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**Coping, Anxiety and Depression in Caregivers of People With
Alzheimer's Disease**

Claudia Cooper

University College London

Submitted for examination for PhD in May 2007

Supervised by Professors Gill Livingston & Martin Orrell

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ABSTRACT

Background: There have been few longitudinal studies investigating the impact of coping on psychological morbidity in caregivers of people with dementia (CG), and those have conflicting or unreplicated findings. About a quarter of caregivers of people with dementia (CG) experience clinically significant anxiety, but anxiety is relatively neglected in this group.

Main Hypothesis: The relationship between burden at baseline (T1) and anxiety a year later will be mediated by more dysfunctional coping strategies, and less emotion-focussed and problem-focussed coping strategies at T1.

Methods: 126 people with Alzheimer's disease and their family carers were recruited, of whom 93(73.8%) were re-interviewed a year later. Sampling was designed to ensure that the participants were representative of people living in the UK with Alzheimer's disease in terms of dementia severity, gender and care setting. I used the Hospital Anxiety and Depression Scale to measure carer anxiety, and the Brief COPE to measure coping strategies, to explore our hypothesis that the relationship between carer burden and anxiety and depression is mediated by coping style.

Results: Using relatively fewer emotion-focussed strategies and more problem-focussed strategies mediated the relationship between caregiver burden and anxiety a year later, after controlling for potential confounders. Using fewer emotion focussed strategies also predicted higher psychological morbidity in general. More use of dysfunctional coping strategies mediated this relationship cross-sectionally but not on longitudinal analysis.

Conclusion: Carers who used more emotion-focussed coping strategies in response to carer burden were protected from having higher anxiety levels a year later, while those using problem-focussed strategies were not. Most current psychological interventions

are based on problem-solving coping strategies, but our results suggest that a psychological intervention package to encourage emotion-focussed coping may be a rational approach to reduce anxiety in dementia carers. Studies are needed to test such interventions.

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LIST OF ABBREVIATIONS

AD = Alzheimer's Disease

ADAS-COG = The Alzheimer's Disease Assessment Scale-Cognition

ADCS-ADL = The Alzheimer's Disease Co-Operative Study Inventory - Activities Of Daily Living Scale

ADA = Alzheimer Disease Association

ADL = Activities Of Daily Living

ApoE4 = Apolipoprotein ε4 allele

BAI = Beck Anxiety Inventory

BEHAVE-AD = Behavioral pathology in Alzheimer's Disease Scale

BSI = Brief Symptom Inventory

CAMCOG = Cambridge Cognitive Examination

CEBM = Centre For Evidence Based Medicine

CG = Caregivers Of People With Dementia

CI = Confidence Interval

CIBIC = Clinician's Interview Based Impression of Change

CIDI = Composite International Diagnostic Interview

CMHT= Community Mental Health Team

CBT= Cognitive Behavioural Therapy

COPE Scale = Coping Orientations To Problems Experienced Scale

CR = Care Recipient

DSM= Diagnostic And Statistical Manual Of Mental Disorders

ESEMeD = European Study Of The Epidemiology Of Mental Disorders

GAD= Generalised Anxiety Disorder

GHQ= General Health Questionnaire

GMS= Geriatric Mental State

GR = Grade of Recommendation

GWBS= General Well-Being Adjustment Scale

HAS = Hamilton Anxiety Scale

HADS = Hospital And Anxiety Depression Scale

HSQ = Health Status Questionnaire

IADL= Instrumental Activities Of Daily Living

ICD= International Classification of Diseases

KSQ = Kellner Symptom Questionnaire

LE=Level Of Evidence

LTE = List Of Threatening Experiences

MMSE= Mini Mental State Examination

NINCDS-ADRDA = National Institute of Neurological and Communicative Disorders
and Stroke/Alzheimer's Disease and Related Disorders Associations

NICE = National Institute of Clinical Excellence

NFI = Normed Fit Index

NNT = Numbers Needed to Treat

NPI= Neuropsychiatric Inventory

OCD= Obsessive Compulsive Disorder

PMS = Psychiatric Morbidity Survey

POMS= Profile Of Mood States

QoL-AD = Quality of Life - Alzheimer's Disease scale

RCT= Randomised Controlled Trials

REACH Study = Resources For Enhancing Alzheimer's Caregiver's Health Study

SF-36 = Short Form-36

SPSS= Savage Personality Screening Scale

STAI= Spielberger State-Trait Anxiety Inventory

SD= Standard Deviation

SCL= Symptom Checklist

SRRS = Social Readjustment Rating Scale

T1 = Time 1

T2 = Time 2

TMAS= Taylor Manifest Anxiety Scale

WCCL= Ways Of Coping Checklist

Z = Wilcoxon signed rank statistic

1 INTRODUCTION

“Once, if there had been little traffic about, we would have swum at once the hundred yards or so across the river and back. Now it is too much trouble, and a possible producer of that endless omnipresent anxiety of Alzheimer’s, which spreads to the one who looks after the sufferer.” (Bayley 1998)

Dame Iris Murdoch, a novelist of international repute, was diagnosed with Alzheimer’s disease aged 76, in 1995. In his novel ‘Iris’, her husband John Bayley (1998) described his caregiving experiences. His and other high profile memoirs have highlighted the problems faced by spouses, children, friends and neighbours who provide care for people with Alzheimer’s disease. Such caregivers are likely to have to cope with cognitive and behavioural decline and increased dependency of the person they care for, as well as the loss of their relationship with that person as they used to be, and many experience high levels of burden and stress. Some caregivers manage these difficulties without experiencing mental health problems and report that caregiving can be a rewarding, positive experience (Roff et al. 2004) but a significant proportion experience increased psychological and physical morbidity. This morbidity may also impact deleteriously on the person they care for, as it is likely to affect their ability to care and has been associated with elder abuse (Compton et al. 1997) and the institutionalisation of the person with dementia (Gaugler et al. 2003).

The purpose of my study has been to explore the role of coping strategies in predicting anxiety and depression in Care Givers of people with dementia (CG). Anxiety has been selected as the primary outcome measure because it is a common psychiatric morbidity in this group, and yet the subject of far less investigation than other psychological outcomes such as depression and overall psychological morbidity. I was interested in the role of coping because there was preliminary evidence (Neundorfer 1991; Vedhara

et al. 2000; Vedhara et al. 2001) that the type of strategies family caregivers use to cope, rather than the nature or degree of problems they are required to cope with, may determine whether caregiver psychological morbidity develops subsequently. If confirmed, this hypothesis would suggest that a rational psychological treatment package for CG could usefully target their coping styles, and this study could then inform the development of such an intervention.

In this chapter, I will first introduce the topics of dementia including Alzheimer's disease, family caregivers, anxiety and coping. Next I shall focus specifically on family caregivers for people with dementia, and introduce the literature related to their mental health, the coping strategies they have reported using and treatments based on modifying coping strategies that have been tested in this group. Because anxiety was the primary outcome measure, I have undertaken a systematic review, described in Chapter 2, to explore the current evidence base regarding the prevalence and associates of anxiety, and the effectiveness of interventions targeting anxiety symptoms in CG. Chapter 3 sets out my hypotheses and objectives, and the main body of this thesis (Chapters 4-7) describes my prospective cohort study exploring the role of coping strategies in predicting the development of anxiety and depression in caregivers of people with Alzheimer's disease. The results of this study have already informed the development of protocols for further work, and I will discuss these in Chapter 8, before drawing final conclusions from the work of this thesis in Chapter 9.

1.1 Dementia

Dementia is defined by the International Classification of Diseases (ICD-10) (World Health Organisation 1992) as: "a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation,

learning capacity, language, and judgement. While impairments of cognitive function are the most common symptom, they are commonly accompanied by deterioration in emotional control, social behaviour, or motivation.” Functional and executive impairments are often prominent and their inclusion in future definitions has been advocated (Katona et al. 2007).

In the UK, the number of people aged 75 and over is projected to rise from 4.4 million in 2001 to 6.9 million in 2031 (from 8 to 11% of the UK population) (Wheller 2006). The prevalence of dementia increases with age. Dementia currently accounts for 11.2% of years lived with disability in people aged over sixty, which is more than stroke, cardiovascular disease and all forms of cancer (World Health Organisation 2003). The worldwide prevalence of dementia is expected to double over the next 20 years to 81.1 million cases by 2040 (Ferri et al. 2005). The potential economic and health consequences of this rise are compounded by a forecast decrease in the working-age population. In the year 2000, there were 7.1 million people with dementia and 493 million people of working-age in Europe, a ratio of 69.4 people of working age for every person with dementia. By the year 2050, this ratio will decrease to only 21.1 (Wancata et al. 2003). Thus, the financial and emotional burden placed by dementia on the working-age population is projected to rise over the next fifty years, taking into account the impact of migration, and many more people may be called upon to care for family members and friends with dementia.

1.1.1 Alzheimer’s disease

It is 100 years since Alois Alzheimer first described his eponymous disorder, and Alzheimer’s disease (AD) is now recognised as the leading cause of dementia in Caucasian populations, accounting for 30%-60% of all dementia cases in large prevalence studies (Blennow et al. 2006; Kukull et al. 2002; Stevens et al. 2002). Onset is insidious, and symptoms include memory loss, language deterioration, impaired

ability to mentally manipulate visual information, poor judgment, confusion, restlessness, and emotional lability. Estimates for the rate of cognitive decline in AD range from 2.7-4.5 points on the Mini Mental State Examination (MMSE) per year (Aguero-Torres et al. 1998). The relative risk of death in people with AD compared to those without is estimated to be between 1.4 and 2.8. Shorter survival time has been associated with older age, greater levels of functional disability and higher levels of education in people with Alzheimer's disease. The latter probably relates to delayed identification of the disease in this group (Aguero-Torres et al. 1998). The classic neuropathology of amyloid plaques and fibrillary tangles can only be confirmed on autopsy. However, accepted clinical guidelines for possible or probable AD that incorporate clinical features, blood test and neuroimaging results have increased diagnostic accuracy. Rasmusson and colleagues (1996) found, for example that diagnoses made according to the criteria of the National Institute of Neurological Disorders and Stroke/Alzheimer Disease and Related Disorders Association (NINDS/ADRDA) were 90% accurate when compared with autopsy diagnoses.

