age: 71.9 (5.4)	Cross-sectional study derived	Memory complaints, at least	Individuals who	Anxiety Depression	Goldberg Anxiety Scale (GAS;	The proportion of conversion from MCI to

		from the PAQUID Study	one error on the MMSE three word recall task, or a score of <29 on the Isaac-Set Test (Isaacs et al., 1973)	developed dementia of Alzheimer type (DAT): 26.9 (1.1) Stable MCI: 27.6 (1.3)		Goldberg & Hillier, 1979) Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979)	dementia of Alzheimer type (DAT) was higher for participants with symptoms of apathy. 91.7% of the participants who developed DAT had at least one symptom of apathy compared to 26.4% of non-converted participants
Robert et al., (2002)	19 Control Age: 70.68 (8.21) 24 MCI Age: 71.67 (5.92) 12 PD Age: 64.1 (11.9) 60 AD Age: 74.90 (7.11)	Reliability and validity assessment of the Apathy Inventory	ICD-10 criteria	Control: 29 MCI: 28.2 (1.06) PD: 27.2 (3.5) AD: 22.55 (3.98)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	Scores on these measures for participants with MCI were between the scores for those with AD and control participants. The largest difference between the control participants and participants with MCI was for the lack of initiative dimension
Rosenberg et al., (2012)	1779 MCI Age: 75.4 (9.6)	Multi-centre population study	Objective or subjective evidence of cognitive impairment but no significant functional impairment to meet criteria for dementia	27.8 (7.5)	Neuropsychiatric symptoms Depression	Neuropsychiatric Inventory (NPI; Cummings et al., 1994) 15-item Geriatric Depression Scale (GDS-15; Yesavage et al., 1982)	Participants with greater levels of executive dysfunction had increased symptoms of NPS. 27.3% of participants had depressive symptoms.
Rozzini et al., (2007)	94 a-MCI Age: 71.7 (8.3) 26 na-MCI Age: 68.8	Longitudinal clinic based	Artero et al., (2006)	a-MCI: 26.2 (1.8) na-MCI: 27.4 (1.8)	Anxiety Neuropsychiatric symptoms Depression	Geriatric Depression Scale 15 item version (GDS-15; Yesavage et al., 1982) Hamilton Anxiety Scale (Hamilton, 1967) Neuropsychiatric Inventory (NPI;	83% of those with a-MCI and 73% of those with na-MCI had depressive symptoms. 75% of those with a-MCI and 73% of those with na-MCI had symptoms of anxiety. 99 participants were re-evaluated one year later and

						Cummings et al., 1994)	42 of these had progressed to dementia.
Rozzini et al., (2009)	57 outpatients with cognitive complaints Age: 71.2 (7.3)	Validation of Geriatric Anxiety Inventory	Cognitive complaint, no dementia, change from normal functioning in IADL/ADL, preserved general functioning, cognitive functioning 1.5 SD below means	27.7 (1.9)	Anxiety Neuropsychiatric symptoms Depression	Geriatric Anxiety Inventory (Pachana et al., 2007) Neuropsychiatric Inventory (NPI; Cummings et al., 1994) Geriatric Depression Scale (Yesavage et al., 1982) Anxiety Status Inventory (Zung, 1971)	44 participants had MCI and anxiety. Those with anxiety showed more behavioural and psychological disturbances, more depressive symptoms and were more compromised in instrumental activities of daily living. Executive functions were independently related to anxiety disorders in participants.
Ryu et al., (2011)	241 MCI Age: 72.9 (5.7)	Population based study	Petersen's criteria (Petersen, 2004) of cognitive concern expressed by an informant or the participant, cognitive impairment in one domain or more, intact activities of daily living, and no dementia	22.5 (3.3)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994) Korean version of the Geriatric Depression Scale (GDS-K; Cho et al., 1999) Quality of Life-AD (QoL-AD; Logsdon et al., 1999)	At six month follow up 46.6% of participants had at least one NPS with 30.9% having clinically significant symptoms. Those with more symptoms at baseline were more likely to have persistent symptoms and a poorer quality of life. Depression, anxiety and sleep disturbances were the most common symptoms
Solfrizi et al., (2007)	2963 including 139 MCI	Longitudinal community	Petersen et al., (1999) criteria but without requirement for subjective memory complaints	Those scoring high on depression: 21.3 (4.2) Without depression: 21.7 (4.2)	Depression	Geriatric Depression Scale (Yesavage et al., 1982)	63.3% of participants with MCI had high levels of depression. 36 participants completed a second analysis and all scored highly on the measure of depression.

Teng et al., (2007)	51 MCI Age of those who progressed to AD: 75.8 (6.0) Age of those who did not progress to AD: 71.9 (7.3)	Longitudinal Clinic based	Petersen et al., (2004) criteria	Those who progressed to AD: 26.3 (2.8) Those who did not progress to AD: 28.0 (1.7)	Neuropsychiatric symptoms	Neuropsychiatric Inventory (NPI; Cummings et al., 1994)	12 participants progressed to AD over 2.1 years. Baseline NPI symptoms were higher in those who progressed than in those who did not. Participants who progressed were more likely to have depression but this was not significant after corrections.
Van der Linde et al., (2010)	389 MCI aged 73.8 (0.43)	MRC-CFAS Longitudinal	Subjective memory complaint, performance on tests of memory or other cognitive domains below 16th percentile, no impairment in general cognitive function	25.4 (0.14)	Behavioural and psychological symptoms	Structured interviews with participants and informants which include the Cambridge Mental Disorders of the Elderly Examination (CAMDEX; Roth et al., 1986)	Depression increased as cognitive function worsened but there was no difference between those with MCI and healthy controls in the prevalence of anxiety. 61% of participants with MCI had depression.
Vicini Chilovi et al., (2009)	124 including 50 without depression Age: 71.6 (8.5) 38 with depression Age: 70.8 (7.6)	Longitudinal Clinic based	Winblad et al., (2004) criteria	Without depression: 26.8 (1.9) With depression: 26.7 (1.8)	Depression	DSM-IV Criteria Neuropsychiatric Inventory (NPI; Cummings et al., 1994) Geriatric Depression Scale 15 item version (GDS-15; Yesavage et al., 1982) Hamilton Anxiety Scale (Hamilton, 1967)	24% of those with MCI but not depression progressed from MCI to dementia. 7.9% of those with MCI and depression progressed to dementia. Depression appeared to have a protective effect on progression from MCI to dementia.
Zhang et al., (2012)	38 MCI Age: 71.0 (8.0) 49 controls	Observational	Petersen et al., (1999) criteria	28.0 (1.0)	Neuropsychiatric symptoms	Neuropsychiatric Inventory Chinese Version (Xie et al., 2004)	81.6% of participants with MCI had at least one NPS. Common symptoms were depression (28.9%) and anxiety (26.3%)

Zihl et al., (2009)	24 MCI Age: 65.8 (5.8) 50 Depressed Age: 64.1 (6.4) 20 Control Age: 63.4 (1.0)	Cross-sectional study	Winblad et al., (2004) revised diagnostic criteria	MCI: 27.8 (1.8) Depressed: 28.3 (1.6) Control: 29.8 (0.4)	Depressive symptoms	Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979)	Participants with MCI and participants with depression plus cognitive impairments have a very similar neuropsychological pattern in the domains of attention, memory and executive functions. Cognitive dysfunction remained in participants with depression even after remission of depressive symptomology

Quality Assessment

Table 3.3 shows the quality score for each study. The score in each case represents the number of unmet criteria, and hence lower scores indicate higher quality. Fifteen studies met all seven quality criteria, eighteen studies failed to meet one, eighteen studies failed to meet two, eight studies failed to meet three and only one study failed to meet four (Lee, Potter, Wagner, Welsh-Bohmer, & Steffens, 2006).

Table 3.3: Quality assessment of included studies

	Representative sample	Was an appropriate sample size used?	Acceptable classification of MCI	Acceptable measures of mood	No confounding factors	Reporting of withdrawals	Statistical methods appropriate for the study design	Score
Adler et al., (2004)	×	×	✓	✓	N/A	×	✓	3
Artero et al., (2008)	✓	✓	✓	✓	✓	×	✓	1
Baiyewu et al., (2012)	✓	×	×	✓	✓	✓	✓	2
Barnes et al., (2006)	✓	✓	×	✓	✓	×	✓	2
Bhalla et al., (2009)	×	✓	✓	✓	×	N/A	✓	1
Brodaty et al., (2012)	✓	✓	✓	✓	✓	✓	✓	0
Caracciolo et al., (2012)	✓	✓	✓	✓	✓	×	✓	1
Chan et al., (2003)	✓	✓	✓	✓	✓	N/A	✓	0
Cherbuin et al., (2009)	✓	✓	✓	✓	✓	×	✓	1
Clement et al., (2009)	×	×	✓	✓	×	N/A	✓	3
Collie et al., (2002)	✓	✓	✓	✓	✓	×	✓	1
Devier et al., (2009)	×	✓	×	✓	×	✓	✓	3
Di Iulio et al., (2010)	×	✓	✓	✓	×	N/A	✓	2
Dotson et al., (2010)	✓	✓	✓	✓	✓	×	✓	1

Edwards et al., (2009)	×	✓	✓	×	N/A	×	✓	3
Elfgren et al., (2010)	×	×	✓	✓	✓	✓	✓	2
Fernandez-Martinez et al., (2010)	×	✓	✓	✓	×	N/A	✓	2
Forsell et al., (2003)	✓	✓	×	✓	✓	N/A	✓	1
Gabryelewicz et al., (2006)	✓	✓	✓	✓	N/A	✓	×	1
Gallagher et al., (2011)	×	✓	✓	×	N/A	×	✓	3
Gallassi et al., (2007)	×	✓	✓	✓	×	N/A	×	3
Geda et al., (2006)	✓	✓	✓	×	N/A	×	✓	2
Geda et al., (2008)	✓	✓	✓	×	N/A	N/A	✓	1
Goveas et al., (2011)	×	✓	✓	✓	✓	×	✓	2
Hidaka et al., (2012)	✓	✓	✓	×	N/A	✓	✓	1
Huddon et al., (2008)	×	✓	✓	×	✓	N/A	✓	2
Houde et al., (2008)	×	✓	✓	✓	N/A	N/A	×	2
Hwang et al., (2004)	×	✓	✓	✓	✓	N/A	✓	1
Johnson et al., (2012)	✓	✓	✓	✓	✓	N/A	✓	0
Kruger et al., (2012)	✓	✓	✓	✓	×	N/A	✓	1
Kumar et al., (2006)	✓	✓	✓	✓	✓	N/A	✓	0
Lee et al., (2006)	×	✓	×	✓	×	×	✓	4
Lopez et al., (2005)	×	✓	✓	✓	×	N/A	✓	2
Luppa et al., (2012)	✓	✓	✓	✓	✓	N/A	✓	0
Lyketsos et al., (2002)	✓	✓	✓	✓	✓	×	✓	1
McDougall et al., (2006)	✓	✓	✓	✓	×	N/A	✓	1
McIlvane et al., (2008)	×	×	×	✓	N/A	N/A	✓	3
Muangpaisan et al., (2008)	✓	✓	✓	✓	✓	N/A	✓	0
Palmer et al., (2007)	✓	✓	✓	✓	✓	✓	✓	0
Palmer et al., (2010)	✓	✓	✓	✓	✓	✓	✓	0
Panza et al., (2008)	✓	✓	✓	✓	✓	✓	✓	0
Panza et al., (2008)	✓	✓	✓	✓	✓	✓	✓	0
Ramakers et al., (2009)	×	✓	×	✓	N/A	✓	✓	2

Ravaglia et al., (2008)	✓	✓	✓	✓	✓	✓	✓	0
Robert et al., (2002)	×	✓	✓	✓	✓	N/A	✓	1
Robert et al., (2006)	×	✓	×	✓	✓	✓	✓	2
Rosenberg et al., (2011)	✓	✓	✓	✓	✓	N/A	✓	0
Rozzini et al., (2007)	×	✓	✓	✓	✓	×	✓	2
Rozzini et al., (2009)	×	✓	✓	✓	N/A	N/A	✓	1
Ryu et al., (2011)	✓	✓	✓	✓	✓	×	✓	1
Shahnawaz et al., (2012)	✓	✓	✓	✓	✓	N/A	✓	0
Solfrizi et al., (2007)	✓	✓	✓	✓	✓	N/A	✓	0
Spira et al., (2012)	×	✓	✓	×	N/A	×	✓	3
Steenland et al., (2012)	×	✓	✓	✓	✓	×	✓	2
Teng et al., (2007)	×	✓	✓	✓	N/A	×	✓	2
Van der Linde et al., (2010)	✓	✓	✓	✓	✓	N/A	✓	0
Vicini Chilovi et al., (2009)	×	✓	✓	✓	N/A	×	✓	2
Wilson et al., (2007)	×	✓	✓	✓	N/A	×	✓	2
Zhang et al., (2012)	×	✓	✓	✓	✓	N/A	✓	1
Zihl et al., (2009)	×	✓	✓	✓	✓	×	✓	2

Key	
✓	Criterion met
×	Criterion not met
N/A	Criterion not applicable

Participant characteristics

The included studies describe either clinical or community samples. In the clinical studies the concept of MCI was applied to individuals presenting at memory clinics or experiencing memory problems, whether self-referred or referred by General Practitioners (GPs). In the community studies MCI criteria were applied to samples of older people drawn from the general population.

Mean MMSE scores were specified for the majority of the clinical studies, although in some cases the Modified Mini Mental State Exam (3MS) was used instead (D. E. Barnes et al., 2006; Goveas, Espeland, Woods, Wassertheil-Smoller, & Kotchen, 2011; Lyketsos et al., 2002), and in one case the Thai version of the MMSE was used (Muangpaisan, Intalapaporn, & Assantachai, 2008). Mean MMSE scores ranged from 22.5 (Ryu, Ha, Park, Yu, & Livingston, 2011) to 28.7 (Hwang, Masterman, Ortiz, Fairbanks, & Cummings, 2004) and the mean across studies where data were available was 27.2 for the clinical studies. Mean MMSE scores were given for nine of the twenty-four community samples and ranged from 17.3 (Baiyewu et al., 2012) to 28.8 (Collie, Maruff, & Currie, 2002). The mean across studies where data were available was 25.8 for community samples.

The number of participants ranged from 18 (Cherbuin et al., 2009) to 8855 (Steenland et al., 2012). In studies where data regarding the age of participants were available, the age of participants ranged from 55.5 years to 86.9 years (mean across studies: 72.6 years).

MCI definitions used

Various classification systems for MCI were used. Twenty-seven studies used the Petersen et al (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999) criteria which require a subjective memory complaint, deficits in cognitive function compared to age and education norms, intact activities of daily living and intact global cognition, and stipulate that the individual should not meet criteria for dementia.

Twenty-two studies used criteria similar to those of Petersen (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999) in terms of deficits on neuropsychological test batteries. One study required a deficit of 1.5SD (standard deviation) below the mean on any single test or 1SD below the mean on two or more tests of cognitive function (Chan et al., 2003). Other research required that participants had an MMSE score of 1SD below age- and education-

specific means (Forsell, Palmer, & Fratiglioni, 2003). Other studies (Devier et al., 2009; G. J. McDougall et al., 2006; Rozzini et al., 2009) did not specify the cut-off scores for the neuropsychological tests used. Of the twenty-two studies, ten required a subjective memory complaint in order to classify participants as having MCI (Devier et al., 2009; Elfgren, Gustafson, Vestberg, & Passant, 2010; Hidaka et al., 2012).

ICD-10 criteria which refer to mild cognitive disorder (Robert et al., 2002) were used in one study. These criteria require that an individual must have difficulties in new learning, memory, concentration, thinking, or language, and stipulate that there should be abnormality or decline in performance on neuropsychological tests.

Seven studies (Kruger et al., 2012; Luppa et al., 2012) used revised diagnostic criteria for MCI (Winblad et al., 2004). These criteria specify that an individual should not meet criteria for dementia and should show cognitive decline through a subjective memory complaint in conjunction with deficits on objective cognitive tests. Basic ADLs should be preserved and complex instrumental functions should be minimally impaired.

Criteria used in one study were derived from previous investigations of the same sample (Wilson et al., 2007). The National Alzheimer's Coordinating Center Codebook (2006), which is a comprehensive assessment that considers an individual's cognitive functioning along with health and demographic factors, was used in another study (Steenland et al., 2012).

Definitions of mood

The studies reviewed used several terms to describe mood. Most studies directly investigated either depression (D. E. Barnes et al., 2006; Geda et al., 2006) or anxiety

(Rozzini et al., 2009). Several studies investigated both anxiety and depression (G. J. McDougall et al., 2006; Steenland et al., 2012).

The term neuropsychiatric symptoms was used in nineteen of the studies (Lyketsos et al., 2002; Palmer et al., 2010; Ryu et al., 2011). Neuropsychiatric symptoms are typically measured with the NPI and the term encompasses symptoms in the domains of delusions, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, aberrant motor behaviour, sleep and night time behaviours, and appetite and eating disorders. This review is concerned with depression/dysphoria and anxiety, and so measurements of these aspects of neuropsychiatric symptoms were considered where information was given. One study referred to 'psychosocial stress' (Elfgren et al., 2010). The term refers to patient reports of experiences of daily stress during the last three months. This was included here due to its association with anxiety.

Selection of measures for assessment of mood

A range of measures was used to assess mood and these are summarised in Table 4. Five studies (Adler et al., 2004; Bhalla et al., 2009; Devier et al., 2009; Lopez et al., 2006; Ramakers et al., 2009) used the Hamilton Depression Scale (HAM-D). Sixteen studies (Chan et al., 2003; Di Iulio et al., 2010; Lyketsos et al., 2002; Palmer et al., 2010) used the Neuropsychiatric Inventory (NPI; Cummings et al., 1994). In addition, two studies (Geda et al., 2008; Rosenberg et al., 2013) used the shortened form of the NPI, the Neuropsychiatric Inventory Questionnaire (NPI-Q). Seven studies (Artero et al., 2008; D. E. Barnes et al., 2006; Collie et al., 2002; Dotson, Beydoun, & Zonderman, 2010; Goveas et al., 2011; G. J. McDougall et al., 2006; McIlvane, Popa, Robinson, Houseweart, & Haley, 2008) used the Center for Epidemiologic Studies Depression Scale (CES-D;). Four studies (Elfgren et al., 2010; Gabryelewicz et al., 2007; Robert et al., 2006; Zihl, Reppermund, Thum, & Unger,

2010) used the Montgomery Asberg Depression Scale (MADRS). Nine studies used the full version of the Geriatric Depression Scale (GDS-30), six studies used the fifteen-item version of the Geriatric Depression Scale (GDS-15;) two studies (Huddon, Belleville, & Gauthier, 2008; Steenland et al., 2012) used the shortened five-item version (GDS-5) and one study (Ryu et al., 2011) used the Korean version (GDS-K). One study used the Comprehensive Psychopathological Rating Scale (Forsell et al., 2003) which contains mostly self-report items but also includes some observer-rated items, and another used the BEHAVE-AD scale (Gallagher et al., 2011). One study used the Goldberg Depression Scale and the depression section of the PRIME-MD Patient Health Questionnaire (PHQ) (Johnson et al., 2012). One study used a self-report rating of perceived sadness (Caracciolo et al., 2011).

Several measures were used to assess anxiety, such as the State-Trait Anxiety Inventory (STAI) (G. J. McDougall et al., 2006) and the Goldberg Anxiety Scale (GAS) (Robert et al., 2006). One study used both the Geriatric Anxiety Inventory (GAI) and the Anxiety Status Inventory (ASI) (Rozzini et al., 2009).

Relationship between MCI and mood

A meta-analysis was conducted to investigate whether people with MCI were more likely to have low mood than those who are not cognitively impaired (Figure 3.2) and this shows that the odds of having depressive symptoms are increased in people with a classification of MCI (odds ratio [OR] = 2.01; 95% CI: 1.50, 2.69).

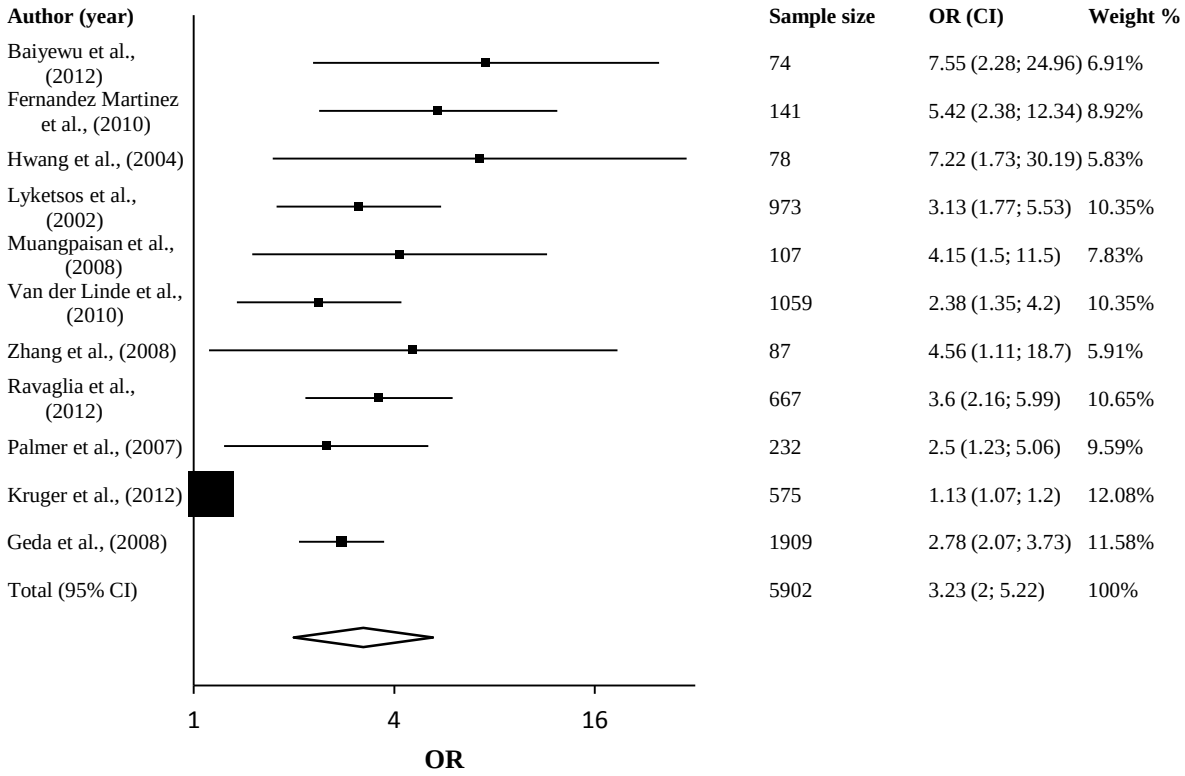

Figure 3.2: The odds of having depressive symptoms in individuals with MCI.

A further meta-analysis (Figure 3.3) was conducted to ascertain whether symptoms of anxiety were more prevalent in people classified as having MCI than in those without cognitive impairment. In seven of the eight studies included in this analysis, the odds of having symptoms of anxiety are increased by 1.43 to 3.6 if an individual is classified as having MCI. One study (Hwang et al., 2004) showed an increase in the odds of having symptoms of anxiety of 16.5. The overall result shows an increase in the likelihood of symptoms of anxiety in people with MCI (OR = 2.50; 95% CI: 1.69, 3.71).

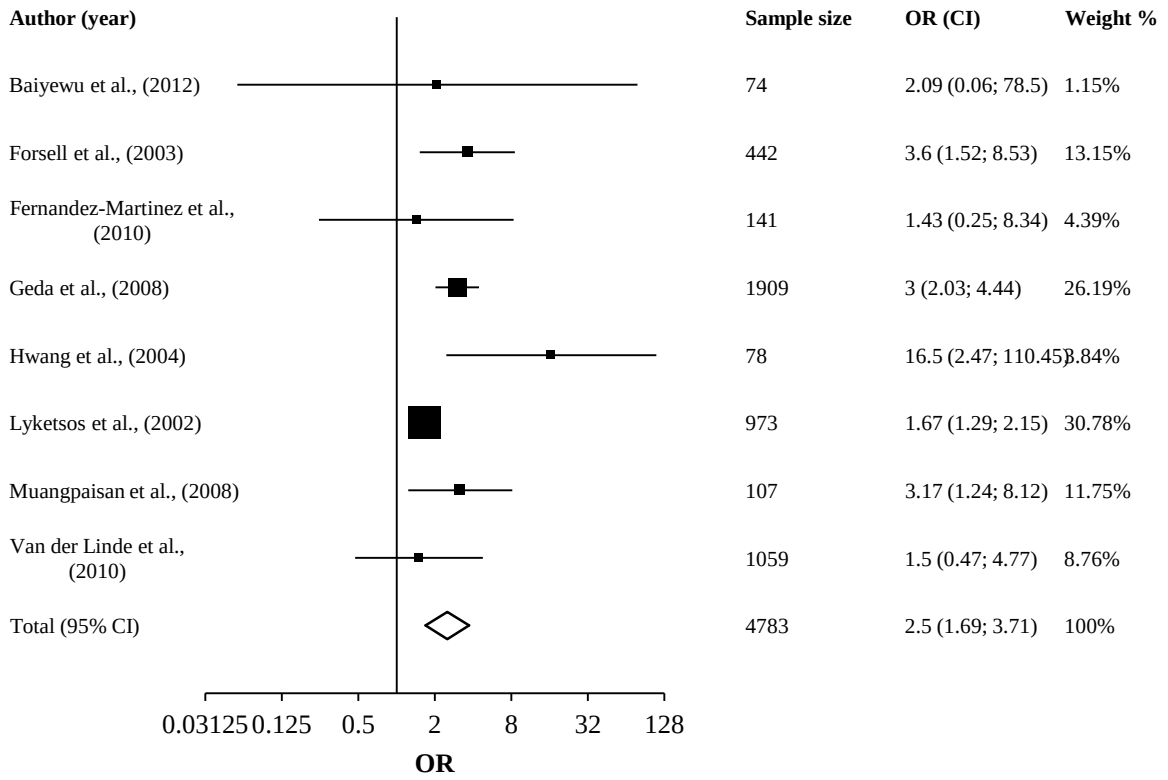

Figure 3.3: The odds of having symptoms of anxiety in individuals with MCI.

Four studies examined the relationship between the subtype of MCI and symptoms of depression or anxiety. Individuals with multiple-domain MCI experienced a similar frequency of depressive symptoms to individuals with Alzheimer's disease, which is greater than older people with normal cognitive functioning, although the symptoms were likely to be milder (Di Iulio et al., 2010). One study showed that more individuals with non-amnestic MCI than individuals with the amnestic subtype of MCI had depressive symptoms,(Johnson et al., 2012) whereas another reported there were similar levels of symptoms of depression and anxiety for the amnestic and non-amnestic subtypes (Rozzini et al., 2008).

Temporal relationship

Follow up times ranged from 2.1 years (Teng, Lu, & Cummings, 2007) to 12 years (Wilson et al., 2007). Three studies commented on the effect of the time of onset of mood

problems. Two studies reported that the risk of MCI was greater for people with newly developed depression rather than a life history of depression (Bhalla et al., 2009; Geda et al., 2006) and one study found that past depression was not related to an increase in the risk of incident MCI (Steenland et al., 2012).

Several studies investigated the progression from not cognitively impaired to a classification of MCI, and five studies showed that depressive symptoms or low mood increased the risk of being classified as having MCI. Those with low mood were 2.5 times more likely to progress to a classification of MCI over six years (Caracciolo et al., 2011). Two studies concluded that a diagnosis of depression was associated with a greater incidence of MCI (Goveas et al., 2011; Kumar, Jorm, Parslow, & Sachdev, 2006). Taking medication for symptoms of anxiety or depression was found to be significantly predictive of a progression from not cognitively impaired to MCI over four years (Cherbuin et al., 2009). Self-report of anxiety or depression was only mildly predictive of MCI. One study followed participants for 3.5 years and found no significant association between depressive symptoms and the rate of incident MCI (Panza et al., 2008). A further study reported that the risk of MCI increased by approximately 6% for each symptom of depression endorsed by participants, but this did not remain significant when proneness to distress was controlled for (Wilson et al., 2007). A meta-analysis was conducted using studies where data were available to examine the risk of progressing from not cognitively impaired to having MCI when symptoms of depression are present. Figure 3.4 shows an increase in the risk of progression from no cognitive impairment to MCI when depressive symptoms are present (hazard ratio [HR] = 2.40; 95% CI: 191, 3.02).

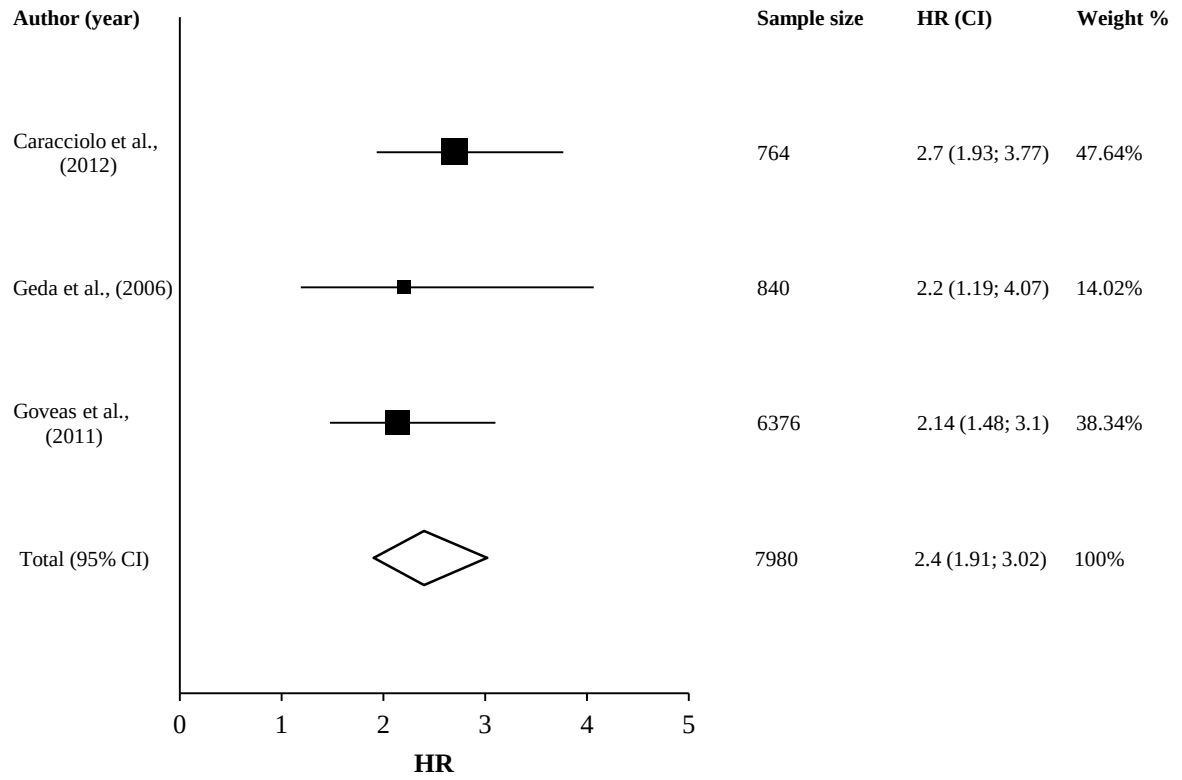

Figure 3.4: The effect of depressive symptoms on risk of progression from not cognitively impaired to a classification of MCI.

Progression from MCI to dementia

Eight studies investigated the risk of progression from MCI to dementia over time and most found that depression was not a risk factor. Only one study found that a higher score on measures of depression was significantly more frequent in individuals who progress from MCI to dementia (Gabryelewicz et al., 2007). One study found that whilst there was no difference in the baseline levels of depressive symptoms between individuals who progressed to dementia and those who did not, the persistence of depressive symptoms increased risk of progression (Houde et al., 2008). A further study followed participants for 2.1 years and found that baseline NPI scores for depression were higher in those who progressed from MCI to dementia than in those who continued to be classified as having MCI, although this did not remain significant after correction for multiple

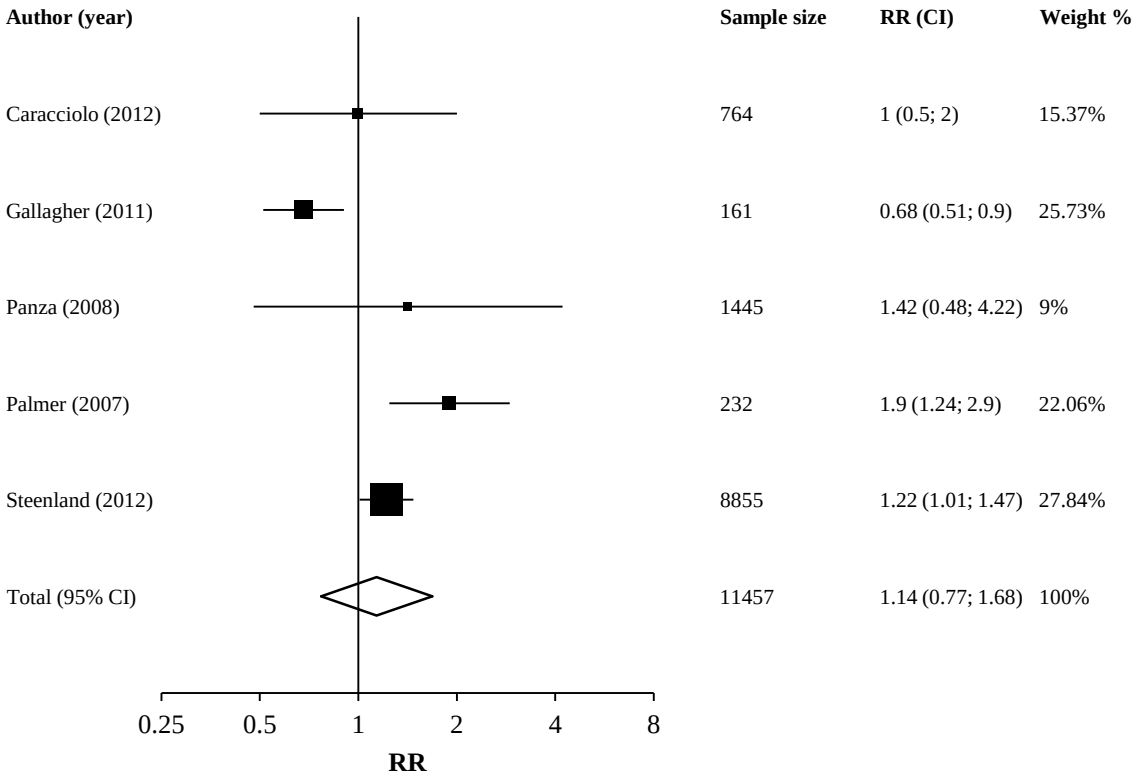

Figure 3.5: The effect of depressive symptoms on risk of progression from a classification of MCI to a diagnosis of dementia.

comparisons (Teng et al., 2007). A protective effect of depression on the progression from MCI to dementia has also been reported (Vicini Chilovi et al., 2009). A meta-analysis was conducted using studies where data were available to examine the effect of depressive symptoms on the risk of progression to dementia from MCI. Figure 3.5 shows an overall increase in risk of progressing from MCI to dementia when depressive symptoms are present (relative risk [RR] = 1.14; 95% CI: 0.77, 1.68).

Only a small number of studies considered anxiety and it was not possible to conduct a meta-analysis to examine the effect of anxiety on progression from MCI to dementia. One study found that as the number of anxiety symptoms increased, the risk of progression from MCI to dementia almost doubled. (Palmer et al., 2007) However, another study found that

higher levels of trait anxiety were significantly associated with a lower risk of conversion to Alzheimer's disease (Gallagher et al., 2011).

Discussion

This review aimed to explore the relationship between mood and MCI through investigating whether symptoms of depression and anxiety are more likely in individuals who have been classified as having MCI and examining the effect of such symptoms on the risk of progression from no cognitive impairment to MCI or from MCI to dementia. To the best of our knowledge, this review is the first to synthesise studies investigating mood and MCI, assess the effects of mood on progression, and conduct meta-analyses using available data to clarify the relationships explored.

The meta-analyses showed that symptoms of depression or anxiety were more common in people classified as having MCI compared to people with normal cognitive functioning. Having symptoms of depression increased the risk of progression from not cognitively impaired to MCI, and from MCI to dementia. Data were not available to calculate whether there was an increase in risk associated with symptoms of anxiety.

There are several issues that should be considered when interpreting the findings of this review. Firstly, the source of the study population can be problematic when applying the concept of MCI. Clinical samples tend to be drawn from individuals who have presented at memory clinics for a detailed assessment, allowing the identification of subtle difficulties, whereas when applying MCI criteria retrospectively in community samples, individuals with more subtle impairments may not be identified and so results may be biased towards those who show a greater level of impairment (Chertkow, 2002). Research suggests that there are differences between clinical samples and community samples in the rate of conversion from

MCI to dementia (Bruscoli & Lovestone, 2004), with research showing that 15% of clinical samples but only 7.5% of community dwellers converted to dementia (Baars et al., 2009).

MMSE scores were provided for the majority of the studies reviewed and whilst most scores fall within expected ranges, some studies report MMSE scores that are much lower that would be anticipated for individuals who have been classified as having MCI (Forsell et al., 2003). It could be suggested that individuals showing this level of cognitive function may be more impaired than other individuals who have been classified as having MCI and hence may not be directly comparable.

A number of studies included a small number of participants (Elfgren et al., 2010; Rozzini et al., 2009) and these may not be as representative of the MCI population as studies using larger samples (Goveas et al., 2011; Steenland et al., 2012). The age of participants in the included studies was within the expected range except for one study in which the youngest participants were aged 55.5 years (Dotson et al., 2010). This is younger than would be expected, as studies investigating MCI typically consider participants who are over 65 years old.

Several different definitions of MCI were used in the included studies. A recent study found that the application of different classification systems resulted in the same individuals being concurrently classed as having MCI according to certain definitions and healthy according to others (Matthews et al., 2008), highlighting the need for agreement on which definition to use. The heterogeneity of the definitions of MCI used in the included studies could suggest that participants from different studies may not have the same levels or types of cognitive impairment.

The majority of studies included in this review either did not specify which subtype of MCI was investigated or included only participants with the amnestic subtype. This may

mean that individuals with other subtypes were unaccounted for, or where the subtype of MCI was not specified, participant groups could be considered to be overly heterogeneous, which may have attenuated any effects. The subtype of MCI investigated may also have an impact on the relationship between MCI and depression or anxiety. Only four of the studies included in this review investigated the effect of MCI subtype, and the results were mixed.

Several of the included studies required a subjective memory complaint as part of the MCI definition, although there is controversy as to the usefulness of this. Research has recommended that subjective memory complaint should not be a diagnostic criterion because it lacks accuracy (Lenehan et al., 2012). Instead objective evidence for the stability or decline of cognitive function over time should be sought. Corroboration by an informant is not a requirement, but it is valuable as it can help to ensure the accuracy of the subjective memory complaint. Furthermore, increased levels of subjective memory complaints were found to be correlated with increased levels of anxiety and depression, independent of whether an individual was classified as having MCI, suggesting that mood may influence the accuracy with which people appraise their memory. The presence of depression may inflate memory problems by enhancing negative attributions. (Roberts et al., 2009) The association between subjective memory complaints and depression is stronger than the association between subjective memory complaints and objective memory impairments (Minett et al., 2008). Research has shown that including subjective memory complaints in the criteria for MCI classification does not increase predictive ability (Baars et al., 2009). Subjective memory complaints may therefore be unnecessary and could potentially contribute to identification of more false positives or false negatives (Lenehan et al., 2012).

The findings may also have been affected by the use of several different measures of mood. The NPI is well established for use with individuals who have impairments in cognitive functioning; however, the shortened version of the NPI (NPI-Q) should be

interpreted with caution as it contains fewer questions than the original NPI. In addition, both versions of the NPI are based on informant report rather than being directly administered to the participant, which could allow for symptoms to be wrongly estimated or misattributed.

A further issue is the overlapping nature of depression and anxiety. These frequently coexist and may interact with each other. Research has found that anxiety symptoms were significantly and directly associated with depressive symptoms. In one study, taken together, symptoms of anxiety and depression were associated with a decline in cognitive function but the association did not hold for depressive symptoms alone (Stillman, Rowe, Arndt, & Moser, 2012). Therefore, studies that consider only depression or anxiety may be missing participants with milder symptoms of one mood problem that interact with symptoms of the other.

The use of neuropsychological tests to quantify cognitive functioning is not straightforward. Neuropsychological models of memory indicate that there are several different systems of memory, with different processes and modalities involved. However, memory impairments are often treated much more simply in the context of MCI. Aspects and processes of memory may be affected in MCI in different ways, with some preserved and others impaired. In addition, depression or anxiety may differentially affect some aspects or processes compared to others. The use of neuropsychological tests is complex as different tests assess different aspects of memory and use different modalities, and therefore the results of tests may not be directly comparable. In addition, interpreting the results from neuropsychological tests is difficult as simple cut-off scores are not used. Instead, individual performance is assessed in relation to age- and education-specific norms (Clare, 2008). Relying on one single test may be problematic, and research suggests that instead of requiring marked impairment on one single test it may be more appropriate to focus on a pattern of

performance across a range of tests that indicate milder, but more widespread impairment (Fisk & Rockwood, 2005; Jak, Bondi, Delano-Wood, Wierenga, & Corey-Bloom, 2009).

The review highlights additional issues that should be considered. This review only included articles published in English and so relevant articles published in other languages may have been missed. One article published in Spanish was excluded. In addition, this review only included published items as the search methods did not reveal any unpublished literature; hence there may be a publication bias towards studies that have found an association between MCI and mood.

This review has several implications. From a theoretical viewpoint the review demonstrates that systems for classifying MCI should take symptoms of depression and anxiety into account. At present, classification systems often exclude individuals with mood problems, which may distort prevalence and incidence rates for MCI. In a practical sense, there is a need to help individuals overcome symptoms of depression and anxiety. At present the direction of the relationship between symptoms of depression or anxiety and MCI has not been established, but this review has shown that the odds of having MCI are increased in those with depressive symptoms. Further research may be able to clarify this relationship and hence allow interventions to be targeted accordingly. This review has implications for clinical practice, general practitioners and front-line medical staff who need to recognise subtle symptoms in older people, in relation to both mood and cognitive function, and to encourage older people to talk about their concerns.

This review has demonstrated that evidence exists for a relationship between MCI and mood. Whilst the direction of the relationship cannot be firmly established at the moment, there is scope for further investigation involving participants with either mood problems, cognitive impairment, or both. The findings of this review also suggest that symptoms of

depression may have an effect on the progression of cognitive impairment and such findings could be used to increase awareness amongst older people and general practitioners. More knowledge in this area may provide a foundation for attempts to slow or prevent progression from MCI to dementia in order to afford a better quality of life for those affected by cognitive impairment and their families.

Chapter 4: Subjective memory complaints, mood and MCI: A follow-up study

Summary

Subjective memory complaints (SMC) form part of the criteria for many accepted definitions of mild cognitive impairment (MCI), and occur frequently in older people. Research has suggested that SMC may impact on the quality of life for older people and consequently they are an important area of research. However, there is no consensus at present on the necessity of including SMC as a requirement for a classification of MCI, and some researchers suggest that SMC are unrelated to objective measures of cognitive function. SMC may instead be related to the presence of mood problems. This chapter investigates the idea that SMC are related to mood rather than cognition and comments on the inclusion of SMC as a criterion for MCI.

In this chapter, participants in the Medical Research Council Cognitive Function and Ageing Study (MRC-CFAS I) were categorised according to cognitive status into three distinct groups; of no cognitive impairment, MCI (including SMC) and MCIW (MCI without SMC). Analyses were conducted to compare the groups for anxiety and depression at two time points, and found that symptoms of anxiety and depression were significantly more likely in participants categorised as MCI and were significantly less likely in those categorised as MCIW. SMC were also found to increase the odds of symptoms of anxiety and depression regardless of cognitive status. Analyses were conducted using the two time points to establish a temporal relationship between mood and cognition, and results suggested that a change from a classification of no cognitive impairment to MCI over two years was associated with the development of depressive symptoms, suggesting that depressive symptoms occurred after the onset of cognitive problems.

The findings of this chapter suggest that SMC are indeed related to mood, and potentially more so than to objective cognitive functioning. A change in cognitive status from

not cognitively impaired to MCI may also be associated with the development of depressive symptoms.

Introduction

Subjective memory complaints (SMC) are reports of problems with, or changes in, memory and are common in older people (Balash et al., 2013; Dux et al., 2008). Assessments of SMC range from brief questions concerning individuals' perceived memory function or how memory changes may have affected activities of daily living (Cook & Marsiske, 2006) to more in-depth questionnaires such as the Memory Functioning Questionnaire (Gilewski, Zelinski, & Schaie, 1990) or the Metamemory in Adulthood Questionnaire (Dixon, Hultsch, & Hertzog, 1988). SMC are associated with a lower quality of life in older people (Iliffe & Pealing, 2010; Mol, van Boxtel, Willems, & Jolles, 2006).

Petersen et al, (2001) make a connection between SMC and mild cognitive impairment (MCI); a concept developed to describe a transitional phase between age-appropriate cognitive functioning and pathological decline (Matthews et al., 2008). However, this has proved controversial with several researchers suggesting that SMC are not an essential criterion for MCI and may lack both specificity and sensitivity as a diagnostic criterion (Lenehan et al., 2012). Accordingly, SMC are included as a criterion in only ten of the nineteen MCI definitions identified by the MRC-CFAS I study (Matthews et al., 2008; Stephan et al., 2008) alongside the requirement for an objective impairment in memory or other cognitive domains such as language, absence of dementia, intact general cognitive functioning and intact activities of daily living (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999).

Including SMC as a criterion for classification of MCI reduces the prevalence estimates of MCI (Matthews et al., 2008), in that as many as 62% of individuals who experience cognitive decline do not report SMC (Iliffe & Pealing, 2010). Possible reasons for such a discrepancy may include individual variations in adapting to cognitive change, where

some individuals may not perceive such changes as significant or requiring action. However, progression to dementia in one study was predicted better by the presence of memory complaints than by global cognitive impairment without dementia or by domain-specific cognitive impairments. Palmer et al. (2003) found that 51% of future dementia cases in a sample drawn from a population-based study had memory complaints.

SMC are also related to symptoms of depression and anxiety (G. J. McDougall et al., 2006). Depression or anxiety may influence the expression of SMC. Depression is positively associated with SMC (Minett et al., 2008; Zandi, 2004) and may enhance negative attributions (Roberts et al., 2009) so that individuals may experience a distorted subjective appraisal of their memory function in the presence of depressive symptoms. SMC without objective impairment may be a manifestation of depressive symptoms (Balash et al., 2013). An increase in anxiety has also been associated with an increase in SMC despite no decrease in objective memory performance (Dux et al., 2008). Anxiety was found to be higher in individuals with SMC who have lower Mini Mental State Examination scores (MMSE) (Balash et al., 2013; Folstein et al., 1975). Symptoms of depression and anxiety are increased in individuals who have been classified as having MCI (D. E. Barnes et al., 2006; Bhalla et al., 2009; Chan et al., 2003; Geda et al., 2006; Yates et al., 2013), potentially indicating a risk factor for the development of MCI, a reaction to the onset of cognitive decline or a circular relationship involving both possibilities. Depression may also form part of a prodromal phase of dementia, which would justify a triple relationship between depression, SMC and cognitive decline (Minett et al., 2008).

This study aimed to investigate the complex relationship between SMC, mood, and MCI by answering the following research questions:

1. Are people with MCI more likely to have symptoms of anxiety or depression than people with normal cognitive functioning?
2. Are people with SMC more likely to report symptoms of anxiety or depression than people without SMC?
3. Does anxiety or depression at baseline predict the presence of SMC two years later?
4. Is anxiety or depression at baseline associated with a change in cognitive status over two years?
5. Will a change in cognitive status over two years predict the presence of anxiety or depression at the end of the two year period?

Methods

Design

Mood and the presence of subjective memory complaints were assessed longitudinally in a sample of older people who were participating in the Medical Research Council Cognitive Function and Ageing Study (MRC-CFAS I). MRC-CFAS I is a longitudinal population-based study involving participants drawn from five centres which represent rural and urban areas of England and Wales, investigating changes that affect people as they age. Fuller details can be found in Chapter 2. Participants were initially screened regarding their general health and day-to-day activities, with 20% of participants completing a more detailed assessment, selected on the basis of age, geographical location and cognitive ability. Participants were assessed again after approximately 24 months. Ethical approval was granted by University and NHS Ethics Committees. This chapter presents analysis of baseline and follow-up data from MRC-CFAS I.

Participants

Individuals over 65 years and living in the Gwynedd, Cambridge, Nottinghamshire, Newcastle and Oxford areas of the UK were randomly sampled from 1990 to 1991. Fuller details are reported elsewhere (Brayne, McCracken, Matthews, & MRC-CFAS, 2006) and in Chapter 2 of this thesis. The participants investigated in the present study consisted of the 20% subsample who took part in the detailed assessment, drawn from the larger baseline sample. Data from the first assessment and two-year follow up interviews were used in this analysis. Participants were excluded from the analysis if they had objective cognitive impairment beyond the criteria for MCI (dementia n=587; other cognitive impairment no dementia [OCIND] n=234) or impaired ADLs (n=475) at baseline resulting in 1344 participants included at the first assessment. There were no restrictions on cognitive status at the follow-up time point, resulting in the inclusion of 896 participants at follow-up after a two year period.

Definition of subjective memory complaints

A subjective memory complaint was indicated by a self-report of memory problems by the participant. This was assessed using two questions from the baseline screening interview, "Have you ever had difficulty with your memory?" and "Have you tended to forget things recently?", and one question from the combined screen and interview "Have you had any difficulty with your memory?" A positive answer to any of the above questions resulted in a participant being categorised as having an SMC at baseline, with SMC being a dichotomous category. A subjective memory complaint at follow-up was identified by a positive answer to either of two questions from the assessment: "Have you had any difficulty with your memory?" or "Have you tended to forget things recently?" Again, SMC was a dichotomous category.

Assessment of mood

A structured interview was used to assess various aspects of mood. This paper focuses on anxiety and depression. Anxiety and depression were defined by the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) (Copeland et al., 1986) algorithm, where a score of two indicated mild symptoms and a score of three or above indicated a case of anxiety or depression. The symptoms were assessed using a structured interview that incorporated questions from the GMS-AGECAT, History and Aetiology Schedule and the CAMDEX and can be found online (http://www.cfas.ac.uk).

Classification of MCI

MCI was defined using an algorithm based on traditional criteria that had been used in previous studies using data from MRC-CFAS I (See Chapter 2, Figure 2.2 for details). Participants with a classification of MCI were expected to have an objective cognitive impairment in either memory or a non-memory domain such as language, no dementia, intact ADLs, intact general cognitive function (indicated by a score of 22 or higher on the MMSE), and SMC. Objective cognitive complaints were defined using the CAMDEX Cambridge Cognitive Examination (CAMCOG), where a score falling one standard deviation below age-adjusted norms represented impairment. Memory impairment was defined using the memory domains of the CAMCOG and impairment in other cognitive domains was defined according to impairments in any other domain of the CAMCOG. For the purpose of this analysis, a further group of participants was identified which included participants who met all the criteria for MCI, except that they did not report a subjective memory complaint. These participants were categorised as MCI-without (MCIW; see Chapter 2, Figure 2.2).

At follow-up, participants could be categorised as having MCI, MCIW, or dementia, or could be classified in two further categories. Some participants were classified as having

other cognitive impairment no dementia (OCIND) which comprised individuals who had general cognitive decline, but did not meet criteria for dementia and had intact ADLs. This group included participants with and without SMC. Participants could also be classified in the ADL category, which included people who had general cognitive decline, impairments in ADLs but did not meet criteria for dementia. Again, this category included participants with and without SMC. Participants were allocated to each category using the cognitive status algorithm (See Chapter 2, Figure 2.2).

Statistical analyses

Analyses were conducted using SPSS 20.0. Differences between participants with and without subjective memory complaints were described for both time points. Logistic regression was used to calculate odds ratios for symptoms of anxiety or depression at baseline and follow-up according to cognitive status and presence of SMC. Pearson's chi squared test was used to calculate changes in SMC, cognitive status and symptoms of anxiety and depression over the two year period.

Results

Table 4.1 summarises the characteristics of the study sample at baseline according to whether SMC were reported. At baseline, 787 participants from a total of 1344 (58.6%) participants reported SMC. There did not appear to be differences between those with SMC and those without in terms of age, MMSE scores, years in full time education or gender. Table 4.2 summarises the cognitive status of the participants according to whether or not SMC were reported. Due to the definitions used to create the cognitive classifications, all participants classified as having MCI reported SMC, and none of the participants classified as having MCIW reported SMC. The cognitive status of some participants changed between baseline and follow-up and this is shown in Figure 4.1. According to the definitions for

cognitive impairment used in this study, 49.5% of participants were classified as having MCI or MCIW at baseline and 28.6% of participants were classified as having MCI or MCIW at follow-up.

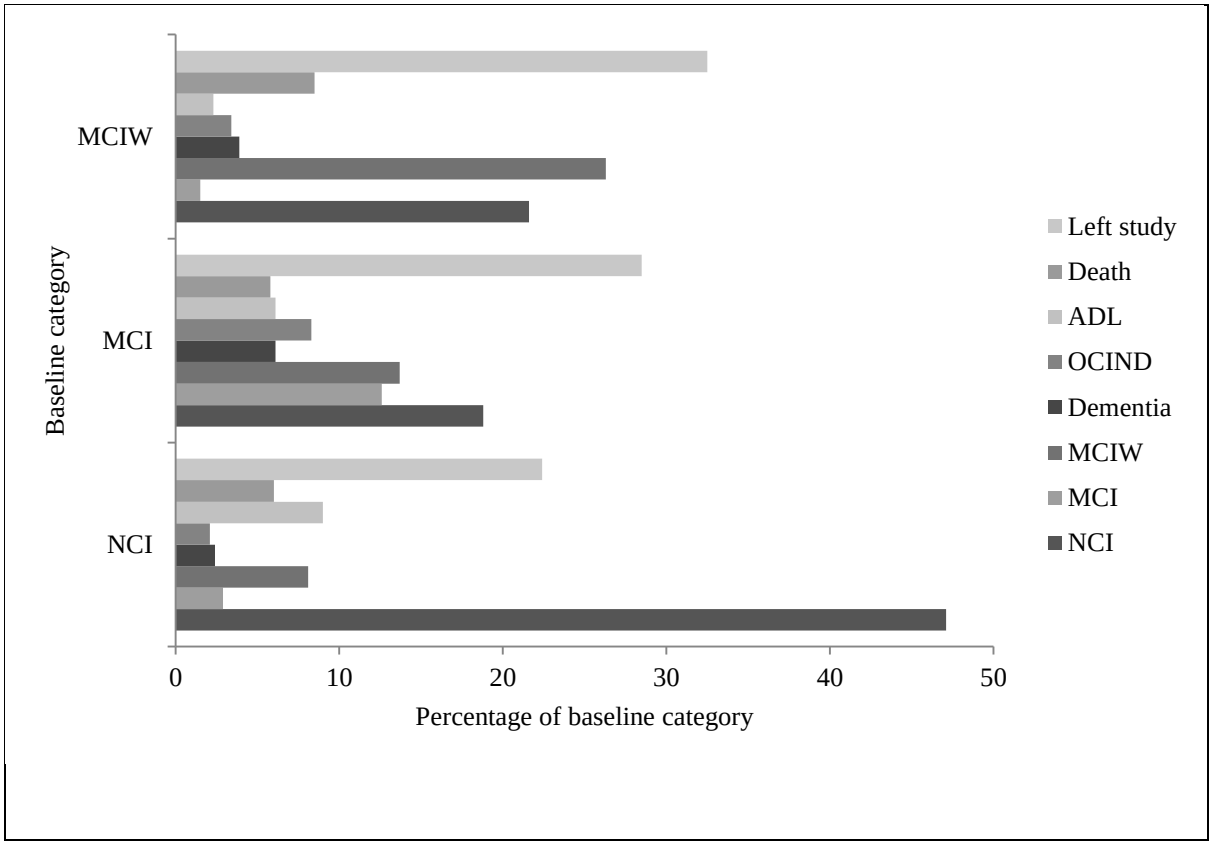

Figure 4.1: Changes in cognitive status between baseline and follow-up. Baseline category is shown on the Y-axis and each bar shows the percentage of participants who have moved to each category at follow-up.

Table 4.1: Sample characteristics for participants with and without subjective memory complaints at baseline.

	Baseline			Follow-up		
	No SMC	SMC	Total	No SMC	SMC	Total
Age mean(sd)	73.69 (6.15)	74.56 (6.50)		75.41 (6.17)	76.68 (6.62)	
MMSE mean (sd)	25.13 (3.69)	24.86 (3.49)		25.40 (3.47)	25.07 (3.13)	
Female N(%)	501 (63.7)	360 (64.6)		433 (65.7)	151 (63.7)	
Years in FT Education mean (sd)	9.86 (2.13)	10.03 (2.23)		9.98 (2.12)	10.12 (2.32)	
Without depression (%)	629 (79.9)	370 (66.4)	1344 (100)	546 (82.9)	141 (59.5)	896 (100)
With depression (%)	158 (20.1)	187 (33.6)		113 (17.1)	96 (40.5)	
Without anxiety (%)	766 (97.3)	514 (92.3)		651 (98.8)	214 (90.3)	
With anxiety (%)	21 (2.7)	43 (7.7)		8 (1.2)	23 (9.7)	
Total (%)	787 (58.6)	557 (41.4)		659 (73.5)	237 (26.5)	

Table 4.2: Cognitive status according to SMC at baseline

	Baseline			Follow-up		
N(%)	No SMC	SMC	Total	No SMC	SMC	Total
NCI	399 (50.7)	280 (50.3)	679 (50.5)	360 (54.6)	94 (39.7)	456 (50.9)
MCI	0 (0.0)	277 (20.6)	277 (20.6)	0 (0.0)	61 (6.8)	61 (6.8)
MCIW	388 (49.3)	0 (0.0)	388 (28.9)	195 (29.6)	0 (0.0)	195 (21.8)
OCIND				35 (5.3)	15 (6.3)	50 (5.6)
ADL				47 (7.1)	39 (16.5)	86 (9.6)
Dementia				22 (3.3)	26 (11.0)	48 (5.4)
Total	787 (58.6)	557 (44.4)	1344 (100)	659 (73.5)	237 (26.5)	896 (100)

NCI = not cognitively impaired
MCI = objective cognitive impairment, intact general cognition, intact ADLs, absence of dementia and a report of SMC
MCIW = participants who would otherwise be classified as MCI but do not report SMC
OCIND = other cognitive impairment, no dementia where participants indicate general cognitive decline but have intact ADLs and do not meet criteria for dementia
ADL = participants who show general cognitive decline and impaired ADLs but do not meet criteria for dementia.
Dementia = Participants who have been classified as having dementia.

Are people with MCI more likely to have symptoms of anxiety or depression compared to people with normal cognitive functioning?

Logistic regressions were conducted for each cognitive status group to investigate the odds of the presence of symptoms of anxiety or depression and the results are shown in Table 4.3. The odds of experiencing symptoms of anxiety or depression at baseline were significantly increased in participants in the MCI category, but were significantly decreased in participants who were categorised as MCIW. There were no significant changes in odds for participants without cognitive impairment. Cognitive status at baseline was not associated with an increase or a decrease in the odds of experiencing anxiety at follow-up. However, being categorised as having MCI at baseline increased the odds of reporting depressive symptoms at follow-up. Participants in the ADL cognitive status category at follow-up had significantly increased odds of reporting anxiety at follow-up. Participants categorised as MCI and ADL at follow-up had significantly increased odds of reporting depression at follow-up.

Table 4.3: Logistic regressions to show odds of having anxiety or depression at baseline or follow-up dependent on cognitive status at baseline or follow-up.

Baseline cognitive status			
Anxiety at baseline	OR	CI	P
NCI	0.75	0.45-1.25	.268
MCI	**3.22**	**1.93-5.38**	**.000**
MCIW	**0.34**	**0.16-0.72**	**.005**
Depression at baseline			
NCI	1.04	0.82-1.33	.736
MCI	**1.71**	**1.28-2.27**	**.000**
MCIW	**0.58**	**0.44-0.78**	**.000**
Anxiety at follow-up			
NCI	0.90	0.44-1.85	.775
MCI	1.64	0.74-3.62	.224
MCIW	0.69	0.28-1.71	.423
Depression at follow-up			
NCI	0.82	0.60-1.11	.198
MCI	**1.87**	**1.30-2.67**	**.001**
MCIW	0.72	0.50-1.05	.089
Follow-up cognitive status			
Anxiety at follow-up			
NCI	0.52	0.25-1.10	.086
MCI	1.49	0.44-5.05	.521
MCIW	0.24	0.06-1.02	.052
Dementia	1.23	0.29-5.31	.783
OCIND	0.00	0.00	.997
ADL	**7.84**	**3.69-16.63**	**.000**
Depression at follow-up			
NCI	**0.54**	**0.39-0.74**	**.000**
MCI	**2.28**	**1.33-3.91**	**.003**
MCIW	0.72	0.48-1.07	.105
Dementia	1.10	0.56-2.16	.778
OCIND	1.59	0.86-2.95	.139
ADL	**2.96**	**1.87-4.68**	**.000**

Are people with SMC more likely to report symptoms of anxiety or depression than people without SMC?

Logistic regression using baseline data showed that the odds of having symptoms of anxiety or depression were higher in participants who reported SMC compared to those who did not report SMC (anxiety: OR=3.05, CI=1.79-5.20, p<.001; depression: OR=2.01, CI=1.57-2.58, p<.001).

Is anxiety or depression at baseline associated with the presence of SMC at follow-up?

A significant association was found between the presence of anxiety at baseline and the presence of SMC at follow-up (χ^2 (1) = 12.56, p<.001). Based on the odds ratio, having anxiety at baseline increased the odds of having SMC at follow-up by a factor of 2.95. Partial correlation showed that the relationship between anxiety at baseline and SMC at follow-up remained significant when anxiety at follow-up was controlled for (r=.66, p (one-tailed) =.025) with anxiety at baseline accounting for 44% of the variance in SMC at follow-up. The association between the presence of depression at baseline and the presence of SMC at follow-up was also significant (χ^2 (1) = 18.01, p<.001). Having depression at baseline increased the odds of having SMC at follow-up by a factor of 2.00 according to the odds ratio. Partial correlation showed that the relationship between depression at baseline and SMC at follow-up was significant when depression at follow-up was controlled for, with depression at baseline accounting for 41% of the variation in SMC at follow-up (r=.064, p (one tailed) =.027).

Is anxiety or depression at follow-up associated with the presence of SMC at follow-up?

A significant association was found between the presence of anxiety at follow-up and the presence of SMC at follow-up (χ^2 (1) = 37.62, p<.001). Based on the odds ratio, having

anxiety at follow-up increased the odds of having SMC at follow-up by a factor of 8.75. The association between the presence of depression at follow-up and the presence of SMC at follow-up was also significant (χ^2 (1) = 53.18, p<.001). This resulted in increased odds of having SMC at follow-up by a factor of 3.29 when depression was present at follow-up.

Is anxiety or depression at baseline associated with a change in cognitive status over two years?

The presence of symptoms of anxiety or depression at baseline was not associated with progression from no cognitive impairment to MCI, OCIND, MCIW or dementia, or from MCI to dementia, over two years (see Table 4.4).

Is anxiety or depression at follow-up associated with a change in cognitive status over two years?

Symptoms of anxiety at follow-up were not associated with a change in cognitive status from no cognitive impairment to MCI, OCIND, MCIW or dementia, or from MCI to dementia, over two years. Symptoms of depression at follow-up were associated with a change in cognitive status from not cognitively impaired to a classification of MCI between baseline and follow-up (χ^2 (1) = 9.72, p=.002) resulting in an increase in odds by a factor of four. However, symptoms of depression at follow-up were not associated with a change in cognitive status from no cognitive impairment to OCIND, MCIW or dementia, or from MCI to dementia, over two years (see Table 4.4). Depression at baseline and anxiety and depression at follow-up were associated with an increase in risk of developing ADL impairment in those with no cognitive impairment at baseline.

Table 4.4: Associations between symptoms of anxiety or depression and changes in cognitive status over two years

		Pearson Chi Square	P
Anxiety at baseline			
Baseline	Follow-up		
NCI	MCI	0.14	.710
NCI	MCIW	0.52	.470
NCI	Dementia	0.37	.544
NCI	OCIND	0.56	.453
NCI	ADL	2.02	.155
MCI	Dementia	0.50	.480
MCIW	Dementia	0.36	.549
Depression at baseline			
Baseline	Follow-up		
NCI	MCI	0.02	.902
NCI	MCIW	0.27	.603
NCI	Dementia	0.01	.913
NCI	OCIND	0.17	.681
NCI	**ADL**	**10.42**	**.001**
MCI	Dementia	0.38	.537
MCIW	Dementia	0.46	.499
Anxiety at follow-up			
Baseline	Follow-up		
NCI	MCI	0.19	.664
NCI	MCIW	2.12	.146
NCI	Dementia	0.56	.452
NCI	OCIND	0.49	.483
NCI	**ADL**	**21.61**	**.000**
MCI	Dementia	0.04	.851
MCIW	Dementia	1.03	.310
Depression at follow-up			
Baseline	Follow-up		
NCI	**MCI**	**9.88**	**.002**
NCI	MCIW	2.91	.088
NCI	Dementia	0.82	.366
NCI	OCIND	0.00	.984
NCI	**ADL**	**18.98**	**.000**
MCI	Dementia	0.11	.743
MCIW	Dementia	2.06	.151

Discussion

The study aimed to determine whether there is an association between subjective memory complaints, objective cognitive impairment and symptoms of anxiety or depression using data from a large population study of older people.

The odds of having symptoms of anxiety or depression were increased in participants in the MCI category but were decreased for participants in the MCIW category. Symptoms of anxiety or depression were increased in participants reporting SMC compared to participants who did not report them, regardless of cognitive status. Symptoms of anxiety and depression at baseline were significantly associated with the presence of SMC at follow-up but were not associated with a change in cognitive status between baseline and follow-up. Symptoms of depression at follow-up were significantly associated with a change in cognitive status from not cognitively impaired to a classification of MCI over two years, but symptoms of anxiety at follow-up did not show such an association.

The finding that people classified as having MCI have increased odds of experiencing symptoms of anxiety or depression compared to people without cognitive impairment is in line with previous literature which has suggested that anxiety and depression are common comorbidities of MCI (Kruger et al., 2012; Ravaglia et al., 2008; Van der Linde et al., 2010). However, the odds of having symptoms of anxiety or depression were decreased in people classified as MCIW. This might suggest that the increase in odds for people with MCI is related to the subjective memory complaint component of the MCI definition, as SMC are not a requirement for the MCIW category. This is in contrast with some research (Cook & Marsiske, 2006), which suggests that depression does not drive the relationship between subjective beliefs and objective cognitive performance. However, no participants in the study

by Cook and Marsiske endorsed depressive symptoms to a clinical level, whereas the present study includes participants with clinical levels of depressive symptoms.

The odds of reporting symptoms of anxiety or depression are increased in participants reporting SMC compared to participants who did not report SMC. Again, this is in line with previous literature (Balash et al., 2013; Caselli et al., 2013; Dux et al., 2008; Minett et al., 2008; Schmand, Jonker, Geerlings, & Lindeboom, 1997) and suggests that SMC and symptoms of anxiety or depression are related.

Data from two time points were used to investigate the relationship between SMC and symptoms of anxiety or depression over time, and participants who reported both anxiety and depression at baseline were more likely to have SMC two years later even after anxiety and depression at follow-up was controlled for. This suggests that anxious or depressive symptomology could influence how an individual appraises their memory or cognitive abilities, a possibility that has also been considered by other researchers (Dux et al., 2008; Jorm et al., 1997; Roberts et al., 2009).

Symptoms of anxiety and depression at baseline, and anxiety at follow-up, were not associated with changes in cognitive status between baseline and follow-up for either type of cognitive impairment (MCI or MCIW), with changes from normal cognitive functioning to dementia, or with changes from MCI to dementia. Symptoms of depression at follow-up were only associated with a change from not cognitively impaired to a classification of MCI. This contradicts previous research which has found that anxiety and depression are risk factors for cognitive decline (Caracciolo et al., 2011; Geda et al., 2006; Goveas et al., 2011) but supports other research which has found that anxiety and depression may not be risk factors for progression from MCI to dementia (Gallagher et al., 2011; Vicini Chilovi et al., 2009).

The present study has a number of limitations. Firstly, the sample size at follow-up is considerably smaller than at baseline which led to a relatively small number of participants reporting symptoms of anxiety and depression at follow-up. This may have impacted on statistical power and could explain why significant associations were not found. Only data from participants who took part at both time points were used when assessing changes over the two year period. Participants left the study between baseline and follow-up for several reasons, such as moving away from the study area, elective withdrawal and death.

Two years may not be enough time to track development of cognitive decline, SMC, or the development of symptoms of anxiety or depression. A longer follow-up time may have allowed for subtle changes in cognitive functioning or mood to be observed and analysed. However, studies with longer follow-up periods have reported similar results (Comijs, Deeg, Dik, Twisk, & Jonker, 2002; Jorm et al., 1997).

The definitions of cognitive impairment used in this study rely on participants' performance on an objective cognitive task, which provides only a snapshot of cognitive performance rather than assessing subtle changes over frequent time points. Such testing can be affected by mood, medication and fatigue, and therefore it is not surprising that participants did not necessarily progress from no cognitive impairment to a type of cognitive impairment in a straightforward direction. The results show that 18.8% of participants in the MCI category and 21.6% of participants in the MCIW category at baseline are classified as having normal cognitive functioning at follow-up, showing that many participants' cognitive performance had improved. This suggests that the categories of cognitive impairment used may lack stability. Presence of SMC was also found to be unstable, with 38.1% of participants who had reported SMC at baseline no longer reporting them at follow-up.

The questions used to assess anxiety and depression in the present study may not be sensitive enough to draw out participants who are experiencing less severe or less frequent symptoms. Efforts were made to address this by including participants who scored as having borderline symptoms on the AGECAT algorithm as well as those who were classed as a definite case.

Despite these possible limitations, the present study has several strengths: the CAMCOG, is well-established as a cognitive assessment tool for dementia and milder levels of cognitive impairment, and is widely used in this area of research. The criteria used to create the MCI classification here are consistent with established definitions of MCI (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999). The procedure for assessment of mood-related symptoms used in this study has also previously been used to produce prevalence calculations for anxiety and depression which are in line with previous research and can be considered to be robust (Van der Linde et al., 2010). Lastly, the present study uses a subsample drawn from a larger population sample, which is representative of the older population as participants were not identified through attendance at health services.

The findings of this study have several implications. From a theoretical perspective, the MCIW category shows that a large number of participants who would otherwise meet criteria for MCI are missed from this classification on the basis of not reporting SMC. Individuals categorised as MCIW may benefit from assistance or intervention but would most likely go unnoticed by health professionals until their cognitive problems worsen. In addition, SMC may be more strongly related to anxiety or depression than to objective memory problems, as shown by the lack of association with anxiety or depression in people categorised as MCIW. Clinical implications are that health professionals could spend more time with older people who report SMC to investigate the presence of cognitive decline or symptoms of anxiety or depression. This could help to make sure that older people are

receiving the correct information and are benefitting from any help that is available to them. Lastly, there are implications for future research, such as conducting a longer study with more frequent time points that may be more sensitive to detecting change in cognitive function. Cognitive function could be analysed as a continuous measure and classifications of cognitive status could be retrospectively applied in order to analyse variance within each classification of cognitive functioning. Lastly, questions that are more sensitive to less severe or less frequent feelings of anxiety or depression could be used to assess older people who are experiencing milder symptoms.

The findings of this study imply that a large number of participants who would otherwise meet criteria for MCI are missed, if SMC are seen as an essential criterion, and so may not receive appropriate support. More attention may also be needed for anxiety and depression in the context of MCI. This study suggests that SMC contributes significantly to the relationship between MCI and mood.

Chapter 5: Subjective memory complaints are involved in the relationship between mood and MCI

Summary

This chapter builds on the work of Chapter 4 by continuing the investigation into the role of subjective memory complaints (SMC) in the relationship between MCI and mood. In the last chapter, the presence of SMC was found to change the relationship between symptoms of anxiety or depression and cognitive impairment, and SMC were shown to be related to mood regardless of cognitive status.

The previous chapter included data from the Medical Research Council Cognitive Function and Ageing Study (MRC-CFAS I), collected in the early 1990s. This chapter has updated the investigation with a more recent cohort using data collected as part of the Cognitive Function and Ageing Study Wales (CFAS Wales), and mediation analyses were added to clarify how SMC operate in relation to cognition and mood. Data were collected from structured interviews with community dwellers aged over 65, in both urban and rural areas of Wales. The interviews assessed cognitive functioning, reports of SMC and mood (anxiety and depression). Participants were then categorised into one of three cognitive status categories using an algorithm; of no cognitive impairment, MCI including SMC and MCI without SMC (MCIW). The odds of experiencing symptoms of anxiety and depression were increased for people categorised as MCI but did not change for those without cognitive impairment or in the MCIW category. The odds of having symptoms of anxiety and depression were also increased in people who reported SMC, regardless of cognitive status. Mediation analyses suggested that SMC do partially mediate the relationship between cognition and mood and this raises questions about whether SMC should form a criterion in the MCI definition.

The results of this chapter confirm and add to those of Chapter 4, and raise the question about the requirement for SMC to be included in the MCI definition.

Introduction

Mild cognitive impairment (MCI) is a categorisation that may be applied to older people who experience a level of cognitive decline considered more severe than normal ageing but not thought sufficient in extent or severity to constitute dementia (Matthews et al., 2008). The broader MCI definition encompasses the following criteria: an objective impairment in memory or other cognitive domains such as language, a subjective memory complaint, absence of dementia, intact general cognition and intact activities of daily living (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999). Currently, several variants of this definition exist, and such variations differ in the extent to which they endorse the criteria above (Stephan et al., 2008).

The role of subjective memory complaints (SMC) in the MCI definition is questioned by researchers as some studies have found it to lack accuracy as a diagnostic criterion (Lenehan et al., 2012). SMC are common in the healthy older population (Podewils, McLay, Rebok, & Lyketsos, 2003) but show little relationship with either informant reports or cognitive test results (Jorm et al., 1997). Previous research has also found that as many as 62% of individuals experiencing cognitive decline do not report it (Iliffe & Pealing, 2010), suggesting that SMC can be experienced by those without impairments, and often may not be experienced by those with impairments.

Investigating SMC is important as evidence has shown a link between SMC and future cognitive decline. Schmand et al., (1997) found that SMC were associated with greater odds of having a dementia diagnosis after four years. There is also a growing body of research investigating subjective cognitive decline as a distinct stage on the cognitive continuum between normal ageing and dementia. Subjective cognitive decline is thought to

occur before MCI and potentially represents a stage when the person is aware of changes in cognitive functioning, but these changes are not detected by formal testing.

One explanation for the discrepancy in the relationship between SMC and cognitive decline could be the influence of mood, such as symptoms of anxiety or depression. Anxiety and depression are related to MCI (D. E. Barnes et al., 2006; Yates et al., 2013) and also to SMC (Dux et al., 2008; Minett et al., 2008).

The previous chapter found that SMC are linked to symptoms of anxiety and depression but not necessarily to objective cognitive impairment. This study aims to update this research using data that were collected more recently from a sample that matched the demographic of the original study as closely as possible. This study will answer the following questions:

1. Are people with MCI more likely to have symptoms of anxiety or depression than people without cognitive impairment?
2. Are people with SMC more likely to report symptoms of anxiety and depression than those without SMC?
3. Do SMC mediate the relationship between cognitive impairment and symptoms of anxiety or depression?

Methods

Design

Mood, cognitive functioning and SMC were examined using cross-sectional data from a large sample of older people who participated in the Cognitive Functioning and Ageing Study Wales (CFAS Wales). CFAS Wales is a longitudinal population-based study which has gathered information about participants drawn from two research centres in urban and rural

areas of Wales, investigating changes that people may experience as they age. Participants took part in face-to-face interviews, which were usually conducted in their own homes, with trained interviewers through the medium of English or Welsh, depending on the participant's preference. Ethical approval was granted by the appropriate NHS Ethics committee. Further information can be found in Chapter 2. This paper presents data from the first wave of interviews.