Familial AD is a rare autosomal dominant disorder with early onset, caused by amyloid precursor protein and presenilin genes. By contrast, sporadic AD is very common. Besides ageing, epidemiological studies have suggested that factors associated with development of sporadic AD include those related to decreased passive brain reserve capacity (e.g. low educational and occupational attainment, and low mental ability early in life) and reduced active brain reserve (mental and physical activity) during late life. Risk factors for vascular disease (e.g. smoking, obesity, hypertension) also seem to increase the risk of AD, but it is not yet clear whether this is a true causal mechanism (i.e. these factors result in AD pathology) or whether cerebrovascular pathology increases the likelihood that AD-related cerebral damage will exceed the threshold for dementia (Blennow et al. 2006).

A large population based twin study showed that the extent of heritability for sporadic Alzheimer's disease is 80% (Gatz et al. 2006). In practical terms, the risk to the first-degree relatives of patients with sporadic AD who developed the disorder at any time up to the age of 85 years is increased some threefold to fourfold relative to the risk in controls. This translates to an actual risk of developing AD of between one in five and one in six, once death from other causes is taken into consideration (Liddell et al. 2001). The Apolipoprotein $\epsilon 4$ (ApoE4) allele has been calculated to account for most of the genetic risk in sporadic AD. ApoE acts as a cholesterol transporter in the brain, with ApoE4 being less efficient than the other variants in reuse of membrane lipids and neuronal repair. An individual who is homozygous for ApoE4 is fifteen times more likely to develop AD than someone without an ApoE4 allele.

1.2 Caregivers

According to the UK government, a caregiver is: 'one who provides regular and/or substantial care to another person who is dependent on them for help' (Department of Health 1999a). Six million people (11% of the population aged over five years) identified themselves as unpaid caregivers in the 2001 Great British census, of whom one fifth were providing more than fifty hours of care per week (Wheller 2006). Compared with the remainder of the general population, unpaid caregivers were more likely to be female. Although the majority were aged between 34 and 65, older caregivers were more likely to be providing over fifty hours care per week. The 2001 census does not give information on people cared for, but we know from the 2000 General Household Survey that over half of unpaid caregivers were providing care to a parent or parent-in-law and a fifth were caring for a spouse (Wheller 2006). All were caring for either a relative, friend or neighbour. Unpaid caregivers are sometimes called informal caregivers to distinguish them from professional caregivers. From this point I

will use the term ‘family caregiver’ to refer to all unpaid caregivers who look after a relative, friend or neighbour.

1.2.1 Economic, legal and political aspects of caring

Based on 2000 care costs, it has been calculated that family caregivers collectively save the UK economy £57 billion a year (Carers UK 2002). This calculation is based on replacement costs, that is the cost of replacing all informal care with paid care. An alternative strategy for costing caregiver time is to calculate the cost to the individual of providing the care, including loss of potential earnings (termed the opportunity cost). Estimates for replacement costs are usually higher than for opportunity costs, and there is no current consensus regarding which system of calculation is preferable.

Increasing recognition of the central role of family caregivers in the nation’s health and social care and the help that should be provided for them has been reflected in government legislation, including The Caregivers’ (Recognition and Services) Act (Department of Health 1995); The Caregivers and Disabled Children Act (Department of Health 2000); and The Caregivers’ (Equal Opportunities) Act (Department of Health 2004). The first National Caregivers’ Strategy (Department of Health 1999a); and the National Service Frameworks for Mental Health (Department of Health 1999b) and Older People (Department of Health 2001) also prioritised the needs of caregivers. Collectively these initiatives have given family caregivers the right to expect care, information and support for themselves and to be consulted about health and social plans regarding the person for whom they care. Under the Mental Capacity Act (Department of Health 2005) some caregivers will be able to accept rights and responsibilities to make decisions on behalf of the person they care for when they are no longer able to do so themselves.

1.2.2 Morbidity in caregivers

Alongside the recognition and political prioritisation of care for family caregivers, there has been a burgeoning of research regarding the problems, physical and psychological illnesses they face. Before focusing on caregivers for people with Alzheimer's disease, it is important to acknowledge that being a family caregiver for someone who needs help for any reason may be a risk factor for mental illness. Among family caregivers identified by the 2000 General Household Survey, 21% of women and 12% of men reported significant mental health problems; those caring for someone living in the same household, or caring for more than twenty hours a week were at particular risk (Singleton et al. 2002). More recently, the Caregivers Speak Out Project (Keely & Clarke 2002) surveyed 3800 caregivers to assess progress three years after the National Caregivers' Strategy was launched. They noted some improvements, with increased information provided and new caregivers reporting more positive experiences, but nonetheless 90% of those interviewed reported stress, depression, anxiety or insomnia. Most care recipients are older people (Singleton et al. 2002); evidence synthesis from studies of caregivers for frail elders has conclusively demonstrated that they report increased levels of caregiver burden and psychological morbidity (Pinquart & Sorensen 2003b).

1.3 Anxiety

1.3.1 Symptoms

Everyone experiences anxiety and worry sometimes, and some anxiety can be helpful and necessary. A recent longitudinal study found that children with low levels of anxiety were more likely to die from an accidental cause (Lee et al. 2006). In anxiety disorders, symptoms are persistent, severe, pervasive or difficult to control to an extent

causing significant distress or interference with daily life. Symptoms of Generalised Anxiety Disorder (GAD) include feelings of worry and fear that are excessive or not realistic, muscular tension and somatic symptoms including trembling, feeling shaky, aching in the back and shoulders, tension headaches, chest tightness, restlessness, exaggerated startle, irritability, insomnia, fatigue, dry mouth, sweating, urinary frequency, difficulty swallowing, nausea, and diarrhoea. These symptoms must be present most days for at least three weeks according to ICD-10 (World Health Organisation 1992), while Diagnostic and Statistical Manual of Mental Disorders (DSM) IV (American Psychiatric Association 1994) requires that they are present for at least six months. Other anxiety disorders defined by ICD-10 include panic disorder, agoraphobia, simple and social phobias, Obsessive Compulsive Disorder (OCD) and Post Traumatic Stress Disorder (PTSD).

1.3.2 Prevalence

Anxiety disorders are currently among the most common mental illnesses in the UK. In the 2001 Great British Psychiatric Morbidity Survey (PMS) (which interviewed adults aged 16-74), 4.4% of people interviewed met criteria for GAD, 1.8% of people met criteria for phobia, 1.1% for OCD and 0.7% for Panic Disorder in the last two weeks, measured using the Revised Clinical Interview Schedule (CIS-R) and defined according to ICD-10 diagnostic criteria (Singleton et al. 2001). The overall rate of any anxiety disorder was 6.5% (from my own calculations from PMS database). This compares with a prevalence of 2.6% for any depressive episode in the same survey. The European Study of the Epidemiology of Mental Disorders (ESEMeD) project (Alonso et al. 2004) interviewed a representative random sample of 21,425 adults aged 18 or over from Belgium, France, Germany, Italy, the Netherlands and Spain in 2001-2003, using the Composite International Diagnostic Interview (CIDI) to make DSM IV diagnoses. Any anxiety disorder was diagnosable in 6.4% of people interviewed; specific phobia

(affecting 3.5%) was the most common anxiety diagnosis. By comparison 3.9% were diagnosed with major depression, and 4.2% with any mood disorder. Collectively these prevalence studies indicate that anxiety disorders may be more prevalent than depressive disorders in the general population, affecting over 6% of all adults (Alonso et al. 2004; Singleton et al. 2001).

1.3.3 Anxiety in older adults

Because many CG are older people, it is also important to consider the prevalence of anxiety disorders in the older general population. Anxiety prevalence estimates from three studies of the older general population have ranged from 10-15%, which is slightly higher than prevalence rates in the adult population (aged 18-75) discussed above. Beekman and colleagues (1998) interviewed 3107 people aged 55-85 for the Longitudinal Aging Study Amsterdam (LASA study) using the Diagnostic Interview Schedule (DIS). They found an overall prevalence of anxiety disorders meeting DSM-III criteria of 10.2% (n=137), of whom 7.3% had GAD, 3.1% had phobic disorders, 1.0% panic disorder and 0.6% OCD. The prevalence of major depression in the same cohort was 2.02%, that of minor depression 12.9%, while 14.9% had clinically relevant levels of depressive symptoms (Beekman et al. 1995). Results from a representative survey of 700 people over the age of 65 living in the UK (Islington, London) yielded similar results; 14.9% fulfilled criteria for depression, 15.0% fulfilled criteria for any anxiety disorder (4.7% met criteria for GAD and the remainder were diagnosed with phobic anxiety) (Livingston et al. 1996). Anxiety was measured using a scale validated against clinical diagnosis. Thirdly, in a probability sample of 860 Black and 214 Caucasian people aged 55 years and over living in Brooklyn, New York, collected between 1996 and 1999, 14% experienced clinically significant anxiety, defined using the Anxiety Status Inventory Scale, which is validated for use in older adults (Cohen et al. 2006). The two studies that also reported the prevalence of depression found

comparable rates for anxiety and depression (Beekman et al. 1998; Livingston et al. 1996). Different surveys of older and younger adults have reported that GAD (Beekman et al. 1998; Singleton et al. 2001) and specific phobias (Alonso et al. 2004) are the most common anxiety diagnoses.

1.3.4 Natural history

Anxiety disorders are often chronic and persistent, although two longitudinal studies have indicated that a third to a half of people experiencing them have recovered 2½ to 6 years later. Livingston and colleagues (1996) reinterviewed 86 people from their cohort of 165 people aged 65+ with anxiety or depression living in Islington 2.5 years after their initial survey. Of those not reinterviewed, 25 had died, 23 had moved out of the area and 23 refused to be interviewed. Half of those diagnosed with GAD at initial interview had recovered and half had not. Of the 50 people initially diagnosed with phobic anxiety, 16.4% had recovered, 65.6% remained unwell and 18% had died. Women and those who did not initially have a comorbid diagnosis of depression were less likely to have recovered, perhaps because those with comorbid depression were more likely to have received treatment.