Participants

Individuals over 65 years and living in the Gwynedd, Ynys Môn and Neath Port Talbot areas of Wales were randomly sampled from general practice lists between 2011 and 2013, with equal numbers drawn from the age groups 65-74 and 75 and above. Fuller details are reported in Chapter 2. Participants were excluded from the analysis if they had a diagnosis of dementia (n=129), impaired activities of daily living (ADLs; n=52) or cognitive decline greater than that expected for a classification of MCI, but not meeting the criteria for dementia for other reasons (other cognitive impairment no dementia; OCIND; n=152) resulting in n=3173 participants included in this analysis.

Definition of subjective memory complaints

Subjective memory complaints were indicated by a self-report of memory problems by the participant. This was assessed using the following questions asked during the structured interview: "Have you ever had any difficulty with your memory?" and "Have you tended to forget things recently?" A positive answer to either question resulted in a participant being categorised as having SMC, which was a dichotomous category.

Assessment of mood

Symptoms of anxiety and depression were assessed during the structured interview. Anxiety and depression were defined using the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) algorithm (Copeland et al., 1986), where a score of two indicated mild symptoms and a score of three or above indicated case-level anxiety or depression. This study excluded all participants with a score less than two.

Classification of cognitive status

MCI was defined using the cognitive status algorithm (see Chapter 2, Figure 2.2). Participants classified as having MCI displayed an objective cognitive impairment, intact general cognitive functioning (indicated by a score of equal to or greater than 22 on the MMSE), intact ADLs, an absence of dementia, and SMC. Objective cognitive impairment was defined using the CAMDEX CAMCOG (Huppert et al., 1995) which formed a section of the structured interview. A score falling one standard deviation below age-adjusted norms on any cognitive domain measured in the CAMCOG represented impairment.

A further group of participants was created using the cognitive status algorithm (See Chapter 2, Figure 2.2) that included all participants who would otherwise meet criteria for MCI, except that they did not report SMC. This group was referred to as MCI-without (MCIW).

Participants in the OCIND, ADL or dementia categories, defined using the cognitive status algorithm (See Chapter 2, Figure 2.2.) were excluded from analyses as they represented a level of impairment greater than would be expected for a classification of MCI.

For use in mediation analyses, a median split on the total CAMCOG score was used adjusting for age, gender and education (See Appendix P and Chapter 2).

Statistical analyses

Analyses were conducted using SPSS 20.0. Differences between participants with and without SMC were described. Logistic regression was conducted to determine the odds of experiencing symptoms of anxiety or depression for each cognitive status and for participants with and without SMC.

A mediation analysis using logistic regression was conducted using the median split of the CAMCOG, symptoms of anxiety or depression as the outcome variable and the presence of SMC as the mediating variable. Sobel Tests were used to determine if the partial mediation effects were significant.

Sensitivity Analyses

Sensitivity analyses were conducted to determine the most appropriate measure of cognition for use in the mediation model. Various measures of cognition were assessed using logistic regression to investigate the relationship with anxiety and depression. The results of the logistic regressions are shown in Table 5.1. The CAMCOG median split measure of cognition was the only measure of cognition that showed significant relationship with anxiety, and also yielded a significant Sobel test statistic. Table 5.2 shows the sensitivity analyses conducted using logistic regression to investigate the relationship between cognition and depression.

Table 5.1: Sensitivity analyses using logistic regression to show the relationship between different measures of cognition and anxiety and results of the Sobel test for mediation with SMC as a mediating variable

	OR	CI	P	Sobel test	P
MCItotal	1.14	0.76-1.71	.542	2.25	.025
CAMCOG total score	0.99	0.98-1.00	.176	-0.98	.327
CAMCOG median split	0.65	0.47-0.89	.008	-2.29	.021
MCItotal groups MCI and MCIW together and compares them to no cognitive impairment CAMCOG total score is the total score achieved by each participant on the CAMCOG questions asked in the interview CAMCOG median split is a dichotomous variable created from splitting the CAMCOG scale into two groups using the median of the scale					

Table 5.2: Sensitivity analyses using logistic regression to show the relationship between different measures of cognition and depression and results of the Sobel test for mediation with SMC as a mediating variable

	OR	CI	P	Sobel test	P
MCItotal	1.39	1.13-1.71	.002	2.40	.016
CAMCOG total score	0.98	0.98-0.99	.000	-0.99	.320
CAMCOG median split	0.70	0.59-0.82	.000	-2.48	.013
MCItotal groups MCI and MCIW together and compares them to no cognitive impairment CAMCOG total score is the total score achieved by each participant on the CAMCOG questions asked in the interview CAMCOG median split is a dichotomous variable created from splitting the CAMCOG scale into two groups using the median of the scale					

Results

The characteristics of the study sample are shown in Table 5.3. Data were analysed from 3173 participants who were classified according to cognitive status as having no cognitive impairment (NCI), MCI or MCIW. SMC were reported by 1050 participants (33.1%), with 200 participants (6.3%) meeting criteria for MCI and 329 participants (10.4%) being categorised as MCIW.

Table 5.3: Sample characteristics for participants with and without SMC

	No SMC	SMC	Total (%)
Age mean (SD)	74.34 (6.89)	74.34 (6.79)	
MMSE mean (SD)	27.55 (2.19)	27.22 (2.30)	
CAMCOG mean (SD)	85.20 (10.65)	84.83 (8.47)	
Years in FT Education mean (SD)	11.73 (2.69)	11.73 (2.83)	
Female N (%)	1205 (56.8)	524 (50.1)	1729 (54.5)
With anxiety N (%)	79 (3.7)	84 (8.0)	163 (5.1)
Without anxiety N (%)	2044 (96.3)	966 (92.0)	3010 (94.9)
With depression N (%)	431 (20.3)	357 (34.0)	788 (24.8)
Without depression N (%)	1692 (79.7)	693 (66.0)	2385 (75.2)
Total (%)	2123 (66.9)	1050 (33.1)	3173 (100)

Are people with MCI more likely to have symptoms of anxiety or depression compared to people without cognitive impairment?

Logistic regression showed that the odds of experiencing symptoms of anxiety were significantly increased in people who had been classified as having MCI (OR=1.93, CI=1.16-3.22, p=.012) but not for people classified as MCIW (OR=0.68, CI=0.37-1.23, p=.199) or people without cognitive impairment (OR=0.88, CI=0.59-1.32, p=.542). The same pattern was found for the odds of experiencing symptoms of depression, where the risks were significantly increased in people who had been classified as having MCI (OR=2.04, CI=1.52-2.74, p<.000) but not for people classified as MCIW (OR=1.01, CI=0.77-1.31, p=.968), and the odds were significantly decreased in participants with no cognitive impairment (OR=0.72, CI=0.59-0.88, p=.002).

Are people with SMC more likely to report symptoms of anxiety and depression than those without SMC?

The odds of experiencing symptoms of anxiety and depression were significantly increased in participants who had reported subjective memory complaints (anxiety OR=2.25,

CI=1.64-3.09, p<.001; depression OR=2.02, CI=1.71-2.39, p<.001), regardless of their cognitive status. The number of people reporting SMC for each AGECAT level of anxiety and depression are shown in Table 5.4. Logistic regression showed that the odds of both anxiety (OR=2.17, CI=1.53-3.08, p<.001) and depression (OR=2.02, CI=1.68-2.43, p<.001) were significantly increased in participants without cognitive impairment who reported SMC.

Table 5.4: SMC reported for each AGECAT level of anxiety and depression

	No SMC	SMC
Anxiety Level 0	1352	518
Anxiety Level 1	692	448
Anxiety Level 2	32	27
Anxiety Level 3	37	37
Anxiety Level 4	10	15
Anxiety Level 5	0	5

	No SMC	SMC
Depression level 0	1617	620
Depression level 1	75	73
Depression level 2	270	239
Depression level 3	122	81
Depression level 4	39	37

Do SMC mediate the relationship between cognition and symptoms of anxiety or depression?

Logistic regression was used to investigate whether SMC mediate the relationship between cognition and anxiety. Sensitivity analyses conducted prior to mediation analyses indicated that using cognition as a dichotomous variable created by an age-, education- and gender-adjusted median split of the total CAMCOG score would be most appropriate, as this variable had a relationship with anxiety (OR=0.65, CI=0.47-0.89, p=.008), whereas cognition as a continuous variable did not (Table 5.1). Mediation analyses suggested that the association between cognition and anxiety is partially mediated by the presence of SMC (Figure 5.1A), and the results of the Sobel test suggest that the mediation effect was significant, z'=-2.30, p=.021.

The CAMCOG median split variable was also used as the measure of cognition in testing for mediation between cognition and depression in order to maintain continuity, although other measures of cognition were assessed in sensitivity analyses (Table 5.2). In this analysis, the total effect of cognition on depression was significant (OR=0.70, CI=0.59-0.82,

p<.000). Mediation analyses show that the association between cognition and depression was partially mediated by the presence of SMC (Figure 5.1B) and the results of the Sobel test suggest that this mediation was also significant, z'=-2.48, p=.013.

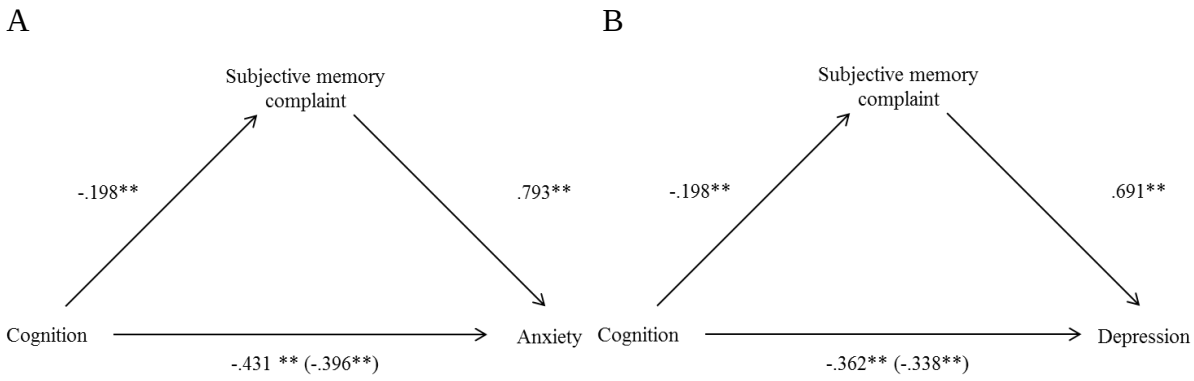

Figure 5.1: The relationships between cognition and anxiety (A) and cognition and depression (B) are partially mediated by subjective memory complaints (*p<.05, **p<.01, ns = non-significant).

Discussion

This study aimed to investigate the relationship between MCI, mood and SMC, using data from a large population study of people over 65 years old living in Wales. The findings suggest that the odds of experiencing symptoms of both anxiety and depression are significantly increased in people categorised as having MCI (where SMC are part of the criteria), but the odds are not increased for people with no cognitive impairment or for those otherwise meeting criteria for MCI who do not report SMC. Reports of SMC were also associated with increased odds of having symptoms of anxiety and depression across all cognitive status groups compared to people who did not report SMC. Mediation analyses suggested that SMC partially mediates the relationship between cognition and mood.

The findings from the present study echo the results of previous studies that have also shown an association between MCI and mood (Fernandez-Martinez, Molano, Castro, & Zarranz, 2010; Kruger et al., 2012; Lyketsos et al., 2002; Van der Linde et al., 2010). SMC

may occur due to an individual's attributional style and may therefore be related to depression as a function of negative attributions, rather than due to cognitive impairment (Dux et al., 2008; Jorm et al., 1997). The relationship between MCI and anxiety may operate in two directions. On one hand, concerns over memory may influence general levels of anxiety, as memory problems can be frightening and anxiety provoking (Antikainen et al., 2001). However, anxiety could be a risk factor for reports of SMC (Derouesne, Lacomblez, Thibault, & LePoncin, 1999) as older people may become more vigilant about their cognitive processes and aware of very subtle changes that are not detected by neuropsychological tests. Previous research has also shown that people reporting SMC were also more likely to report symptoms of anxiety and depression even after controlling for actual cognitive performance (Comijs et al., 2002). The findings of this study are in line with this research, as participants reporting SMC were more likely than those without SMC to experience mood problems regardless of cognitive status.

The MCIW category and mood problems were not significantly related, suggesting that it is likely that SMC mediate the relationship between MCI and mood, as the only difference between the MCI and MCIW categories is the presence of SMC. This idea is confirmed by mediation analyses, although it is probable that other factors also influence the relationship as the analyses suggest that SMC operate only as a partial mediator.

There are several limitations to the present study. The response rate to the interviews from which the data were collected was approximately 46% and it could be suggested that potential participants with anxiety, depression or cognitive impairment may have refused to participate, leaving a sample that is not entirely representative, however for this analysis which uses relative rather than absolute differences this effect is attenuated.

The number of participants reporting symptoms of anxiety was small and this could indicate that the questions included in the interview to assess anxiety may not have been sensitive enough. In addition, the AGECAT algorithm (Copeland et al., 1986) used to categorise the level of anxiety may not be effective at classifying people with less severe but more frequent anxiety problems and consequently may miss individuals with sub-clinical levels of anxiety. In addition, older people may not report anxiety, as they may trivialise the symptoms or regard these as a normal part of the ageing process.

The present study does, however, have several strengths. Firstly, the data were collected from a large sample which incorporated community dwellers and older people living in institutions, from both urban and rural areas in Wales. In addition, the measures used within the interview to assess cognition such as the MMSE (Folstein et al., 1975) and the CAMCOG (Huppert et al., 1995) are very well established tools for use with older people. Lastly, the use of the MCI and MCIW categories for classifying the cognitive status of the participants made it possible to directly compare how SMC operate in relation to mood. This chapter builds on the previous chapter and adds to the literature regarding the questionable value of including SMC in the MCI definition.

The findings from this chapter have several possible applications. From a theoretical perspective, the results raise questions regarding the inclusion of SMC as a criterion within the MCI definition. By insisting on the presence of SMC, many people with objective cognitive impairment who could benefit from timely intervention may go undetected by healthcare professionals. In addition, the MCI and MCIW categories may represent different points on the continuum between normal ageing and pathological ageing. Research suggests that symptoms of anxiety and depression are associated with progression from MCI to dementia, and the lack of a relationship between mood and the MCIW category compared to the relationship shown with the MCI category could indicate that MCI is a step further along

on the pathway to pathological ageing. Alternatively, the MCIW category may represent a separate trajectory, on which participants may progress to further cognitive decline, remain stable or even improve their cognitive performance. It would be informative to follow this sub-sample of participants over time and observe their cognitive journey.

Clinical applications of the findings could include the identification of symptoms of anxiety or depression in older people who report SMC, as the present study suggests that SMC may be related to mood rather than objective cognitive performance. Previous research found that an improvement in mood was associated with a decline in the reporting of SMC (Antikainen et al., 2001). Coupled with research that suggests that SMC are related to a lower quality of life (Mol et al., 2006), this could mean that detecting and addressing mood problems could reduce SMC and in turn improve quality of life. Interventions to improve mood problems may in turn also help to reduce the chances of progression from MCI to dementia.

The findings of this study highlight the requirement for more research in this area. The association between MCI and anxiety could be investigated with more comprehensive measures of anxiety, such as a scaled measurement tool, instead of using the AGECAT algorithm (Copeland et al., 1986). Further investigation could aim to determine the nature of anxiety in older people, and the worries or concerns that affect them. Understanding anxiety better in older people may help to develop a better understanding of how mood, cognitive function and SMC interact.

This study has shown that the odds of experiencing symptoms of anxiety and depression are increased in participants categorised as having MCI, but the odds are not increased in those without cognitive impairment, or those categorised as MCIW, suggesting that SMC are more likely to be related to mood problems rather than objective cognitive

impairment. The results suggest that SMC may play a mediating role in the relationship between cognition and mood problems. Awareness of the interplay between SMC and mood may help older people to obtain targeted assistance for both memory and mood problems which may in turn positively affect their quality of life.

Chapter 6: What role does the health of older people have in the relationship between mood and MCI?

Summary

Health has well documented links to mood, perhaps due to medical burden, or due to metacognitive processes related to the subjective appraisal of health. Health problems are common in older people, and the likelihood of experiencing one or more health problems increases with age. Health is associated with cognitive functioning, in that vascular changes related to poorer health can impact on cognitive performance, or that health problems may limit the ability to take part in beneficial lifestyle behaviours such as physical exercise.

Health is difficult to measure as a concept, and often in health-related research proxy measures are used. This chapter includes an analysis of data from the Cognitive Function and Ageing Study Wales (CFAS Wales), in which structured interviews with community dwellers and older people in residential care captured measures of cognition, mood and health. Health measures included perceived health, co-morbid health conditions, physical activity, health service use and instrumental activities of daily living (IADLs). Each measure of health was assessed independently in relation to cognitive functioning, anxiety and depression, and then combined to form a latent health variable and tested using structural equation modelling. All measures of health were associated with differences in anxiety and depression, with participants who reported anxiety and depression being less likely to engage in physical activity and more likely to report poor or fair health, have more comorbid health conditions, use more services and experience more difficulties with IADLs. Perceived health was associated with cognitive status, with participants classified as having MCI being more likely to report fair or poor health and participants who were not cognitively impaired being less likely to report fair or poor health. Participants with cognitive impairment were less likely to engage in physical activity. Structural equation modelling confirmed the association between health and cognition, with depression acting as a mediator in this relationship.

Introduction

Mild cognitive impairment (MCI) is regarded as a transitional state between normal and pathological ageing (Matthews et al., 2008) and the prevalence is thought to range from 3-20% in older people (Busse, Bischkopf, Reidel-Heller, & Angermeyer, 2003). Currently, several variations of the criteria used to classify MCI have been proposed (Stephan et al., 2008), but broadly they encompass the following: an objective impairment in memory or other cognitive domain, a subjective memory complaint, intact activities of daily living (ADLs), intact general cognition and no dementia (Petersen, 2004; Petersen et al., 2014; Petersen et al., 2001; Petersen et al., 1999). Individuals who experience MCI are at increased risk of progressing to dementia, at a rate of 10-15% per year compared to 1-2% of people without cognitive impairment per year (Petersen et al., 2001) and so MCI is seen as a useful concept that can help to identify people who may be able to benefit from intervention.

In addition to experiencing cognitive changes, older people also frequently experience health problems with risk increasing sharply with age (Brayne et al., 2001; Parker & Thorslund, 2007). The prevalence of chronic disease in old age is generally high. Previous research conducted in a community setting with older people found that 35.6% of participants had one chronic disease and 20.5% of participants had two or more chronic diseases (Bisschop, Kriegsman, Beekman, & Deeg, 2004). The health problems faced in later life can be numerous and wide ranging, and can cause older people to experience functional difficulties which may in turn impact on well-being by diminishing a person's ability to carry out certain tasks.

There are currently well-established links between health problems in later life and cognitive impairment, with vascular diseases being the second most common cause of cognitive decline after Alzheimer's disease (Elwood et al., 2002). Previous research has

found associations between cognitive decline and poorer folate status in older adults (Ebly, Schaefer, Campbell, & Hogan, 1998), and between cognitive impairment and lower levels of vitamin B-12 (Morris, Jacques, Rosenberg, & Selhub, 2007). However, the link between other health problems, such as cancer or arthritis, and cognitive impairment is less clear and is in need of further investigation.

Health problems have also been linked to problems with mood, such as anxiety or depression in older adults, as previous research has found that more depressive symptoms were associated with poorer subjective and objective ratings of health (Williamson & Schulz, 1992b). Late life depressive syndromes frequently occur in conjunction with medical and neurological disorders (Alexopoulos et al., 2002). Depression may be linked to changes in the vascular system, as research suggests that the risk of stroke in older hypertensive people who reported depressive symptoms was more than twice that of older hypertensive people who did not report symptoms of depression (Simonsick, Wallace, Blazer, & Berkman, 1995). In addition, older men who reported psychosocial distress were more likely to suffer from chronic diseases (one or more of ischemic heart disease, diabetes or respiratory disease) or to have retired due to ill-health (May et al., 2002). Depression could be related to the pain experienced (Williamson & Schulz, 1992a) in relation to chronic conditions.

However, health as a concept can be difficult to measure and consequently proxy measures are often used in health research. Physical activity may serve as a marker for health (Laurin, Verreault, Lindsay, MacPherson, & Rockwood, 2001) and was found to improve health related quality of life (Lim & Taylor, 2005) and the mental well-being of people aged over 65 years (Windle, Hughes, Linck, Russell, & Woods, 2010). Being regularly active is associated with better physical and psychological health (Booth, Owen, Bauman, Clavisi, & Leslie, 2000), and was associated with enhanced mood (US Department of Health and Human Services, 1996). Physical activity in later life was found to have a beneficial effect

across a range of outcomes such as anxiety (Lim & Taylor, 2005), minor and major episodes of depression (Sjosten & Kivela, 2006), and it is thought that people who are not engaging in physical activity are twice as likely to have symptoms of depression (US Department of Health and Human Services, 1996). Furthermore, physical activity was linked to a reduced risk of cognitive impairment and dementia, especially Alzheimer's disease (Laurin et al., 2001), and may provide a significant protective effect or even improve cognitive functioning (Angevaren, Aufdempkampe, Verhaar, Aleman, & Vanhees, 2008). A recent randomised controlled trial found that exercise improved cognitive function in older people with MCI over an 18-month follow-up period (Lautenschlager et al., 2008).

Older people are the main users of health and social care in the UK accounting for approximately one third of total hospital admissions (Howse, 2007), and in 2012 46% of adult hospital admissions were for those aged over 65 years (Age UK, 2013). Self-rated health was shown to have an effect on health service use, with general practitioner consultation rates rising as perceived health decreases. In addition, community nurse and home help visits were associated with poor self-rated health, and having a less than excellent rating of perceived health was strongly associated with having had recent contact with health and social services (Bath, 1999). Health service use may act as an indicator for overall health, particularly as it is associated with self-rated health which was found to correlate well with actual health in older people (Stoddart, Whitley, Harvey, & Sharp, 2002).

Instrumental activities of daily living (IADLs) involve complex daily activities, such as household finances or using public transport. IADLs can be affected by anxiety and depression, with symptoms being a potential risk factor for disability (Livingston, Seeman, Merrill, & Blazer, 1994; Stuck et al., 1999). However, the relationship may operate bi-directionally, with functional decline increasing the risk for subsequent depression, perhaps due to the onset of disability impacting on perceived control and self-esteem (Lenze, Rogers,

et al., 2001) or anxiety. A small research study found that when depression in older people is successfully treated, functional ability can improve (Oakley, Khin, Parks, Bauer, & Sunderland, 2002). IADLs may also be related to cognitive functioning. Currently, intact activities of daily living (ADLs) are used as a criterion in the MCI definition and can be used to differentiate between MCI and dementia (Perneczky, Pohl, Sorg, Hartmann, et al., 2006). However, there is less guidance regarding how IADLs should be considered as a criterion and many people with MCI do show some impairment in IADLs. Research suggests a strong correlation between patients' level of cognitive decline and ability to carry out everyday tasks, with tasks involving memory and reasoning especially affected (Perneczky, Pohl, Sorg, Hartmann, et al., 2006; Perneczky, Pohl, Sorg, Hatmann, et al., 2006). The relationship between IADLs, mood and MCI may operate in different ways, whereby cognitive decline may lead to impaired IADLs and in turn depression or anxiety. However, it may be the case that impaired IADLs pose a risk factor for depression or anxiety, which then leads to cognitive decline and the development of MCI.

The link between mood and cognitive changes is well documented. Several studies have found that symptoms of anxiety or depression are more common in people with a classification of MCI than in older people without cognitive impairment (Forsell et al., 2003; Lyketsos et al., 2002; Van der Linde et al., 2010; Yates et al., 2013). The presence of symptoms of anxiety or depression is thought to increase the risk of progression from not cognitively impaired to a classification of MCI (Caracciolo et al., 2011; Geda et al., 2006), and in turn progression from MCI to dementia (Palmer et al., 2007; Panza et al., 2008). The relationship may also be bi-directional, as research has shown that having a classification of MCI may increase the risk of experiencing symptoms of anxiety or depression (Chan et al., 2003; Devier et al., 2009; Muangpaisan et al., 2008).

This chapter aims to investigate the following questions:

1. Are people with MCI more likely to experience health problems than people without cognitive impairment?
2. Are people with health problems more likely to experience mood problems than individuals who do not report health problems?
3. Is the relationship between MCI and mood mediated by health?

Methods

Design

Mood, cognitive functioning and health were examined using cross-sectional data from a large sample of community dwelling older people who participated in the Cognitive Functioning and Ageing Study Wales (CFAS Wales). Fuller details are presented in Chapter 2 of this thesis. CFAS Wales is a longitudinal population-based study which has gathered information about participants drawn from two research centres in urban and rural areas of Wales, investigating changes that people may experience as they age. Participants took part in face-to-face interviews, which were usually conducted in their own homes, with trained interviewers through the medium of English or Welsh, depending on the participant's preference. It was planned that participants would be followed up after 24 months to complete the interview again; this chapter presents analyses from the first wave of data collection. Ethical approval was granted by the relevant NHS Ethics committees.

Participants

Individuals aged over 65 years living in the Gwynedd, Ynys Môn and Neath Port Talbot areas of Wales were randomly sampled between 2011 and 2013. Fuller details are

reported in Chapter 2. Participants were excluded from the analysis if they had a diagnosis of dementia (n=129), impaired ADLs (n=52), or cognitive decline greater than that expected for a classification of MCI, but not meeting the criteria for dementia for other reasons (other cognitive impairment no dementia; OCIND; n=152) resulting in n=3173 participants included in this analysis.

Assessment of health

Five measures of health and health-related behaviour were used to assess participants' overall health. The five measures used questions asked during the CFAS Wales interview.

Perceived health: Subjectively-rated health was assessed with the question: "Would you say that for someone of your age, your own health in general is: Excellent/good/fair/poor/don't know?"

Total health conditions: Participants were asked whether or not they had the following health conditions: angina, intermittent claudication, high/low blood pressure, cancer, diabetes, Parkinson's disease, stroke, heart attack, fits/epilepsy, serious head injury, chronic bronchitis, asthma (excluding childhood asthma), arthritis, peptic ulcers, pernicious anaemia, transient ischaemic attack (TIA), thyroid problems, meningitis and shingles. These questions were mapped on to the Charlson Co-morbidity Index (Charlson et al., 1987). In line with the scoring system of the Charlson Co-Morbidity Index, a summary score was created by scoring each positive answer as one, except for cancer which scored two or three depending on whether the cancer was a past or current problem. The total score had a range from 0 to 21, with higher scores reflecting higher levels of illness.

Total physical activity: The physical activity score was calculated by asking how frequently participants took part in various activities with a total score that ranged from 0 to 72.

Service Use: Health service usage was investigated by asking participants if they had used certain services and how frequently. Positive answers were summed and adjusted for frequency, with higher scores indicating increased usage of services.

Instrumental activities of daily living: IADLs were assessed using five questions in the CFAS Wales interview. Participants responded by reporting if they needed help, had some difficulty or did not have any difficulty with each activity. The total IADL score used in this analysis ranged from 0 to 10 and higher scores reflected less functionality.

Assessment of mood

This study focuses on anxiety and depression. Anxiety and depression were defined using the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) algorithm (Copeland et al., 1986), where a score of two indicated mild symptoms and a score of three or above indicated a case of anxiety or depression. This study considers all participants with a score of two or above.

Classification of cognitive status

Cognitive status categories were defined using the cognitive status algorithm (See Chapter 2, Figure 2.2). Participants classified as having MCI displayed an objective cognitive impairment, an absence of dementia, intact ADLs, intact general cognition (demonstrated by a score of equal to or greater than 22 on the MMSE) and the presence of subjective memory complaints (SMC). The MCIW category included all participants who would otherwise meet criteria for MCI, except that they did not report SMC. Objective cognitive impairment was defined using the CAMCOG (Huppert et al., 1995), which formed a section of the CFAS Wales interview, with scores falling one standard deviation below age-adjusted norms on any of the cognitive domains representing cognitive impairment.

Participants with cognitive impairment beyond what would be expected for a classification of MCI or MCIW (See Chapter 2, Figure 2.2) were excluded from analyses.

Statistical analyses

Descriptive analyses were conducted using SPSS 20.0. Analysis of variance with planned contrasts and post hoc procedures and chi squared analyses were used to investigate the associations between health problems, cognitive status, and presence of symptoms of anxiety or depression. Logistic regression analyses were used to investigate changes in odds of experiencing mood problems according to health and cognitive status. Health was investigated as a latent variable between cognitive functioning and symptoms of anxiety or depression using structural equation modelling procedures in Mplus Version 7.

Results

Data from 3173 participants were analysed and their characteristics are shown in Table 1. The participants were categorised as having no cognitive impairment (NCI), MCI or MCIW. There did not appear to be differences between the cognitive groups in age, gender or years in full time education. Differences between the cognitive status categories on each measure of health were investigated and are shown in Table 6.1. Differences between participants with and without anxiety or depression are shown in Table 6.2.

Table 6.1: Descriptive statistics separated by cognitive status group

		NCI	MCI	MCIW
Age mean (SD)		74.31 (6.95)	73.88 (6.12)	74.87 (6.50)
Female N (%)		1444 (54.6)	89 (44.5)	196 (59.6)
Years in full time education mean (SD)		11.83 (2.80)	11.44 (2.40)	11.08 (2.31)
Perceived health N (%)	Excellent	590 (22.3)	30 (15.0)	75 (22.8)
	Good	1255 (47.5)	78 (39.0)	134 (40.7)
	Fair	607 (23.0)	60 (30.0)	82 (24.9)
	Poor	159 (6.0)	26 (13.0)	17 (5.2)
Physical activity mean (SD)		16.50 (10.37)	12.60 (10.09)	13.96 (10.37)
Service use mean (SD)		4.09 (7.39)	4.26 (8.91)	3.88 (6.99)
Health conditions mean (SD)		2.95 (2.01)	3.32 (2.27)	2.60 (1.89)
IADL score (SD)		1.39 (1.74)	2.08 (2.09)	1.50 (1.96)
Anxiety N (%)		133 (5.03)	18 (9.0)	12 (3.6)
Depression N (%)		628 (23.8)	78 (39.0)	82 (24.9)
Subjective memory complaint N (%)		850 (32.1)	200 (100)	0 (0.0)
Total		2644	200	329

NCI: no cognitive impairment
MCI: Objective cognitive impairment, intact general cognition, intact activities of daily living, subjective memory complaint reported by the participant, absence of dementia
MCIW: Objective cognitive impairment, intact general cognition, intact activities of daily living, absence of subjective memory complaint, absence of dementia

Table 6.2: Mean scores for measures of health for participants with and without anxiety or depression

	No Anxiety	Anxiety	No Depression	Depression
Health conditions mean (SD)	2.87 (1.99)	4.11 (2.24)	2.75 (1.94)	3.49 (2.16)
Physical activity mean (SD)	16.21 (10.39)	12.01 (10.08)	16.80 (10.36)	13.53 (10.18)
Service use mean (SD)	3.96 (7.44)	6.18 (7.44)	3.88 (7.56)	4.66 (7.09)
IADL score (SD)	1.38 (1.76)	2.67 (2.06)	1.23 (1.68)	2.09 (1.98)

Perceived health

Pearson's chi square and likelihood ratios showed that there was a significant difference in perceived health between participants classified as NCI, MCI and MCIW, ($\chi^2(6) = 28.80$, $p<.001$). Logistic regression was used to investigate the association further using perceived health collapsed into two categories of excellent/good and fair/poor to allow for the calculation of risk for each cognitive status. The odds of reporting fair/poor health were

significantly decreased for participants without cognitive impairment (OR=0.71, CI=0.58-0.87, p=.001), but was significantly increased for participants in the MCI category (OR=1.89, CI=1.41-2.54, p<.001). The odds were not significantly changed for participants in the MCIW category (OR=1.09, CI=0.84-1.40, p=.523). Perceived health was found to be related to anxiety, (χ^2 (3) =126.37, p<.001) and depression (χ^2 (3) = 151.73, p<.001). Perceived health was again collapsed into two categories to calculate risk and the association between anxiety and perceived health remained, (χ^2 (1) = 85.86, p<.001). Based on the odds ratio, the odds of having anxiety were 4.31 times higher when participants reported fair/poor health. The association between depression and perceived health also remained (χ^2 (1) = 114.04, p<.001) when perceived health was collapsed into two categories, with the odds of having depression 2.48 times for participants who reported fair/poor health.

Total health conditions

A significant effect of cognitive status was found on health conditions, *F*(2, 384.74) =8.25, p<.001 (equal variances not assumed). Planned contrasts revealed a significant difference in number of health conditions between participants with MCI and those categorised as MCIW, *t*(363.30) =-3.81, p<.001 (equal variances not assumed) and this was confirmed by post hoc testing using the Games-Howell procedure (M=3.33, SE=0.16). Planned contrasts failed to show significant differences between participants with cognitive impairment and those categorised as NCI, *t*(492.23) =0.10, p=.918 (equal variances not assumed). However, further post hoc testing with the Games-Howell procedure revealed a significant mean difference between the MCIW category (M=2.60, SE=0.10) and participants without cognitive impairment (M=2.95, SE=0.04). Participants with anxiety were more likely to suffer from health conditions (M=4.11, SE=0.18) than those without anxiety (M=2.87, SE=0.04), a difference that was statistically significant, *t*(176.07) =-6.90, p<.001, *r*=.46 (equal variances not assumed). Participants with symptoms of depression were also more

likely to suffer from health conditions (M=3.49, SE=0.08) than those without depression (M=2.75, SE=0.04), and this difference was also statistically significant, $t(1234.31) = -8.47$, $p<.001$, $r=.23$ (equal variances not assumed).

Total physical activity

A one-way ANOVA showed that there was a significant effect of cognitive status on levels of physical activity, $F(2, 3172) = 20.34$, $p<.001$. Planned contrasts revealed that having cognitive impairment (either MCI or MCIW) was associated with decreased physical activity score compared to people with NCI, $t(3170) = -6.38$, $p<.001$, $r=.11$. However, there was no significant difference in physical activity score between people with MCI and MCIW, $t(3170) = 1.47$, $p=.142$. Post hoc tests confirmed that the means were significantly different between NCI and MCI, and NCI and MCIW, but not between the MCI and MCIW groups. Participants without anxiety were more likely to engage in physical activity (M=16.21, SE=0.19) than those with anxiety (M=12.01, SE=0.79). This difference was significant, $t(3171) = 5.04$, $p<.001$, $r=0.09$. The same pattern was shown for symptoms of depression, as participants without depression were more likely to engage in physical activity (M=16.80, SE=0.21) compared to those with depression (M=13.53, SE=0.36). This difference was also significant, $t(3171) = 7.72$, $p<.001$, $r=0.14$.

Service use

Cognitive status was not found to be related to service use, as the difference between groups was not significant, $F(2, 3170) = 9.80$, $p=.838$. However, significant differences in service use were found between participants with anxiety (M=6.18, SE=0.58) and those without anxiety (M=3.96, SE=0.14), $t(180.00) = -3.71$, $p<.001$, $r=.27$ (equal variances not assumed). Participants with depression had a higher service use score (M=4.66, SE=0.25)

than participants who were not depressed (M=3.88, SE=0.16) and this difference was significant, $t(1423.86) = -2.62$, p=.009, r=.06 (equal variances not assumed).

Instrumental activities of daily living

A significant difference between participants categorised as NCI, MCI and MCIW was found for IADL score, $F(2, 369.83) = 10.25$, p<.001 (equal variances not assumed). Planned contrasts showed that participants with MCI and MCIW experienced more difficulties with IADLs than participants without cognitive impairment, and that this difference was significant, $t(507.78) = 4.05$, p<.001, r=.19 (equal variances not assumed). The difference in IADL score between participants with MCI and MCIW was also significant, $t(394.81) = -3.11$, p=.002, r=.15 (equal variances not assumed). Games-Howell procedures confirmed that there were significant mean differences between participants in the NCI and MCI categories, and between participants categorised as MCI and MCIW, but there was no significant difference in IADL score between participants without cognitive impairment and those categorised as MCIW. There was a significant difference in IADL score between participants with anxiety (M=2.67, SE=0.16) and those without (M=1.38, SE=0.03), $t(175.10) = -7.84$, p<.001, r=.51 (equal variances not assumed). Similarly, participants with depression experienced more IADL difficulties (M=2.09, SE=0.07) than those without depression (M=1.23, SE=0.03) and this difference was significant, $t(1176.27) = -10.88$, p<.001, r=.30 (equal variances not assumed).

Health as mediating variable

Structural equation modelling was used to assess health as a latent variable that combined the various health-related measures outlined above. The participants were randomly allocated into two groups to allow for a model calibration group and a model validation group. The hypothesised model included total health conditions, total physical

activities, service use, IADL score and perceived health collapsed into two categories as observed variables that loaded on to a latent health variable. Preliminary sensitivity analyses suggested that the reliability for three IADL items (managing money, checking change and following TV programmes; see supplementary results) was poor and consequently it was decided to remove these from the SEM analyses to increase the fit of the model. On calibration of the model, total physical activities was found to reduce the fit of the model and this was subsequently removed. The final model included two IADL items (heavy housework, and shopping and carrying heavy bags), total health conditions, service use and perceived health which loaded on to the latent health variable. The loadings of the observed variables can be seen in Table 4. The latent health variable was regressed upon cognitive status and mood, with mood acting as a mediating variable between health and cognitive status (Figure 6.1). Anxiety and depression were tested separately for each of the three cognitive status categories, with each model being compared to a null model that specified no relationships between the variables. Model fitting statistics can be seen in Table 6.3.

The results of the SEM analyses suggested that health had a direct effect on being categorised as having MCI (b=0.07, p=.021), but not on being categorised as MCIW (b=-0.049, p=.186) or not cognitively impaired (b=-0.01, p=.893). Anxiety was not associated with being categorised as not cognitively impaired (b=-0.03, p=.613) or MCIW (b=-0.01, p=.914), or MCI (b=0.04, p=.372). Anxiety did not mediate the relationships between health and MCI (b=0.02, p=.374), health and MCIW (b=0.00, p=.914) or health and not cognitively impaired (b=-0.01, p=.614).

The risk of experiencing symptoms of depression was significantly decreased in people categorised as not cognitively impaired (b=-0.08, p=.017), but was slightly increased in those classified as having MCI (b=0.09, p=.003), and did not significantly change for people in the MCIW category (b=-0.02, p=.618). Depression significantly mediated the

relationship between health and MCI (b=0.30, p=.005) and between health and NCI (b=-0.03, p=.021), but was not a mediator of the relationship between health and MCIW (b=-0.01, p=.618).