Schuurmans et al (2005) followed up 84% of 112 people aged 55 or over recruited for the LASA study who had an anxiety disorder at baseline; 23% still met criteria for an anxiety disorder six years later, another 47% suffered from subclinical anxiety symptoms, while 31% were in full remission. Persistence of anxiety was associated with a high baseline neuroticism score, use of benzodiazepines and less use of mental health care facilities and antidepressants, suggesting that effective treatment might increase rates of remission.

1.3.5 Comorbidity

Symptoms of anxiety and depression frequently co-occur. Estimates for the proportion of people in the general population with anxiety disorders who are also depressed have

ranged from 13% (van Balkom et al. 2000) to 60.4% (Schoevers et al. 2003) in large epidemiologically representative studies. The prevalence of anxiety disorders is also increased in people diagnosed with other anxiety disorders (Krueger 1999), substance misuse (Conway et al. 2006), avoidant or dependent personality disorders (Kantjarvi et al. 2006), eating disorders (Kaye et al. 2004) and physical disorders (Sareen et al. 2005a).

1.3.6 Secondary disability

Anxiety disorders cause considerable disability and stress. In the ESEMeD study, anxiety disorders were second only to heart disease in the total amount of disability they caused in the population studied; they resulted in more disability than mood disorders, arthritis, or alcohol disorders (Buist-Bouwman et al. 2006). In a large epidemiological study in Australia, people with anxiety disorders reported: reduced labour force participation, and impaired work performance and career progression, compared to people without disabilities or long-term health conditions (Waghorn et al. 2005).

People with anxiety disorders also experience more disability associated with comorbid physical health problems. Among respondents with one or more physical disorders interviewed for the USA National Comorbidity survey, a large household population survey, a comorbid anxiety disorder diagnosis was associated with an increased likelihood of physical disability even after adjusting for severity of pain, comorbid mood, and substance use disorders (Sareen et al. 2005a). Those with anxiety disorders also use more medical resources for physical disorders. In a large (n=3726) nationally representative probability survey conducted in Germany from 1997 to 1999, the prevalence of anxiety disorders was 11.9% among those demonstrating normal health service utilisation, and 29.3% among high services users (Schmitz & Kruse 2002). The personal cost of anxiety disorders is also great. In the USA National Comorbidity survey, those with anxiety disorders were over twice as likely to think about and to

attempt suicide compared with those who did not have an anxiety disorder (Sareen et al. 2005b).

1.3.7 Aetiology

The aetiology of anxiety disorders is multifactorial, resulting from the interaction of genetic and environmental factors.

1.3.7.1 Genetic factors

In a family study, GAD (but not other anxiety disorders) defined according to DSM-III criteria was five times more prevalent (19.5% versus 3.5%) among first-degree relatives of patients with GAD than among relatives of controls (Noyes et al. 1987). Kendler et al (1995) concluded that two main genetic factors, the first loading heavily on phobia, panic disorder, and bulimia nervosa and the second on major depression and GAD best explained the genetic component of aetiology. This suggests that the anxiety disorders are not, from a genetic perspective, aetiologically homogeneous, and consequently that the interaction of genetic and environmental factors is likely to play a critical part in determining the nature of any psychiatric disorder that develops, and if it develops at all.

1.3.7.2 Environmental factors

Many studies have demonstrated that stresses and traumatic life events can increase the likelihood of developing an anxiety disorder. As for genetic factors, the experience of stressful life events is thought to increase one's likelihood of experiencing a range of psychiatric disorders rather than being specifically aetiologically related to the development of anxiety disorders. For example, child sexual abuse was associated with a greater risk of developing anxiety disorders, major depression, conduct disorder, substance use disorder, and suicidal behaviours in a cohort of adults followed since birth in New Zealand (Fergusson et al. 1996). Similarly, in the US National Comorbidity Survey, retrospectively reported childhood adversities, including parental divorce, maternal depression, rape and natural disaster, were consistently associated with onset

of DSM-III-R mood, anxiety, addictive and acting out disorders in adulthood (Kessler et al. 1997). Possible mechanisms for this relationship might be that childhood adversity causes: hyperactivity of the hypothalamus-pituitary-adrenal axis (Rinne et al. 2002); interferes with development of social skills (Johnson et al. 2002) and can result in having fewer close relationships and feeling more emotionally isolated as an adult (Wilson et al. 2006), as all these factors increase vulnerability to psychiatric disorders.

Stresses endured as an adult also appear to increase the likelihood of experiencing a subsequent psychiatric disorder including an anxiety disorder. Several studies have found that stressful or traumatic life events including chronically dysfunctional marital and family relationships increase the incidence of GAD (Gelder et al. 2001). Anxiety disorders have been associated with a range of markers of socio-economic deprivation and stress in cross-sectional surveys, including being divorced or separated and living alone or as a single parent (Singleton et al. 2001). They are also more prevalent in women and those aged between 35 and 54 (Singleton et al. 2001).

1.3.8 Management

Andrews and colleagues (2004) compared the effectiveness of treatment in terms of number of years of living with disability avoided for a range of psychiatric disorders, using data from the Australian National Survey of Mental Health and Well-being. They found that anxiety disorders were the most treatable illnesses, with two-thirds of the burden of GAD, and half the burden of all anxiety disorders theoretically avoidable. Despite this, few people with anxiety disorders were receiving treatment at the time of the survey. Roth and Fonagy (1996) concluded in their seminal review of psychotherapy that Cognitive Behavioural Therapy (CBT) delivered by experienced therapists has demonstrated good efficacy for treating anxiety disorders, and that two-thirds to three-quarters of people could be expected to show clinically significant improvements at six months follow-up. A recent meta-analysis established that CBT

reduced anxiety and increased quality of life in people with GAD, and that its effectiveness was comparable to pharmacotherapy (the majority of comparisons were with benzodiazepines) but with a lower drop out rate (Mitte 2005). In a second meta-analysis by the same author, pharmacotherapy was superior to placebo for treatment of GAD. Azapirones (eg buspirone) and benzodiazepines were the main drug treatments evaluated in the studies reviewed (the most recent of which was published in May 2002) and these were equally effective (Mitte et al. 2005). A number of studies have also demonstrated that Selective Serotonin Reuptake Inhibitors (SSRIs) are effective in treating anxiety disorders (Schuurmans et al. 2006; van der Linden et al. 2000). Antidepressants (imipramine, venlafaxine and paroxetine) were found to be superior to placebo in treating GAD in a recent Cochrane review. The calculated Numbers Needed to Treat (NNT) for antidepressants in GAD was 5.15 (Kapczinski et al. 2006). Recent guidelines issued by the National Institute of Clinical Excellence (NICE) (2004) advocate CBT as first line treatment for GAD, panic disorder and agoraphobia. Pharmacotherapy with SSRIs (or imipramine or clomipramine if these are not effective after twelve weeks) and self help are also recommended.

1.4 Coping

Coping is the process by which people manage stress. It has long been accepted that different people exposed to the same stress may react in very different ways. The Ancient Greeks observed that while most soldiers managed in the face of battle, a minority experienced disabling fear responses. For example, Herodotus records that Aristodemus, a soldier of the hand-picked elite Spartan unit “finding his heart failed him,” remained safely in the rear and did not join the fight with other soldiers, and was subsequently nicknamed “the trembler”. In the First World War, according to one estimate, mental breakdowns represented forty percent of British battle casualties. The

British psychologist Charles Myers first used the diagnosis “shell shock” for such cases (Anderson 2006).

Lazarus and Folkman (1984) outlined a transactional model to explain why some people develop clinically significant psychiatric morbidity and others do not when exposed to comparable stressors. It views coping as a process that begins with appraisal of the situation one is faced with. First an individual evaluates the stressful situation with regard to their values, beliefs and intentions (primary appraisal). Next they consider what can be done about the situation, and whether they believe they have the resources to cope with it. This secondary appraisal forms the basis of the coping response.

1.4.1 Classifying coping

Lazarus and Folkman (1984) classified coping strategies as either problem-focussed or emotion-focussed. Problem-focussed coping strategies involve defining the problem, generating alternative solutions, considering their relative costs and benefits, choosing among them and acting. John Bayley describes coping in various ways in his care for Iris Murdoch, including the use of problem-based planning approaches:

‘[A television programme is] part of the morning ritual, as I try to make it. I have to insist a bit, as Alzheimer’s now seems to have grown inimical to routines. Perhaps we all know by instinct that an adopted routine preserves sanity?’ (Bayley 1998 page 242)

Emotion-focussed strategies seek to lessen the emotional distress associated with a situation through attempting to change one’s own feelings about it. One example is humour:

‘I can’t reply in the way I used to do then but only in the way she speaks to me now. I reply with the jokes or nonsense that still makes her laugh. So we are still part of each other.’ (Bayley 1998 page 249)

Not all coping strategies are helpful. One example of a strategy that is likely to be unhelpful to the caregiver and person with dementia is venting:

‘Violent irritation possesses me and I shout out before I can stop myself, ‘Don’t keep asking me where we are going!’ (Bayley 1998 page 251)

There has been disagreement about how best to classify coping strategies. Carver (1997) criticised Lazarus and Folkman’s dichotomous classification into emotion-focussed and problem-focussed coping as being too simplistic. He described thirteen different types of strategy, that were classified into problem-focussed, emotion-focussed and dysfunctional strategies, thus separating potentially helpful (problem-focussed and emotion-focussed) and unhelpful (dysfunctional) strategies. This is the system of classification I have used in this thesis. Other classificatory systems have divided coping strategies into: approach coping, where a person engages with the problem and thinks actively about what to do to resolve it, or avoidance coping, which describes the opposite of this. Using the previous classification, approach coping involves a combination of problem-focussed and emotion-focussed approaches, while avoidance coping would be a dysfunctional coping strategy. Other authors have described active behavioural, active cognitive and avoidance coping. Active cognitive coping involves using cognitive strategies such as “looking on the positive side” or “telling oneself things to feel better” and would thus appear to equate with emotion-focused coping. Active behavioural coping involves responding to a stressor with practical actions and is more akin to problem-focussed coping, although it may also involve seeking out emotion support (Powers et al. 2002).

The most beneficial coping response will vary with the nature of the stressor. Lazarus and Folkman (1984) suggested that those who perceive they have the resources to alleviate a stressful situation are most likely to respond to it with a problem-focussed coping strategy (an action to change the situation) and those who do not are more likely

to respond to the stressor with an emotion-focussed strategy (to change their way of thinking about the situation). In coping with any situation, most people use a mixture of strategies, so it is the predominant style that is generally considered in coping research. Powers et al (2002) found that avoidance, active behavioural and active cognitive coping strategies used in dementia caregivers at four six month intervals were highly correlated ($r=0.52-0.69$) for each type of strategy. They hypothesised from these results that coping style is a trait rather than a state variable, because even though the people with dementia in their study were becoming more dependent, the caregivers did not change the strategies they used. This is contradicted by intervention studies in dementia caregivers that have succeeded in changing the type of coping strategies they used to more helpful ones (Chiverton & Caine 1989; Lavoie et al. 2005).

1.4.2 The relationship of coping to mental health

Numerous longitudinal studies have investigated how respondents' coping response to a range of stressors, acute and chronic, impacted upon levels of subsequent psychological morbidity. Most have reported that use of dysfunctional strategies predicts worse mental health. In a large longitudinal epidemiological USA study, Silver and colleagues (2002) found that responding to stress induced by the September 11th, 2001 terrorist attacks with more dysfunctional (denial and self-distraction) coping strategies predicted a worse psychological outcome. In two further representative prospective cohort studies, use of dysfunctional (avoidant, withdrawal) strategies were associated with decreased psychological wellbeing a year later in USA citizens living with HIV (Fleishman et al. 2003), and lower mood scores over the subsequent two years in patients from an Australian melanoma unit (Brown et al. 2000).

1.4.3 Measuring coping in caregivers

There is a debate about whether researchers should measure a person's dispositional coping style (the style that participants report using most frequently in their lives) or

their situational coping style (the style used for a specific stressor). Carver and Scheier (1994) compared dispositional, and situational coping style, both measured using the Coping Orientations To Problems Experienced (COPE) scale, in 156 undergraduate students. They were first asked how they usually coped with difficulties, and then to recall a recent stressful event and to report the strategies they used to cope with it. A disadvantage of this study was that the stressor was not standardised. The factor structure was very similar for the scale when used in these two different ways, but internal consistency of the scale tended to be better for situational coping. Most of the situational coping subscales correlated with their dispositional counterparts significantly at a low-moderate level. The authors suggest that personality traits and coping dispositions both play a role in determining situational coping, and that coping strategies may be reported most accurately when people are asked about a more specific situation.

Most studies of CG coping have asked specifically about coping as it relates to caregiving stresses (Kneebone & Martin 2003). By asking about all stresses and problems associated with caregiving, it is intended that the caregiver will bring to mind those aspects they found most difficult. A few studies have asked CG about coping with greater specificity, using well-defined stressors. In one study 107 CG were asked to complete a generic coping measure about how they coped with each of three stressors: loss of memory and ability to communicate, and the gradual decline of a loved one (Williamson & Schulz 1993). Whilst I considered this approach, a difficulty is that caregivers are likely to have encountered different challenges and the meaning of a single stressor may vary greatly between caregivers. In addition, CG may become anxious or depressed for several reasons, both related to caregiving and other factors, and how they cope with all of these stressors is relevant clinically. I therefore decided to

use a generic measure of coping and to ask about stresses associated with caregiving but not to specify the stressors further.

While some studies in CG have used coping scales designed specifically for caregiving, the majority have used generic measures (Kneebone & Martin 2003). Many of these have the advantages of published, acceptable psychometric properties and that findings are generalisable to other coping research. Two of the most frequently used general coping measures are the WCCL (Figure 1.1, page 34) and the COPE scale (see Figure 4.2, page 114 for more details).

1.4.3.1 The Ways of Coping Checklist

The WCCL is the instrument used most frequently to measure coping in CG and other populations. It was developed (Folkman & Lazarus 1980), and subsequently revised (Folkman & Lazarus 1988) and is based on their now widely influential model of stress and coping (Lazarus 1966; Lazarus & Folkman 1984). Respondents are asked about a stressor and then to indicate the degree to which they have utilized each particular coping method to deal with it. Responses to the statements are subsequently factor-analysed to identify more general patterns of coping. The authors found that in a representative community study that employed this measure, eight distinct coping strategies emerged, from which subscales were developed: seeking social support, positive reappraisal, planful problem solving, self-controlling, distancing, accepting responsibility, confrontative and escape avoidance coping (Figure 1.1, page 34).

Figure 1.1 Coping Factors Measured by the Ways of Coping Checklist

(Mindgarten website 2006)

1. **Confrontive Coping:** describes aggressive efforts to alter the situation and suggests some degree of hostility and risk-taking.
2. **Distancing:** describes cognitive efforts to detach oneself and to minimize the significance of the situation.
3. **Self-Controlling:** describes efforts to regulate one's feelings and actions.
4. **Seeking Social Support:** describes efforts to seek informational support, tangible support, and emotional support.
5. **Accepting Responsibility:** acknowledges one's own role in the problem with a concomitant theme of trying to put things right.
6. **Escape-Avoidance:** describes wishful thinking and behavioral efforts to escape or avoid the problem. Items on this scale contrast with those on the Distancing scale, which suggest detachment.
7. **Planful Problem Solving:** describes deliberate problem-focused efforts to alter the situation, coupled with an analytic approach to solving the problem.
8. **Positive Reappraisal:** describes efforts to create positive meaning by focusing on personal growth. It also has a religious dimension.

1.4.3.2 Development of the COPE

Carver (1989) suggested a number of difficulties with the WCCL. Firstly, it has only two subscales, for problem-focussed and emotion-focussed strategies which do not enable researchers to distinguish between coping styles that are likely to be helpful and unhelpful; perhaps because of this the WCCL has been employed idiosyncratically across different studies, with most studies using factor analysis to further reduce the eight scales reported above. A second suggested difficulty is its empirical design, meaning that items were initially chosen as being diverse and representative samples of potential coping resources, rather than because they represented theoretically interesting categories of coping. Thirdly he suggested that some of the items are ambiguous and unfocussed, citing two items from the confrontative coping subscale as examples: “Took a big chance or did something risky” and “I did something I didn’t think would work, but at least I was doing something”. The first of these could be emotion-focussed or problem-focussed depending on the respondents’ interpretation, while the coping style described in the second example could be appropriate or not depending on the situation. Carver and colleagues (1989) aimed to overcome these problems in the COPE (see section 4.4.1.4.1, page 111 for details of the COPE and section 4.4.1.4.2, page 112 for details of the Brief COPE).

1.4.3.3 Analysis of coping scores

Early coping research analysed scores on scales representing different coping responses (e.g. approach and avoidant coping). This strategy has been criticised, because the use of different types of coping relative to each other is likely to be important. Possible alternative strategies are to explore the use of different types of coping style relative to each other, for example using multivariate statistical analyses, the method I will employ in this study. An alternative approach that has been used previously is cluster analysis to

develop a typology of coping configurations among respondents (Fleishman et al. 2003), although such an approach suggests that there are a finite number of discrete coping approaches which probably does not reflect reality, and in my study would have reduced power to examine associates of coping.

1.4.3.4 Problems with existing coping literature

Gottlieb and Wolfe (2002) reviewed the CG coping literature (1984-2000), and found 17 studies exploring the relationship of coping to health outcomes in caregivers for people living in the community with dementia. They noted a number of limitations in the current literature. Although six of the studies they found used the WCCL, the items were analysed in such a variety of ways, dividing them on an *a priori* or empirical basis, that the evidence could only be synthesized to a limited extent. The lack of clearly defined coping subscales that are meaningful was a major limitation of earlier coping studies (see section 1.4.3.1, page 33).

While most (14/17) cited Lazarus and Folkman's transactional model as the basis for their study, none drew on the model to formulate hypotheses about how particular stressors might interact with pre-specified coping styles to impact upon CG health. A second criticism was a failure to: "make predictions about differential effects of specific types of coping on different aspects of health and wellbeing." A lack of evidence from longitudinal studies was also observed.

1.5 Morbidity in caregivers for people with dementia

1.5.1 Comparison with non-caregivers and other caregivers

There is consistent evidence that caregiving for people with dementia is associated with poorer health outcomes. Dementia caregivers have reported reduced wellbeing (Rose-

Rego et al. 1998) and poorer physical health (Schulz et al. 1995), and are at increased risk of mortality (Schulz & Beach 1999) compared with non-caregivers. Dementia caregiving has also consistently been linked with psychological problems, usually in terms of caregiver burden, general psychological distress and depressive symptomatology (Pinquart & Sorensen 2003a). Caregivers for people with dementia appear to be at higher risk of developing mental health problems than caregivers for people with other illnesses, including: cancer (Clipp & George 1993); AIDS or terminal cancer (Flaskerud et al. 2000) and Parkinson's disease without cognitive impairment (Hooker et al. 2000). Livingston and colleagues (1996) found that among elderly people and their caregivers living at home, 3% (n=1) of caregivers for those with physical health problems had depression, compared with 30% (n=9) and 47% (n=7) of those caring for someone with a psychiatric disorder or dementia respectively.

There are a number of reasons why caregiving for a person with dementia might be particularly stressful. Livingston et al. (1996) suggested that the loss of a confiding relationship with the cared for person may have explained the higher rates in those caring for people with dementia, whereas in other caring situations, confiding is likely to be less affected or even increased. Bertrand et al (2006) examined the reasons for greater stress among 106 dementia caregivers compared with 243 caregivers for people without dementia in their prospective cohort study of women over 65 originally recruited for the Caregiver Study of Osteoporotic Fractures. They found that the higher incidence of behavioural problems in people with dementia was the most important factor, and that increased role captivity (feeling trapped by the illness of the person for whom they were caring) mediated this relationship in the dementia caregivers. Using data from the 1996 National Caregiver Survey, Ory et al (1999) reported that dementia caregivers spend significantly more hours per week providing care, report more employment complications and family conflict, and less time for leisure and other

family members than other caregivers, and these factors might also explain their higher levels of morbidity. Other possible reasons why caring for someone with dementia is particularly stressful could be that there are fewer caregiving rewards (for example, satisfaction from caring), the care recipient is less likely to understand sacrifices made by the caregiver and give appreciation; and the stress of making decisions for someone who has lost the capacity to do so for themselves.