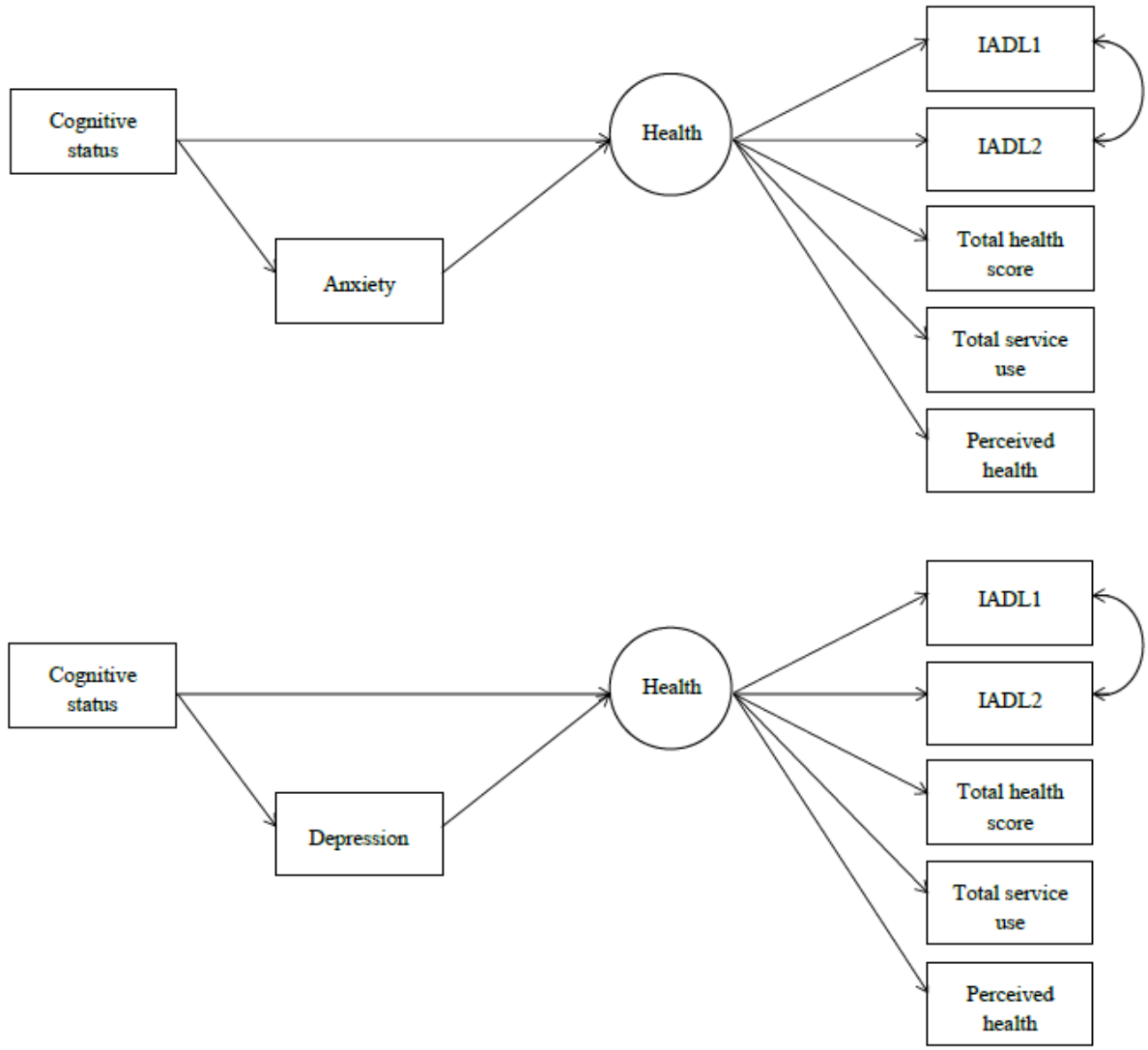

Figure 6.1: Final structural equation model solution showing anxiety (top) and depression (bottom) as mediators.

Table 6.3: Model fitting statistics for each structural equation model

Model		$\chi 2$	*p*-value	*df*	RMSEA	CFI
Anxiety	NCI	26.75	.008	12	.028	.989
	MCI	14.81	.248	12	.012	.998
	MCIW	28.69	.044	12	.029	.988
Depression	NCI	31.14	.002	12	.031	.986
	MCI	19.17	.085	12	.019	.995
	MCIW	34.24	.001	12	.035	.986

Table 6.4: Factor loadings of observed measures of health on to the latent health variable

	Estimate	Standard error	*p*-value
IADL1	0.63	.026	.000
IADL2	0.62	.025	.000
Total health conditions	0.64	.019	.000
Total service use	0.26	.009	.000
Perceived health	0.57	.020	.000

Discussion

This study aimed to explore the influence of various measures of health on the relationship between mood and mild cognitive impairment. The measures of health investigated were perceived health, health conditions, physical activity, health service use, and instrumental activities of daily living (IADLs).

There were differences on all measures of health between people with and without anxiety and depression. Participants with anxiety or depression had more comorbid health conditions than those without mood problems. This could be due to the association between overall medical burden and increased risk of depression (Alexopoulos, 2005). Those with anxiety and depression reported using more health services than participants who did not report symptoms. Participants with anxiety and depression had more difficulties with IADLs compared to those not reporting symptoms, reflecting previous research that suggests that depression is associated with functional decline (Stuck et al., 1999). Older people reporting

anxiety and depression were found to have a lower level of participation in physical activities than those without mood problems.

However, the differences across the measures of health between the three cognitive status groups of NCI, MCI and MCIW are less clear cut. Participants without any cognitive impairment had less IADL difficulties than those with MCI or MCIW, which reflects previous research (Perneczky, Pohl, Sorg, Hatmann, et al., 2006), and participated in more physical activities than those categorised as MCI or MCIW. There were no significant differences in service use score between the cognitive groups, although the mean scores showed a trend for participants categorised as MCI scoring slightly higher. This is in line with previous literature which found that participants with cognitive impairment were more likely to be hospitalised and stay in for longer (Weiler, Lubben, & Chi, 1991). Participants categorised as MCI and NCI did not differ in the number of comorbid health conditions. It is interesting that participants in the MCIW category reported the least number of co-morbid health conditions. Participants categorised as MCIW may be less likely to report health problems, suggesting a link to underlying metacognitive processes.

Perceived health was found to be related to an increased risk of anxiety and depression, and showed an association with cognitive status. The proportion of participants reporting fair or poor health is higher in the MCI category than for participants without cognitive impairment, or those categorised as MCIW. This suggests that perceived health may be linked with the subjective memory complaint element of the MCI criteria. Previous research has shown that poor reported health is associated with higher general practitioner (GP) consultation rates and the use of health and social services (Bath, 1999), whilst better self-rated health is predictive of better functional status and lower service use (Bond, Dickinson, Matthews, Jagger, & Brayne, 2006). It is widely acknowledged that if mood problems are treated there are likely to be positive effects on how people perceive their own

health which in turn could improve functional status and reduce health and social service requirement. Improvements to cognitive functioning could also improve self-perception of health, however, this is more difficult to achieve. Public health initiatives targeted at younger adults to adopt lifestyle interventions that may enhance or preserve cognitive functioning, such as improving cardiovascular health may be beneficial.

Structural equation modelling showed that the latent variable of health was associated with being classified as having MCI, but not with being in the no cognitive impairment or MCIW categories. Anxiety was not associated with the MCI, MCIW or no cognitive impairment categories and did not mediate the relationship between health and cognitive status. The odds of experiencing symptoms of depression were decreased for people without cognitive impairment, but were increased in those categorised as having MCI. The odds of having depression did not change for participants in the MCIW category. Depression was also found to be a mediator in the relationship between health and MCI and between health and no cognitive impairment, but mediation analyses were not significant between health and the MCIW category. This may suggest that the relationship between health and MCI arises because health and mood are inter-related, and as this relationship only occurs in people with MCI it could point to the involvement of SMC. The findings regarding symptoms of anxiety remain unclear and further investigation with a larger sample is needed.

This study has several limitations. Firstly, the number of participants reporting anxiety is very small and this may have resulted in low statistical power. In addition, the numbers of participants in the cognitive status groups is unequal which resulted in unequal variances across several statistical tests and may have contributed to the small effect size some of the analyses. However, the statistical tests used are robust which supports confidence in the findings.

A further limitation is that the questions regarding anxiety used in the CFAS Wales interview and the AGECAT algorithm (Copeland et al., 1986) used to classify participants as having anxiety may not be sensitive enough to elicit the true nature of anxiety in older people. Anxiety in older people is difficult to measure and questions using a scaled response may have provided a better measure. However, participants classified as a sub-case of anxiety according to the AGECAT algorithm were considered to have anxiety in this study in order to capture milder and less frequent symptoms.

The measures of physical activity and health service use do not have a validated scoring system. Instead, positive answers to questions asked in the CFAS Wales interview were summed to create composite scores. Validated measures of physical activity and health service use may have elicited clearer responses in order to create a more accurate picture of health in older people. In addition, the measure of physical activity was developed approximately 25 years ago. Due to different opportunities for physical activity and changing tastes or fashions over time, this measure may benefit from being refreshed to include activities that a modern cohort may endorse. For example, there was not a great deal of 'dancing' or 'heavy housework' reported. The measure of health conditions was derived from the Charlson Co-Morbidity Index using the questions asked in the CFAS Wales interview. Recent research (Quan et al., 2011) has reported that the weightings for some health conditions should be adjusted to reflect the ageing population. However, the reliability of our health measure using the original Charlson weightings (Charlson et al., 1987) was found to be good and so the weightings were not adjusted in this study. Furthermore, the Charlson Co-morbidity Index was developed for use with hospital administration data (Chaudhry, Jin, & Meltzer, 2005), but research suggests that it is applicable to self-report and questionnaire data (Katz, Chang, Sangha, Fossel, & Bates, 1996) and the measure of health conditions used in these analyses may be treated confidently.

This study has several strengths. The overall sample size is very large and due to sampling procedures employed, the sample was as representative as possible, as it included both community dwellers and those living in residential care and had a response rate of approximately 50%. In addition, extensive efforts were made to contact potential participants living in very rural and isolated areas, and people over 75 years of age were over-sampled to ensure that the oldest old were well represented.

This study has brought together several proxy measures of health to assess the contribution of each measure to the relationship between mood and mild cognitive impairment. Health has many dimensions to it, and using several aspects of health and health-related behaviours has added to the detail of the analysis.

The use of well-defined cognitive categories is a further strength of this study. The MCI cognitive status group is based on criteria similar to those of Petersen (Petersen, 2004) which will allow the results of this study to be compared to other studies. The MCIW cognitive status group allowed for investigation of the differences experienced by those who do not report subjective memory complaints by comparing participants in this group to those with MCI, which has added to the emerging literature on subjective cognitive impairment.

The results of this study could be used to provide an evidence base for interventions addressing the health of older people. Improvements in health may assist with preventing or reducing mood problems, which will also benefit cognition. In reducing mood problems, fewer burdens may be placed on health and social services which would benefit the wider community in freeing up health service resources. In addition, older people in receipt of health and social services are also likely to be cared for by family members (Luker & Perkins, 1987; Wenger, 1985). Consequently, in helping to decrease the effects of anxiety and depression and need for services, the burden placed on family members could be

reduced. Carers can develop avoidable health problems (Simon, 2001) which may be prevented through supporting those with anxious and depressive symptomology.

This chapter has brought together several measures of health to provide a picture of the relationship between MCI, mood and health in greater detail than has been seen in other research, allowing different conceptualisations of health to be investigated in relation to mood and cognition. The use of the MCI and MCIW categories has shown that perceptions of health extend to include cognitive functioning, which is an important finding given that physical and cognitive health are often treated very separately by patients and doctors alike. The finding that participants in the MCIW category, without SMC, reported less health problems than participants with MCI and those with normal cognitive functioning is particularly interesting and this is thought to be the first research to show this finding. Overall, this chapter has clarified the link between health and mood, which in turn influences cognitive functioning; suggesting that with careful intervention and encouragement to maintain healthy lifestyles as people age both mood problems and cognitive decline may be prevented.

Chapter 7: Do social networks help to explain the relationship between mood and MCI?

Summary

Social networks can change as people grow older, for various reasons that may be adaptive or unwanted. Social interactions are thought to be beneficial to mental health, and consequently changes to social networks may be associated with symptoms of anxiety or depression.

This chapter reports an investigation into the role that social networks might play in the relationship between mild cognitive impairment (MCI) and mood and includes an analysis of data collected as part of the Cognitive Function and Ageing Study Wales (CFAS Wales). CFAS Wales involved conducting a structured interview with community dwelling older people which included measures of mood, cognitive functioning and social networks. The findings of this chapter showed that having a smaller social network was associated with being classified as having MCI and with experiencing symptoms of anxiety and depression. However, moderation effects of social networks on the relationship between MCI and mood could not be established. This suggests that whilst social networks may not change this association, maintaining a social network can positively influence both mood and cognitive functioning. Maintaining social networks is an area that could benefit from intervention through befriending schemes or local volunteering initiatives.

Introduction

Social networks can be conceptualised as the web of social relationships surrounding a person, taking into account the nature of the interpersonal ties involved (Berkman et al., 2000). Most older people have a significant number of relationships, although previous research suggests that there is a negative association between age and social network size (van Tilburg, 1998) as older people may experience a reduction in the size of their social networks, and are more likely to disengage socially than younger people (Wenger, 1997). There are many reasons for this, including the death of friends and family members, problems getting out of the house, a loss of confidence, or a lack of opportunities for social interaction. However, it has also been suggested that older people perform a selective 'pruning' process where contact is lost with peripheral members of social networks in order to focus on more meaningful relationships with emotionally closer members of the network (Carstensen et al., 2003).

Mood-related problems, such as symptoms of depression, are common in older people (Beekman, Copeland, & Prince, 1999; G. J. McDougall et al., 2006). Previous research found depression to be prevalent in 9.3% of community dwelling older people, and in 27.1% of those living in institutions (F. A. McDougall et al., 2007). Anxiety in older people is less well researched and estimates suggest that the prevalence is 0.2% (Kvaal et al., 2008).

Previous research has shown a relationship between symptoms of anxiety or depression and changes to social networks. People with fewer social interactions are more likely to have symptoms of anxiety or depression (Prince, Harwood, Blizard, Thomas, & Mann, 1997). On the other hand, having multiple social roles can help to promote self-esteem, which in turn may prevent depression (Berkman et al., 2000; Fratiglioni, Paillard-Borg, & Winblad, 2004). Some studies have indicated that people who experience greater

levels of social interaction and support have better mental health outcomes (Seeman, 1996; Seeman et al., 2001) and significantly decreased psychological distress (Wenger, 1997). Social cognitive theory (Bandura, 1998) suggests that experiencing anxiety or depression may reduce feelings of efficacy necessary to create and maintain relationships, leading to a decline in social network size.

In addition to changes in social networks, older people may also experience changes in their cognitive functioning, with some meeting criteria for classification as having mild cognitive impairment (MCI). MCI is thought to represent a transitional phase on a continuum between normal cognitive functioning and pathological decline (Matthews et al., 2008). Research suggests that 10-15% of those classified as having MCI will progress to a diagnosis for dementia each year, compared to only 1-2% of people without cognitive impairment (Petersen et al., 2001). There are several variations on the criteria used to classify MCI (Stephan et al., 2008), but the broad definition includes an impairment in memory or another cognitive domain, a subjective memory complaint, intact activities of daily living (ADLs), intact general cognition and no dementia (Petersen, 2004; Petersen et al., 2001; Petersen et al., 1999).

The link between symptoms of MCI and symptoms of anxiety and depression is well established (Forsell et al., 2003; Van der Linde et al., 2010)(Chapter 3), with several studies suggesting that mood problems pose a risk factor for the development of MCI (Caracciolo et al., 2011; Geda et al., 2006) and for progression from MCI to dementia (Palmer et al., 2007; Panza et al., 2008). This evidence base highlights the need for further research into the MCI concept as it is an area well placed for the development of interventions to delay further cognitive decline.

There is also evidence for a link between cognitive function and social networks (Beland, Zunzunegui, Alvarado, Otero, & del Ser, 2005; Berkman et al., 2000). Social isolation or disengagement is thought to accelerate cognitive decline in ageing (Fratiglioni et al., 2004; Wang et al., 2002). A rich social network was reported to have a protective effect against dementia (Wang et al., 2002). However, it is not clear in which direction the association may operate as cognitive impairment may make it difficult for older people to maintain social networks, leading to a withdrawal from social interactions and in turn an increase in anxious or depressive symptomatology. On the other hand, increased symptoms of anxiety or depression may lead to fewer social interactions, increasing the risk of a classification of MCI.

This chapter aims to examine the three-way relationship between MCI, mood and social networks, but will first examine associations between MCI and mood, MCI and social networks, and social networks and mood, in a large sample of older people recruited from primary care lists. Moderation analyses are used to assess the three-way nature of the relationship between cognitive status and mood, as it is expected that social network score will alter the strength of the relationship between cognition and mood depending on which cognitive status category participants belong to.

Methods

Design

Mood, cognitive functioning and social networks were examined using cross-sectional data from a large sample of older people who participated in the Cognitive Functioning and Ageing Study Wales (CFAS Wales). Fuller details can be found in Chapter 2 of this thesis. CFAS Wales is a longitudinal population-based study which has gathered information about participants drawn from two research centres in urban and rural areas of Wales, investigating

changes that people may experience as they age. Participants took part in face-to-face interviews, which were usually conducted in their own homes, with trained interviewers through the medium of English or Welsh, depending on the participant's preference. Participants are followed up after 24 months to complete a number of measures again. Ethical approval was granted by the relevant NHS Ethics committees. This chapter presents baseline data.

Participants

Individuals over 65 years and living in the Gwynedd, Anglesey and Neath Port Talbot areas of Wales were randomly sampled between 2011 and 2013 (See Chapter 2 for details). Participants were excluded from the analysis if they had a diagnosis of dementia (n=129) or impaired ADLs (n=52) or cognitive decline greater than that expected for a classification of MCI, but not meeting the criteria for dementia for other reasons (other cognitive impairment no dementia; OCIND; n=152) resulting in 3173 participants being included in this analysis.

Social network score

Social networks were assessed in the interview by ascertaining participants' contact with friends and relatives using the Lubben Social Network Scale six-item version (LSNS-6; Appendix O) (Lubben et al., 2006). The LSNS-6 comprises two subscales investigating the level of contact with family and friends and has a total score of 30, and was included in the CFAS Wales interview.

Assessment of mood

Anxiety and depression were assessed in the CFAS Wales interview. Anxiety and depression were defined using the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) algorithm (Copeland et al., 1986),

where a score of two indicated mild symptoms and a score of three or above indicated a case of anxiety or depression. This study considers all participants with a score of two or above.

Classification of cognitive status

MCI was defined using the cognitive status algorithm (See Chapter 2, Figure 2.2). Participants classified as having MCI displayed an objective cognitive impairment, intact ADLs, intact general cognition (indicated by a score equal to or greater than 22 on the MMSE), an absence of dementia and reports of subjective memory complaints (SMC). A further cognitive status group of those otherwise meeting criteria for MCI but who did not report subjective memory complaints was also created (MCIW). Objective cognitive impairment was defined as scores falling one standard deviation below age-adjusted norms on one or more of the subscales of the CAMCOG (Huppert et al., 1995), a well-established scale designed to asses different domains of cognitive functioning that formed a section of the CFAS Wales interview. Participants with cognitive impairment more severe than would be expected for a classification of MCI or MCIW were identified using the cognitive status algorithm (See Chapter 2, Figure 2.2) and were excluded from analyses.

Statistical analyses

Statistical analyses were conducted using SPSS 20.0. Logistic regression analyses were used to investigate the change in odds of experiencing symptoms of anxiety and depression dependent on cognitive status and social network score, and to investigate the interaction of these factors. The relationship between social network score and cognitive status was also investigated using analysis of variance (ANOVA) and correlation analyses. Planned contrasts were used in the ANOVA to investigate differences in social network score which were confirmed using post-hoc procedures. Moderation analyses were conducted by

investigating the interaction effects of the target variables.

Sensitivity analyses

Logistic regressions were conducted on each subtype of MCI to test for robustness and are presented in Supplementary Table S7.1. In predicting the odds of symptoms of anxiety, only the non-amnestic subtype was significant, and both the amnestic and non-amnestic subtypes were significantly associated with depression. The multiple-domain subtype was not significantly associated with anxiety or depression. The MCI and MCIW categories were combined to create MCItotal, which includes participants who meet all criteria for MCI, both with and without SMC. Logistic regression was used to assess the relationship with mood and the results can be found in Table S7.1. The relationship between MCItotal and depression was significant, but MCItotal was not found to significantly increase the odds of anxiety.

Table 7.1: Sensitivity analyses investigating the relationship between cognitive category and mood

	OR	CI	P
Anxiety			
MCIA	0.86	0.37-1.98	.724
MCIN	**5.40**	**2.63-11.08**	**.000**
MCIM	2.07	0.48-8.98	.333
MCItotal	1.14	0.76-1.71	.542
Depression			
MCIA	**1.98**	**1.39-2.84**	**.000**
MCIN	**1.97**	**1.08-3.58**	**.026**
MCIM	2.03	0.83-4.98	.123
MCItotal	**1.39**	**1.13-1.71**	**.002**

MCIA: Amnestic-MCI subtype (objective cognitive impairment is in memory only)
MCIN: Non-amnestic-MCI subtype (objective cognitive impairment is in a non-memory domain of cognitive functioning, e.g. language)
MCIM: multiple-domain-MCI subtype (objective cognitive impairment is in more than one domain of cognitive functioning and may include memory and non-memory domains)
MCItotal: Objective cognitive impairment, intact general cognition, intact ADLs, absence of dementia, SMC may or may not be present

Further sensitivity analyses focused on the definition of anxiety and depression. An AGECAT score of two is considered a ‘subcase’ and a score of three is considered a ‘case’. Cases and subcases were analysed separately and the results are shown in Table S7.2.

Table 7.2: Sensitivity analyses investigating the relationship between cognitive category and subcases or cases of mood

	OR	CI	P
Anxiety Case Level			
NCI	0.95	0.57-1.60	.860
MCI	**2.00**	**1.08-3.71**	**.028**
MCIW	0.52	0.23-1.20	.124
Depression Case Level			
NCI	0.69	0.51-0.93	.015
MCI	1.53	0.99-2.37	.058
MCIW	1.32	0.91-1.90	.147
Anxiety Subcase Level			
NCI	0.78	0.41-1.48	.447
MCI	1.70	0.72-4.01	.223
MCIW	0.98	0.42-2.29	.960
Depression Subcase Level			
NCI	0.80	0.63-1.02	.068
MCI	**1.99**	**1.43-2.77**	**.000**
MCIW	0.84	0.60-1.16	.283

Sensitivity analyses were also conducted using each level of the AGECAT score separately. AGECAT scores for anxiety range from 0 to 5 and from 0 to 4 for depression. The results are presented in Table S7.3 and few analyses show significant results, confirming the reason that grouping levels two and above together is the most effective way of analysing this data.

Table 7.3: Odds ratios showing the relationship between cognitive category and each AGECAT level of anxiety or depression

		OR	CI	P
Anxiety Level 0	NCI	1.00	0.83-1.21	.982
	MCI	0.76	0.57-1.01	.057
	MCIW	1.21	0.95-1.53	.121
Anxiety Level 1	NCI	0.76	0.85-1.25	.761
	MCI	1.13	0.84-1.51	.434
	MCIW	0.89	0.70-1.13	.320
Anxiety Level 2	NCI	0.78	0.41-1.48	.447
	MCI	1.70	0.72-4.01	.223
	MCIW	0.98	0.42-2.29	.960
Anxiety Level 3	NCI	0.85	0.47-1.54	.600
	MCI	**2.11**	**1.03-4.30**	**.040**
	MCIW	0.62	0.25-1.55	.307
Anxiety Level 4	NCI	1.47	0.44-4.93	.532
	MCI	1.30	0.30-5.53	.727
	MCIW	0.36	0.05-2.66	.315
Anxiety Level 5	NCI	0.80	0.09-7.17	.842
	MCI	3.73	0.42-33.53	.240
	MCIW	Unable to compute due to lack of cases		
Depression Level 0	**NCI**	**1.33**	**1.09-1.62**	**.005**
	MCI	**0.49**	**0.36-0.65**	**.000**
	MCIW	1.07	0.83-1.38	.605
Depression Level 1	NCI	1.09	0.69-1.72	.705
	MCI	1.33	0.73-2.45	.356
	MCIW	0.68	0.37-1.28	.233
Depression Level 2	NCI	0.80	0.63-1.02	.067
	MCI	**1.99**	**1.43-2.77**	**.000**
	MCIW	0.84	0.60-1.16	.283
Depression Level 3	**NCI**	**0.64**	**0.46-0.90**	**.011**
	MCI	1.39	0.83-2.34	.211
	MCIW	**1.55**	**1.03-2.32**	**.034**
Depression Level 4	NCI	0.88	0.49-1.59	.679
	MCI	1.78	0.84-3.76	.130
	MCIW	0.74	0.32-1.71	.476

An independent samples t-test was used to compare the mean social network score between the no cognitive impairment group and the MCItotal group (MCI+MCIW) and the

results showed that there was a significant difference in social network score between the groups, $t(725.63)=3.68$, $p<.001$ (one tailed; equal variances not assumed), $r=0.13$. The total CAMCOG score was split into two groups using the median value, and an independent samples t-test was used to compare the mean social network score between the low scoring CAMCOG group and the high scoring CAMCOG group. The analysis showed that there was a significant difference in social network score between the two CAMCOG groups, $t(3171)=-7.08$, $p<.000$ (one tailed), $r=0.12$.

Logistic regressions were conducted to assess the relationship between social network score and mood using either the subcase or the case definitions of anxiety and depression and are presented in Table S7.4. The analyses show that the odds of case level anxiety or depression are significantly reduced, but the relationship between subcase level anxiety or depression and social network scale are not significantly changed. The results are similar to those included in the main analyses using anxiety and depression level two and above.

Table 7.4: Odds ratios showing the relationship between anxiety and depression cases and subcases and social network score

	OR	CI	P
Anxiety subcase	1.00	0.96-1.04	.904
Depression subcase	1.00	0.98-1.01	.533
Anxiety case	**0.96**	**0.92-0.99**	**.006**
Depression case	**0.94**	**0.92-0.96**	**.000**

Results

Data were analysed from 3173 participants who were classified as having no cognitive impairment (NCI), MCI or MCIW and their characteristics are shown in Table 7.5. There did not appear to be differences between the cognitive groupings in age, gender, years in full time education or marital status.

Table 7.5: Descriptive statistics separated by cognitive status group

		NCI	MCIP	MCIW
Age mean (SD)		74.31 (6.95)	73.88 (6.12)	74.87 (6.50)
Female N (%)		1444 (54.6)	89 (44.5)	196 (59.6)
Years in full time education mean (SD)		11.83 (2.80)	11.44 (2.40)	11.08 (2.31)
Marital status N (%)	Married	1657 (62.7)	132 (66.0)	183 (55.6)
	Cohabiting	41 (1.6)	2 (1.0)	6 (1.8)
	Single	97 (3.7)	6 (3.0)	19 (5.8)
	Widowed	667 (25.2)	40 (20.0)	97 (29.5)
	Divorced/Separated	181 (6.8)	20 (10.0)	24 (7.3)
LSNS6 score mean (SD)		15.58 (5.82)	14.15 (6.13)	14.71 (6.26)
Anxiety N (%)		133 (5%)	18 (9.0)	12 (3.6)
Depression N (%)		628 (23.8)	78 (39.0)	82 (24.9)
Subjective memory complaint N (%)		850 (32.1)	200 (100)	0 (0.0)
Total		2644	200	329

NCI: no cognitive impairment
MCI: Objective cognitive impairment, intact general cognition, intact activities of daily living, subjective memory complaint reported by the participant, absence of dementia
MCIW: Objective cognitive impairment, intact general cognition, intact activities of daily living, absence of subjective memory complaint, absence of dementia

Is there an association between MCI and mood?

Logistic regression analyses showed the odds of having symptoms of anxiety were significantly increased in people categorised as MCI (OR=1.93, CI=1.16-3.22, p=.012) but not in those categorised as MCIW (OR=0.68, CI=0.37-1.23, p=.199) or NCI (OR=0.88, CI=0.59-1.32, p=.542). The odds of having symptoms of depression were also increased in participants categorised as MCI (OR=2.04, CI=1.52-2.74, p<.001) but not in people categorised as MCIW (OR=1.01, CI=0.77-1.31, p=.968). The odds of depressive symptoms were decreased in participants without cognitive impairment (OR=0.72, CI=0.59-0.88, p=.002).

Is there an association between MCI and social networks?

A one-way ANOVA showed a significant effect of cognitive status on social network score, $F(2, 381.882) = 7.35$, $p < .005$. A significant Levene's statistic revealed unequal variances between cognitive status groups so the Welch statistic was used to increase the robustness of the analysis. Planned contrasts revealed that the social network score significantly decreased for both MCI and MCIW categories compared to no cognitive impairment, $t(578.99) = -3.83$, $p < .001$ (one-tailed), $r = 0.5$, but that there were no significant differences in social network score between the MCI and MCIW categories $t(426.96) = -1.01$, $p = .155$ (one-tailed), $r = 0.05$, (equal variances not assumed).

Is there an association between social networks and symptoms of anxiety or depression?

Logistic regression analyses were conducted using social network score as a continuous variable to investigate the association with mood. The analyses showed that social network score was associated with a small decrease in risk of having symptoms of anxiety (OR=0.96, CI=0.93-0.99, p=.003) and the risk of having symptoms of depression (OR=0.97, CI=0.95-0.98, p<000), and significance remained after age and gender were controlled for. Correlation analysis showed that social network score was significantly inversely related to both anxiety ($r = -0.41$, p[one-tailed] =.011) and depression ($r = -0.75$, p[one-tailed] <.000) suggesting that as social network score decreases, anxiety and depression increase. Table 7.6 shows the mean social network scores for each AGECAT level of anxiety and depression and suggests a general trend of decreasing social network score as severity of anxiety and depression increase.

Table 7.6: Mean social network score for each AGECAT level of anxiety and depression

Anxiety	N(%)	Mean Social Network Score (SD)
0	1870	15.67 (5.82)
1	1140	15.09 (5.94)

Depression	N(%)	Mean Social Network Score (SD)
0	2237	15.72 (5.83)
1	148	14.57 (6.52)

2	59	15.31 (5.62)
3	74	13.89 (6.07)
4	25	14.00 (6.08)
5	5	12.20 (6.61)

2	509	15.25 (5.68)
3	203	13.67 (6.44)
4	76	13.09 (5.37)

What is the nature of the three-way relationship between MCI, mood and social networks?

Logistic regression was used to investigate the relationship between the cognitive categories, social network score, the interaction of each cognitive category with the social network score, and mood. In testing for anxiety it was found that there were no main effects for cognitive status or social network score and no interaction between the two for participants with no cognitive impairment compared to the participants categorised as MCI or MCIW. In participants categorised as MCI, there was a significant main effect of social network score on anxiety (OR=0.96, CI=0.92-1.00, p=.046) but the main effect of cognitive status and the interaction term were not significant. There were no significant main effects of cognitive status or social networks, and there was no significant interaction between the two for participants categorised as MCIW.

There was a significant main effect of social network score for participants with no cognitive impairment on the relationship with depression (OR=0.97, CI=0.96-0.99, p=.001) but there was not a significant main effect of cognitive status or a significant interaction between the two. In participants with MCI, cognitive status and social network score both showed main effects (OR=2.59, CI=1.22-5.48, p=.013; OR=0.97, CI=0.94-0.99, p=.005 respectively) but there was no significant interaction. Participants categorised as having MCIW did not show a main effect for cognitive status, but there was a significant main effect for social network score (OR=0.98, CI=0.96-1.00, p=.035). There was no interaction between cognitive status and social network score for participants with MCIW.

The role of subjective memory complaints

In order to investigate this relationship between MCI and mood more thoroughly, analyses were conducted to assess the role of subjective memory complaints. SMC increased the odds of anxiety (OR=2.25, CI=1.64-3.09, p<.001) and depression (OR=2.02, CI=1.71-2.39, p<.001). There was no significant difference in social network score between participants who reported SMC and those who did not, $t(3171)=1.06$, p=.145 (one tailed), $r=0.02$. Logistic regression was used to determine main and interaction effects of social network score and SMC on anxiety and only social network score showed a significant main effect (OR=0.97, CI=0.95-0.99, p=.027). However, for depression, both SMC and social network score showed main effects (OR=2.03, CI=1.30-3.19, p=.002; OR=0.97, CI=0.96-0.99, p<.001, respectively) but there was no interaction between the two.

Discussion

This study aimed to investigate the relationship between MCI and mood, and to explore the effect of social networks on this relationship. Anxiety and depression were significantly increased in participants classified as having MCI, but not in those categorised as MCIW or NCI. The social network score was significantly less in the MCI and MCIW groups compared to participants in the NCI category, and correlation analyses suggested that as the social network score increased, anxiety and depression decreased. Moderation analyses revealed that social network score had an effect on mood, and being categorised as having MCI had an effect on depression. However, there were no interactions between cognitive status, social network score and mood. This suggests that whilst cognitive status and social network score are important factors in whether participants experience mood problems, the relationship between cognitive status and mood is not moderated by social network score.

The relationship between MCI and mood was explored, on the basis of previous research identifying that anxiety and depression may be potential risk factors for the development of MCI (Caracciolo et al., 2011; Goveas et al., 2011), and the progression from MCI to dementia (Palmer et al., 2007; Panza et al., 2008; Steenland et al., 2012). The findings of this study are in line with the existing literature and findings of the previous chapters of this thesis, in that participants who were classified as having MCI had increased odds of experiencing symptoms of both anxiety and depression compared to participants without cognitive impairment (Fernandez-Martinez et al., 2010; Hwang et al., 2004; Van der Linde et al., 2010). However, participants in the MCIW group, who met the criteria for MCI except for reporting SMC, did not show significantly increased odds of anxiety or depression. This suggests that mood problems may be related to the subjective element of the MCI definition rather than objective cognitive impairments, and may reflect underlying metacognitive processes that warrant further investigation. Underlying metacognitive processes may operate in a similar way to social cognitive theory, which emphasises the role of self-efficacy in creating and maintaining social relationships (Bandura, 1998). Self-efficacy can be disrupted by feelings of anxiety and depression. This may mean that metacognition is similarly disrupted, and that in experiencing anxiety or depression, people lose the feeling of competence in their cognitive processes leading to reports of memory complaints, regardless of objective evidence.

The analyses identified that there was a significant difference in the social network score between the cognitive status groups, and further statistical procedures identified that the MCI and MCIW groups were significantly different to participants without cognitive impairment, but were not different from each other. Previous evidence has suggested that a rich social network (Wang et al., 2002) and a greater number of confidants (Seidler, Benhardt, Neinhaus, & Frolich, 2003) can have a protective effect against dementia and this

could suggest that a smaller social network may be a risk factor for MCI. The social environment could affect cognitive ageing (Beland et al., 2005) and a smaller social network could have an effect on cognitive decline. The findings of this study showed that whilst there was no significant differences in social network score between the MCI and the MCIW groups, the mean score for the MCIW group was slightly higher than that of the MCI group. This may mean that an effect is present, but is too small to be detected in this sample.

An increase in social network score was found to slightly decrease the odds of experiencing both anxiety and depression. Correlation analyses showed a strong, inverse relationship between social network score and anxiety or depression, suggesting that as the social network score increased anxiety or depression decreased. This follows previous findings, which have also suggested that social integration can lead to better mental health outcomes (Seeman et al., 2001) and that social isolation can increase the risk of depression (Berkman et al., 2000). However, the reverse may also be true that a reduced social network may be determined by depressive symptoms (Fratiglioni et al., 2004), and it is difficult to investigate the direction of this relationship in this study because it is cross-sectional in design.

Main effects of being categorised as having MCI and social network score were found when testing for moderation in the relationship between cognitive status and depression, although no significant interaction effects were found between any cognitive group and social network score. This suggests that whilst social network score and the MCI classification are related to the odds of experiencing depression, with social network score showing a decrease and MCI showing an increase, the relationship is not moderated. Main effects were found for social network score in participants categorised as having MCI when investigating the relationship between cognitive status and anxiety, although the interaction between cognitive status and social network score was not significant for any category.

The present study does have some methodological limitations. The questions regarding anxiety may not be sensitive enough to capture mild anxiety and every day worries experienced by older people. In addition, anxiety may be underreported due to older people attempting to minimise anxious feelings or worries. This study used the AGECAT algorithm (Copeland et al., 1986) to calculate mood and this may yield different results to those of a scaled anxiety questionnaire or clinical judgement. In addition, the sample sizes for NCI, MCI and MCIW were different, with over ten times as many participants in the NCI category as in the MCI category, which may have affected the statistical power in the analyses. Furthermore, the participant recruitment process may have biased the study sample slightly, as potential participants with anxiety or depression may have refused to participate.

However, there are many strengths of this study. The overall sample used in the analyses is large and draws from both urban and rural populations. The sampling frame was designed to over sample for people over the age of 75 to ensure that the oldest old were well represented within the sample and the participation rate was almost 50%.

The study also uses clear operationalised definitions of the cognitive categories, and in particular MCI (See Chapter 2, Figure 2.2), which allows for comparison with other studies using the same criteria. In addition to the MCI category, participants who meet criteria without exhibiting SMC (MCIW) were also investigated to see how they differ to participants in the MCI category, and this has added to the emerging evidence base on subjective cognitive impairment.

The Lubben Social Network Scale six-item version (LSNS-6; Appendix O) (Lubben et al., 2006) was used as the measure of social networks in this study and is a reliable and valid measure. The LSNS-6 was found to have good internal consistency (α=0.83) and

discriminant validity, of the whole measure and for both subscales (Lubben et al., 2006), and showed good internal consistency when used in this study (α=0.73).

In order to capture mild and borderline symptoms of depression and anxiety, AGECAT scores of two and above have been considered. An AGECAT score of three is considered a case, with a score of two constituting a sub-case, and so by including sub-cases in the analyses milder or less frequent symptoms were taken account of.

In order to counteract the unequal sample sizes for the difference cognitive status groups robust statistical techniques were used. A more conservative statistic was reported from the ANOVA, with conservative post-hoc procedures also used. Logistic regression techniques also perform well in cases of unequal sample sizes and consequently the findings of this study can be treated with confidence.