1.5.2 Prevalence and aetiology of caregiver morbidity

A recent review found ten studies investigating the prevalence and incidence of major depressive disorder in CG, with a mean prevalence of 22.3% (Cuijpers 2005). Studies that have measured the prevalence of clinically significant anxiety and depression in CG have reported similar rates for anxiety (10-35%) and depression (10-34%) (Coope et al. 1995; Dura et al. 1991; Mahoney et al. 2005; Neundorfer 1991; Russo et al. 1995; Vitaliano et al. 1991), but despite this far fewer studies have investigated the prevalence and correlates of anxiety than depression in CG. Schulz and colleagues (1995) found twenty-nine studies which measured the prevalence and correlates of depression in CG in a systematic review (1989-1995) but only seven measuring anxiety, and commented on the need for more studies on anxiety in CG. Correlates of depression were: more patient problem behaviours and perceived stress; decreased life satisfaction, income, self-rated health, satisfaction of social support and quality of the past relationship between the caregiver and the person with dementia; female CG gender, lack of information, as well as identifying fewer positive aspects of caring such as companionship and rewards. Anxiety is also relatively neglected in intervention studies. Selwood and colleagues (2007) found that only five of sixty-six studies of psychological interventions for CG reported anxiety as an outcome.

There are a number of reasons why this relative neglect of anxiety symptoms may be important. There is considerable comorbidity between anxiety and depression in the

general population, and this has also been demonstrated in populations of dementia caregivers (Russo et al. 1995). In a large study of people with AD and their caregivers living in London and South-East England (the LASER-AD study of which this thesis is part) our research group found that 36.1% of anxiety cases were also depressed, and 81.3% of depression cases were also anxious (Mahoney et al. 2005). Factors associated with or causing depression may not bear the same relationship to anxiety, and similarly interventions that reduce depression may not necessarily reduce anxiety. Pinquart and colleagues (2006) found that effects of cognitive-behavioral therapy, support, counselling, day care, training of people with dementia, and multicomponent interventions were domain specific (i.e. those directed at reducing depression cannot be presumed to also reduce anxiety), and concluded that clinicians must tailor interventions according to the specific needs of the individual caregivers.

1.5.3 Relationship of morbidity to coping strategies

While it is accepted that coping strategies are important predictors of affective illnesses in the general population, they tend to be considered less than the stresses of caring and the clinical characteristics of the person with dementia in existing CG research. Nonetheless, there is some evidence that coping style can influence the vulnerability of dementia caregivers to adverse health effects. In some studies coping strategies have been investigated as mediators of the impact of stressors on health outcomes (e.g. Goode et al. 1998; Mausbach et al. 2006b), in line with the Lazarus and Folkman model of stress and coping, rather than as direct predictors of health outcomes. This seems rational, as coping response in caregiving is inevitably a product of the stressors that need to be coped with by an individual and is the analytic approach I have used in my study. Below I will discuss studies exploring the relationship of coping strategies to caregiver burden and a range of health outcomes in CG, including anxiety and

depression. In the next chapter I will focus specifically on the evidence for the outcome anxiety (see page 70).

1.5.3.1 Problem-Focussed Strategies

Results from cross-sectional studies examining the relationship between use of problem-based coping strategies and health status and caregiver burden are inconsistent, with different authors reporting no association, positive and negative correlations. Hinrichsen et al. (1994) reported that active management strategies (planning) were associated with increased caregiver burden. Neundorfer (1991) found that planful problem-solving was significantly but weakly ($r=0.22$, $p<0.05$) positively correlated with anxiety but not with depression or physical health scores, while Vedhara (2001) reported that it did not predict anxiety or depression; both authors used the Ways of Coping Checklist (WCCL) to measure coping (see page 34). Vedhara (2000; 2001) recruited CG from a memory clinic in Bristol. They are the only group to have previously reported correlates of emotion-focussed, problem-focussed and dysfunctional coping strategies cross-sectionally and prospectively (at 6, 12 and 18 month). Because of this, I will refer to their study throughout this chapter and the next, although it has a number of limitations, including a small sample size ($n=50$) and omission of a number of potentially important factors including caregiver burden. Morano (2003) concluded that problem-focussed coping neither mediated nor moderated the relationship between patient problem behaviour and a range of psychological outcomes including depression and life satisfaction.

Other cross-sectional studies have reported, by contrast, an association between problem-focussed coping and positive health outcomes in CG. Mckee et al. (1997) used the WCCL to measure coping in 228 caregivers for elderly people, only half of whom had dementia. They found that more use of problem-focussed coping was associated with better self-perceived and interviewer rated coping. This may, however, be more

informative of the perception of family caregivers and health professionals about how one should cope than the actual effects of coping. More use of instrumental coping or problem-solving coping has also been associated with increased positive affect in 315 CG for spouses with AD (Pruchno & Resch 1989); less distress in 78 caregivers of people with AD (Rose et al. 1997); and higher self-reported health in 54 CG (Haley et al. 1996).

In the only two longitudinal studies to use validated subscales of problem-based coping strategies, they did not predict higher caregiver burden scores 15-18 months later (Vitaliano et al. 1991) or anxiety, depression or stress six or twelve months later (Vedhara et al. 2001). By contrast, Wright (1994) found that the strategy of “actively trying to change the situation” was associated with fewer depressed moods in seven CG who cared for someone who had moved to a care home over the two years of the study, but not in those who continued to care at home.

In summary, in cross-sectional studies, problem-focussed coping was consistently unrelated to depression, while results for anxiety were inconsistent in two small studies. Other health outcomes and their association to problem-focussed coping have been explored in single studies, and results are inconsistent. In unreplicated prospective studies, use of problem-focussed coping strategies were not associated with caregiver burden, stress, anxiety or depression between 6-18 months later in unreplicated prospective studies. A clear consensus is therefore lacking about the relationship of problem-focussed coping to health outcomes or caregiver burden, because no adequately powered prospective study of these relationships have been undertaken.

1.5.3.2 Emotion-Focussed Strategies

The literature is complicated by a tendency to group helpful (acceptance, humour, religion, positive reframing) and non-helpful (venting, denial) emotion-focussed strategies together. Carver et al. (1989) separated these in the COPE (see Figure 4.2,

page 114). Exploring the content of emotion-focussed coping scales has enabled me to synthesise the evidence for helpful emotion-focussed strategies separately. From this point I will use the term emotion-focussed coping to mean helpful emotion-focussed strategies, as defined in the COPE (see Figure 4.2, page 114, for a description of emotion-focussed, problem-focussed and dysfunctional coping strategies as defined by the COPE).

Emotion-focussed coping strategies and their relationship to dementia caregiver burden and health outcomes have been explored in a number of cross-sectional studies which I will describe below, and most have found they are beneficial. Seeking spiritual support and reframing problems have been associated with decreased caregiver burden (Pratt et al. 1985); acceptance with more CG positive adjustment (Pruchno & Resch 1989); and management of meaning (which includes elements of acceptance, humour and positive reframing) with less role overload (a perception that caregiving demands exceed one's personal resources) (Gallagher et al. 1994) and depression in CG (Saad et al. 1995). Morano (2003) found that among 204 family caregivers for people with AD, more use of emotion-focussed coping (reduction of expectations, use of positive comparisons, and a search for a larger meaning) moderated the relationship between more problematic patient behaviour and less depression and greater life satisfaction. Williamson and Schulz (1993) reported that using the strategy of acceptance to manage "loss of ability to communicate" and "gradual decline of a loved one" was associated with less depression. Gottlieb and Gignac (1996) asked 51 CG about their coping responses to "the most upsetting symptom of the disease" and "a deprivation occasioned by the caregiving role". They classified responses to open questions using content analysis techniques. Positive reframing was associated with better health and fewer psychiatric symptoms. CG reported finding religious coping strategies helpful in a descriptive study

(Stolley et al. 1999) although they were not related to caregiver mental health in a cross-sectional survey (Mausbach et al. 2006a).

In two other cross-sectional studies results were less consistent. Positive reappraisal was not associated with anxiety, depression (Neundorfer 1991; Vedhara et al. 2001) or stress (Vedhara et al. 2001). Neundorfer found that self-controlling coping (see Figure 1.1, page 34 for content of this scale) positively correlated with anxiety but not with depression or physical health scores. Vedhara reported that self-controlling coping did not correlate with anxiety or depression on multivariate analyses. As discussed earlier. Both these studies were small (n=50,60) and may have lacked the power to detect a clinically significant association.

There is inconsistent evidence regarding the impact of emotion-focussed coping strategies from three longitudinal studies. Two used the WCCL to measure coping. In the first and largest of these, the emotion-focussed strategy of “counting one’s blessings” predicted less caregiver burden 15-18 months later in 95 CG (Vitaliano et al. 1991). Positive reappraisal did not predict subsequent anxiety, depression or stress in a second, smaller (n=50) longitudinal study (Vedhara et al. 2001). Finally, Winslow (1997) found that the single coping style they measured using a non-validated method, management of meaning, was not associated with anxiety a year later.

In summary, most evidence from cross-sectional studies is that emotion-focussed coping is associated with decreased CG depression, burden, role overload and greater satisfaction and positive adjustment reported. Depression was included as an outcome measure in five studies; three reported an association with lower levels of emotion-focussed coping, and two no association. One study found that emotion-focussed coping was associated with reduced anxiety and one found no such association. Evidence regarding emotion-focussed coping and health outcomes from longitudinal studies is scarce and inconsistent, but more emotion-focussed coping was associated

with decreased burden subsequently in the larger of two studies that used a validated measure of coping.

1.5.3.3 Combined Problem-Focussed And Emotion-Focussed Strategies

Several authors have used scales that include problem-focussed coping strategies together with emotion-orientated factors; most have found these styles of coping are associated with better health outcomes. Pratt et al. (1985) reported that “confidence in problem-solving” which also measures sense of mastery was associated with decreased burden. Five further cross-sectional studies examined coping styles that combined problem-solving with emotion-focussed coping strategies. In two, these measures (that included problem-solving and acceptance and positive reappraisal respectively) were associated with increased CG life satisfaction and decreased depression (Haley et al. 1996) and not experiencing burnout (Almberg et al. 1997). In the third study, Powers et al (2002) administered the Beck Depression Inventory (BDI) and the Indices of Coping Responses at four time points and compared mean values on each measure; active behavioural coping which is comparable to problem solving but also includes seeking emotional support, did not correlate with depression scores.

Seeking social support is a subscale of the WCCL which is probably best classified as a combination of problem-focussed and emotion-focussed coping. In the instrument used in my study (the COPE) this concept was divided into seeking emotional support (emotion-focussed coping) and seeking instrumental support (problem-focussed coping). Seeking social support was positively associated with depression and anxiety (Neundorfer 1991) in one study using the WCCL, but in a second there was no association of this scale with anxiety, and conflicting results for depression and stress (Vedhara et al. 2001). Interestingly, combined use of problem-focussed and emotion-focussed coping strategies have also been associated with lower plasma levels of D-dimer, an end-product of the coagulation cascade associated with increased

cardiovascular risk (Aschbacher et al. 2005). The authors suggest that this coping style buffered the impact of acute psychological stressors on procoagulant activity. In the only prospective study of combined problem and emotion-focussed coping strategies, Goode and colleagues (1998) found that this coping style mediated an effect between primary stressors (e.g. patient self-care and behavioural problems) and decreased depression and less deterioration in physical health a year later in 122 caregivers of people with AD.

In summary, combined problem-focussed and emotion-focussed coping has been associated with not experiencing burnout and increased life satisfaction, but results for depression and anxiety were conflicting. They were associated with decreased depression a year later in a single prospective study.

1.5.3.4 Dysfunctional Coping Strategies

Dysfunctional coping strategies have also been investigated in cross-sectional studies. Avoidance coping has been associated with increased depression (Ashley & Kleinpeter 2006; Haley et al. 1996), increased caregiver burden (Pett et al. 1988) and less life satisfaction (Haley et al. 1996). In addition, in one study it mediated the relationship between patient problem behaviours and caregiver depressive symptoms (Mausbach et al. 2006b). Wishing-emotive/wishfulness coping (comparable to denial) has been associated with reduced physical health and increased anxiety (Neundorfer 1991), increased depression (Neundorfer 1991; Williamson & Schulz 1993) and decreased psychological adjustment (Pruchno & Resch 1989); regressive coping styles were associated with increased caregiver burden and low life satisfaction (Pett et al. 1988); grieving, worrying and self-accusation strategies with greater burnout (Almberg et al. 1997) and passivity (behavioural disengagement) (Pratt et al. 1985); and criticism (comparable to venting) (Hinrichsen & Niederehe 1994) with increased caregiver burden. Gottlieb and Gignac (1996) found that while “changing and avoiding

distressing topics” was associated with increased psychiatric symptoms and decreased life satisfaction, perhaps surprisingly “admonishing oneself not to express emotion” was associated with increased life satisfaction (Gottlieb & Gignac 1996). Perhaps people who do not like to openly express emotion are more prone to social desirability bias when completing questionnaires.

Dysfunctional coping strategies have only been investigated in two longitudinal studies. Using more of the coping strategy *escape-avoidance* predicted greater anxiety, depression and self-perceived stress and decreased vitality and self-perceived emotional functioning six months later; while using *confrontative coping* predicted anxiety and self-perceived stress six months and a year later (Vedhara et al. 2001). Distancing was not associated with subsequent anxiety or depression on multivariate analyses. Secondly, McClendon and colleagues (2004) found that higher CG wishfulness-intrapsychic (but not avoidance or instrumental) coping scores on an unvalidated measure were associated with decreased survival time of the person with dementia for whom they were caring (after controlling for morbidity factors of the person with dementia) in a cohort of 193 people with probable or possible AD and their CG recruited to an AD research centre from 1993 to 1997, who were followed-up until 2002. They suggest as a possible mechanism for this unreplicated finding that caregivers engaging in wishfulness-intrapsychic coping are less psychologically available to the person with dementia, provide less person-centred care, and thus they may inadvertently contribute to excess disability and consequent accelerated decline. They comment that interventions to enhance coping skills among caregivers have focused primarily on increasing problem solving and acceptance coping, but including components to reduce wishfulness-intrapsychic approaches may benefit the CG and person with dementia.

In summary, there is good evidence that dysfunctional coping strategies are associated with more caregiver burden and a range of adverse caregiver health outcomes cross-sectionally, including consistent evidence for a positive association with anxiety and depression. They have been associated with more CG depression, anxiety and stress as well as other adverse health outcomes six to twelve months later in one longitudinal study with significant limitations that I have discussed previously. In a second cohort study that used an unvalidated coping measure, they were associated with decreased survival time of the person with dementia.

1.5.3.5 Interventions Targeting Coping

Many trials of interventions for caregivers have now been evaluated some of which have attempted to modify coping. Roth and Fonagy (1996) reported mixed but promising results for psychological interventions aimed at improving coping strategies of CG; including: psychoeducation, psychodynamic and cognitive-behavioural treatments addressing depression, behavioural management techniques for the person with dementia, and coping skills training (stress reduction, assertiveness, and problem-solving skills). They concluded that no single intervention could be identified as a treatment of choice. Three recent reviews of the CG intervention literature have concluded that: psychoeducational and psychotherapeutic interventions showed consistent short-term effects on all outcome measures (Sorensen et al. 2002); the overall mean effect size for psychosocial interventions with CG was 0.3 for reduction in CG psychological morbidity, but there was insufficient evidence to make recommendations regarding what type of interventions might be most helpful (Brodaty et al. 2003); and that psychoeducational interventions that require active participation of caregivers had the broadest effects (Pinquart & Sorensen 2006).

A difficulty with these reviews is that they classified the different types of intervention into very broad categories, and do not distinguish in their conclusions, for example,

between psychoeducational interventions specifically targeting coping skills and those teaching behavioural management techniques. This is partly due to the heterogeneity of the interventions. Selwood et al (2007) classified interventions according to their predominant component, and found that there was evidence that teaching caregivers coping strategies either individually or in a group reduced levels of depression. An important question is what type of coping strategies were encouraged or discouraged in these studies, and to explore this I reviewed all of the coping interventions they included in their review that were considered to be of good or excellent validity (i.e. CEBM criteria for Level 1 or 2 studies (see Figure 1.2, page 58). I also searched the electronic databases MEDLINE (1951-) and PsychINFO (1887-) for all coping intervention studies in CG published after the period of their review (July 2003 – August 2006).

Figure 1.2 Oxford Centre for Evidence-based Medicine Levels of Evidence

(Centre of Evidence Based Medicine 2006)

Level	Therapy/Prevention, Aetiology/Harm	Differential diagnosis/symptom
		prevalence study
1a	SR (with homogeneity) of RCTs	SR (with homogeneity) of prospective cohort studies
1b	Individual RCT (with narrow Confidence Interval)	Prospective cohort study with good follow-up****
1c	All or none	All or none case-series
2a	SR (with homogeneity) of cohort studies	SR (with homogeneity) of 2b and better studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study, or poor follow-up
2c	“Outcomes” Research; Ecological studies	Ecological studies
3a	SR (with homogeneity) of case-control studies	SR (with homogeneity) of 3b and better studies
3b	Individual Case-Control Study	Non-consecutive cohort study, or very limited population
4	Case-series (and poor quality cohort and case-control studies)	Case-series or superseded reference standards
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or “first principles”	Expert opinion without explicit critical appraisal, or based on physiology, bench research or “first principles”

1.5.3.5.1 The “Coping with Caregiving” Programme

Four of the studies reported by Selwood and colleagues (all Level 2, i.e. studies of good quality) evaluated a caregiver training programme developed by Gallagher-Thompson and colleagues, delivered as a group intervention in three studies (Coon et al. 2003; Gallagher-Thompson et al. 2001; Gallagher-Thompson et al. 2003) and comparing a video based training package delivered in a group and individual setting in the fourth (Steffen 2000). This programme, entitled “Coping with Frustration” and subsequently “Coping with caregiving” involved eight to ten weekly sessions, which included CBT cognitive change strategies to manage anger and frustration by identifying and challenging dysfunctional thoughts; relaxation; assertiveness training to help CG avoid passive-aggressive, avoidant styles of communication; and encouragement through positive self statements. This heterogeneous intervention therefore involves promotion of problem-solving, and emotion-focussed strategies and avoidance of dysfunctional coping strategies. Depression scores were significantly decreased in all the study treatment groups compared with controls, although in the video based study the reduction was only significant in the individual but not the group treatment group when the intervention groups were analysed separately. Anger intensity was reduced in the two studies measuring this (Coon et al. 2003; Steffen 2000) and Steffen and colleagues (2000) also found that self-efficacy scores increased. Only Gallagher-Thompson (2001) measured burden and found it was not significantly decreased. This could support a hypothesis that coping strategies mediate the impact of burden on CG mental health but do not change the levels of burden experienced, although burden does include a subjective component that might be expected to respond to the intervention. Subsequent analysis from results of the trial by Gallagher-Thompson (2003) indicated that low

baseline self-efficacy scores predicted a better response to the Coping with Caregiving programme (Rabinowitz et al. 2006).

1.5.3.5.2 The “Taking Care of Myself” programme

The conceptual framework for this intervention was derived from Lazarus and Folkman’s transactional theory of stress and coping, and the main focus was to promote use of problem solving, positive reframing and seeking social support coping strategies (Levesque et al. 2002). It has been evaluated in two RCTs. Hebert et al (2003) found no difference in levels of depression, anxiety and burden in the intervention group compared to the controls immediately after delivery of the intervention in CG, over 80% of whom were living with the person for whom they cared. The second RCT involved daughters caring for their elderly parents with dementia who were living in a long term care facility; those who took part in the experimental programme demonstrated a significant reduction in perceived threat and role overload, compared with those in a comparison programme offered by the Quebec Alzheimer Society (n = 51), and a control group (n = 41). They also demonstrated increased use of the coping strategy positive reframing in the experimental group post-intervention that was maintained three months later, while perceived availability of informal and formal support was a persistent effect in both the experimental and Alzheimer’s Society group (Ducharme et al. 2005). The authors also asked caregivers about their recollections of the intervention in semi-structured interviews, and found that they most frequently recalled reframing as the aspect they found most helpful, while problem-solving coping and seeking social support were less frequently endorsed as helpful (Lavoie et al. 2005).