The findings from this study have several applications. From a clinical point of view, clinicians and healthcare staff could increase their awareness of older people's social networks as this has an impact on both mood and cognitive status. Health and social care workers may be able to identify older people with smaller social networks and refer them to interventions such as befriending schemes to try to increase their social network size. Befriending schemes are available in many areas and the emotional support provided by befriending schemes may provide a preventative strategy for people at risk of mood problems, as evidence suggests that befriending can reduce depressive symptoms (Mead, Lester, Chew-Graham, Gask, & Bower, 2010). From a theoretical perspective, the inclusion of the MCIW category raises interesting questions regarding the subjective element of the MCI definition and suggests that SMC may be the link between MCI and mood, or could potentially differentiate between stages of cognitive decline. It is likely that social cognitive processes operate as part of this relationship, and that feelings of self-efficacy required in

maintaining social networks work may extend to how competent people feel with regards to their memory. These processes can be disrupted by anxiety and depression (Conner & Norman, 2005), potentially leading to subjective memory complaints. In terms of practical applications, awareness could be raised amongst older people of the importance of maintaining a social network and the benefits that it has to their mood and cognitive functioning. However, whilst encouraging older people to seek out social opportunities would be advantageous, there are often a number of practical barriers such as lack of adequate transport or convenient places to meet others, as many reasons why older people are lonely are beyond their control (Findlay, 2003). Organisations, local government and charities could be encouraged to facilitate opportunities for social participation such as providing a space for people to meet or increasing the availability of transport for older people who cannot drive or live in rural areas.

This chapter aimed to investigate the link between MCI and anxiety and depression, with a particular focus on social networks as a moderator of the relationship. People with MCI are at greater risk of anxiety and depression, and smaller social networks were found to be associated with both mood problems and cognitive decline. However, whilst both factors are important, the findings of this study do not suggest that social networks and cognitive status interact in a moderated relationship.

Chapter 8: Discussion

Summary

This chapter aims to draw together the findings of Chapters 3-7 of this thesis and use the conclusions drawn from them to answer the research questions outlined in Chapter 1. Included in this chapter is commentary on the methodological considerations encountered through the development of the included studies, and the potential implications of their findings. The chapter provides ideas for future research directions and about how future studies may address some of the limitations of this research.

Introduction

The relationship between mild cognitive impairment (MCI) and mood was explored in this thesis through the examination of existing literature and the analysis of two large data sets. MCI is thought to exist on a continuum between normal ageing and pathological ageing, such as dementia, and may represent an intermediate stage of cognitive decline (Matthews et al., 2008). Previous literature suggests that anxiety and depression, which are common in older people (Beekman et al., 1999), are related to MCI (D. E. Barnes et al., 2006). However, the nature of the relationship is unclear and warrants further investigation.

Chapter 3 of this thesis comprises a systematic review and meta-analysis of the literature regarding the relationship between MCI and anxiety or depression. The review provided a solid foundation for the hypothesis that MCI and mood are related, and indicated that symptoms of anxiety and depression are more common in people with MCI than those with normal cognitive functioning. Symptoms of depression were associated with an increase in the progression from not cognitively impaired to a classification of MCI, and from MCI to dementia. However, the literature was lacking regarding the relationship between MCI and anxiety, and changes in risk for people with symptoms of anxiety could not be calculated. The systematic review highlighted the need to look more deeply into the relationship between MCI and mood, and the empirical chapters of this thesis (Chapters 4-7) build on the conclusions of the systematic review by investigating factors that may be associated with or influential to this relationship.

Three topic areas were identified from previous literature as being of interest and in need of investigation, as their influence on the relationship between MCI and mood may help to clarify the association. The three topics of subjective memory complaints (SMC), the health of older people, and social networks were investigated in further detail in Chapters 4-7

using data collected as part of the Medical Research Council Cognitive Functioning and Ageing Study I (MRC-CFAS I; Chapter 4) and the Cognitive Functioning and Ageing Study Wales (CFAS Wales; Chapters 5-7).

Presented in the following sections of this chapter are the main findings of the empirical studies, which investigated the relationship between MCI and mood through SMC (Chapters 4 & 5), health (Chapter 6) and social networks (Chapter 7), within the context of existing literature and in relation to each of the research questions posed in Chapter 1. The methodological considerations, strengths and implications of the findings of this thesis are presented, and recommendations for future research are suggested.

Discussion of findings in relation to each research question

Are MCI and mood problems related?

This question was addressed in this thesis with the systematic review (Chapter 3) and with the empirical studies that have used both follow-up (Chapter 4) and cross-sectional (Chapters 5-7) data. The systematic review and meta-analyses showed that the odds of experiencing symptoms of anxiety and depression are increased in people with MCI compared to people without cognitive impairment (Fernandez-Martinez et al., 2010; Forsell et al., 2003; Hwang et al., 2004; Ravaglia et al., 2008). Depression was also found to be associated with an increase in the risk of progression from no cognitive impairment to MCI, which reflects previous work (Caracciolo et al., 2011; Geda et al., 2006), and from MCI to dementia, where previous research has disagreed (Gallagher et al., 2011; Palmer et al., 2007; Panza et al., 2008). There are possible reasons for such disagreement in past literature, and it is likely that the heterogeneous nature of the MCI definition has contributed to the differences in the results. The findings of this thesis show that when MCI is subdivided into participants with SMC and those without the results are different. Furthermore, the MCI definition is

unstable, as shown in Chapter 4 where participants who were classified as having MCI at one time point were then classified as having no cognitive impairment at the second time point. Matthews, et al, (2008) discuss how different definitions of MCI show varying progression rates to dementia, and potentially until the definition of MCI can be refined into a more stable concept results of progression will be different in different studies. However, the risks posed by anxiety are less clear, with studies suggesting conflicting results (Gallagher et al., 2011; Palmer et al., 2007), highlighting the need for further research in this area.

Chapter 4 investigated the role of subjective memory complaints (SMC) in the relationship between MCI and mood using data from two time points, and in order to do this is was necessary to establish whether MCI and mood were related in this sample. Analyses showed that the presence of MCI increased the odds of depression and anxiety at baseline, which reflects previous literature outlined above and the findings of Chapter 3. A classification of MCI at baseline also increased the odds of reporting depressive symptoms at follow-up. This again suggests that MCI and mood are related and hints at the potential for a temporal element to the relationship, as the presence of MCI at baseline had an influence on the presence of depression at follow-up. However, mood problems at baseline were not associated with a change from no cognitive impairment to MCI, which reflects previous research (Panza et al., 2008; Steenland et al., 2012), or from MCI to dementia over the two year period, which again fits with some previous literature (Devier et al., 2009; Houde et al., 2008; Vicini Chilovi et al., 2009), but contrasts with other research findings (Gabryelewicz et al., 2007).

Chapters 5 to 7 included analyses of data from CFAS Wales and also showed that MCI and mood were related in a more recent community cohort. The odds of experiencing symptoms of anxiety and depression were increased for participants categorised as having MCI, again adding to the literature outlined in Chapter 3, but not for those with a

classification of MCIW or those without cognitive impairment (See Chapter 2, Figure 2.2 for details of the cognitive status categories). The category of MCIW has not been used before in previous research and so it is difficult to relate these findings to the literature. The data used in these analyses were from a single time point and so cannot point towards a temporal relationship between MCI and mood, but can contribute evidence to suggest an association.

The findings in relation to this research question have added to an already growing body of literature that suggests that a relationship between MCI and mood exists. The work presented in this thesis shows that the relationship between MCI and mood is different for participants with SMC and those without, and this is the first time that the two definitions of MCI were directly compared to each other. The relationship appears to hinge on the definition of MCI used, and the findings suggest that subjective memory complaints may be a key factor in the presence of mood problems in those with cognitive impairment.

It may be the case that health and social networks of older people operate through the presence of SMC (Figure 8.1) to alter the relationship between MCI and mood. Social networks and health may also influence each other. Older people in better health have higher levels of self-efficacy required to maintain social networks, and having larger social networks may lead to more encounters with people who lead healthy lifestyles, which in turn could increase self-efficacy for adopting healthy behaviours. The presence of SMC may represent a breakdown in metacognitive processes, and may be alter the effect that health and social networks have on the relationship between MCI and mood through social cognitive processes, which may be similarly disturbed.

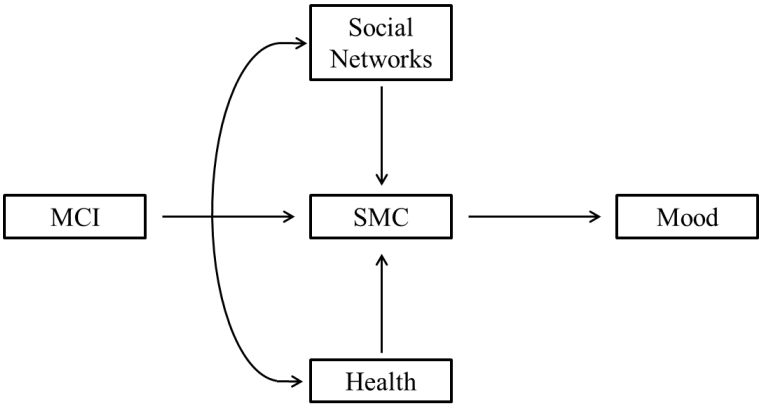

Figure 8.1: SMC alter the relationship between MCI and mood

Do subjective memory complaints modify the relationship between MCI and anxiety or depression?

Chapters 4 and 5 investigated the role of SMC with regard to the relationship between MCI and mood using data from MRC-CFAS I (Chapter 4) and CFAS Wales (Chapter 5). In Chapter 4, analyses suggested that participants categorised as having MCI were more likely to have symptoms of anxiety and depression compared to participants without cognitive impairment or those categorised as having MCIW. Interestingly, the risk of anxiety or depression was decreased for participants with MCIW. This suggests that the symptoms may be related to the subjective memory component of the MCI definition, as this was the only difference between the MCI and MCIW groups. In addition, participants reporting SMC regardless of cognitive status were also more likely to report anxiety and depression, which was shown in previous literature (Antikainen et al., 2001; Comijs et al., 2002), and provides further evidence to support the link between meta-cognition and mood. This chapter directly compared participants with MCI that included SMC, and participants with MCI who did not report SMC, and this is thought to be the first time this approach has been used. Chapter 4 also includes data from two time points, and showed how participants may change between the cognitive categories over the course of two years. Research has looked into how varying definitions of MCI may operate over time (Matthews et al., 2008), but this is the first study

that has directly compared the role of SMC in people categorised as having MCI to people who would otherwise meet criteria for MCI, but do not report SMC.

These findings were echoed in Chapter 5, as participants who reported SMC were again more likely to report symptoms of anxiety and depression. Participants categorised as having MCI had increased odds of experiencing anxiety and depression, but the odds did not change for participants who were not cognitively impaired or categorised as MCIW. Mediation analyses confirmed that SMC partially mediated the relationship between cognition and mood, suggesting that symptoms of anxiety and depression may be related to metacognitive processes as well as objective cognitive performance. Mediation analyses similar to those conducted in Chapter 5 have not been seen in previous literature and consequently this chapter adds an interesting element to the discussion surrounding the usefulness of SMC in the MCI definition.

Is the relationship between MCI and anxiety or depression mediated by perceived health or health state?

The second topic area explored in this thesis was how the health of older people could influence the relationship between MCI and mood (Chapter 6). Health as a concept is difficult to measure and in order to give as detailed a picture as possible several proxy measures were used. These included self-perceived health, number of health conditions, level of physical activities, health service use, and instrumental activities of daily living (IADLs). There were differences across all measures of health between participants with mood problems and without, where participants with anxiety or depression reported worse self-perceived health, more comorbid health conditions, a lower level of physical activities, increased health service use, and more difficulties with IADLs use than participants who did not report anxiety or depression. This is in line with previous literature (Alexopoulos, 2005;

Bisschop et al., 2004; Lenze, Rogers, et al., 2001; Stuck et al., 1999), and the inclusion of the different measures of health provide a holistic picture of the relationship between mood and health, which is seldom seen as many studies investigate only a single aspect of health in older people, such as exercise (Windle et al., 2010). This provides further evidence for the relationship between the health of older people and the presence of anxious or depressive symptoms, and resonates with existing literature. It is likely that poor health increases the likelihood of anxiety and depression for several reasons, for example, the pain related to particular health conditions (Williamson & Schulz, 1992a), anxiety relating to medication use, the effects of particular medicines themselves, and the restrictions that illness may place on older people by curtailing opportunities to engage in physical and social activity (Fagerstrom, Holst, & Hallberg, 2007) as these are known to ameliorate the effects of mood problems (Dungan, Brown, & Ramsey, 1996).

Participants without cognitive impairment reported fewer difficulties with IADLs and participated in more physical activities than those categorised as MCI and MCIW, suggesting that some measures of health may be linked to cognitive functioning (Perneczky, Pohl, Sorg, Hatmann, et al., 2006). Participants categorised as having MCI had increased odds of reporting fair or poor perceived health than participants with no cognitive impairment, whose odds were found to be decreased, and those classified as MCIW, whose odds did not change. This reflects the findings in relation to SMC and provides further evidence for the need to question the importance of subjective appraisal and metacognitive processes in the MCI definition. This also echoes previous literature, which suggests that self-reported health is a good predictor for cognitive impairment (Bond et al., 2006), but this chapter is one of the only studies to date to look at the relationship between subjective cognitive appraisals and self-perception of health in participants with MCI (Marri et al., 2001), and is the only study to investigate it with a large sample. From a metacognitive perspective, SMC and perceived

health may represent related concepts, and potentially when people view their health as poor they may extend this appraisal to their cognitive function, or vice versa. Again, this idea has links with social cognitive theory (Bandura, 1998), where feelings of self-efficacy or competence may be driven by how people feel about their health or memory, and extended to include all aspects of their functioning. People may experience lapses in their memory, which diminish feelings of competence in their functioning, and may then extend to feeling negative about their health. In addition, depression and anxiety can reduce feelings of self-efficacy (Conner & Norman, 2005), which may lead to worse perceptions of health and memory. Perceived health, SMC and mood may all be part of particular way of thinking that should be considered when categorising someone as having MCI or investigating cognitive impairment. As the stigma surrounding dementia and emotional problems is reduced, people may begin to include emotional and cognitive health in their global view of their overall health, leading to an overlap between perceptions of physical health and cognition.

Structural equation modelling was used to demonstrate whether health mediated the relationship between MCI and mood and, after calibration of the model, the results showed that, for participants categorised as having MCI, health did partially mediate the relationship between MCI and both anxiety and depression. For participants categorised as MCIW and those without cognitive impairment, the path between health and cognitive status was not significant, which may again point back to the subjective aspect of MCI, in that when people with MCI acknowledge their memory problems, they are acknowledging a more general sense of poor health, which may not occur in those with MCIW or no cognitive impairment. In all models, the path between health and mood was significant, suggesting that health impacts on mood. A possible interpretation might be that symptoms of anxiety or depression increase in response to poor health, and this in turn impacts only on people with MCI who report SMC, providing further evidence for the unique association between MCI and mood

that is not present in those without cognitive impairment or people in the MCIW category. The evidence for the link between mood and MCI is demonstrated further by the finding of a significant path between mood and cognitive status for people with MCI but not for people categorised as MCIW or those without cognitive impairment.

What is the nature of the three-way relationship between MCI, mood and social networks?

The influence of social networks on the relationship between MCI and mood was investigated in Chapter 7 of this thesis. The social network score was significantly lower for the MCI and MCIW categories compared to participants without any cognitive impairment. Furthermore, an increase in social network score was associated with a decrease in anxiety and depression. However, moderation analyses did not show any interaction effects, suggesting that whilst social networks are important to both cognitive status and mood, they do not moderate the relationship between MCI and mood. Previous literature has suggested that social relationships throughout the life course and in later years may contribute to continued mental stimulation and better cognitive strategies (Zunzunegui, Alvarado, Del Ser, & Otero, 2003) and our findings complement this. Again, the distinction between participants with MCI that included SMC and those with MCI who did not report SMC is new in relation to investigating social networks in older people, but there was no difference found in the relationship between cognitive status, mood and social network score between the MCI and MCIW groups. It was expected that social network score would moderate the relationship between cognitive status and mood in participants classified as MCI only, reflecting an underlying social cognitive or metacognitive process where individuals who had reported SMC may have decreased self-efficacy and in turn smaller social networks due to reduced feelings of competence in maintaining or creating social ties (Bandura, 1998). However, these results were not seen, and future research may be needed to discover why, as there are

many factors other than self-efficacy that determine the nature of social networks, including family size, living situation, and location.

What implications do the findings of this thesis have for the concept of MCI for the future?

The findings of this thesis demonstrate that there is a link between cognition and mood and this is in line with previous literature (Lyketsos et al., 2002; Van der Linde et al., 2010). People with mood problems are often excluded from research into MCI and this is likely to be inappropriate, due to the common occurrence of MCI with comorbid mood problems. Furthermore, there is considerable evidence to suggest that the relationship is influenced by the presence of SMC, which are frequently a criterion of MCI definitions in spite of disagreement over their usefulness (Lenehan et al., 2012). In fact, the inclusion of SMC may be a hindrance, as this thesis has demonstrated that there are people who would otherwise meet the criteria for MCI, but could potentially be missed from diagnoses or helpful intervention due to the non-reporting of SMC.

The relationship between SMC and mood problems was a particularly interesting development during the course of preparing this thesis. The MCIW category was initially created to investigate the role of SMC in Chapters 4 and 5, and to make it possible to directly compare the impact of cognitive impairment on mood between participants meeting traditional criteria for MCI and those who did not report SMC. However, the category proved useful in further analyses and it became interesting to look at this subsample in more detail. There were differences found between the MCI and MCIW groups in both health and social networks, highlighting that there is a distinction between the two groups and suggesting that participants in the MCIW category may be on a different trajectory between normal ageing and dementia than participants who meet criteria for MCI including SMC. Research is emerging in the area of subjective cognitive impairment, as subjective complaints of

cognitive impairment can emerge up to fifteen years before a person meets criteria for a classification MCI (Reisberg et al., 2008), although it should be acknowledged that some people may report cognitive complaints and never develop MCI. People who could be considered to have subjective cognitive impairment are likely to perform within the normal range on cognitive tests. Subjective cognitive impairment was found to be a significant predictor of future cognitive decline, and people reporting subjective cognitive complaints were found to have a reduction in grey matter similar to people with MCI, but different to people who did not report cognitive complaints (Reisberg & Gauthier, 2008). Identification of risk states are vital for targeted dementia prevention, and evidence suggests that subjective cognitive impairment is associated with an increased risk of future decline (Jessen et al., 2014).

The interesting finding that the MCI category and mood are related, but the MCIW category and mood do not seem to show the same association, raises the question of whether SMC are a function of anxiety and depression rather than being related to objective cognitive performance itself (Dux et al., 2008). This has implications for the concept of MCI and whether SMC should be included in diagnostic criteria, as SMC may not be representing memory problems and instead may be suggestive of mood problems. This is an area for further research, as previous research remains divided over the usefulness of SMC in predicting further cognitive decline. Anxiety and depression are thought to be risk factors for progression to dementia, but as mood appears to be involved in the reporting of SMC, it is likely that mood and the subjective appraisal of cognitive function is relevant to the likelihood of progression to dementia.

Methodological considerations

Secondary data analysis

The method of analysis used in Chapters 4-7 was that of secondary analysis and this posed a number of limitations and strengths. A major limitation was that I was unable to contribute to the design of the study or choose which questions were asked during the MRC-CFAS I and CFAS Wales interviews, and I was only able to make use of certain measures that were included in the interviews. There are aspects of the design that I would change, such as how depression and anxiety were measured, and this is outlined in the section below. I would also have liked to include a more comprehensive measure of SMC, such as the Memory Functioning Questionnaire, to increase the robustness of the measure of SMC.

However, conducting secondary analysis of the MRC-CFAS I and CFAS Wales datasets had a number of positive outcomes. Firstly, it allowed for access to two large datasets from a representative community sample, which was particularly useful when investigating a phenomenon such as MCI that only occurs in approximately 3% of the population (Fisk et al., 2003). Furthermore, the older people who participated in the studies have invested a considerable amount of their time and effort in taking part, and it is the responsibility of the researchers involved to extract as much information from this resource as possible. I have achieved this by identifying and answering several research questions, which will contribute to our understanding of the relationship between MCI and mood. Taking part in the data collection for CFAS Wales has provided me with experience of participating in a large research study and I have gained knowledge of data cleaning, operationalization of variables, analysis and working as part of a multi-centre team with varied research interests.

Measuring depression and anxiety

The AGECAT algorithm (Copeland et al., 1986) which was used to determine which participants had symptoms of anxiety and depression was included as a variable in the MRC-CFAS I and CFAS Wales data that I received from the University of Cambridge. The questions asked in the MRC-CFAS I and CFAS Wales interviews that are used in calculating the AGECAT algorithm may not be sensitive to less severe or less frequent incidences of anxiety and depression and may miss participants with milder symptoms. In addition, these questions were designed over 25 years ago, and the nature of older peoples' worries or concerns may be different in the present day, which could suggest that the anxiety and depression questions may benefit from updating.

The nature of the questions asked in the MRC-CFAS I and CFAS Wales interviews constrained the way in which anxiety and depression could be identified. The use of scaled measures of depression and anxiety would have made the results of the analyses included in this thesis more comparable with other studies investigating the relationship between MCI and mood. In addition, the AGECAT algorithm results in a categorical outcome. In this thesis, the categories were collapsed into dichotomous outcomes, but typically there are four levels for depression and five levels for anxiety. The use of categorical outcomes meant that particular analysis techniques needed to be used, and mediation analyses especially should be interpreted with caution.

The cognitive status algorithm

The cognitive status algorithm was originally created by Dr Blossom Stephan (Newcastle University) and updated by me (see Chapter 2 for details) and was used throughout this thesis to determine which participants fall into each cognitive category. The algorithm was effective in creating distinct cognitive groups, with observed numbers for each

cognitive category approximating what previous research has suggested are the expected numbers. The cognitive categories and how they were created can be clearly seen (see Chapter 2, Figure 2.2) which allows for ease of interpretation and replication by future studies using CFAS Wales or similar data.

The MCIW cognitive status category

The MCIW category was originally created for use in Chapters 4 and 5 to investigate the role of SMC in the relationship between MCI and mood. However, the differences between the MCI and MCIW categories suggested that the MCIW category was worth retaining for future analyses to discover if there were differences between the groups in other areas of interest. It has proved to be interesting as differences were found across several measures between the MCI and MCIW groups which suggests that the MCIW group is either at a separate point on a continuum between normal ageing and dementia, for example as in the diagram proposed by Reisberg, et al. (2008), or following a different trajectory (Figure 8.2). It is unclear at present what the risks for progression to dementia are for the MCIW group and whether this group is different to people with MCI or without cognitive impairment in other ways than the presence or absence of SMC. The analyses in Chapter 4 showed that over two years 6. 1% of participants in the MCI category progressed to dementia, compared to 3.9% of those categorised as MCIW, and 2.4% of those with no cognitive impairment, suggesting that participants in the MCIW group progressed at a decreased rate to those categorised as MCI. Almost the same amount of participants in the MCIW category at the baseline analysis in Chapter 4 were classified as not cognitively impaired, as those who remained in the MCIW category, at the follow up time point. A very small proportion (1.5%) progressed to the MCI category over the two years, suggesting that the development of SMC over a two-year time period is not common. However, 13.7% of participants categorised as MCI at baseline converted to MCIW at follow-up, suggesting that

the loss of SMC over two years is possible, and may reflect a change in thought processes. It is also possible that this could reflect people adjusting to changes experienced in their cognitive functioning, or a loss of subjective awareness of the objective cognitive problems observed. It is a group of participants that warrant further investigation in the future and it would be very interesting to see which cognitive category they fall in to at the follow-up time point in CFAS Wales. The findings of that analysis may well alter the composition of Figure 8.2.

It is also important to acknowledge that subjective evaluations of memory depend on what was asked, and how it was asked. Different patterns of awareness of metacognitive processes may depend on the level or type of awareness assessed. This is a complex issue, and there may be several possible explanations as to the presence or absence of particular cognitive evaluations.

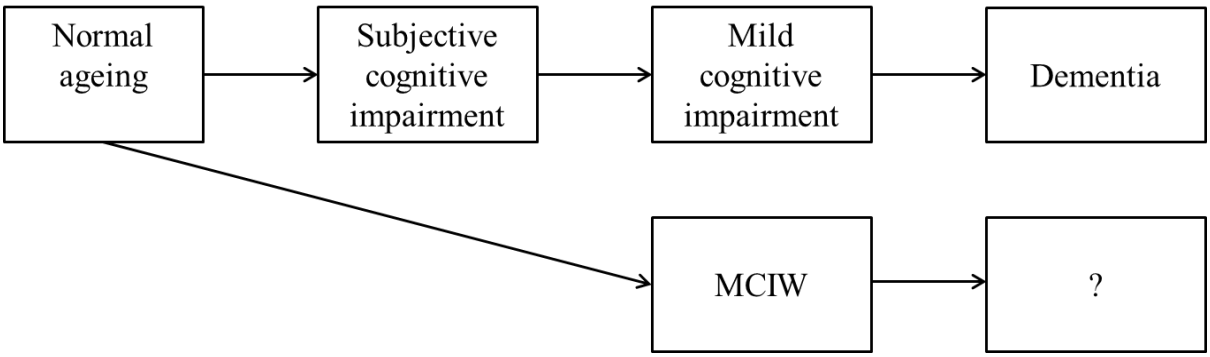

Figure 8.2: Potential trajectories between normal ageing and dementia

Future research directions

Longitudinal analyses

Chapter 4 demonstrated that the cognitive status categories and the presence of SMC were unstable over a two-year period. CFAS Wales is a longitudinal study and in the future

data will become available to conduct analyses using more than one time point. It would be interesting to see if patterns similar to those shown in Chapter 4 occur in the CFAS Wales data, as demonstrating that the definitions of MCI are still unstable in more recent cohorts may provide evidence to prompt a review of the definitions.

Cognitive categories

A review of cognitive categories such as MCI and MCIW, and the criteria used to create them, is necessary. The categories used during this thesis were created using cut off scores calculated from the CAMCOG (Huppert et al., 1995) and the MMSE (Folstein et al., 1975), and the criteria were used to allow this work to align with previous CFAS research. However, it is unclear how appropriate these criteria are and future research should investigate whether these criteria should be updated for newer cohorts.

Measures of health

The use of more measures of health could add greater depth and detail to assist in clarifying the relationship between cognition, mood and health. Physical measures such as blood pressure, weight and the results of blood tests could provide an objective measure of health functioning. This could also be combined with medical records to gain insight into the level of comorbidity experienced by participants that is not captured by the questions asked in the interview. Lastly, hospital admissions data and social care usage data could be linked to provide an overview of the intensity of engagement with health and social services as this may indicate health needs. Research involving analysis of linked data is emerging. The ability to link valuable datasets is very exciting and will offer a very detailed picture of overall functioning.

The subjective experience

Qualitative research could be used to help to understand the subjective experience of MCI and how ratings of perceived health operate as part of a global metacognitive process. Qualitative research suggests that attitudes towards cognitive impairment are associated with loss, and that the self-concept may be changed with a label of MCI (Corner & Bond, 2006). The MCIW group may therefore represent a group of individuals striving to retain their sense of self. Qualitative studies have also shown that older people may be reluctant to contact healthcare professionals about memory problems (Corner & Bond, 2004). It would also be interesting to gain insight from participants with different ratings of perceived health, as research suggests that concurrent health problems may be key contextual factors that form a backdrop to establishing the meaning of being categorised as having MCI (Lingler et al., 2006), and those with and without SMC to see the level of cross-over between SMC and perceived health, and to investigate how this makes a person feel overall.

Implications of the findings

The findings of this thesis have highlighted the need to review and update how MCI is categorised, and how the categories are applied in clinical practice. Currently, working groups exist to refine the definitions used for MCI, but clarity is yet to be achieved. Reaching a consensus on what criteria should be included in the definition, and applying agreed criteria consistently could help to reduce the ambiguity surrounding the label of MCI. Varying definitions have an effect on the overall prevalence rates for MCI in the United Kingdom and make it difficult for research studies to be homogenous enough to pool results effectively. This impacts on how evidence regarding the best practice in interventions with MCI can be presented in order to direct health service resources and research budgets. Additionally, this research has highlighted that participants with anxiety and depression should not be excluded

from research studies into MCI, as cognitive decline and mood problems are often comorbid. Excluding participants with mood problems potentially biases samples of participants with MCI, and does not represent a true picture of cognitive decline or associated mood problems.

The findings of this thesis show that people who report SMC are more likely to experience anxiety and depression, and consequently it is important that SMC are acknowledged and taken seriously, as reports of SMC may represent a useful time for intervention to bring long-term benefits in slowing further cognitive decline. Many older people may perceive SMC as a normal part of ageing, however SMC may be an indicator of other problems, and increased vigilance towards SMC may allow for early detection of potential mood or cognitive issues. This could be achieved through awareness campaigns using traditional media and social media; similar to campaigns that raise awareness of particular types of cancer, or to promote smoking cessation. In terms of social cognitive theory, hearing stories and seeing videos of how other people have dealt with memory problems may increase feelings of self-efficacy in people experiencing SMC, so that they feel more capable of seeking help. Opportunities to increase feelings of self-efficacy associated with managing cognitive functions may in turn increase feelings of self-efficacy required to engage in positive health behaviours and maintain social networks. It is likely that improvements in any domain of social, cognitive or physical functioning may lead to improvements in other domains, representing a positive feedback loop (Butler, Forette, & Greengoss, 2004).

Adequate provision of information may also help to alleviate anxieties that older people may have about cognitive changes. Establishing signpost routes to relevant services that may be able to offer more information, assistance or intervention may help older people to come to terms with changes that they face in the future and provide them with valuable skills to assist them in planning and coping.

Raising awareness of SMC, cognitive changes and mood problems may also extend to people of all ages, alongside targeting information at older people. Family, friends and neighbours of older people may notice changes in their cognitive functioning, mood, or hear them report SMC, and being fully informed may provide the opportunity to signpost older people to their GP or other relevant services. A similar campaign to the NHS Keep Warm, Keep Well awareness campaign that encourages people to check that their older neighbours and friends are staying well in the winter could be useful.

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) (Kivipelto et al., 2013), is a multi-domain study to prevent or delay the onset of cognitive decline. Participants are provided with nutritional guidance, an exercise training programme, cognitive training, social stimulation through numerous group meetings, and monitoring of metabolic and cardiovascular risk factors through both group and one-to-one sessions. Participants in the FINGER study have not experienced cognitive decline at enrolment and this intervention may represent an excellent opportunity to show how support at an early stage, before the development of cognitive decline, may be beneficial. Similar interventions may prove beneficial to older people who report SMC, as these can occur for a long time before the onset of cognitive problems (Reisberg et al., 2008).

As Chapter 6 showed, there is a link between MCI, mood and health, and that perceived health may be part of a metacognitive process involved in this relationship. Consequently, simple exercise interventions that are easy to be successful at may be effective in increasing perceived health, through providing opportunities for older people to increase their levels of self-efficacy. Fisher and Li (2004) found small positive effects on mental health and life satisfaction after participation in a community-based neighbourhood walking programme for older people. The walking routes in this study were easy-going, which may have enabled the participants to feel successful without placing too much pressure on them,

and created a chance to increase feelings of competence. Also, as this intervention was a group exercise, seeing other older people enjoying physical activity may have further helped to increase feelings of self-efficacy.

Whilst the findings of Chapter 7 are mixed regarding the nature of the three-way relationship between mood, MCI and social networks, interventions to provide social opportunities for older people have found to be effective in reducing cognitive decline and increasing well-being (Stevens, 2001). Research suggests that those with the most extensive social networks experience the lowest rates of cognitive decline (L. L. Barnes, Mendes de Leon, Wilson, Bienias, & Evans, 2004) and so interventions in this area should be encouraged. However, it must acknowledged that interventions comprising activities to enhance social engagement are difficult to develop and hard to control for (Flicker, 2009).

Conclusion

This thesis has reported on recent literature and empirical evidence in the topic area of MCI and mood in older people. Data from two large epidemiological studies were analysed and findings showed that there is a relationship between MCI and mood. An interesting investigation into the role of SMC emerged and developed through the course of this thesis, and the results of the analyses demonstrated that mood is related to SMC, potentially more so than to objective cognitive performance. The findings of this thesis also highlighted the role of health problems in the relationship between MCI and mood, suggesting that interventions to improve the health of older people may in turn reduce mood problems and benefit cognitive functioning. The findings regarding the role of social networks were less clear cut; but having more social contact had a positive effect on both mood and cognition in older people. This thesis has added to the literature regarding MCI and mood, and whilst it has raised new questions and further avenues for research, it has helped to clarify the role of

influential factors in this relationship and show that there is significant room for intervention to improve the quality of life for older people.

References

Adler, G., Chwalek, K., & Jajcevic, A. (2004). Six-month course of mild cognitive impairment and affective symptoms in late-life depression. *European psychiatry : the journal of the Association of European Psychiatrists, 19*(8), 502-505. doi: 10.1016/j.eurpsy.2004.09.003

Age UK. (2013). Later Life in the United Kingdom. In A. UK (Ed.), *Later Life in the United Kingdom* (December 2013 ed.). United Kingdom: Age UK.

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

Alexopoulos, G. S., Buckwalter, K., Olin, J., Martinez, R., Wainscott, C., & Krishnan, K. R. (2002). Comorbidity of late-life depression: an opportunity for research in mechanisms and treatment. *Biological Psychiatry, 52*, 543-558.

Alzheimer's Society. (2013). Dementia 2013: The hidden voice of loneliness. UK: Alzheimer's Society.

Angevaren, M., Aufdempkampe, G., Verhaar, H. J. J., Aleman, A., & Vanhees, L. (2008). Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database of Systmeatic Reviews*(3). doi: 10.1002/14651858.CD005381.pub 3.

Antikainen, R., Hanninen, T., Honkalampi, K., Hintikka, J., Koivumaa-Honkanen, H., Tanskanen, A., & Viinamaki, H. (2001). Mood improvement reduces memory complaints in depressed patients. *European Archives of Psychiatry and Clinical Neuroscience, 251*(1), 6-11. doi: 10.1007/s004060170060

Artero, S., Ancelin, M.-L., Portet, F., Dupuy, A., Berr, C., Dartigues, J.-F., . . . Ritchie, K. (2008). Risk profiles for mild cognitive impairment and progression to dementia are gender specific. *Journal of Neurology, Neurosurgery and Psychiatry, 79*(9), 979-984. doi: 10.1136/jnnp.2007.136903

Baars, M. A. E., van Boxtel, M. P. J., Dijkstra, J. B., Visser, P. J., & van den Akker, M. (2009). Predictive value of mild cognitive impairment for dementia. *Dementia and Geriatric Cognitive Disorders, 27*, 173-181. doi: 10.1159/000200465

Baiyewu, O., Unverzagt, F. W., Ogunniyi, A., Smith-Gamble, V., Gureje, O., Lane, K. A., & Hendrie, H. C. (2012). Behavioural symptoms in community-dwelling elderly Nigerians with dementia, mild cognitive impairment and normal cognition. *International Journal of Geriatric Psychology, 27*, 9. doi: 10.1002/gps.2804

Balash, Y., Mordechovich, M., Shabtai, H., Giladi, N., Gurevich, T., & Korczyn, A. D. (2013). Subjective memory complaints in elders: depression, anxiety, or cognitive decline? *Acta Neurologica Scandinavica*, *127*(5), 344-350. doi: 10.1111/ane.12038

Bandura, A. (1998). Health promotion from the perspective of social cognitive theory. *Psychology and Health, 13*, 623-649.

Bandura, A. (2004). Health promotionnby social cognitive means. *Health Education & Behavior, 31*, 143-164. doi: 10.1177/1090198104263660

Barnes, D. E., Alexopoulos, G. S., Lopez, O. L., Williamson, J. D., & Yaffe, K. (2006). Depressive symptoms, vascular disease, and mild cognitive impairment: findings from the Cardiovascular Health Study. *Archives of General Psychiatry, 63*(3), 273-279. doi: 10.1001/archpsyc.63.3.273

Barnes, L. L., Mendes de Leon, C. F., Wilson, R., Bienias, J. L., & Evans, D. A. (2004). Social resources and cognitive decline in a population of older African Americans and whites. *Neurology, 63*(12), 2322-2326. doi: 10.1212/01.WNL.0000147473.04043.B3

Bath, P. A. (1999). Self-rated health as a risk factor for prescribed drug use and future health and social service use in older people. *Journal of Gerontology, 54A*(11), 565-570.

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

Beland, F., Zunzunegui, M. V., Alvarado, B., Otero, A., & del Ser, T. (2005). Trajectories of cognitive decline and social relations. *Journal of Gerontology: Psychological Sciences, 60B*(6), 320-330.

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

Bhalla, R. K., Butters, M. A., Becker, J. T., Houck, P. R., Snitz, B. E., Lopez, O. L., . . . Reynolds, C. F., 3rd. (2009). Patterns of mild cognitive impairment after treatment of depression in the elderly. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 17*(4), 308-316. doi: 10.1097/JGP.0b013e318190b8d8

Bisschop, M. I., Kriegsman, D. M. W., Beekman, A. T. F., & Deeg, D. J. H. (2004). Chronic diseases and depression: the modifying role of psychosocial resources. *Social Science & Medicine, 59*, 721-733.

Bond, J., & Carstairs, V. (1982). Services for the Elderly *Scottish Health Service Studies*. Scotland.

Bond, J., Dickinson, H. O., Matthews, F., Jagger, C., & Brayne, C. (2006). Self-rated health as a predictor of death, functional and cognitive impairment: A longitudinal cohort study. *European Journal of Ageing, 3*, 193-206. doi: 10.1007/s10433-006-0039-8

Booth, M. L., Owen, N., Bauman, A., Clavisi, O., & Leslie, E. (2000). Social-cognitive and perceived environment influences associated with physical activity in older Australians. *Preventive Medicine, 31*, 15-22. doi: 10.1006/pmed.2000.0661

Brambati, S. M., Belleville, S., Kergoat, M. J., Chayer, C., Gauthier, S., & Joubert, S. (2009). Single- and multiple-domain amnestic mild cognitive impairment: Two sides of the same coin? *Dementia and Geriatric Cognitive Disorders, 28*(6), 541-549. doi: 10.1159/000255240

Brayne, C., Matthews, F. E., McGee, M., & Jagger, C. (2001). Health and ill-health in the older population in England and Wales. The Medical Research Council Cognitive Function and Ageing Study (MRC CFAS). *Age and Ageing, 30*, 53-62.