1.5.3.5.3 Other interventions involving emotion- and problem-focussed coping

Selwood and colleagues found two Level 1 (the highest quality evidence: see Figure 1.2) involving interventions that promoted use of emotion-focussed and problem-focussed coping, and both demonstrated significant decreases in depression levels as well as

improvements in other psychological outcomes. In the first, Hepburn et al. (2001) found that depression and burden decreased significantly in a group receiving weekly two hour group training sessions over the course of seven weeks, which included information giving sessions and coping training. Caregivers were guided to develop coping strategies that were tailored to the stage of dementia. The workshop emphasised that the caregiver's role did not include goals associated with rehabilitation or delaying the course of the disease, and encouraged them to care for their own needs and to consider the emotional impact of their actions on the person with dementia realistically. An example of this would be understanding that making decisions the person with dementia can no longer make will probably lower their levels of frustration and not damage their self-esteem. Caregivers received problem-solving suggestions, as well as encouragement to strengthen their beliefs in their own abilities. The ability to view the caregiving situation with some distance and thereby develop strategies for dealing with immediate and recurring caregiving situations was emphasised. The coping strategies taught by this intervention include acceptance, seeking emotional support, positive reframing, unspecified problem-solving techniques, and possibly also distancing (which Carver (1989) classified as a dysfunctional strategy).

The second study (Marriott et al. 2000) found that a cognitive-behavioural family intervention of 14 fortnightly sessions of caregiver education, stress management and coping skills training delivered by an experienced consultant clinical psychologist, improved caregiver psychological distress and depression both immediately and three months later. The stress management involved a thorough assessment of the caregiver's current appraisal and response to stressors, including avoidance, self-sacrificing and isolating behaviour. More adaptive methods of managing personal stress were then taught, including self-monitoring, relaxation training and cognitive and behavioural responses. The coping skills sessions included advice and role-play concerning more

effective ways to respond to problematic patient behaviours, and exercises to address caregivers' feelings of loss concerning changes in the patient or alterations to their own quality of life. This intervention therefore combined promoting acceptance and problem-solving coping strategies and discouraging dysfunctional strategies including avoidance.

1.5.3.5.4 Interventions involving emotion-focussed coping only

Two studies which promoted use of emotion-focussed strategies led to a significant decrease in depression. The first involved emotional support and relaxation training, and written information about managing resentment, grief, guilt and isolation (Sutcliffe & Lerner 1988). The second included a complex programme for the CG and person with dementia, including psychotherapeutic individual and art therapy, relaxation, social work consultation, support groups and an educational programme for the CG (Romero & Wenz 2001).

1.5.3.5.5 Interventions involving problem-focussed coping

Only two studies reported that the coping intervention they evaluated was ineffective and these were the only two that did not include an emotion-focussed coping component. Gendron (1996) found that there was no difference in depression, anxiety or burden in an RCT of an intervention that appeared very similar to the "Coping with caregiving" training. It included components from that programme that focussed on reducing dysfunctional and promoting problem-focussed strategies but omitted the relaxation and encouragement of positive self statements modules that constituted the emotion-focussed aspects (see Table 2.3, page 86 for more details of this study). Secondly, an RCT of an intervention that taught problem-focussed coping found no difference in burden scores between intervention and control groups (Roberts et al. 1999).

1.5.3.5.6 Interpretation of Intervention studies

The interventions predominantly based on coping strategies that have demonstrated efficacy in decreasing depression all included strategies to promote emotion-focussed coping skills and all but two also promote problem-focussed strategies, so it is difficult to ascertain whether emotion-focussed strategies alone or both of these components are effective. The most conclusive evidence was in favour of a training programme that included promotion of emotion-focussed and problem-focussed strategies and discouragement of dysfunctional coping strategies, which appeared to decrease depression but not caregiver burden. The only two interventions that involved coping modification as their primary intervention that failed to demonstrate efficacy involved either promoting problem-focussed coping alone (Roberts et al. 1999) or together with discouraging dysfunctional coping strategies (Gendron et al. 1996). Interestingly, Morris et al. (1992) evaluated a problem-solving course on coping for CG compared with attendance at seminars on dementia, and found that both groups showed a significant increase in problem-focused strategies and a decrease in distancing coping strategies but that there was no change in levels of depression or strain. This would suggest that the failure of interventions focussing on problem-focussed and dysfunctional strategies alone to reduce morbidity is not due to a failure to modify coping.

Virtually all of the interventions combined didactic teaching of coping skills with some kind of interactive component to the intervention, supporting previous findings that active CG participation is associated with greater efficacy for coping and other interventions (Pinquart & Sorensen 2006; Selwood et al. 2007).

In this chapter I have discussed the current literature regarding the association of coping style with a range of psychological outcomes in CG, and the impact of interventions that attempt to modify coping on their psychological morbidity. In chapter two I will focus

on anxiety, my proposed primary outcome measure and explore the prevalence, correlates and potential treatments for anxiety in CG in a systematic literature review.

2 ANXIETY PREVALENCE, CORRELATES AND TREATMENT IN DEMENTIA CAREGIVERS: A SYSTEMATIC REVIEW

(see publications in Appendix F).

2.1 Method

2.1.1 Search strategy

I searched:

- Electronic databases namely: Allied & Complementary Medicine (1985-); British Nursing Index (1994-); CINAHL (1982-); EMBASE (1974-); MEDLINE (1951-); and PsycINFO (1887-) for studies published up to June 2005, using the terms “carer” or “caregiver”, combined with “dementia” or “Alzheimer’s disease” and “anxiety”.
- Reference lists of all included papers and relevant systematic reviews.

Five experts in the mental health of CG were contacted, to ask if they knew of further studies and I included them even if they were published after this date.

2.1.2 Inclusion and Exclusion Criteria

I included primary research studies with quantitative outcome measures of anxiety in informal (friend and family) caregivers of people with any type of dementia, published in English, that reported prevalence, correlates, predictors or the effects of an intervention for anxiety. I excluded qualitative studies, dissertation abstracts and secondary research, and single case studies. I also excluded studies that were rated as the lowest Level of evidence (Level 5) by the Oxford Centre for Evidence Based Medicine (CEBM) (see Figure 1.2, page 49), i.e. results that were not tested statistically and did not include information to enable me to do so.

2.1.3 Assessing validity

I extracted data from all papers meeting my inclusion criteria, dividing them into prevalence, correlate and treatment studies.

2.1.3.1 Prevalence Studies

Validity of prevalence studies was evaluated using the following checklist (Boyle 1998).

With my supervisor (GL), I determined how many of seven criteria for rating the validity of prevalence studies were met. These were:

A. Sampling - Does the survey design yield a sample of respondents representative of a defined target population?

1. Was the target population defined clearly?
2. Was probability sampling used to identify potential respondents?
3. Did the characteristics of respondents match the target population?

B. Measurement - Did the survey instruments yield reliable and valid measures of psychiatric disorder and other key concepts?

4. Were the data collection methods standardised?
5. Were the survey instruments reliable?
6. Were the survey instruments valid?

C. Analysis

7. Were special features of the sampling design accounted for in the analysis?

We discussed each study and resolved discrepancies through discussion to reach consensus. I also calculated confidence intervals for the study prevalence estimates, using standard statistical software.

2.1.3.2 Correlate And Treatment Studies

I assigned all other studies to a Level of evidence according to CEBM guidelines (http://www.cebm.net/levels_of_evidence.asp#levels) (see Figure 1.2, page 49). Levels of evidence range from 1-5 with lower numbers indicating higher quality. I included studies rated Level 1b to Level 4 in this review.

For correlate studies examining levels of anxiety symptoms the levels assigned to papers included were:

Level 1b - Prospective cohort studies with good (>80%) follow-up with adequate time for alternative diagnoses to emerge (eg 1-6 months acute, 1 - 5 years chronic)

Level 2b - Retrospective cohort studies

Level 2c - Ecological studies

Level 3b - individual case-control studies with: clearly defined comparison groups, blinded or self rated measures of anxiety and other outcomes, that controlled for known confounders

Level 4 – Case series, poor quality (i.e. not meeting above criteria) cohort and case control studies

For treatment studies the levels assigned to papers included were:

Level 1b - Good quality Randomised Controlled Trials (RCTs) that were randomised with concealment, double-blinded, had complete follow-up (over 80%), intention-to-treat analyses, and narrow confidence intervals

Level 2b - Prospective cohort studies with good (>80%) follow-up with adequate time for alternative diagnoses to emerge (eg 1-6 months acute, 1 - 5 years chronic) and RCTs not meeting criteria for Level 1b

Level 4 - Cohort studies not meeting the above criteria

2.1.3.3 Procedure

A second rater (TB) also assigned levels of evidence to each study independently and if disagreements occurred then the reasons behind each decision were discussed among both raters and my supervisor (GL) until a conclusion was agreed. Each category of association was then given an overall Grade of evidence ranging from A to D according to the CEBM criteria. A Grade of A which represents consistent Level 1 studies indicates the best evidence; a Grade of B represents consistent Level 2 or 3 studies; a Grade of C represents evidence from Level 4 studies, extrapolations from Level 2 or 3 studies or findings from a single Level 1 or Level 2 study, where no other Level 1 or 2 study existed. A Grade of D is the lowest and represents troublingly inconsistent or inconclusive studies at any Level. These grades indicate the confidence with which any conclusion can be drawn, about whether a factor is associated with anxiety or not, or whether a treatment is effective or ineffective for alleviating anxiety in CG.

2.2 Results

I found 530 references; 451 could be excluded from the title and abstract as not relating to prevalence, correlates or treatment of anxiety in caregivers of people with dementia, leaving 89 abstracts. I included 56 of these (23 treatment and 33 prevalence and correlate studies), after excluding those that did not include: results for anxiety (n=10) or CG separately (n=8); quantitative anxiety measurement (n=10); current caregivers (n=1); or original research (n=2) and those rated as Level 5 studies (n=2).

2.2.1 Prevalence studies

Eight studies reported the prevalence of anxiety disorders or caseness, and validity of these studies is reported in Table 2.1 (page 62). Prevalences ranged from 3.7% to 76.5% depending on the time period covered, the population interviewed and the definition of anxiety caseness used.