Brayne, C., McCracken, C., Matthews, F. E., & MRC-CFAS. (2006). Cohort profile: the Medical Research Council Cognitive Function and Ageing Study (CFAS). *International Journal of Epidemiology, 35*(5), 1140-1145. doi: 10.1093/ije/dyl199

Bruscoli, M., & Lovestone, S. (2004). Is MCI really just early dementia? A systematic review of conversion studies. *International Psychogeriatrics, 16*, 129 - 140. doi: 10.1017/S1041610204000092

Bryant, C., Jackson, H., & Ames, D. (2008). The prevalence of anxiety in older adults: Methodological issues and a review of the literature. *Journal of Affective Disorders, 109*, 233-250. doi: 10.1016/j.jad.2007.11.008

Buchtemann, D., Luppa, M., Bramesfeld, A., & Riedel-Heller, S. (2012). Incidence of late life depression: A systematic review. *Journal of Affective Disorders, 142*, 172-179. doi: 10.1016/j.jad.2012.05.010

Busse, A., Bischkopf, J., Reidel-Heller, S. G., & Angermeyer, M. C. (2003). Mild cognitive impairment: prevalence and incidence according to different diagnositic criteria: results of the Leipzig Longitudinal Study of the Aged (LEILA75+). *The Brisith Journal of Psychiatry, 182*, 449-454.

Butler, R. N., Forette, F., & Greengoss, S. (2004). Maintaining cognitive health in an ageing society. *Journal of the Royal Society for the Promotion of Health, 124*(3), 119-121.

Butters, M. A., Bhalla, R. K., Andreescu, C., Wetherell, J. L., Mantella, R., Begley, A. E., & Lenze, E. J. (2011). Changes in neuropsychological functioning following treatment for late-life generalised anxiety disorder. *British Journal of Psychiatry, 199*(1472-1465), 211 - 218. doi: 10.1192/bjp.bp.110.090217

Byers, A. L., Yaffe, K., Covinsky, K. E., Friedman, M. B., & Bruce, M. L. (2010). High occurrence of mood and anxiety disorders among older adults: The National Comorbidity Survey replication. *Archives of General Psychiatry, 67*(5), 489-496. doi: 10.1001/archgenpsychiatry.2010.35

Caracciolo, B., Backman, L., Monastero, R., Winblad, B., & Fratiglioni, L. (2011). The symptom of low mood in the prodromal stage of mild cognitive impairment and dementia: a cohort study of a community dwelling elderly population. *Journal of neurology, neurosurgery, and psychiatry, 82*(7), 788-793. doi: 10.1136/jnnp.2010.225003

Carstensen, L. L., Fung, H. H., & Charles, S. T. (2003). Socioemotional selectivity theory and the regulation of emotion in the second half of life. *Motivation and Emotion, 27*(2), 103-123. doi: 0146-7239/03/0600-0103/0

Caselli, R. J., Chenb, K., Lockec, D. E. C., Leeb, W., Roontivab, A., Bandyb, D., . . . Reiman, E. M. (2013). Subjective cognitive decline: Self and informant comparisons. *Alzheimer's & Dementia, In press*, 1-6. doi: 10.1016/j.jalz.2013.01.003

Chan, D. C., Kasper, J. D., Black, B. S., & Rabins, P. V. (2003). Prevalence and correlates of behavioral and psychiatric symptoms in community-dwelling elders with dementia or mild cognitive impairment: the Memory and Medical Care Study. *International Journal of Geriatric Psychiatry, 18*(2), 174 - 182. doi: 10.1002/gps.781

Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Disease, 40*(5), 373-383.

Chaudhry, S., Jin, L., & Meltzer, D. (2005). Use of a self-report-generated Charlson Comorbidity Index for predicting mortality. *Medical Care, 43*(6), 607-615.

Chen, Y. F., Dewey, M. E., & Avery, A. J. (2001). Self-reported medication use for older people in England and Wales. *Journal of Clinical Pharmacy and Therapeutics, 26*(2), 129-140. doi: 10.1046/j.1365-2710.2001.00333.x

Cherbuin, N., Reglade-Meslin, C., Kumar, R., Jacomb, P., Easteal, S., Christensen, H., & Anstey, K. J. (2009). Risk factors of transition from normal cognition to mild cognitive disorder: The PATH through Life Study. *Dementia and Geriatric Cognitive Disorders, 28*, 47 - 55. doi: 10.1159/000229025

Chertkow, H. (2002). Mild cognitive impairment. *The Canadian Alzheimer Disease Review*, 15 - 20.

Clare, L. (2008). Neuropsychological Assessment. In R. Woods & L. Clare (Eds.), *Handbook of the Clinical Psychology of Ageing* (2nd ed., pp. 363-383). England: John Wiley & Sons Ltd.

Collie, A., Maruff, P., & Currie, J. (2002). Behavioral characterization of mild cognitive impairment. *Journal of clinical and experimental neuropsychology, 24*(6), 720-733. doi: 10.1076/jcen.24.6.720.8397

Comijs, H. C., Deeg, D. J., Dik, M. G., Twisk, J. W., & Jonker, C. (2002). Memory complaints; the association with psycho-affective and health problems and the role of personality characteristics. A 6-year follow-up study. *Journal of Affective Disorders, 72*(2), 157-165.

Conner, M., & Norman, P. (2005). Predicting Health Behaviour: A social cognition approach. In M. Conner & P. Norman (Eds.), *Predicting Health Behaviour: Research and practice with social cognition models* (2nd ed., pp. 1-27). England: Open University Press.

Cook, S. E., & Marsiske, M. (2006). Subjective memory beliefs and cognitive performance in normal and mildly impaired older adults. *Aging and Mental Health, 10*, 413-423. doi: 10.1037/0882-7974.20.3.390

Copeland, J. R. M., Dewey, M. E., & Griffiths-Jones, H. M. (1986). A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. *Psychological Medicine, 16*(1), 89-99. doi: 10.1017/S0033291700057779

Corner, L., & Bond, J. (2004). Being at risk of dementia: Fears and anxieties of older adults. *Journal of Aging Studies, 18*, 143-155. doi: 10.1016/j.jaging.2004.01.007

Corner, L., & Bond, J. (2006). The impact of the label of mild cognitive impairment on the individual's sense of self. *Philosophy, Psychiatry, & Psychology, 13*(1), 3-12. doi: 10.1353/ppp.2006.0036

de Jong-Gierveld, J., & Kamphuis, F. H. (1985). The development of a Rasch-type loneliness scale. *Applied Psychological Measures, 9*, 289-299.

Derouesne, C., Lacomblez, L., Thibault, S., & LePoncin, M. (1999). Memory complaints in young and elderly subjects. *International Journal of Geriatric Psychiatry, 14*(4), 291-301. doi: 10.1002/(SICI)1099-1166(199904)14:4<291::AID-GPS902>3.0.CO;2-7

Devier, D. J., Pelton, G. H., Tabert, M. H., Liu, X., Cuasay, K., Eisenstadt, R., . . . Devanand, D. P. (2009). The impact of anxiety on conversion from mild cognitive impairment to Alzheimer's disease. *International journal of geriatric psychiatry, 24*(12), 1335-1342. doi: 10.1002/gps.2263

Di Iulio, F., Palmer, K., Blundo, C., Casini, A. R., Gianni, W., Caltagirone, C., & Spalletta, G. (2010). Occurrence of neuropsychiatric symptoms and psychiatric disorders in mild Alzheimer's disease and mild cognitive impairment subtypes. *International psychogeriatrics / IPA, 22*(4), 629-640. doi: 10.1017/S1041610210000281

Diener, E., Emmons, R. A., Larsen, R. J., & Griffin, S. (1985). The satisfaction with life scale. *The Journal of Personality Assessment, 49*(1), 71-75.

Dixon, R. A., Hultsch, D. F., & Hertzog, C. (1988). The Metamemory in Adulthood (MIA) questionnaire. *Psychopharmacology Bulletin, 24*, 671-688.

Dotson, V. M., Beydoun, M. A., & Zonderman, A. B. (2010). Recurrent depressive symptoms and the incidence of dementia and mild cognitive impairment. *Neurology, 75*(1), 27-34. doi: 10.1212/WNL.0b013e3181e62124

Dubois, B., & Albert, M. L. (2004). Amnestic MCI or prodromal Alzheimer's disease? *The Lancet Neurology, 3*, 246 - 248. doi: S1474442204007100

Dungan, J. M., Brown, A. V., & Ramsey, M. A. (1996). Health maintenance for the indepdent frail older adult: Can it improve physical and mental well-being? *Journal of Advanced Nursing, 23*, 1185-1193.

Dux, M. C., Woodard, J. L., Calamari, J. E., Messina, M., Arora, S., Chik, H., & Pontarelli, N. (2008). The moderating role of negative affect on objective verbal memory performance and subjective memory complaints in healthy older adults. *Journal of the International Neuropsychological Society, 14*, 327-336. doi: 10.10170S1355617708080363

Ebly, E. M., Schaefer, J. P., Campbell, N. R. C., & Hogan, D. B. (1998). Folate status, vascular disease and cognition in elderly Canadians. *Age and Ageing, 27*, 485-491.

Elfgren, C., Gustafson, L., Vestberg, S., & Passant, U. (2010). Subjective memory complaints, neuropsychological performance and psychiatric variables in memory clinic attendees: a 3-year follow-up study. *Archives of Gerontology and Geriatrics, 51*(3), e110-114. doi: 10.1016/j.archger.2010.02.009

Elwood, P. C., Pickering, J., Bayer, A., & Gallacher, J. E. J. (2002). Vascular disease and cognitive function in older men in the Caerphilly cohort. *Age and Ageing, 31*, 43-48.

Fagerstrom, C., Holst, G., & Hallberg, I. R. (2007). Feeling hindered by health problems and functional capacity at 60 years and above. *Archives of Gerontology and Geriatrics, 44*, 181-201.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods, 41*, 1149-1160.

Fernandez-Martinez, M., Molano, A., Castro, J., & Zarranz, J. J. (2010). Prevalence of neuropsychiatric symptoms in mild cognitive impairment and Alzheimer's disease, and its relationship with cognitive impairment. *Current Alzheimer research, 7*(6), 517-526. doi: 10.2174/156720510792231748

Findlay, R. A. (2003). Interventions to reduce social isolation amongst older people: where is the evidence? *Ageing & Society, 23*, 647-658. doi: 10.1017/S0144686X03001296

Fisher, K. J., & Li, F. (2004). A community-based walking trial to improve neighbourhood quality of life in older adults: A multilevel analysis. *Annals of Behavioural Medicine, 28*(3), 186-194.

Fisk, J. D., Merry, H. R., & Rockwood, K. (2003). Variations in case definition affect prevelance but not outcomes of mild cognitive impairment. *Neurology, 61*, 1179-1184.

Fisk, J. D., & Rockwood, K. (2005). Outcomes of incident mild cognitive impairment in relation to case definition. *Journal of Neurology, Neurosurgery and Psychiatry, 76*, 1175 - 1177. doi: 10.1136/jnnp.2004.053751

Flicker, L. (2009). Lifestyle interventions to reduce the risk of dementia. *Maturitas, 63*, 319-322. doi: 10.1016/j.maturitas.2009.06.008

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.

Forsell, Y., Palmer, K., & Fratiglioni, L. (2003). Psychiatric symptoms/syndromes in elderly persons with mild cognitive impairment. Data from a cross-sectional study. *Acta neurologica Scandinavica.Supplementum, 179*, 25-28.

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.

Frerichs, R. J., & Tuokko, H. A. (2006). Reliable change scores and their relation to perceived change in memory: Implications for the diagnosis of mild cognitive impairment. *Archives of Clinical Neuropsychology, 21*, 109-115. doi: 10.1016/j.acn.2005.08.003

Gabryelewicz, T., Styczynska, M., Luczywek, E., Barczak, A., Pfeffer, A., Androsiuk, W., . . . Barcikowska, M. (2007). The rate of conversion of mild cognitive impairment to dementia: predictive role of depression. *International journal of geriatric psychiatry, 22*(6), 563-567. doi: 10.1002/gps.1716

Gale, C. R., Aihie Sayer, A., Cooper, C., Dennison, E. M., Starr, J. M., Whalley, L. J., . . . Deary, I. J. (2011). Factors associated with symptoms of anxiety and depression in five cohorts of community-based older people: The HALCyon (Healthy Ageing across the Life Course) Programme. *Psychological Medicine, 41*, 2057-2073. doi: 10.1017/S0033291711000195

Gallagher, D., Coen, R., Kilroy, D., Belinski, K., Bruce, I., Coakley, D., . . . Lawlor, B. A. (2011). Anxiety and behavioural disturbance as markers of prodromal Alzheimer's disease in patients with mild cognitive impairment. *International journal of geriatric psychiatry, 26*(2), 166-172. doi: 10.1002/gps.2509; 10.1002/gps.2509

Geda, Y. E., Knopman, D. S., Mrazek, D. A., Jicha, G. A., Smith, G. E., Negash, S., . . . Rocca, W. A. (2006). Depression, apolipoprotein E genotype, and the incidence of mild cognitive impairment: a prospective cohort study. *Archives of Neurology, 63*(3), 435-440. doi: 10.1001/archneur.63.3.435

Geda, Y. E., Roberts, R. O., Knopman, D. S., Petersen, R. C., Christianson, T. J., Pankratz, V. S., . . . Rocca, W. A. (2008). Prevalence of neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging: population-based study. *Archives of General Psychiatry, 65*(10), 1193-1198. doi: 10.1001/archpsyc.65.10.1193

Gilewski, M. J., Zelinski, E. M., & Schaie, K. W. (1990). The Memory Functioning Questionnaire for assessment of memory complaints in adulthood and old age. *Psychology and Aging, 5*, 482-490.

Glaesmer, H., Riedel-Heller, S., Braehler, E., Spangenberg, L., & Luppa, M. (2011). Age- and gender-specific prevalence and risk factors for depressive symptoms in the elderly: A population-based study. *International Psychogeriatrics, 23*(8), 1294-1300. doi: 10.1017/S1041610211000780

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*(1), 57-66. doi: 10.1111/j.1532-5415.2010.03233.x; 10.1111/j.1532-5415.2010.03233.x

Hidaka, S., Ikejima, C., Kodama, C., Nose, M., Yamashita, F., Sasaki, M., . . . Asada, T. (2012). Prevalence of depression and depressive symptoms among older Japanese people: comorbidity of mild cognitive impairment and depression. *International journal of geriatric psychiatry, 27*(3), 271-279. doi: 10.1002/gps.2715; 10.1002/gps.2715

Houde, M., Bergman, H., Whitehead, V., & Chertkow, H. (2008). A predictive depression pattern in mild cognitive impairment. *International Journal of Geriatric Psychiatry, 23*, 1028 - 1033. doi: 10.1002/gps.2028

Howse, K. (2007). Health and social care for older people in the UK: a snapshot view. In K. Howse (Ed.), *Working Paper 607*. Oxford, England: Oxford Institute of Ageing.

Huddon, C., Belleville, S., & Gauthier, S. (2008). The association between depressive and cognitive symptoms in amnestic mild cognitive impairment. *International psychogeriatrics / IPA, 20*(4), 710-723. doi: 10.1017/S1041610208007114

Huppert, F. A., Brayne, C., Gill, C., Paykel, E. S., & Beardsall, L. (1995). CAMCOG - a concise neuropsychological test to assist dementia diagnosis: socio-demographic determinants in an elderly population sample. *British Journal of Clinical Psychology, 34*(4), 529-541.

Hwang, T. J., Masterman, D. L., Ortiz, F., Fairbanks, L. A., & Cummings, J. L. (2004). Mild cognitive impairment I associated with characteristic neuropsychiatric symptoms. *Alzheimer Disease and Associated Disorders, 18*, 17 - 21.

Iliffe, S., & Pealing, L. (2010). Subjective memory problems. *BMJ, 340*, 703-706. doi: 10.1136/bmj.c1425

Jak, A. J., Bondi, M. W., Delano-Wood, L., Wierenga, C., & Corey-Bloom, J. (2009). Quantification of five neuropsychological approaches to defining mild cognitive impairment. *American Journal of Geriatric Psychiatry, 17*, 368 - 375. doi: 10.1097/JGP.0b013e31819431d5

Jessen, F., Amariglio, R. E., van Boxtel, M., Breteler, M., Ceccaldi, M., Chetelat, G., . . . Subjective Cognitive Decline Initiative (SCD-I) Working Group. (2014). A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & Dementia*, 1-9. doi: 10.1016/j.jalz.2014.01.001

Johansson, B. (2008). Memory and cognition in ageing. In B. Woods & L. Clare (Eds.), *Handbooks of the Clinical Psychology of Ageing* (2nd ed., pp. 33-55). West Sussex, England: John Wiley & Sons, Ltd.

Johnson, L. A., Mauer, C., Jahn, D., Song, M., Wyshywaniuk, L., Hall, J. R., & O'Bryant, S. E. (2012). Cognitive differences among depressed and non-depressed MCI participants: A project FRONTIER study. *International Journal of Geriatric Psychiatry, 28*(4), 377-382. doi: 10.1002/gps.3835

Jones, D. A., & Peters, T. J. (1992). Caring for elderly dependants: Effects on the carer's quality of life. *Age and Ageing, 21*, 421-428. doi: 10.1093/ageing/21.6.421

Jorm, A. F., Christensen, H., Korten, A. E., Henderson, A. S., Jacomb, P. A., & Mackinnon, A. (1997). Do cognitive complaints either predict future cognitive decline or reflect past cognitive decline? A longitudinal study of an elderly community sample. *Psychological Medicine, 27*, 91-98.

Katz, J. N., Chang, L. C., Sangha, O., Fossel, A. H., & Bates, D. W. (1996). Can comorbidity be measured by questionnaire rather than medical record review? *Medical Care, 34*(1), 73-84.

Kivipelto, M., Solomon, A., Ahtiluoto, S., Ngandu, T., Lehtisalo, J., Antikainen, R., . . . Soininen, H. (2013). The Finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER): Study deisgn and progress. *Alzheimer's and Dementia, 9*, 657-665. doi: 10.1016/j.jalz.2012.09.012

Klekociuk, S. Z., & Summers, M. J. (2014). Exploring the validity of mild cognitive impairment (MCI) subtypes: Multiple-domain amnestic MCI is the only identifiable subtype at longitudinal follow-up. *Journal of Clinical and Experimental Neuropsychology, Advance online publication*, 1-12. doi: 10.1080/13803395.2014.890699

Kral, V. A. (1962). Senescent forgetfulness: Benign and malignant. *Journal of the Canadian Medical Association, 86*, 257 - 260.

Kruger, T. M., Abner, E. L., Mendiondo, M., Schmitt, F. A., Smith, C. D., & Jicha, G. A. (2012). Differential reports of pain and depression differentiate mild cognitive impairment from cognitively intact elderly participants. *Journal of Geriatric Psychiatry and Neurology, 25*, 107 - 112. doi: 10.1177/0891988712445097

Kumar, R., Jorm, A. F., Parslow, R. A., & Sachdev, P. S. (2006). Depression in mild cognitive impairment in a community sample of individuals 60-64 years old. *International psychogeriatrics / IPA, 18*(3), 471-480. doi: 10.1017/S1041610205003005

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

Laurin, D., Verreault, R., Lindsay, J., MacPherson, K., & Rockwood, K. (2001). Physical activity and risk of cognitive impairment and dementia in elderly persons. *Archives of Neurology, 58*, 498-504.

Lautenschlager, N. T., Cox, K. L., Flicker, L., Foster, J. K., van Bockxmeer, F. M., Xiao, J., . . . Almeida, O. P. (2008). Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease. *Journal of the American Medical Association, 300*(9), 1027-1037. doi: ACTRN12605000136606

Lee, J. S., Potter, G. G., Wagner, H. R., Welsh-Bohmer, K. A., & Steffens, D. (2006). Persistent mild cognitive impairment in geriatric depression. *International Psychogeriatrics, 19*, 125 - 135.

Lenehan, M. E., Klekociuk, S. Z., & Summers, M. J. (2012). Absence of a relationship between subjective memory complaint and objective memory impairment in mild cognitive impairment (MCI): is it time to abandon subjective memory complaint as an MCI diagnostic criterion? *International Psychogeriatrics, 24*, 1 - 10. doi: 10.1017/S1041610212000695

Lenze, E. J., Mulsant, B. H., Shear, M. K., Alexopoulos, G. S., Frank, E., & Reynolds, C. F. (2001). Comorbidity of depression and anxiety disorders in later life. *Depression and Anxiety, 14*, 86-93.

Lenze, E. J., Rogers, J. C., Martire, L. M., Mulsant, B. H., Rollman, B. L., Dew, M. A., . . . Reynolds, C. F. (2001). The association of late-life depression and anxiety with physical disability. *American Journal of Geriatric Psychiatry, 9*(2), 113-135.

Lim, K., & Taylor, L. (2005). Factors associated with physical activity among older people - a population-based study. *Preventive Medicine, 40*, 33-40. doi: 10.1016/j.ypmed.2004.04.046

Lingler, J. H., Nightingale, M. C., Erlen, J. A., Kane, A. L., Reynolds, C. F., Schulz, R., & deKosky, S. T. (2006). Making sense of mild cognitive impairment: A qualitative exploration of the patient's experience. *The Gerontologist, 46*(6), 791-800.

Livingston, B. M., Seeman, T. E., Merrill, S. S., & Blazer, D. G. (1994). The impact of depressive symptomatology on physical disability: MacArthur studies of successful aging. *American Journal of Public Health, 84*(11), 1796-1799.

Lopez, O. L., Becker, J. T., Jagust, W. J., Fitzpatrick, A., Carlson, M. C., DeKosky, S. T., . . . Kuller, L. H. (2006). Neuropsychological characteristics of mild cognitive impairment subgroups. *Journal of neurology, neurosurgery, and psychiatry, 77*(2), 159-165. doi: 10.1136/jnnp.2004.045567

Lubben, J. (1988). Assessing social networks among elderly populations. *Family & Community Health, 11*(3), 42-52.

Lubben, J., Blozik, E., Gillmann, G., Illife, S., Kruse, W., Beck, J. C., & Stuck, A. E. (2006). Performance of an abbreviated version of the Lubben Social Network Scale among three European community-dwelling older adult populations. *The Gerontologist, 46*(4), 503-513.

Luker, K. A., & Perkins, E. S. (1987). The elderly at home: service needs and provision. *Journal of the Royall College of General Practitioners, 37*, 248-250.

Luppa, M., Sikorski, C., Luck, T., Weyerer, S., Villringer, A., Konig, H. H., & Riedel-Heller, S. G. (2012). Prevalence and risk factors of depressive symptoms in latest life – results of the Leipzig Longitudinal Study of the Aged (Leila 75+). *International Journal of Geriatric Psychiatry, 27*, 286 - 295. doi: 10.1002/gps.2781

Luszczynska, A., & Schwarzer, R. (2005). Social cognitive theory. In M. Conner & P. Norman (Eds.), *Predicting Health Behaviour: Research and practice with social cognition models* (2nd ed., pp. 127-169). England: Open University Press.

Lyketsos, C. G., Lopez, O., Jones, B., Fitzpatrick, A. L., Breitner, J., & DeKosky, S. (2002). Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. *JAMA : the journal of the American Medical Association, 288*(12), 1475-1483.

Marri, L., Modugno, M., Iacono, S., Renzetti, C., de Vreese, L. P., & Neri, M. (2001). Metamemory and self-perceived health in mild cognitive impairment. *Archives of Gerontology and Geriatrics, 7*, 235-244.

Matthews, F. E., Arthur, A., Barnes, L. E., Bond, J., Jagger, C., Robinson, L., & Brayne, C. (2013). A two-decade comparison of the 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, 6736*(13), 61570-61576. doi: 10.1016/s0140-6736(13)61570-6

Matthews, F. E., Stephan, B. C. M., McKeith, I. G., Bond, J., & Brayne, C. (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

May, M., McCarron, P., Stansfeld, S., Ben-Shlomo, Y.,, Gallacher, J., Yarnell, J., Davey Smith, G., . . . Ebrahim, S. (2002). Does psychological distress predict the risk of ischemic stroke and transient ischemic attack? The Caerphilly Study. *Stroke, 33*, 7-12.

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

McDougall, G. J., Becker, H., & Arheart, K. L. (2006). Older adults in the SeniorWISE Study at risk for mild cognitive impairment. *Archives of Psychiatric Nursing, 20*, 126 - 134. doi: 10.1016/j.apnu.2005.09.003

McIlvane, J. M., Popa, M. A., Robinson, B., Houseweart, K., & Haley, W. E. (2008). Perceptions of illness, coping, and well-being in persons with mild cognitive impairment and their care partners. *Alzheimer Disease and Associated Disorders, 22*, 284 - 292. doi: 10.1097/WAD.0b013e318169d714

Mead, N., Lester, H., Chew-Graham, C., Gask, L., & Bower, P. (2010). Effects of befriending on depressive symptoms and distress: systematic review and meta-analyses. *The British Journal of Psychiatry, 196*, 96-101. doi: 10.1192/bjp.bp.109.064089

Mecacci, L., & Righi, S. (2006). Cognitive failures, metacognitive beliefs and aging. *Personality and individual differences, 2006*(40), 1453-1459. doi: 10.1016/j.paid.2005.11.022

Minett, T. S. C., Da Silva, R. V., Ortiz, K. Z., & Bertolucci, P. H. F. (2008). Subjective memory complaints in an elderly sample: a cross-sectional study. *International Journal of Geriatric Psychiatry, 23*, 49-54. doi: 10.1002/gps.1836

Mitchell, A. J., & Shiri-Feshki, M. (2009). Rate of progression of mild cognitive impairment to dementia - a meta-analysis of 41 robust inception cohort studies. *Acta Psychiatrica Scandinavica, 119*, 252-265. doi: 10.1111/j.1600-0447.2008.01326.x

Mol, M. E. M., van Boxtel, M. P. J., Willems, D., & Jolles, J. (2006). Do subjective memory complaints predict cognitive dysfunction over time? A six-year follow-up of the Maastricht Aging Study. *International Journal of Geriatric Psychiatry, 21*, 432–441. doi: 10.1002/gps.1487

Morris, M. A., Jacques, P. F., Rosenberg, I. H., & Selhub, J. (2007). Folate and vitamin B-12 status in relation to anemia, macrosytosis and cognitive impairment in older Americans in the age of folic acid fortification. *American Journal of Clinical Nutrition, 85*, 193-200.

Muangpaisan, W., Intalapaporn, S., & Assantachai, P. (2008). Neuropsychiatric symptoms in the community-based patients with mild cognitive impairment and the influence of demographic factors. *International journal of geriatric psychiatry, 23*(7), 699-703. doi: 10.1002/gps.1963

Nordhus, I. H. (2008). Manifestations of depression and anxiety in older adults. In B. Woods & L. Clare (Eds.), *Handbook of the Clinical Psychology of Ageing* (2nd ed., pp. 97-110). West Sussex: UK: John Wiley & Sons.

Oakley, F., Khin, N. A., Parks, R., Bauer, L., & Sunderland, T. (2002). Improvement in activities of daily living in elderly following treatment for post-bereavement depression. *Acta Psychiatrica Scandinavica, 105*, 231-234.

Office for National Statistics. (2012). Population ageing in the United Kingdom, its constituent countries and the European Union (pp. 1-12): Office for National Statistics.

Office for National Statistics. (2013). What does the 2011 census tell us about older people? (pp. 1-17).

Palmer, K., Backman, L., Winblad, B., & Fratiglioni, L. (2003). Detection of Alzheimer's disease and dementia in the preclinical phase: population based cohort study. *BMJ, 326*, 1-5.

Palmer, K., Berger, A. K., Monastero, R., Winblad, B., Backman, L., & Fratiglioni, L. (2007). Predictors of progression from mild cognitive impairment to Alzheimer disease. *Neurology, 68*(19), 1596-1602. doi: 10.1212/01.wnl.0000260968.92345.3f

Palmer, K., Di Iulio, F., Varsi, A. E., Gianni, W., Sancesario, G., Caltagirone, C., & Spalletta, G. (2010). Neuropsychiatric predictors of progression from amnestic-mild cognitive impairment to Alzheimer's disease: the role of depression and apathy. *Journal of Alzheimer's disease : JAD, 20*(1), 175-183. doi: 10.3233/JAD-2010-1352

Panza, F., D'Introno, A., Colacicco, A. M., Capurso, C., Del Parigi, A., Caselli, R. J., . . . Italian Longitudinal Study on Aging Working, G. (2008). Depressive symptoms, vascular risk factors and mild cognitive impairment. The Italian longitudinal study on aging. *Dementia and geriatric cognitive disorders, 25*(4), 336-346. doi: 10.1159/000119522

Parker, M. G., & Thorslund, M. (2007). Health trends in the elderly population: Getting better and getting worse. *The Gerontologist, 47*(2), 150-158.

Perneczky, R., Pohl, C., Sorg, C., Hartmann, J., Komossa, K., Alexopoulos, P., . . . Kurz, A. (2006). Complex activities of daily living in mild cognitive impairment: Conceptual and diagnostic issues. *Age and Ageing, 35*, 240-245. doi: 0.093/ageing/afj054

Perneczky, R., Pohl, C., Sorg, C., Hatmann, J., Tosic, N., Grimmer, T., . . . Kurz, A. (2006). Impairment of activities of daily living requiring memory or complex reasoning as part of the MCI syndrome. *International Journal of Geriatric Psychiatry, 21*, 158-162. doi: 10.1002/gps.1444

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine, 256*, 183 - 194. doi: 10.1111/j.1365-2796.2004.01388.x

Petersen, R. C., Caracciolo, B., Brayne, C., Gauthier, S., Jelic, V., & Fratiglioni, L. (2014). Mild cognitive impairment: A concept in evolution. *Journal of Internal Medicine, 275*, 214-228. doi: 10.1111/joim.12190

Petersen, R. C., Doody, R., Kurz, A., Mohs, R. C., Morris, J. C., Rabins, P. V., & Winblad, B. (2001). Current concepts in mild cognitive impairment. *Archives of Neurology, 58*, 1985 - 1992. doi: 10.1001/archneur.58.12.1985

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokmen, E. (1999). Mild cognitive impairment: Clinical characterization and outcome. *Archives of Neurology, 56*, 303-308.

Podewils, L. J., McLay, R. N., Rebok, G. W., & Lyketsos, C. G. (2003). Relationship of self-perceptions of memory and worry to objective measures of memory and cognition in the general population. *Psychosomatics, 44*(6), 461-470.

Prince, M. J., Harwood, R. H., Blizard, R. A., Thomas, A., & Mann, H. (1997). Social support deficits, loneliness and life events as risk factors for depression in old age. The Gospel Oak Project VI. *Psychological Medicine, 27*, 323-332.

Quan, H., Li, B., Couris, C. M., Fushimi, K., Graham, P., Hider, P., . . . Sundararajan, V. (2011). Updating and validating the Charlson Comorbidity Index and score for risk adjustment in hospital discharge abstracts using data from six countries. *American Journal of Epidemiology, 173*(6), 676-682. doi: 10.1093/aje/kwq433

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Medicine, 1*, 385-401.

Ramakers, I. H., Visser, P. J., Aalten, P., Kester, A., Jolles, J., & Verhey, F. R. (2009). Affective symptoms as predictors of Alzheimer's disease in subjects with mild cognitive impairment: A 10-year follow-up study. *Psychological Medicine, 40*, 1193 - 1201. doi: 10.1017/S0033291709991577

Ravaglia, G., Forti, P., Lucicesare, A., Rietti, E., Pisacane, N., Mariani, E., & Dalmonte, E. (2008). Prevalent depressive symptoms as a risk factor for conversion to mild cognitive impairment in an elderly Italian cohort. *The American Journal of Geriatric Psychiatry, 16*(10), 834-843. doi: 10.1097/JGP.0b013e318181f9b1

Reisberg, B., & Gauthier, S. (2008). Currrent evidence for subjective cognitive impairment (SCI) as the pre-mild cognitive impairment (MCI) stage of subsequently manifest Azheimer's disease. *International Psychogeriatrics, 20*, 1-16. doi: 10.1017/S1041610207006412

Reisberg, B., Prichep, L., Mosconi, L., John, E. R., Glodzik-Sobanska, L., Boksay, I., . . . du Leon, M. J. (2008). The pre-mild cognitive impairment, subjective cognitive impairment stage of Alzheimer's disease. *Alzheimer's and Dementia, 4*, S98-S108. doi: 10.1016/j.jalz.2007.11.017

Reppermund, S., Sachdev, P. S., Crawford, J., Kochan, N. A., Slavin, M. J., Kang, K., . . . Brodarty, H. (2011). The relationship of neuropsychological function to instrumental activities of daily living in mild cognitive impairment. *International Journal of Geriatric Psychiatry, 26*(8), 843-852. doi: 10.1002/gps.2612

Robert, P. H., Berr, C., Volteau, M., Bertogliati, C., Benoit, M., Sarazin, M., & study., m. o. t. P. (2006). Apathy in patients with mild cognitive impairment and the risk of developing dementia of Alzheimer's disease: A one-year follow-up study. *Clinical Neurology and Neurosurgery, 108*, 733 - 736. doi: 10.1016/j.clineuro.2006.02.003

Robert, P. H., Clairet, S., Benoit, M., Koutaich, J., Bertogliati, C., Tible, O., & Bedoucha, P. (2002). The Apathy Inventory: Assessment of apathy and awareness in Alzheimer's disease, Parkinson's disease and mild cognitive impairment. *International Journal of Geriatric Psychiatry, 17*, 1099 - 1105. doi: 10.1002/gps.755

Roberts, J. L., Clare, L., & Woods, R. T. (2009). Subjective memory complaints and awareness of memory functioning in mild cognitive impairment: A systematic review. *Dementia and Geriatric Cognitive Disorders, 28*, 95 - 109. doi: 10.1159/000234911

Rose, G. A. (1962). The Diagnosis of Ischaemic Heart Pain and Intermittent Claudication in Field Surveys. *Bulletin of the World Health Organisation, 27*, 645-658.

Rosenberg, P. B., Mielke, M. M., Appleby, B. S., Oh, E. S., Geda, Y. E., & Lyketsos, C. G. (2013). The Association of Neuropsychiatric Symptoms in MCI With Incident Dementia and Alzheimer Disease. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 21*(7), 685-695. doi: 10.1097/JGP.0b013e318252e41a

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. *Br J Psychiatry, 149*, 698-709.

Rozzini, L., Chilovi, B. V., Peli, M., Conti, M., Rozzini, R., Trabucchi, M., & Padovani, A. (2009). Anxiety symptoms in mild cognitive impairment. *International journal of geriatric psychiatry, 24*(3), 300-305. doi: 10.1002/gps.2106

Rozzini, L., Vicini Chilovi, B., Conti, M., Delrio, I., Borroni, B., Trabucchi, M., & Padovani, A. (2008). Neuropsychiatric symptoms in amnestic and nonamnestic mild cognitive impairment. *Dementia and geriatric cognitive disorders, 25*(1), 32-36. doi: 10.1159/000111133

Ryu, S. H., Ha, J. H., Park, D. H., Yu, J., & Livingston, G. (2011). Persistence of neuropsychiatric symptoms over six months in mild cognitive impairment in community-dwelling Korean elderly. *International Psychogeriatrics, 23*, 214 - 220. doi: 10.1017/S1041610210001766

Schmand, B., Jonker, C., Geerlings, M. I., & Lindeboom, J. (1997). Subjective memory complaints in the elderly: Depressive symptoms and future dementia. *The British Journal of Psychiatry, 171*, 373-376. doi: 10.1192/bjp.171.4.373

Schoevers, R. A., Beekman, A. T. F., Deeg, D. J. H., Jonker, C., & van Tilburg, W. (2003). Comorbidity and risk-patterns of depression, generalised anxiety disorder and mixed anxiety-depression in later life: Results from the AMSEL study. *International Journal of Geriatric Psychiatry, 18*, 994-1001. doi: 10.1002/gps.1001

Schulz, R., & Martire, L. M. (2004). Family caregiving of persons with dementia. *American Journal of Geriatric Psychiatry, 12*(3), 240-249. doi: 10.1097/00019442-200405000-00002

Seeman, T. E. (1996). Social ties and health: The benefits of social integration. *Annals of Epidemiology, 6*(5), 442-451.

Seeman, T. E., Lusignolo, T. M., Albert, M., & Berkman, L. (2001). Social relationships, social support and patterns of cognitive aging in healthly, high functioning older adults: MacArthur Studies of Successful Aging. *Health Psychology, 20*(4), 249-255. doi: 10.1037//0278-6133.20.4.243

Seidler, A., Benhardt, T., Neinhaus, A., & Frolich, L. (2003). Association between the psychosocial network and dementia - a case-control study. *Journal of Psychiatric Research, 37*, 89-98.

Simon, C. (2001). Informal carers and the primary care team. *British Journal of General Practice, 51*, 920-923.

Simonsick, E. M., Wallace, R. B., Blazer, D. G., & Berkman, L. F. (1995). Depressive symptomology and hypertension-associated morbidity and mortality in older adults. *Psychosomatic Medicine, 57*, 427-435.

Sjosten, N., & Kivela, S. R. (2006). The effects of physical exercise on depressive symptoms among the aged: A systematic review. *International Journal of Geriatric Psychiatry, 21*, 410-418.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *Manual for the State-Trait Anxiety Inventory (self-evaluation questionnaire)*. Palo Alto, CA: Consulting Psychologists Press.

Spira, A. P., Rebok, G. W., Stone, K. L., Kramer, J. H., & Yaffe, K. (2011). Depressive Symptoms in Oldest-Old Women: Risk of Mild Cognitive Impairment and Dementia. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry*. doi: 10.1097/JGP.0b013e318235b611

Steenland, K., Karnes, C., Seals, R., Carnevale, C., Hermida, A., & Levey, A. (2012). Late-life depression as a risk factor for mild cognitive impairment or Alzheimer's disease in 30 US Alzheimer's disease centers. *Journal of Alzheimer's disease : JAD, 31*(2), 265-275. doi: 10.3233/JAD-2012-111922

Stephan, B. C. M., Brayne, C., McKeith, I. G., Bond, J., & Matthews, F. E. (2008). Mild cognitive impairment in the older population: Who is missed and does it matter? *International Journal of Geriatric Psychiatry, 23*, 863 - 871. doi: 10.1002/gps.2013

Stephan, B. C. M., Matthews, F. E., Hunter, S., Savva, G. M., & Bond, J. (2012). Neuropathological profile of mild cognitive impairment from a population perspective. *Alzheimer's Disease and Associated Disorders, 26*, 205-212. doi: 10.1097/WAD.0b013e31822fc24d

Stephan, B. C. M., Matthews, F. E., McKeith, I. G., Bond, J., & Brayne, C. (2007). Early cognitive change in the general population: How do different definitions work? *Journal of the American Geriatrics Society*, 1534-1540. doi: 10.1111/j.1532-5415.2007.01386.x

Stevens, N. (2001). Combating loneliness: A friendship enrichment programme for older women. *Ageing & Society, 21*, 183-202.

Stillman, A. N., Rowe, K. C., Arndt, S., & Moser, D. J. (2012). Anxious symptoms and cognitive function in non-demented older adults: An inverse relationship. *International Journal of Geriatric Psychiatry, 27*, 792 - 798. doi: 10.1002/gps.2785

Stoddart, H., Whitley, E., Harvey, I., & Sharp, D. (2002). What determines the use of home care services by elderly people? *Health and Social Care in the Community, 10*(5), 348-360.

Stuck, A. E., Walthert, J. M., Nikolaus, T., Bula, C. J., Hohmann, C., & Beck, J. C. (1999). Risk factors for functional status decline in community-living elderly people: A systematic literature review. *Social Science and Medicine, 48*, 445-469.

Teng, E., Lu, P. H., & Cummings, J. L. (2007). Neuropsychiatric symptoms are associated with progression from mild cognitive impairment to Alzheimer's disease. *Dementia and geriatric cognitive disorders, 24*(4), 253-259. doi: 10.1159/000107100

Tilvis, R. S., Kahonen-Vare, M. H., Jolkkonen, J., Valvanne, J., Pitkala, K. H., & Strandberg, T. E. (2010). Predictors of cognitive decline and mortality of aged people over a 10-year period. *Journal of Gerontology: Medical Sciences, 59A*(3), 268-274. doi: 10.1093/gerona/59.3.M268

US Department of Health and Human Services. (1996). Physical activity and health: a report from the surgeon general (pp. 1-278). Atlanta, GA: US: National Center for Chronic Disease Prevention and Health Promotion.

Van der Linde, R., Stephan, B. C. M., Matthews, F. E., Brayne, C., & Savva, G. M. (2010). Behavioural and psychological symptoms in the older population without dementia – relationship with socio-demographics, health and cognition. *Biomed Central Geriatrics, 10*. doi: 10.1186/1471-2318-10-87

van Tilburg, T. (1998). Losing and gaining in old age: Changes in personal network size and social support in a four-year longitudinal study. *Journal of Gerontology: Social Sciences, 53B*(6), S313-S323.

Vicini Chilovi, B., Conti, M., Zanetti, M., Mazzu, I., Rozzini, L., & Padovani, A. (2009). Differential impact of apathy and depression in the development of dementia in mild cognitive impairment patients. *Dementia and geriatric cognitive disorders, 27*(4), 390-398. doi: 10.1159/000210045

Vink, D., Aartsen, M. J., & Schoevers, R. A. (2008). Risk factors for anxiety and depression in the elderly: A review. *Journal of Affective Disorders, 106*, 29-44. doi: 10.1016/j.jad.2007.06.005

Wahlund, L. O., Pihlstrand, E., & Jonhagen, M. (2003). Mild cognitive impairment: Experience from a memory clinic. *Acta Neurologica Scandinavica, 107*, 21 -24.

Wang, H. X., Karp, A., Winblad, B., & Fratiglioni, L. (2002). Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: A longitudinal study from the Kungsholmen Project. *American Journal of Epidemiology, 155*(12), 1081-1087.

Weiler, P. G., Lubben, J. E., & Chi, I. (1991). Cognitive impairment and hospital use. *American Journal of Public Health, 81*(9), 1153-1157.

Wenger, G. C. (1985). Care in the community. Changes in dependency and use of domiciliary service: a longitudinal perspective. *Ageing and Society, 5*, 143-159.

Wenger, G. C. (1989). Support networks in old age: Constructing a typology. In M. Jefferys (Ed.), *Growing Old in the Twentieth Century* (1st ed., pp. 166-185): Routledge.

Wenger, G. C. (1997). Social networks and the prediction of elderly people at risk. *Aging & Mental Health, 1*(4), 311-320.

Werner, P., & Korczyn, A. D. (2008). Mild cognitive impairment: Conceptual, assessment, ethical and social issues. *Clinical Interventions in Aging, 3*, 413 - 420.

Whiting, P., Rutjes, A. W. S., Reitsma, J. B., Bossuyt, P. M. M., & Kleijnen, J. (2003). The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology, 3*. doi: 10.1186/1471-2288-3-25

Williamson, G. M., & Schulz, R. (1992a). Pain, activity restriction and symptoms of depression among community-residing elderly adults. *Journal of Gerontology: Psychosocial Sciences, 47*(6), 367-372.

Williamson, G. M., & Schulz, R. (1992b). Physical illness and symptoms of depression among elderly outpatients. *Psychology and Aging, 7*(3), 343-351.

Wilson, R. S., Schneider, J. A., Boyle, P. A., Arnold, S. E., Tang, Y., & Bennett, D. A. (2007). Chronic distress and incidence of mild cognitive impairment. *Neurology, 68*(24), 2085-2092. doi: 10.1212/01.wnl.0000264930.97061.82

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., & Wahlund, L. O. (2004). Mild cognitive impairment – beyond controversies, towards a consensus: Report of the International Working Group on mild cognitive impairment. *Journal of Internal Medicine, 256,* 240 - 246. doi: 10.1111/j.1365-2796.2004.01380.x

Windle, G., Hughes, D., Linck, P., Russell, I., & Woods, B. (2010). Is exercise effective in promoting mental well-being in older age? A systematic review. *Aging and Mental Health, 14*(6), 652-669. doi: 10.1080/1360781003713232

Windle, G., Markland, D. A., & Woods, R. T. (2008). Examination of a theoretical model of psychological resilience in older age. *Aging & Mental Health, 12*(3), 285-292. doi: 10.1080/13607860802120763

Wolf, H., Grunwald, M., Ecke, G. M., Zedlick, D., Bettin, S., & Dannenberg, C. (1998). The prognosis of mild cognitive impairment in the elderly. *Journal of Neural Transmission, 54,* 31 - 50.

Yates, J. A., Clare, L., & Woods, R. T. (2013). Mild cognitive impairment and mood: a systematic review. *Reviews in Clinical Gerontology, 23*(4), 317-356. doi: 10.1017/S0959259813000129

Yesavage, J. A., Brink, T. I., Rose, T. I., Lum, O., Huang, V., Adey, M., & von Leirer, O. (1983). Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research, 17,* 37-49.

Zanardo, F., De Beni, R., & Moe, A. (2006). Influence of other-beliefs on self-beliefs and on everyday memory self-report in the elderly. *Aging Clinical and Experimental Research, 18*(5), 0-8.

Zandi, T. (2004). Relationship between subjective memory complaints, objective memory performance and depression among older adults. *American Journal of Alzheimer's Disease and Other Dementias, 19*(6), 353-360. doi: 10.1177/153331750401900610

Zihl, J., Reppermund, S., Thum, S., & Unger, K. (2010). Neuropsychological profiles in MCI and in depression: Differential cognitive dysfunction patterns or similar final common pathway disorder? *Journal of psychiatric research, 44*(10), 647-654. doi: 10.1016/j.jpsychires.2009.12.002

Zunzunegui, M., Alvarado, B. E., Del Ser, T., & Otero, A. (2003). Social networks, social integration, and social engagement deterime cognitive decline in community-dwelling Spanish older adults. *Journal of Gerontology, 58B*(2), S93-S100.

Appendix A

ETHICAL APPROVAL

NHS
Pwyllgor Moeseg Ymchwil Gogledd Cymru (Y Orllewin)
North Wales Research Ethics Committee (West)

PRIVATE & CONFIDENTIAL
Professor Robert Woods
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01 September 2010

Dear Professor Woods,

Study Title: **Maintaining function and well-being in later life**
REC reference number: **10/WNo01/37**
Protocol number: **1 dated 31/05/2010**

Thank you for your letter of 27 August 2010, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chairman.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Mental Capacity Act 2005

I confirm that the committee has approved this research project for the purposes of the Mental Capacity Act 2005. The committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance

arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where the only involvement of the NHS organisation is as a Participant Identification Centre (PIC), management permission for research is not required but the R&D office should be notified of the study and agree to the organisation's involvement. Guidance on procedures for PICs is available in IRAS. Further advice should be sought from the R&D office where necessary.

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		04 June 2010
REC application 40092/125963/1/582		24 May 2010
Protocol	1	31 May 2010
~~Participant Information Sheet: Patient~~ superseded	~~1~~	~~24 May 2010~~
Participant Information Sheet: Patient	2	05 July 2010
~~Participant Information Sheet: Relative/Carer Information Sheet~~ superseded	~~1~~	~~24 May 2010~~
Participant Information Sheet: Relative/Carer	2	05 July 2010
Participant Information Sheet: Brain Donation Information Sheet	1	24 May 2010
~~Participant Consent Form~~ superseded	~~1~~	~~24 May 2010~~
Participant Consent Form	2	05 July 2010
Participant Consent Form: Saliva Sample	1	24 May 2010
Participant Consent Form: Access to Medical Records	1	24 May 2010
Participant Consent Form: Hearing Test	1	24 May 2010
Participant Consent Form: Blood Sample	1	24 May 2010
~~Participant Consent Form: Brain Donation~~ superseded	~~1~~	~~24 May 2010~~
Participant Consent Form: Brain Donation	2	05 July 2010
~~Participant Consent Form: Consultee~~ superseded	~~1~~	~~24 May 2010~~
Participant Consent Form: Consultee	2	05 July 2010
~~Participant Consent Form: Consultee consent to Informant Interview~~ superseded	~~1~~	~~24 May 2010~~
Participant Consent Form: Consultee consent to Informant Interview	2	05 July 2010
Participant Consent Form: Consultee Brain Donation	1	24 May 2010
Letter of invitation to GP	1	24 May 2010
GP/Consultant Information Sheets	1	24 May 2010
Questionnaire: Part 1 - Respondent	2	04 June 2010
Questionnaire: Part 2 - Informant	1	04 June 2010
Lettter from CMO (Wales)		19 October 2010
Letter from Caldicott Guardian BCUHB		27 August 2010
Latter from Caldicott Guardian ABMUHB		04 August 2010
Supporting paper re: recruitment strategy		27 August 2010
Evidence of insurance or indemnity		01 August 2009
Referees or other scientific critique report		09 January 2009
Investigator CV		24 May 2010

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

10/WNo01/37	**Please quote this number on all correspondence**

Yours sincerely

Rossela Roberts

Mr David Owen
Chairman

Email: rossela.roberts@wales.nhs.uk

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Sponsor's Representative:* Dr Gill Windle, Bangor University
R&D office for Betsi Cadwaladr University Health Board - West

Appendix B

MRC-CFAS I DATA REQUEST FORM

FOR CFAS OFFICE USE
Project no. .....

APPLICATION TO USE DATA FROM THE MRC COGNITIVE FUNCTION AND AGEING STUDY

FOR CONSIDERATION BY THE CFAS COOPERATIVE MANAGEMENT COMMITTEE

This form should be completed in consultation with the CFAS Core Team in the first instance.

Please use type or use BLOCK CAPITALS.

Proposed Study Title
The role of subjective memory complaints in the relationship between mild cognitive impairment and mood

SECTION A: PROJECT STAFF DETAILS

Head of proposed study

Title: Miss Initials: J A

Surname: Yates

Position: PhD Student

Organisation: Bangor University

Address: 45, College Road, Bangor, Gwynedd, LL57 2DG

Telephone No: 01248 383485 Fax No:

Email: j.yates@bangor.ac.uk

Names of collaborators and Organisation(s)

.....

.....

.....

Expected duration of project

From January 2013 to January 2014

CFAS Sponsor: ESRC PhD studentship to CFAS Wales

SECTION B: BACKGROUND AND AIMS OF STUDY (attach full proposal if relevant)

1. Give a brief account of the background to the study (maximum 200 words).

Subjective memory complaints form part of several of the classification systems used to identify individuals who may have MCI (Stephan et al., 2008). Increasing levels of subjective memory complaints correlated with increased levels of anxiety and depression, independent of whether an individual was classified as having MCI, suggesting that mood can influence the accuracy with which a person appraises their memory (Lenehan et al., 2012; van der Linde et al., 2010). The presence of depression may inflate memory problems by enhancing negative attributions (Roberts, Clare & Woods, 2009). Research has shown that the association between subjective memory complaints and depression is stronger than the association between subjective memory complaints and objective memory impairments (Minett et al., 2008). Subjective memory complaints could be influenced by mood in that people with depressive symptoms are more likely experience memory problems, and individuals who are anxious may be more aware of subtle changes in their memory. In turn, being aware of memory problems could cause anxiety and depression due to a potential change in status and self concept.

2. Summarise the aims of the study (maximum 200 words).

The study seeks to investigate possible reasons for changes in mood between the prevelance assessment (A0) and the combined screen and assessment (C2).

It is hypothesised that depressive or anxious symptoms will be more prevalent when there is a greater frequency of subjective memory complaints. An increase in the number in the number of subjective memory complaints should occur with an increase in the prevelance of depressive or anxious symptoms.

A further hypothesis concerns the relationship with mild cognitive impairment. It is expected that subjective memory complaints are more likely in those with mild cognitive impairment, and therefore mood problems are more likely in those with mild cognitive impairment. It is thought that a decline in cognitive function from not cognitively impaired to a classification of mild cognitive impairment will result in a higher prevalence of depressive and anxious symptoms.

Depression and anxiety are defined by an AGECAT score of 3 and above but this project will also consider individuals with an AGECAT score of 2.

Questions relating to memory that will be included in the analysis are: A0 Q55-63 and C2 Q64-78C.

MCI will be defined using an algorithm that does not include subjective memory complaints for the purpose of this analysis.

3. Proposed Funding body (Please attach grant proposal to document)

ESRC PhD studentship to CFAS Wales

4. Has this proposal been peer-reviewed YES
(please provide any comments with proposal)

This proposal has been reviewed by the PhD Committee, School of Psychology, Bangor.

If no, are there plans for review?

SECTION C: Data request form.

Below is a list of all data available from the CFAS data archive. Individuals wanting data are recommended to ask for specific questions that address their research as each interview has about 300 variables and can therefore be very large. Researchers will only be given information required for their proposal. Details of the interviews, and the sections (e.g. health) within, can be found on the website (http://www-cfas.medschl.cam.ac.uk/questionnaires.htm).

Data released will be of a versioned number (e.g. 6.3). All researchers should give this version number in publications. Subsequent releases can be requested.

All researchers will get the main audit data that contains refusal codes, death information (fact and date), participation data on each interview and the audit code data on the 13,004 individuals.

AGECAT diagnosis is embedded into the screen interviews for individuals selected for assessment, if just diagnosis is needed the whole assessment interview is not required.

Interview(s) wanted		Individual (specify later)	Sections (e.g. health, etc)	Complete (rarely given)
Wave 1 interviews				
Prevalence screen	(s0)			
Prevalence assessment	(a0)		Worry, general anxiety, depression, memory, MCI status	
Annual follow-up 1	(f1)			
Wave 2 interviews				
Combined screen and assessment	(c2)		Worry, general anxiety, depression, memory, MCI status	
Incidence screen	(s2)			
Incidence assessment	(a2)			
Annual follow-up 2	(f3)			
Wave 3 interviews				
Combined screen and assessment	(c6)			
* *Twice screened group (Cambs only)*	(s6)			
Wave 5 interviews				
Combined screen and assessment	(cx)			
Complete in sample audit data		Not available	Not available	
* *RIS data (4 centres only)*		Not available	Not available	
* *ESRC data (2 centres only)*		Not available	Not available	
* *Young cohort data (1 centre only)*		Not available	Not available	
Medication data (each interview as above)		Not available	Not available	
Informant information (interviews a0, c2, a2, c6, cx)		Not available	Not available	
Liverpool data				
Wave 1 Phase 1	(w1p1)		Not available	
Wave 1 Phase 2	(w1p2)		Not available	
Wave 2 Phase 1	(w2p1)		Not available	
Wave 2 Phase 2	(w2p2)		Not available	
Wave 3 Phase 1	(w3p1)		Not available	
Wave 3 Phase 2	(w3p2)		Not available	
Wave 4	(w4)		Not available	
Wave 5	(w5)		Not available	
Wave 6	(w6)		Not available	
Neuropathology data (6 centres) *Complete tissue page*				
CERAD information		Not available	Not available	

DOI follow-up interviews (c8)	Not available	Not available	
RINI information	Not available	Not available	
Genetic data (4 centres only) *Complete blood page*			
ApoE information	Not available	Not available	
ACE information	Not available	Not available	

* This data whilst held at the CFAS data archive requires separate permission from the original investigators – will obtained with this form.

2. Are you intending to carry out the analysis yourself? YES

If YES: Where? Bangor University
Approval is for this place only

Details of data required

Format SPSS
Version of software
System PC

All data will be given on CD unless requested otherwise.

If NO: Do you intend to provide funds for analysis at BSU/CAMS? YES / NO

Note: Individuals requiring central statistical support must discuss their needs with the CFAS core group.

3. Are any funds available to pay for implied central computing resources? YES / NO

SECTION D: PUBLICATION AND DISSEMINATION OF CFAS DATA

Please identify how you will publicise and disseminate the findings of your proposed study with deadlines.

i . Submit papers to academic journal(s) - give details of proposed submissions:

ii. Submit findings to a report - please specify:

iii. Present work at conference(s)/seminar(s) - give details of proposed presentations:

iv. Book(s) or contributions to them - please specify:

SECTION E: AUTHORSHIP / ACKNOWLEDGEMENT

The form of authorship is laid down in the CFAS Publication Policy (see Appendix)

Agreed form of authorship / acknowledgement:

A, B, C and MRC CFAS.

FOR CFAS OFFICE USE
Project no. .....

SECTION F: UNDERTAKING FOR USERS OF CFAS DATA

In consideration of the Co-operative Management Committee (CMC) of the MRC Cognitive Function and Ageing Study (CFAS) agreeing to supply me certain data in machine-readable form together with supporting documentation as set out in the Schedule hereto (hereinafter called "the materials", which expression shall include any further or other data or documentation not the subject of a separate agreement) I hereby undertake:

(1) **Purpose:** To use the materials only for the purposes of non-commercial research or teaching specified in the accompanying application and to seek the approval of CFAS CMC for any other proposed use.

(2) **Confidentiality:** To act at all times so as to preserve the confidentiality of individuals and institutions recorded in the materials. In particular I undertake not to attempt or to use the materials to derive information relating to an identified individual or institution nor to claim to have done so.

(3) **Report:** For project of more than one year, write a short (one side A4) progress report for CFAS CMC.

(4) **Acknowledgement:** To acknowledge in any publication, whether printed, electronic or broadcast, based wholly or in part on such materials, the MRC Cognitive Function and Ageing Study (see section E for agreed form of acknowledgement), and to declare in any such work that those who carried out the original data collection and analysis bear no responsibility for the further analysis or interpretation of it.

(5) **Publications:** To conform to the CFAS Publications Policy (see Section E for agreed form of authorship). To distribute an abstract to CFAS CMC of any unpublished CFAS data for presentation at a conference/seminar. Prior to submission to a journal to allow CFAS CMC to comment on any draft paper using CFAS data. To quote the dataset version number in all such papers. To deposit with the CFAS Study Administrator two copies of any published work, conference presentation or report based wholly or in part on such materials.

(6) **Copyright:** Not to distribute copies of the materials to others, nor to make copies of them except as necessary to carry out the purpose specified (see Clause 1).

(7) **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; or in the case of teaching, to give access only to my students who have signed the Students' Undertaking on Conditions of Use Form, a copy of which I will supply to CFAS Study Manager by the end of June each year in which the specified data have been used.

(8) **Derived dataset: deposit:** At the conclusion of my research (or at any time at the request of the CFAS CMC) to deposit in the CFAS data archive, BSU, Cambridge on a suitable medium and at my 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.

(9) **Errors:** To notify CFAS of any errors discovered in the materials.

(10) **Charges:** To meet agreed charges for the supply of materials.

(11) **Liability:** To accept that CFAS CMCs bear no legal responsibility for the accuracy or comprehensiveness of the materials.

(12) **Completion:** To inform CFAS CMC of the completion of the project specified in this application.

(13) **Destruction of data:** After the data has been deposited and verified by the CFAS data archive (see Clause 7), except where an application has been received to use the data for a further project, to destroy or erase irrecoverably all complete, partial or derived copies of the data which have been made available for this application on completion of the specified project and to inform CFAS CMC that this has been done.

Signed:.....

Name (Block Capitals) .....

Date:.....

The completed form should be sent to:

Linda Barnes
Institute of Public Health
Forvie Site
Robinson Way, Cambridge CB2 2SR Phone:O1223 330311 Fax: 01223 330330
email: leb22ATmedschl.cam.ac.uk

Appendix C

CFAS WALES DATA REQUEST FORM

CFAS Wales notification for requests to undertake additional projects, analysis of the data or a bolt on study during the project phase

Related document:
http://cfaswales.bangor.ac.uk/documents/Protocolforrequeststousedatadraft1i.pdf

Proposed title of research:
PhD title: MCI, mood and well-being Papers included: MCI, mood and moderating effects of health and physical factors; MCI mood and the role of subjective memory complaints: a cross sectional study; MCI, mood and moderating effects of social networks.
Investigator name(s):
Jennifer Yates Bob Woods Linda Clare
Names of collaborators and Organisation(s)
Bangor University Swansea University
Proposed funder:
ESRC grant RES060250060
Amount requested (if known) or amount available from funder:
ESRC PhD stipend
Proposed duration (start date/end date):
September 2011 – October 2014
Summary of proposed research (250 words):
Investigating factors that form part of the relationship between mild cognitive impairment and mood. These include subjective memory complaints, health and physical factors, and social networks. Mood will encompass symptoms of anxiety and depression at clinical and borderline levels, and MCI will be considered according to Petersen criteria.
Research aims/objectives/research questions:
1. What is the relationship between MCI, mood and subjective memory complaints? 2. What is the relationship between MCI, mood and health or physical factors? 3. What is the relationship between MCI, mood and social networks?
Which measures do you need to undertake the research? PLEASE LIST
All questions from the interview relating to worry, depression, cognition, social networks, health (subjective and checklist of conditions), service use, functional activities, recreational physical activities
Does this proposal require new/additional interviewing/contacting participants during the project duration?

If so, what is the proposed sample size? PLEASE DESCRIBE THE PROPOSED SAMPLE
No
How does this additional interviewing link directly to, and augment the main project?
Who will undertake the data analysis?
Jennifer Yates
Publication and dissemination – Please detail how disseminate the findings of your proposed study:
Peer review articles, PhD thesis, conference/symposium talks and posters
Authorship and acknowledgement: Please refer to the CFAS Wales publication policy
See CFAS Wales publication policy

Please return to Gill Windle

g.windle@bangor.ac.uk

Appendix D

GP INVITATION LETTER

Institute of Medical & Social Care Research
Bangor University
45 College Road, Bangor,
Gwynedd LL57 2DG

Maintaining function and well-being in later life: A longitudinal cohort study (CFAS Wales)

Dear

This surgery is taking part in a research study conducted by Bangor and Swansea Universities. 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. The project has full NHS ethics approval and R&D approval from Betsi Cadwaladr University Health Board. All the interviewers are fully trained, and have Criminal Records Bureau clearance.

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 (01248) 383050 to discuss your queries. We hope you will take up the opportunity to support this research.

Yours Sincerely

Sefydliad Ymchwil Gofal Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn: Astudiaeth carfan hydredol (CFAS Cymru)

Annwyl

Mae'r feddygfa hon yn cymryd rhan mewn astudiaeth ymchwil sy'n cael ei chynnal gan Brifysgolion Bangor ac Abertawe. Mae heneiddio bellach yn cael ei gydnabod fel un o'r prif heriau sy'n wynebu poblogaethau'r byd. Nod yr astudiaeth hon yw darganfod sut mae iechyd a lles yn newid wrth i bobl fynd yn hŷn. Mae rhai pobl yn cael anawsterau wrth fynd yn hŷn tra bo eraill yn dal yn ffit ac yn egnïol. Mae diddordeb gennym yn yr holl brofiadau er mwyn cael darlun cywir o heneiddio yn y boblogaeth.

Mae'r ymchwil yn rhan o astudiaeth genedlaethol a'i nod yw gwella ein dealltwriaeth o newidiadau sy'n digwydd wrth heneiddio a helpu gwneuthurwr polisi i ddiwallu anghenion cenhedlaeth fodern o bobl hŷn.

Bydd y rhai sy'n cynnal y cyfweliad ar gyfer yr astudiaeth hon yn galw yn ystod yr wythnosau nesaf i ofyn a fyddai modd i chi helpu. Rydych wedi cael eich dewis ar hap ac nid oes unrhyw wybodaeth o'ch cofnodion meddygol wedi ei rhoi i'r ymchwilwyr. Bydd yr ymchwil yn fwy gwerthfawr os bydd cynifer â phosibl o'r rhai a wahoddwyd i gymryd rhan yn fodlon gwneud hynny. Mae'r prosiect wedi cael cymeradwyaeth foesegol lawn y GIG a chymeradwyaeth Ymchwil a Datblygu gan Fwrdd Iechyd Prifysgol Betsi Cadwaladr. Mae pob un o'r rhai fydd yn cyfweld wedi cael eu hyfforddi'n llawn ac wedi eu gwirio gan y Swyddfa Cofnodion Troseddol.

Pan fydd yr unigolyn o'r tîm ymchwil yn galw bydd yn dangos ei gerdyn/cherdyn adnabod ac yn egluro'r astudiaeth yn fanylach. Os bydd yn galw ar adeg anghyfleus, bydd yn fodlon galw eto'n ddiweddarach. Wrth gwrs, mae eich cydweithrediad yn wirfoddol ac ni fydd eich penderfyniad yn effeithio ar eich gofal meddygol. Rwyf wedi amgáu taflen wybodaeth yn egluro'r astudiaeth yn fanylach.

Os oes gennych unrhyw gwestiynau, ffoniwch y tîm ymchwil ar (01248) 383719 i drafod eich ymholiadau. Gobeithio y byddwch yn manteisio ar y cyfle i gefnogi'r gwaith ymchwil hwn.

Yn gywir

Appendix E

PARTICIPANT INFORMATION SHEET

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life (CFAS Wales)

PARTICIPANT INFORMATION SHEET

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, North West Wales, Cambridgeshire and Oxford. The study began in 1991 with 18,000 participants, and it still continues today.

Since the start of the original 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 5000 people in Wales; 2500 people in the original study site of Gwynedd and Anglesey and 2500 at a new site in Neath and Port Talbot. In addition, three centres in England are undertaking a parallel study (Newcastle, Nottingham and Cambridgeshire), which will enable us to compare findings across the different areas.

Why have I been chosen?

You have been randomly selected from National Health Service records. The only information provided to CFAS-Wales is your name, address, sex, and date of birth, all of which 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. If you agree to participate, we will ask for your written consent to look at your medical records, in order to clarify any areas that are uncertain or where additional information is required.

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. We will ask for your consent separately for each aspect of the study, in case there are some parts you would prefer not to participate in.

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 this 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 2-2½ 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, increasing understanding of the genetic influences on diseases related to ageing (e.g. Alzheimer's).

The study includes a follow up and, with your permission, we would hope to ask you to see us again in two years time. Some participants may also be approached before this to take part in a more detailed interview regarding a number of topics, including various life experiences, social life and friendships, lifestyles, activities and interests. This interview would be recorded.

Some participants may be also asked to supply a blood sample which would also be stored for research purposes which would include genetic (DNA) tests as well as relating vitamin levels to nutrition and function. The blood would be taken by a trained researcher. 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; confidentiality would only ever be broken if this became a legal requirement because a person was considered at risk of harm. All information is stored without personal details on secure systems in compliance with the Data Protection Act 1998. Occasionally, as mentioned above, we may ask to tape record an interview; audio tapes are anonymised before the interview is analysed; they may also be used for training and quality control purposes and will be destroyed when no longer required.

Anonymised data collected by the study may be analysed by researchers from other centres, approved either by the CFAS team or by the UK Data Archive, where anonymised data will be held after the study has been completed.

This study has been considered by the North Wales Research Ethics Committee (West).

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 01248 383050 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 Bangor University and the NHS. If you would like any further information or have any questions please contact us on 01248 383719.

Professor Bob Woods
Local Principal Investigator

Dr Gill Windle
Study Coordinator CFAS-Wales

http://cfaswales.bangor.ac.uk/

Sefydliad Ymchwil Gofal
Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn (CFAS Cymru)

TAFLEN WYBODAETH I RAI SY'N CYMRYD RHAN

Hoffem eich gwahodd i gymryd rhan mewn astudiaeth ymchwil. Cyn i chi benderfynu cymryd rhan ai peidio, mae'n bwysig eich bod yn deall pam fod yr ymchwil yn cael ei wneud a beth fydd yn ei olygu. Darllenwch yr wybodaeth ganlynol yn ofalus.

Pwrpas yr astudiaeth

Mae heneiddio bellach yn cael ei gydnabod fel un o'r prif heriau sy'n wynebu poblogaethau'r byd. Mae'n her i wneuthurwyr polisi cenedlaethol a lleol a darparwyr gwasanaeth wrth iddynt gynllunio a darparu gwasanaethau i ddiwallu anghenion y boblogaeth hŷn.

Mae'r astudiaeth hon yn seiliedig ar Astudiaeth Gweithrediadau Gwybyddol a Heneiddio wreiddiol y Cyngor Ymchwil Feddygol a fu'n ymchwilio i heneiddio ac iechyd mewn chwe chanolfan yn y DU: Newcastle, Nottingham, Lerpwl, Gogledd Orllewin Cymru, Swydd Gaergrawnt a Rhydychen. Dechreuodd yr astudiaeth yn 1991 gyda 18,000 o bobl yn cymryd rhan ynddi, ac mae'n dal i barhau heddiw.

Ers dechrau'r astudiaeth wreiddiol bu cynnydd mewn disgwyliad oes ac mae gwelliannau o ran sgrinio, gwneud diagnosis a thrin nifer o anhwylderau cronig. Nod yr astudiaeth hon yw darganfod sut mae iechyd a lles yn newid wrth i bobl fynd yn hŷn. Mae rhai pobl yn cael anawsterau wrth fynd yn hŷn tra bo eraill yn dal yn ffit ac yn egnïol. Mae diddordeb gennym yn yr holl brofiadau er mwyn cael darlun cywir o heneiddio yn y boblogaeth.

Rydym bellach yn awyddus i weld a yw patrymau iechyd yn newid rhwng gwahanol genedlaethau a'r unig ffordd o wneud hyn yw trwy wahodd cenhedlaeth newydd o bobl 65 oed neu fwy i gymryd rhan. Yn yr astudiaeth newydd hon y bwriad yw cysylltu â 5000 o bobl yng Nghymru; 2500 o bobl yn lleoliad yr astudiaeth wreiddiol, sef Gwynedd a Môn a 2500 mewn lleoliad newydd yng Nghastell-nedd a Phort Talbot. Hefyd, mae tair canolfan yn Lloegr yn cynnal astudiaeth gyfochrog (Newcastle, Nottingham a Swydd Gaergrawnt), fydd yn fodd i ni gymharu canlyniadau'r gwahanol ardaloedd.

Pam ydw i wedi cael fy newis?

Rydych chi wedi cael eich dewis ar hap o gofnodion y Gwasanaeth Iechyd Gwladol. Yr unig wybodaeth a roddwyd i CFAS-Cymru yw eich enw, cyfeiriad, rhyw, a'ch dyddiad geni. Mae'r holl wybodaeth wedi cael ei phrosesu gennym yn unol â Deddf Diogelu Data 1998. Ni wyddom unrhyw beth arall amdanoch, ac nid ydym wedi gweld eich cofnodion meddygol. Os byddwch yn cytuno i gymryd rhan, byddwn yn gofyn am eich caniatâd ysgrifenedig i weld eich cofnodion meddygol, er mwyn egluro unrhyw feysydd sy'n ansicr neu os bydd angen mwy o wybodaeth.

Oes raid i mi gymryd rhan?

Nac oes, nid ydych wedi ymrwymo o gwbl i gymryd rhan a gallwch dynnu'n ôl ar unrhyw adeg, heb roi unrhyw reswm. Mae'r astudiaeth yn cael ei chynnal i bwrpas meddygol yn unig, ac ni fydd yn effeithio ar eich gofal meddygol na'ch hawliau cyfreithiol. Byddwn yn gofyn am ganiatâd ar wahân am bob rhan o'r astudiaeth, rhag ofn bod rhai rhannau y byddai'n well gennych chi beidio â chymryd rhan ynddynt.

Beth fydd yn digwydd os byddaf yn penderfynu cymryd rhan?

Os byddwch yn penderfynu cymryd rhan, bydd un o'r tîm ymchwil yn ymweld â chi yn eich cartref. Os nad yw'r amser yn gyfleus bydd yn dychwelyd ar adeg sy'n fwy cyfleus i chi. Bydd yn mynd trwy'r daflen wybodaeth hon gyda chi ac yn ateb unrhyw gwestiynau sydd gennych am yr astudiaeth. Yna bydd yn gofyn i chi lofnodi ffurflen ganiatâd i ddweud eich bod wedi darllen y daflen wybodaeth, wedi cael cyfle i ofyn cwestiynau, a'ch bod yn awyddus i gymryd rhan yn yr astudiaeth.

Yna, byddwn yn gofyn cwestiynau i chi am eich cefndir, iechyd, cyswllt â ffrindiau a theulu a'ch gweithgareddau bob dydd, hefyd bydd rhan ar gof a chanolbwyntio. Bydd y cyfweliad yn cymryd tua 2-2½ awr.

Byddwn yn eich gwahodd i gymryd rhan mewn prawf clyw byr lle byddwn yn gosod dyfais fach wrth ymyl eich clust ac yn anfon sain fer i'r glust er mwyn darganfod os ydych wedi colli eich clyw o gwbl. Bydd y canlyniadau ar gael yn syth, a gyda'ch caniatâd chi, byddwn yn rhoi gwybod i'ch Meddyg Teulu, os yw'r mesuriadau y tu allan i'r lefelau normal ac os nad oes gennych declyn clywed.

Yn ystod y cyfweliad byddwn hefyd yn gofyn i chi os byddech yn fodlon rhoi sampl poer trwy boeri mymryn i gynhwysydd bach. Bydd y sampl yn cael ei gadw er mwyn gwneud gwaith ymchwil i heneiddio, fydd yn cynnwys profion genetig (DNA). Bydd hyn yn gwella'n dealltwriaeth o ddylanwadau genetig ar glefydau sy'n gysylltiedig â heneiddio (e.e. clefyd Alzheimer).

Mae'r astudiaeth yn cynnwys sesiwn ddilynol, a gyda'ch caniatâd chi, gobeithio y gallwn gyfarfod eto ymhen dwy flynedd. Mae'n bosibl y byddwn yn cysylltu â rhai cyn hynny er mwyn eu gwahodd i gymryd rhan mewn cyfweliad manylach i drafod nifer o bynciau, gwahanol brofiadau bywyd, bywyd cymdeithasol a chyfeillgarwch, ffyrdd o fyw, gweithgareddau a diddordebau. Byddai'r cyfweliad hwn yn cael ei recordio.

Mae'n bosibl y byddwn yn gofyn i rai hefyd roi sampl gwaed. Byddai'r sampl hwn hefyd yn cael ei gadw er mwyn gwneud gwaith ymchwil a fyddai'n cynnwys profion genetig (DNA) yn ogystal â lefelau fitaminau sy'n gysylltiedig â maeth a gweithrediadau. Byddai'r prawf gwaed yn cael ei wneud gan aelod hyfforddedig o'r tîm ymchwil. Mae'n annhebygol y bydd gan ganlyniadau'r ymchwiliadau unrhyw oblygiadau personol i'r unigolion sy'n cymryd rhan. Byddwn yn gofyn am ganiatâd ymatebwyr i roi gwybod i'w Meddyg Teulu beth yw eu canlyniadau, os bydd y mesuriadau y tu allan i'r lefelau normal.

Mae rhai o'r bobl yn yr astudiaeth CFAS gwreiddiol wedi cyfrannu ymhellach at yr astudiaeth trwy gytuno i roi eu hymennydd ar ôl marw i bwrpas ymchwil yn y dyfodol. Mae'r rhodd hon yn weithred hael, ac mae wedi ein helpu i wella'n dealltwriaeth o newidiadau yn yr ymennydd wrth heneiddio, e.e. newidiadau sy'n achosi dementia, fel clefyd Alzheimer. Efallai byddwn yn gallu parhau i wneud y gwaith hwn yn y dyfodol, trwy ofyn i'r rhai sy'n cymryd rhan yn yr astudiaeth hon a fydden nhw'n

ystyried Datganiad o Fwriad i roi ymennydd. Os bydd gan y rhai sy'n cymryd rhan ddiddordeb yn yr agwedd hon o'r astudiaeth, bydd ein tîm ymchwil yn rhoi gwybodaeth bellach iddynt.

Yn dibynnu ar gyllid yn y dyfodol mae'n bosibl y byddwn yn gwahodd pobl i gymryd rhan mewn meysydd ymchwil newydd, fel delweddu'r ymennydd. Byddai angen cymeradwyaeth foesegol benodol er mwyn gwneud unrhyw waith ymchwil newydd yn y dyfodol.

Cyfrinachedd

Mae'r holl wybodaeth fydd yn cael ei chasglu gan yr astudiaeth yn gwbl gyfrinachol; yr unig reswm am dorri cyfrinachedd fyddai pe bai'r gyfraith yn ein gorfodi i wneud hynny am reswm cyfreithiol oherwydd bod unigolyn mewn perygl o niwed. Cedwir yr holl wybodaeth heb fanylion personol ar systemau diogel yn unol â Deddf Diogelu Data 1998. O bryd i'w gilydd, fel y soniwyd uchod, efallai byddwn yn gofyn am ganiatâd i recordio cyfweliad; cyn bod y tapiau sain yn cael eu dadansoddi gwneir yn siŵr nad oes enw arnynt; mae'n bosibl y byddan nhw hefyd yn cael eu defnyddio i bwrpas hyfforddi a rheoli ansawdd. Byddan nhw'n cael eu dinistrio pan nad oes eu hangen mwyach.

Mae'n bosibl y bydd data dienw a gasglwyd gan yr astudiaeth hon yn cael ei ddadansoddi gan ymchwilwyr o ganolfannau eraill, a gymeradwywyd naill ai gan dîm CFAS neu gan UK Data Archive, lle cedwir data dienw nes bod yr astudiaeth wedi ei chwblhau.

Mae'r astudiaeth hon wedi cael ei hystyried gan Bwyllgor Moeseg Ymchwil Gogledd Cymru (Gorllewin).

Os nad yw'r sawl y cyfeiriwyd y llythyr ato/ati yn gallu ymateb, byddem yn ddiolchgar pe bai perthynas neu ofalwr yn gallu trafod gyda ni p'un ai y gellir cynnal cyfweliad ai peidio neu p'un ai a fyddai'r perthynas/gofalwr yn fodlon cael ei gyfweld yn ei le/lle.

Os oes gennych unrhyw bryderon neu gwynion ynglŷn ag unrhyw beth sy'n gysylltiedig â'r astudiaeth mae croeso i chi gysylltu â ni ar 01248 383050. Gofynnwch am gael gair gyda Chydlynydd yr Astudiaeth, ac os na fydd yn gallu eich helpu, bydd yn eich cyfeirio at yr unigolyn priodol. Mae trefniadau indemniad ar gyfer yr astudiaeth dan ofal Prifysgol Bangor a'r GIG.

Os hoffech gael gwybodaeth bellach neu os oes gennych unrhyw gwestiynau cysylltwch â ni ar 01248 383050.

Yr Athro Bob Woods
Prif Ymchwilydd Lleol

Dr Gill Windle
Cydlynydd Astudiaeth CFAS-Cymru

http://cfaswales.bangor.ac.uk/

Appendix F

CONSENT FORMS

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life

CONSENT FORM

Respondent identifier: _____

	Please Initial
I confirm that I have read and understood the information sheet (version 3 dated 31/05/2011) 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 may be recorded for later analysis or training and quality control purposes. I agree to this interview being audio recorded.	☐
I understand that confidentiality will only be broken if this becomes a legal requirement because of risk of harm.	☐

All the information collected by the study is completely confidential and is stored anonymously, without personal details. Audio tapes are anonymised and used for analysis and 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 Interviewer…….. Date……

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life

Consent Form for access to medical records

Project No……

Name of Respondent……

CFAS-Wales is a long term study into the health and well-being of the older population. In order to answer some of the research questions one of the research staff may need access to your family doctor's notes or other routine medical records.

Any information collected from these sources will be treated confidentially as per the Data Protection Act 1998.

We would also like to ask for your consent to flag your name at the NHS Information Centre who would then record the date and cause of death of participants in the study, they would also inform us if someone on the study has left the National Health Service i.e. emigrated.

If you would agree please initial the boxes and then sign the form below.

	Please initial
I give my permission to the research staff working on the above study inspecting GP and medical records that relate to me.	☐
I give my permission for any data I supply to CFAS-Wales to be held for long-term storage for health related research purposes (even if I should become incapacitated or in the event of my death).	☐
I agree to CFAS-Wales flagging my name at the NHS Information Centre.	☐

Signature of Respondent……

Signature of Interviewer……

Date……

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life

Consent Form for Hearing Test

Project No.....

Name of Respondent.....

	Please initial
I agree to a research interviewer from the above study conducting a Hearing Test on me by use of the HearCheck Screener.	☐
I understand that the results of any tests are confidential to the research study and that I will not be identified if the results are published.	☐
I agree that my test results can be forwarded to my general practitioner if the measurements lie outside of normal values.	☐

Signature of Respondent.....

Signature of Interviewer.....

Date.....

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life

Consent Form for saliva sample

Project No.....

Name of Respondent.....

	Please initial
I consent to provide a saliva sample to the above study and understand that the saliva sample will be stored for research purposes investigating ageing.	☐
I understand that the sample I provide will be used for tests, which will include genetic studies aimed at understanding the genetic influences on diseases related to ageing such as Alzheimer's, but that the investigations are unlikely to have any implications for me personally. I understand that I will not benefit financially if this research leads to the development of a new treatment or medical test.	☐
I agree that the sample may be used in future for related research projects as approved by a Research Ethics Committee.	☐

Signature of Respondent.....

Signature of Interviewer.....

Date.....

Sefydliad Ymchwil Gofal
Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn

FFURFLEN GANIATÂD

Rhif adnabod yr ymatebydd: _____

Llofnodwch â llythrennau cyntaf eich enw

Rwyf yn cadarnhau fy mod wedi darllen a deall y daflen wybodaeth (fersiwn 3 dyddiedig 31/05/2011) ar gyfer yr astudiaeth uchod a fy mod wedi cael y cyfle i ofyn cwestiynau.	☐
Rwyf yn deall bod fy nghyfraniad yn wirfoddol a bod hawl gennyf i dynnu'n ôl ar unrhyw adeg, heb roi unrhyw reswm, heb i hynny effeithio ar fy ngofal meddygol neu fy hawliau cyfreithiol.	☐
Rwyf yn cytuno i gymryd rhan yn yr astudiaeth uchod.	☐
Rwyf yn deall y gallai'r cyfweliad hwn gael ei recordio i bwrpas dadansoddi neu hyfforddi a rheoli ansawdd yn nes ymlaen. Rwyf yn cytuno y gellir recordio'r cyfweliad hwn ar dâp sain.	☐
Rwyf yn deall mai'r unig reswm am dorri cyfrinachedd yw pe bai'r gyfraith yn gorfodi hynny oherwydd bod perygl o niwed.	☐

Mae'r holl wybodaeth a gesglir gan yr astudiaeth yn gwbl gyfrinachol ac fe'i cedwir ar sail data dienw, heb unrhyw fanylion personol. Mae'r tapiau sain yn ddienw ac fe'u defnyddir i bwrpas dadansoddi a hyfforddi a rheoli ansawdd yn unig ac fe'u dinistrir pan na fydd eu hangen mwyach.

Enw'r Ymatebydd……

Llofnod yr Ymatebydd…….. Dyddiad……

Enw'r Sawl sy'n Cyfweld……

Llofnod y Sawl sy'n Cyfweld…….. Dyddiad……

Sefydliad Ymchwil Gofal Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn

Ffurflen Ganiatâd i gael mynediad at gofnodion meddygol

Rhif Prosiect……

Enw'r Ymatebydd……

Mae CFAS-Cymru'n astudiaeth hirdymor o iechyd a lles pobl hŷn. Er mwyn ateb rhai o'r cwestiynau ymchwil mae'n bosibl y bydd angen i un o aelodau'r tîm ymchwil gael mynediad at y nodiadau gan eich meddyg teulu neu gofnodion meddygol arferol eraill.

Bydd unrhyw wybodaeth a gesglir o'r ffynonellau hyn yn cael ei thrin yn gyfrinachol yn unol â Deddf Diogelu Data 1998.

Hoffem hefyd ofyn am eich caniatâd i amlygu eich enw yng Nghanolfan Wybodaeth y GIG. Byddai'r Ganolfan wedyn yn cofnodi dyddiad ac achos marwolaeth y rhai sydd yn rhan o'r prosiect. Hefyd byddai'n rhoi gwybod i ni os bydd rhywun ar yr astudiaeth yn gadael y Gwasanaeth Iechyd Gwladol h.y. yn allfudo.

Os ydych yn cytuno ynа llofnodwch y blychau a'r ffurflen isod.

Llofnodwch ā llythrennau cyntaf eich enw

Rhoddaf fy nghaniatâd i'r staff ymchwil sy'n gweithio ar yr astudiaeth uchod archwilio fy nghofnodion meddygol a'r cofnodion Meddyg Teulu sy'n berthnasol i mi.	☐
Rhoddaf fy nghaniatâd i unrhyw ddata a roddaf i CFAS-Cymru gael ei gadw am y tymor hir i bwrpas ymchwilio i faterion yn ymwneud ag iechyd (hyd yn oed pe bawn yn analluog neu'n marw).	☐
Rwyf yn cytuno y gall CFAS-Cymru amlygu fy enw yng Nghanolfan Wybodaeth y GIG .	☐

Enw'r Ymatebydd ……

Enw'r Sawl sy'n Cyfweld ……

Dyddiad……

Sefydliad Ymchwil Gofal Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn

Ffurflen Ganiatâd i gynnal Prawf Clyw

Rhif Prosiect……

Enw'r Ymatebydd……

Llofnodwch â llythrennau cyntaf eich enw

Rwyf yn cytuno i gyfwelydd ymchwil o'r astudiaeth uchod gynnal Prawf Clyw arnaf drwy ddefnyddio Offer Sgrinio HearCheck.	☐
Rwyf yn deall bod canlyniadau fy mhrofion yn gyfrinachol i'r astudiaeth ymchwil hon ac na fydd modd fy adnabod os cyhoeddir y canlyniadau.	☐
Rhoddaf fy nghaniatâd i anfon canlyniadau fy mhrawf at fy meddyg teulu os bydd fy mesuriadau y tu allan i'r lefelau normal.	☐

Llofnod yr Ymatebydd……

Llofnod y Sawl sy'n Cyfweld ……

Dyddiad……

Sefydliad Ymchwil Gofal Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn

Ffurflen Ganiatâd ar gyfer sampl poer

Rhif Prosiect……

Enw'r ymatebydd……

Llofnodwch ô llythrennau cyntaf eich enw

Rwyf yn cytuno i roi sampl poer ar gyfer yr astudiaeth uchod ac rwyf yn deall y bydd y sampl poer yn cael ei gadw er mwyn gwneud gwaith ymchwil i heneiddio.	☐
Rwyf yn deall y bydd y sampl a roddaf yn cael ei ddefnyddio ar gyfer profion, fydd yn cynnwys astudiaethau genetig i geisio deall y dylanwadau genetig ar glefydau sy'n gysylltiedig â heneiddio, e.e. clefyd Alzheimer, ond ei bod yn annhebygol y bydd gan yr ymchwiliadau unrhyw oblygiadau i mi'n bersonol. Rwyf yn deall na fyddaf yn elwa'n ariannol os bydd yr ymchwil hwn yn arwain at ddatblygu triniaeth neu brawf meddygol newydd.	☐
Rwyf yn cytuno y gellir defnyddio'r sampl yn y dyfodol ar gyfer prosiectau ymchwil cysylltiedig fel y cymeradwywyd gan Bwyllgor Moeseg Ymchwil.	☐

Llofnod yr Ymatebydd……

Llofnod y Sawl sy'n Cyfweld……

Dyddiad……

Appendix G

INFORMATION FOR RELATIVES

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life

INFORMATION FOR RELATIVES AND CARERS

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, North West Wales, Cambridgeshire and Oxford. The study began in 1991 with 18,000 participants, and it still continues today.

Since the start of the original 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 5000 people in Wales; 2500 people in the original study site of Gwynedd and Anglesey and 2500 at a new site in Neath and Port Talbot. In addition, three centres in England are undertaking a parallel study (Newcastle, Nottingham and Cambridgeshire), which will enable us to compare findings across the different areas.

Why has my relative / friend been approached?

Your relative / friend has been randomly selected from National Health Service records. The only information provided to CFAS-Wales is their name, address, sex, and date of birth, all of which information has been processed by us in accordance with the Data Protection Act 1998. We do not know anything else about them. If your relative / friend agrees to participate, we will ask for written consent to look at their medical records, in order to clarify any areas that are uncertain or where additional information is required.

Do they have to take part?

No, there is no obligation to take part and they can withdraw at any stage, without giving any reason. The study is for medical research only and will not affect their medical care or legal rights. We will ask for consent separately for each aspect of the study, in case there are some parts your relative / friend would prefer not to participate in.

What will happen if my relative/friend should take part?

A research interviewer will arrange a suitable time and date to visit your relative/friend. They will go through the information sheet with them and answer any questions they may have before asking for their consent to take part.

In the event that your friend/relative is unable to give informed consent then you will be asked if in your opinion they would have wished to take part in the research if they had been able to express a view. If you agree that this is the case, you will be asked to sign a consultee consent form on their behalf.

Following this your relative/friend will be asked questions on their background, health, contact with friends and family and day to day activities, there will also be a section on memory and concentration. A full interview will take approximately 2-2½ hours. If your relative is unable to conduct a full interview, an interview based on the most important questions would be conducted which would take no more than 15 minutes.

The interviewer would then seek your consent to conduct an informant interview in which you will be asked to give information on your relative/friend's health and well-being, which would take approximately 1½ hours; this can be arranged at a time convenient to you.

If your relative is able we would ask consent to collect a saliva sample which would be stored for research purposes investigating ageing which would include genetic (DNA) tests, increasing understanding of the genetic influences on diseases related to ageing (e.g. Alzheimer's).

Some participants may also be asked to supply a blood sample which would also be stored for research purposes which would include genetic (DNA) tests, as well as relating vitamin levels to nutrition and function. The results of these investigations are analysed in an anonymised manner. The blood sample would be taken by a trained researcher. 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.

The study includes a follow up and, with your permission, we would hope to ask you to see us again in two years time.

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. Confidentiality would only ever be broken if this became a legal requirement because a person was considered at risk of harm.

Anonymised data collected by the study may be analysed by researchers from other centres, approved either by the CFAS team or by the UK Data Archive, where anonymised data will be held after the study has been completed.

This study has been considered by the North Wales Research Ethics Committee (West).

If you have any concerns or complaints about anything to do with the study please contact us on 01248 383050 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 Bangor University and the NHS. If you would like any further information or have any questions please contact us on 01248 383050.

Professor Bob Woods
Local Principal Investigator

Dr Gill Windle
Study Coordinator CFAS-Wales

http://cfaswales.bangor.ac.uk/

CFASCYMRU
GWEITHREDIAD GWYBYDDOL A HENEIDDIO
CFASWALES
COGNITIVE FUNCTION AND AGEING

PRIFYSGOL
BANGOR
UNIVERSITY

Sefydliad Ymchwil Gofal
Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn

GWYBODAETH I BERTHNASAU A GOFALWYR

Mae heneiddio bellach yn cael ei gydnabod fel un o'r prif heriau sy'n wynebu poblogaethau'r byd. Mae'n her i wneuthurwyr polisi cenedlaethol a lleol a darparwyr gwasanaeth wrth iddynt gynllunio a darparu gwasanaethau i ddiwallu anghenion y boblogaeth hŷn.

Mae'r astudiaeth hon yn seiliedig ar Astudiaeth Gweithrediadau Gwybyddol a Heneiddio wreiddiol y Cyngor Ymchwil Feddygol a fu'n ymchwilio i heneiddio ac iechyd mewn chwe chanolfan yn y DU: Newcastle, Nottingham, Lerpwl, Gogledd Orllewin Cymru, Swydd Gaergrawnt a Rhydychen. Dechreuodd yr astudiaeth yn 1991 gyda 18,000 o bobl yn cymryd rhan ynddi, ac mae'n dal i barhau heddiw.

Ers dechrau'r astudiaeth wreiddiol bu cynnydd mewn disgwyliad oes ac mae gwelliannau o ran sgrinio, gwneud diagnosis a thrin nifer o anhwylderau cronig. Nod yr astudiaeth hon yw darganfod sut mae iechyd a lles yn newid wrth i bobl fynd yn hŷn. Mae rhai pobl yn cael anawsterau wrth fynd yn hŷn tra bo eraill yn dal yn ffit ac yn egnïol. Mae diddordeb gennym yn yr holl brofiadau er mwyn cael darlun cywir o heneiddio yn y boblogaeth.

Rydym bellach yn awyddus i weld a yw patrymau iechyd yn newid rhwng gwahanol genedlaethau a'r unig ffordd o wneud hyn yw trwy wahodd cenhedlaeth newydd o bobl 65 oed neu fwy i gymryd rhan. Yn yr astudiaeth newydd hon y bwriad yw cysylltu â 5000 o bobl yng Nghymru; 2500 o bobl yn lleoliad yr astudiaeth wreiddiol, sef Gwynedd a Môn a 2500 mewn safle newydd yng Nghastell-nedd a Phort Talbot. Hefyd, mae tair canolfan yn Lloegr yn cynnal astudiaeth gyfochrog (Newcastle, Nottingham a Swydd Gaergrawnt), fydd yn fodd i ni gymharu canlyniadau'r gwahanol ardaloedd.

Pam fod fy mherthynas / ffrind wedi ei ddewis?

Mae eich perthynas / ffrind wedi ei ddewis ar hap o gofnodion y Gwasanaeth Iechyd Gwladol. Yr unig wybodaeth a roddwyd i CFAS-Cymru yw eu henw, cyfeiriad, rhyw, a'u dyddiad geni. Mae'r holl wybodaeth wedi cael ei phrosesu gennym yn unol â Deddf Diogelu Data 1998. Ni wyddom unrhyw beth arall amdano ef neu hi. Os bydd eich perthynas / ffrind yn cytuno i gymryd rhan, byddwn yn gofyn am ganiatâd ysgrifenedig i

weld eu cofnodion meddygol, er mwyn egluro unrhyw feysydd sy'n ansicr neu os bydd angen mwy o wybodaeth.

Oes raid iddynt gymryd rhan?

Nac oes, nid oes unrhyw ymrwymiad i gymryd rhan a gallan nhw dynnu'n ôl ar unrhyw adeg, heb roi unrhyw reswm. Mae'r astudiaeth yn cael ei chynnal i bwrpas ymchwil meddygol yn unig, ac ni fydd yn effeithio ar eu gofal meddygol na'u hawliau cyfreithiol. Byddwn yn gofyn am ganiatâd ar wahân am bob rhan o'r astudiaeth, rhag ofn bod rhai rhannau y byddai'n well gan eich perthynas / ffrind beidio â chymryd rhan ynddynt.

Beth fydd yn digwydd os bydd fy mherthynas/ffrind yn cymryd rhan?

Bydd un o'r tîm ymchwil yn trefnu amser a dyddiad addas i ymweld â'ch perthynas/ffrind. Bydd yn mynd trwy'r daflen wybodaeth hon gyda nhw ac yn ateb unrhyw gwestiynau sydd ganddynt cyn gofyn am eu caniatâd i gymryd rhan.

Os na fydd eich ffrind/perthynas yn gallu rhoi caniatâd ar sail penderfyniad cytbwys, yna, byddwn yn gofyn i chi, a fydden nhw wedi dymuno cymryd rhan yn yr ymchwil, yn eich barn chi, pe bydden nhw wedi gallu mynegi barn. Os byddwch yn cytuno y bydden nhw wedi dymuno bod yn rhan ohono, byddwn yn gofyn i chi lofnodi ffurflen ganiatâd ymgynghorai ar eu rhan.

Yna, byddwn yn gofyn cwestiynau i'ch perthynas am eu cefndir, iechyd, cyswllt â ffrindiau a theulu a'ch gweithgareddau bob dydd, hefyd bydd rhan ar gof a chanolbwyntio. Bydd cyfweliad llawn yn cymryd tua 2-2½ awr. Os na fydd modd i'ch perthynas gymryd rhan mewn cyfweliad llawn, byddwn yn cynnal y cyfweliad drwy ofyn y cwestiynau pwysicaf. Ni ddylai gymryd mwy na 15 munud.

Yna, bydd y sawl sy'n cyfweld yn gofyn am eich caniatâd i gynnal cyfweliad gyda chi. Byddwn yn gofyn i chi roi gwybodaeth am iechyd a lles eich perthynas/ffrind. Bydd hyn yn cymryd tua 1½ awr; gellid trefnu'r cyfweliad ar adeg sy'n gyfleus i chi.

Os bydd yn bosibl, byddwn yn gofyn am ganiatâd eich perthynas i gael sampl poer a fyddai'n cael ei gadw er mwyn gwneud gwaith ymchwil i heneiddio, fydd yn cynnwys profion genetig (DNA). Bydd hyn yn gwella'n dealltwriaeth o ddylanwadau genetig ar glefydau sy'n gysylltiedig â heneiddio (e.e. clefyd Alzheimer).

Mae'n bosibl y byddwn yn gofyn i rai hefyd roi sampl gwaed. Byddai'r sampl hwn hefyd yn cael ei gadw er mwyn gwneud gwaith ymchwil a fyddai'n cynnwys profion genetig (DNA) yn ogystal â lefelau fitaminau sy'n gysylltiedig â maeth a gweithrediadau. Caiff canlyniadau'r gwaith hwn ei ddadansoddi ar sail data dienw. Byddai'r prawf gwaed yn cael ei wneud gan aelod hyfforddedig o'r tîm ymchwil. Mae'n annhebygol y bydd gan ganlyniadau'r ymchwiliadau unrhyw oblygiadau personol i'r unigolion sy'n cymryd rhan. Byddwn yn gofyn am ganiatâd ymatebwyr i roi gwybod i'w Meddyg Teulu beth yw eu canlyniadau, os bydd y mesuriadau y tu allan i'r lefelau normal.

Mae'r astudiaeth yn cynnwys sesiwn dilynol, a gyda'ch caniatâd chi, gobeithio y gallwn ofyn i chi ein gweld eto ymhen dwy flynedd.

Mae rhai o'r bobl yn yr astudiaeth CFAS gwreiddiol wedi cyfrannu ymhellach at yr astudiaeth trwy gytuno i roi eu hymennydd ar ôl marw i bwrpas ymchwil yn y dyfodol. Mae'r rhodd hon yn weithred hael, ac mae wedi ein helpu i wella'n dealltwriaeth o newidiadau yn yr ymennydd wrth heneiddio, e.e. newidiadau sy'n achosi dementia, fel clefyd Alzheimer. Efallai byddwn yn gallu parhau i wneud y gwaith hwn yn y dyfodol, trwy ofyn i'r rhai sy'n cymryd rhan yn yr astudiaeth hon a fydden nhw'n ystyried Datganiad o Fwriad i roi ymennydd. Os bydd gan y rhai sy'n cymryd rhan ddiddordeb yn yr agwedd hon o'r astudiaeth, bydd ein tîm ymchwil yn rhoi gwybodaeth bellach iddynt.

Yn dibynnu ar gyllid yn y dyfodol mae'n bosibl y byddwn yn gwahodd pobl i gymryd rhan mewn meysydd ymchwil newydd, fel delweddu'r ymennydd. Byddai angen cymeradwyaeth foesegol benodol er mwyn gwneud unrhyw waith ymchwil newydd yn y dyfodol.

Cyfrinachedd

Mae'r holl wybodaeth fydd yn cael ei chasglu gan yr astudiaeth yn gwbl gyfrinachol a chaiff ei chadw heb fanylion personol ar systemau diogel yn unol â Deddf Diogelu Data 1998. Yr unig reswm am dorri cyfrinachedd fyddai pe bai'r gyfraith yn ein gorfodi i wneud hynny am reswm cyfreithiol oherwydd bod unigolyn mewn perygl o niwed.

Mae'n bosibl y bydd data dienw a gasglwyd gan yr astudiaeth hon yn cael ei ddadansoddi gan ymchwilwyr o ganolfannau eraill, a gymeradwywyd naill ai gan dîm CFAS neu gan UK Data Archive, lle cedwir data dienw nes bod yr astudiaeth wedi ei chwblhau.

Mae'r astudiaeth hon wedi cael ei hystyried gan Bwyllgor Moeseg Ymchwil Gogledd Cymru (Gorllewin).

Os oes gennych unrhyw bryderon neu gwynion ynglŷn ag unrhyw beth sy'n gysylltiedig â'r astudiaeth mae croeso i chi gysylltu â ni ar 01248 383050. Gofynnwch am gael gair gyda Chydlynydd yr Astudiaeth, ac os na fydd yn gallu eich helpu, bydd yn eich cyfeirio at yr unigolyn priodol. Mae trefniadau indemniad ar gyfer yr astudiaeth dan ofal Prifysgol Bangor a'r GIG.

Os hoffech gael gwybodaeth bellach neu os oes gennych unrhyw gwestiynau cysylltwch â ni ar 01248 383050.

Yr Athro Bob Woods
Prif Ymchwilydd Lleol

Dr Gill Windle
Cydlynydd Astudiaeth CFAS-Cymru

Appendix H

CONSULTEE CONSENT FORM

CFASCYMRU
CFASWALES
PRIFYSGOL BANGOR UNIVERSITY

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor, Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life
CONSULTEE CONSENT FORM

Respondent identifier: _____

	Please Initial
I confirm that I have read and understood the information sheet (version 3 dated 31/05/2011) for the above study and have had the opportunity to ask questions.	☐
In my opinion as consultee for ..... I feel that it would be his/her wish to take part in the study if he/she had the capacity to express a view.	☐
I agree to.....(Name and Relationship) taking part in the above study, I understand that he/she is free to withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected.	☐
I understand that research interviews may be taped for analysis, training and quality control purposes. I agree to this interview being audio recorded.	☐
I understand that confidentiality will only be broken if this becomes a legal requirement because of risk of harm.	☐

All the information collected by the study is completely confidential and is stored anonymously, without personal details. Audio tapes are anonymised and used for analysis and training and quality control purposes only and will be destroyed when no longer required.

Name of Consultee..... Signature of Consultee.....

Relationship to participant.....

Address of Consultee.....

.....

Date.....

Interviewers Name..... Interviewers Signature.....

Date.....

Sefydliad Ymchwil Gofal
Meddygol a Chymdeithasol,
Prifysgol Bangor,
45 Ffordd y Coleg, Bangor,
Gwynedd, LL57 2DG

Cynnal lles a gallu'r corff i weithio wrth fynd yn hŷn

FFURFLEN GANIATÂD YMGYNGHORAI

Rhif adnabod yr ymatebydd:_____

Llofnodwch â llythrennau cyntaf eich enw

Rwyf yn cadarnhau fy mod wedi darllen a deall y daflen wybodaeth (fersiwn 3 dyddiedig 31/05/2011) ar gyfer yr astudiaeth uchod a fy mod wedi cael y cyfle i ofyn cwestiynau.	☐
Yn fy marn i fel ymgynghorai ar ran ..... rwyf yn teimlo y byddai ef/hi'n dymuno cymryd rhan yn yr astudiaeth pe bai ganddo/i'r gallu i fynegi barn.	☐
Rwyf yn cytuno y gall.....(Enw a Pherthynas) gymryd rhan yn yr astudiaeth uchod, rwyf yn deall y gall dynnu'n ôl unrhyw adeg, heb roi unrhyw reswm, heb i hynny effeithio ar ei ofal/gofal meddygol neu hawliau cyfreithiol.	☐
Rwyf yn deall y gallai cyfweliadau ymchwil gael eu recordio i bwrpas dadansoddi, hyfforddi a rheoli ansawdd. Rwyf yn cytuno y gellir recordio'r cyfweliad hwn ar dâp sain.	☐
Rwyf yn deall mai'r unig reswm am dorri cyfrinachedd yw pe bai'r gyfraith yn gorfodi hynny oherwydd bod perygl o niwed.	☐

Mae'r holl wybodaeth a gesglir gan yr astudiaeth yn gwbl gyfrinachol ac fe'i cedwir ar sail data dienw, heb unrhyw fanylion personol. Mae'r tapiau sain yn ddienw ac fe'u defnyddir i bwrpas dadansoddi a hyfforddi a rheoli ansawdd yn unig ac fe'u dinistrir pan na fydd eu hangen mwyach.

Enw'r Ymgynghorai..... Llofnod yr Ymgynghorai.....

Perthynas i'r Sawl sy'n Cymryd Rhan.....

Cyfeiriad yr Ymgynghorai.....
Dyddiad.....

Enw'r Sawl sy'n Cyfweld ..... Llofnod y Sawl sy'n Cyfweld.....

Dyddiad.....

Appendix I

THANK YOU LETTER

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor, Gwynedd, Wales, LL57 2DG

Maintaining function and well-being in later life

Dear

Thank you so much for helping with this study, which we hope will be of great value in the years to come.

Each person who takes part makes a difference to the quality of the study so we are enormously grateful to you for your time and hope you will be willing to help us again in the future

If you or your family would like any further information please contact us on any of the following telephone numbers.

Yours sincerely

Professor Bob Woods
Principal Investigator

Professor Bob Woods CFAS-Wales Bangor University 01248 383719	Professor Vanessa Burholt CFAS-Wales Swansea University 01792 602186
Mrs Linda Barnes Study Coordinator MRC CFAS II 01223 330311	Dr Gill Windle Study Coordinator CFAS Wales 01248 383968

http://cfaswales.bangor.ac.uk/

Cyngor Cyllido Addysg Uwch Cymru
Higher Education Funding Council for Wales

Version 1 (31/05/2011)

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor, Gwynedd, Wales, LL57 2DG

Cynnal gallu i weithredu a lles yn ddiweddarach mewn bywyd

Annwyl

Diolch o galon i chi am helpu gyda'r astudiaeth hon. Rydym yn gobeithio y bydd o werth mawr mewn blynyddoedd i ddod.

Mae pob un sydd wedi cymryd rhan wedi gwneud gwahaniaeth i ansawdd yr astudiaeth. Felly, rydym yn hynod ddiolchgar i chi am eich amser a gobeithiwn y byddwch yn fodlon ein helpu eto yn y dyfodol.

Os hoffech chi neu eich teulu gael unrhyw wybodaeth bellach, cysylltwch â ni ar unrhyw un o'r rhifau ffôn canlynol os gwelwch yn dda.

Yn gywir

Yr Athro Bob Woods
Prif Ymchwilydd

Yr Athro Bob Woods CFAS-Cymru Prifysgol Bangor 01248 383719	Yr Athro Vanessa Burholt CFAS-Cymru Prifysgol Abertawe 01792 602186
Mrs Linda Barnes Cydlynydd Astudiaeth MRC CFAS II 01223 330311	Dr Gill Windle Cydlynydd Astudiaeth CFAS Cymru 01248 383968

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Cyngor Cyllido Addysg Uwch Cymru
Higher Education Funding Council for Wales

Version 1 (20/06/2011)

Appendix J

UNABLE TO CONTACT LETTER

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Date.....

We are sorry to have missed you, our interviewer has called to see you on several occasions but unfortunately she has been unable to make contact with you.

She will call again on

.....

to try and arrange an appointment with you. If this is not convenient, please contact us on (01248) 383050

Interviewer Name.....

Institute of Medical & Social Care Research,
Bangor University
45 College Road, Bangor,
Gwynedd, Wales, LL57 2DG

Dyddiad .....

Mae'n ddrwg gennym ein bod wedi eich colli. Fe wnaeth ein cyfwelydd alw i'ch gweld ar sawl achlysur ond, gwaetha'r modd, ni lwyddodd i gysylltu â chi.

Bydd yn galw eto ar

.....

i geisio trefnu apwyntiad gyda chi. Os nad yw hynny'n gyfleus, cysylltwch â ni ar (01248) 383050 os gwelwch yn dda.

Cyfwelydd
Enw .....

Appendix K

DEMOGRAPHIC QUESTIONS

Q4. Are you Married, Single, Widowed or divorced? (If NO are you separated or cohabiting)

1. Married
2. Cohabiting
3. Single
4. Widowed
5. Divorced/separated
7. No answer
6. Not asked.

Q38 What ethnic group do you consider you belong to? Are you…(supply likely options)

A. White
B. Black –Carribbean
C. Black – African
D. Black – Other
E. Indian
F. Pakistani
G. Bangladeshi
H. Chinese
I. Other (specify)
X. Don't know
Y. No answer
Z. Not asked

Q40 How many years did you spend in full time education

Answer in years ___
77. Don't know

Appendix L

MMSE QUESTIONS

(Folstein et al., 1975)

1. Name of city/town/village

2. Day of the week today

3. Date today – day

4. Date today – month

5. Date today – year

6. Season

7. County

8. Name two main streets nearby

9. On what floor of building

10. What is this called (pencil)

11. What is this called (wristwatch)

12. Repeat: ‘No ifs, ands or buts’

13-15. Repeat 3 words: ‘Apple’ ‘Table’ ‘Penny’

16. Serial sevens

17-19. Recall 3 words: ‘Apple’ ‘Table’ ‘Penny’

20. Read and do: ‘Close your eyes’

21. Copy this diagram (pentagon)

22. Write a complete sentence

23. Paper - take in right hand

24. Paper – fold in half

25. Paper – place on lap

26. Address of this place

Appendix M

CAMCOG QUESTIONS

(Huppert et al., 1995; Roth et al., 1986)

Orientation

1. Day
2. Date
3. Month
4. Year
5. Season
6. County
7. Town
8. Two main streets nearby
9. On what floor of building
10. Name of this place

Language Comprehension

1. Nod your head
2. Touch your right ear with your left hand
3. Before looking at the ceiling, please look at the floor
4. Tap each shoulder twice with two fingers keeping your eyes shut
5. Is this place a hotel?
6. Are villages larger than towns?
7. Was there wireless/radio in this country before television was invented?
8. Read this page and then do as it says ('Close your eyes')
9. Read this page and then do as it says ('If you are older than 50 put your hands behind your head')

Language Expression

1. What do you do with a hammer?
2. Where do people usually go to buy medicine?
3. What is a bridge?
4. What is an opinion?

5-11. Name objects shown on picture cards (Shoe, typewriter, scales, suitcase, barometer, table lamp)

12. Fluency (Name as many different animals in one minute)
13. Repeat: 'No ifs, ands or buts'
14. Write address on envelope (George Smith, 38 Mill Road, Blackpool)

Memory (Remote)

For participants born before 1942:

1. Can you tell me when the First World War began?
2. Can you tell me when the Second World War began?
3. Who was the leader of the Germans in the Second World War?
4. Who was the leader of the Russians in the Second World War?
5. What was Mae West famous for?
6. Who was the famous flyer whose son was kidnapped?

For participants born after 1942:

1. Who was the US president who was shot in Texas?
2. What is Yoko Ono famous for?
3. Who was the first man to set foot on the moon?
4. What was Edmund Hilary famous for?
5. Who was the first woman Prime Minister of India?
6. Who was the famous cinema actress who married Prince Ranier of Monaco?

Memory (Recent)

1. What is the name of the present King or Queen?
2. Who will follow her/him
3. What is the name of the Prime Minister?
4. What has been in the news in the past week or two?

Memory (Learning)

1-6. Recall objects shown on picture cards (Shoe, typewriter, scales, suitcase, barometer, table lamp)
7-12. Recognise objects shown on picture cards (Shoe, typewriter, scales, suitcase, barometer, table lamp)
13. Recall address (George Smith, 38 Mill Road, Blackpool)

Attention/Calculation

1. Count backwards from 20
2. Count backwards in sevens from 100 (Serial sevens)
3. Recognise penny without looking (Only included in CFAS Wales)
4. Recognise ten pence piece without looking (Only included in CFAS Wales)
5. How much money does this make? (Penny and ten pence piece; only included in CFAS Wales)
6. If someone gave you this amount (11p) as change from £1, how much did you spend?

Praxis

1. Copy design (Pentagon)
2. Copy design (Spiral)
3. Copy design (3D House)
4-5. Draw a large clock face and put all the numbers in
6. Set the hands to ten past eleven
7. Put paper in an envelope
8. Show how you would wave goodbye
9. Show how you would cut with scissors
10. Show how you would brush teeth

Abstract Thinking

1. In what way are an apple and a banana alike?
2. In what way are a shirt and a dress alike?
3. In what way are a table and a chair alike?
4. In what way are a plant and an animal alike?

Perception

1-2. Who is this (Queen, Pope)
3-8. Recognition of pictures of objects taken from unusual angles (Spectacles, shoe, purse, cup and saucer, telephone, pipe)

Appendix N

HEALTH-RELATED QUESTIONS

Table 1: Scoring system for index of health conditions

Health condition	Score
Angina	1
Intermittent claudication	1
High/low blood pressure	1
Sugar diabetes	1
Parkinson's disease	1
Stroke	1
Heart attack	1
Fits/epilepsy	1
Serious head injury	1
Chronic bronchitis	1
Asthma (excluding childhood asthma)	1
Arthritis	1
Peptic ulcers	1
Pernicious anaemia	1
Transient ischemic attack (TIA)	1
Thyroid problems	1
Meningitis	1
Shingles	1
Cancer (current problems)	2 (plus 1)
Total	21

Table 2: Scoring system for participation in physical activities

Level of energy	Activity	Responses	Score
Vigorous sports or activities	Running or jogging	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Swimming	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Cycling	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Aerobics or gym workout	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Tennis	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Heavy gardening	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Mowing the lawn (manually)	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
Moderately energetic sports or activities	Moderate gardening	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Mowing the lawn (electric mower)	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0

	Cleaning the car	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Walking at a moderate pace	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Dancing	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Floor/stretching exercises	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Heavy Housework	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
Mildly energetic sports or activities	Light gardening	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Bowls	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Light housework	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
	Home repairs	More than once a week Once a week One to three times a month Hardly ever/never No	4 3 2 1 0
			Total: 72

Table 3: Scoring system for service usage

Question	Responses	Score
Local authority or home help	Yes No	1 0
Any nursing services	Yes No	1 0
Chiropodist	Yes No	1 0
Meals on wheels	Yes No	1 0
Physiotherapist	Yes No	1 0
Occupational therapist	Yes No	1 0
Speech therapist	Yes No	1 0
Social worker	Yes No	1 0
Day centre	Yes No	1 0
Day hospital	Yes No	1 0
GP (doctor)	Yes No	1 0
Have you had your sight tested by an optician in the last year?	Yes No	1 0
Have you had a hearing test in the last year?	Yes No	1 0
Have you seen the dentist in the last year?	Yes No	1 0
During the last year have you been in hospital for treatment as a day patient?	Number of separate days	n
During the last year have you been in hospital as an inpatient, overnight or longer?	Number of separate stays x length of each stay in days	n
During the last 3 complete calendar months, did you attend the casualty or outpatients department of a hospital?	Number of occasions	n
		Total:

Appendix O

LUBBEN SOCIAL NETWORK SCALE – 6 (LSNS-6)

FAMILY: *Considering the people to whom you are related by birth, marriage, adoption, etc…*

1. How many relatives do you see or hear from at least once a month?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

2. How many relatives do you feel at ease with that you can talk about private matters?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

3. How many relatives do you feel close to such that you could call on them for help?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

FRIENDSHIPS: *Considering all of your friends including those who live in your neighborhood*

4. How many of your friends do you see or hear from at least once a month?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

5. How many friends do you feel at ease with that you can talk about private matters?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

6. How many friends do you feel close to such that you could call on them for help?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

LSNS-6 total score is an equally weighted sum of these six items. Scores range from 0 to 30

Appendix P

CAMCOG MEDIAN SCORES

Median CAMCOG scores for each age/gender/education group

	Age (years)											
	65-69		70-74		75-79		80-84		85-90		90+	
Education	L	H	L	H	L	H	L	H	L	H	L	H
Female	87	89	83.5	88	86.5	85	82	85	80	80	70.5	78
Male	88	89	86	89	84	87	81	85	81	85	76	80.5
L: Nine or less years in full time education H: Ten or more years in full time education												