Three studies used diagnostic interview schedules to make DSM-III-R (Dura et al. 1991; Russo et al. 1995) or ICD-10 (Coope et al. 1995) diagnoses. A fourth study used the Hospital Anxiety and Depression Scale (HADS) (Mahoney et al. 2005), with a cut off point for determining anxiety caseness (11+) that has demonstrated adequate psychometric properties, although it is higher than the cut point I used in this study (Bjelland et al. 2002). The remaining four studies did not use valid measures of anxiety caseness, because they either did not use accepted cut-off points for defining caseness (Neundorfer 1991; Vitaliano et al. 1991), did not use the measure in the conventional way (Sanson et al. (2004) administered the instrument three times a day for nine days); or used unstandardised diagnoses (reports to an insurance company) (Kolanowski et al. 2004).

Of the four studies reporting prevalence that used valid measures of anxiety, two were prospective studies. The first (Coope et al. 1995) interviewed all CG identified from a case note review of people with mild or moderate dementia newly referred to a UK old age psychiatry service. Caregivers were included if they were in contact with the person with dementia at least once a week and considered themselves caregivers. The second (Mahoney et al. 2005) interviewed CG purposively recruited from London and the surrounding area to be representative of people with dementia living in the community in terms of disease severity, gender and care setting. In fact the Mahoney et al. (2005) study was based on the six month follow-up of the LASER-AD study cohort, while my study is based on the eighteen and thirty month follow-ups from the LASER-AD study. The CG were included in this study if they provided at least four hours care to the person with dementia per week. These surveys reported very different anxiety prevalences (3.7% (Coope et al. 1995) and 23.5% (Mahoney et al. 2005)), probably because Coope et al. (1995) used a hierarchical diagnosis approach so that any person who was depressed could not score as anxious, whereas the other (Mahoney et al. 2005)

examined these diagnoses separately. In the study recording separate diagnoses (Mahoney et al. 2005), 81.3% of depressed cases were also anxiety cases. If these proportions were extrapolated to the hierarchical sample (Coope et al. 1995), then 27.6% would be anxiety cases.

The other two studies that used valid measures of anxiety were retrospective cohort studies carried out in the USA. Both asked CG about anxiety over the entire duration of caregiving, so it is at first perhaps surprising that prevalence rates were lower in these studies. Recall bias may partly explain the lower rates, as may the more stringent criteria for defining cases. Russo et al (1995) reported a 16% prevalence of GAD among spouse CG, over the duration of caregiving, which was for on average four years. Dura et al (1991) reported a 10% prevalence of anxiety disorders in CG caring for parents over the duration of caregiving (average 2.5 years). Both recruited participants from a range of community and clinical sources and did not aim to recruit epidemiologically representative samples.

2.2.1.1 Comparing Caregivers With Non-Caregivers

Three studies compared the prevalence of anxiety disorders in CG with non-caregivers. The two retrospective cohort studies reported above (Dura et al. 1991; Russo et al. 1995) found no significant difference in the prevalence of DSM-III-R anxiety disorders before the onset of caregiving, and in the corresponding period of time in healthy controls, but caregivers experienced significantly more anxiety disorders during caregiving than controls over the same time periods. In addition, a retrospective study (Kolanowski et al. 2004) which did not include a valid measure of anxiety found that among people registered with a private health insurer, the spouses of people with dementia were almost three times more likely to have sought treatment for an anxiety disorder in the past four years than matched controls.

Table 2.1 Studies reporting prevalence of anxiety in dementia caregivers

Study	Population	N	Measure of anxiety	Prevalence period	Prevalence + 95% CI (%)	Validity question answers (see page 57)							
						1	2	3	4	5	6	7	Sum
Mahoney (2005)	Caring \geq 4 hrs/ wk	153	HADS	Week	23.5 (16.8-30.2)	✓	x	✓	✓	✓	✓		5
Coope (1995)	Caregiving \geq once/ week	125	GMS diagnostic interview	Month	3.7 (0.4-7.0)	✓	x	x	✓	✓	✓	x	4
Dura (1991)	Adult caring for parent	78	SCID/ DSM-III-R diagnoses	Caring duration	10 (3.3-16.7)	✓	x	x	✓	✓	✓	x	4
Russo (1995)	Co-resident spouse	82	DIS-III-R diagnoses	Caring duration	16 (8.1-24.1)	✓	x	x	✓	✓	✓	x	4
Neundorfer (1991)	Co-resident spouse	60	Any anxiety symptom on BSI	Week	15 (6.0-24.0)	✓	x	x	✓	✓	x	x	3
Sansoni (2004)	Female co-resident	34	STAI>40	3x /9 days	76.5 (62.2-90.8)	✓	x	x	✓	✓	x	x	3
Vitiliano (1991)	Co-resident spouse	95	SCL-90 score >1 sd \uparrow mean	Week	35.4 (25.8-45.0)	✓	x	x	✓	✓	x	x	3
Kolanowski (2004)	Spouse	979	Diagnosis reported	3 years	7.1 (6.5-8.7)	✓	x	x	x	-	-	x	1

2.2.1.2 Factors Associated With Caregiver Anxiety Caseness Or Diagnosis

There was a marked lack of evidence regarding factors associated with anxiety caseness. This included only one longitudinal study (discussed above), which reported that a past history of depression or anxiety predicted caregiver anxiety caseness (Russo et al. 1995). In addition, two cross-sectional studies were found. Graham et al (1997) found that *more* CG knowledge about dementia was associated with an anxiety disorder diagnosis (using the Geriatric Mental State Schedule) in caregivers of people referred consecutively to a UK memory clinic and old age psychiatry service. The second cross-sectional study by Mahoney et al. (2005) (see Table 2.1, page 62), reported that being a female caregiver, worse subjective physical health, living with and reporting a worse relationship with the person with dementia and caring for someone with more Activities of Daily Living (ADL) impairments, were all associated with being an anxiety case on multivariate analysis. Caregiver factors that were not associated with caregiver anxiety caseness were: employment status, their relationship (spouse, sibling etc.) with the CG and having dependent children.

Summary:

- As no putative predictors or covariates of anxiety caseness have been considered in more than one study there is no conclusive evidence about any of them although preliminary evidence suggests that characteristics relating to both the caregiver and the person with dementia are important.

2.2.2 Studies of factors associated with anxiety

2.2.2.1 Study Quality

I found only two Level 1 studies (the highest Level of evidence) investigating correlates; nine Level 2 studies, eleven Level 3 and three Level 4 studies. They used eight different measures of anxiety. Adequate psychometric properties have been reported for five of

these: the Spielberger Trait Anxiety measure (STAI) (Oei et al. 1990); the HADS (Bjelland et al. 2002); the Brief Symptom Inventory (BSI) (Derogatis 1993), the Symptom Checklist (Derogatis et al. 1973) and the Kellner Symptom Questionnaire (Thompson et al. 2004). The General Health Questionnaire-28 (GHQ-28) was intended as a screening instrument for psychiatric morbidity, and the validity of using the anxiety subscale alone has been questioned (Koeter 1992). For the Savage Personality Screening Scale (SPSS) and the General Wellbeing Adjustment Scale (GWAS) adequate reliability has been reported, but data regarding validity was not available from these or other studies.

Only one study included a power calculation (Croog et al. 2001) (demonstrating a power of 78% to detect a clinically significant reduction in effect), but it is possible that other studies were based on a power calculation that was not reported. The number of CG recruited varied from 34 to 720 (see Table 2.2, page 78) so it is likely that some of the studies were underpowered to detect a clinically significant association with anxiety, and there is also a possibility of Type I errors (studies demonstrating statistically significant differences that are not of clinical significance) in the larger studies. None of the studies explicitly designed their recruitment strategy to ensure that the sample recruited were representative of all CG. Recruitment practices varied widely, and included advertising via local and national media, clinical and community sources such as the National or local Alzheimer's Disease Associations (ADA) and day centres. All of these are subject to bias regarding the CG that are likely to be attending or respond to media adverts. A further variation was that many of the USA-based studies paid subjects (for example average payment to REACH study participants was \$101 (Tarlow & Mahoney 2000), while in UK studies participants were not reported to receive payment.

2.2.2.2 Cohort Studies (Table 2.2, page 78)

I found two Level 1 and two Level 4 studies which examined factors predicting anxiety levels longitudinally. The first Level 1 study recruited co-resident spousal caregivers from a UK memory clinic (Vedhara et al. 2001). Only factors that correlated with anxiety levels on cross-sectional analyses were entered in the regression analysis. *Neuroticism* predicted anxiety six months later. Using more of the dysfunctional coping strategy *escape-avoidance* (see Figure 1.1, page 34 for content of coping scales which are from the WCCL) predicted anxiety six months later but not twelve months later. Using a second dysfunctional strategy *confrontative coping* predicted anxiety six and twelve months later. The emotion-focussed strategies of accepting responsibility and self-controlling coping and the dysfunctional strategy of distancing were included in the multivariate analysis because they were significantly associated with (more) anxiety on univariate cross-sectional analyses but were not predictors of anxiety longitudinally. The second Level 1 study (Stephens et al. 1991) recruited caregivers who visited someone with dementia living in a care home at least once a week, through nursing homes, the ADA and a registry of people who had previously used a respite care program. They investigated the role of caregiver hassles in predicting anxiety. Items on the following subscales were rated by the CG from 0 (not at all a hassle) to 4 (a great deal of a hassle): degree of ADL, behaviour and cognitive impairment of the person with dementia, interactions with nursing home staff and practical problems with visiting. Only caregiver hassles relating to the degree of cognitive impairment of the person receiving care predicted anxiety six months later.

In a Level 4 study (Chang et al. 2001) involving co-resident primary CG recruited from the ADA and dementia clinics, only *the caregivers reporting higher levels of education*, and, in a reduced model containing factors approaching significance in earlier analyses, being a *younger caregiver*, and caring for someone with *more behavioural problems*

predicted anxiety levels eight weeks later. Caregiver gender, marital status, number of roles undertaken (for example employment, motherhood), years they had been caregiving and measures of social support were not associated with anxiety. The age and ADL scores of the person receiving care were also not associated with anxiety.

Another Level 4 study (Winslow 1997) reported data from CG recruited through the ADA, local newspaper advertisements and newsletters for caregiver groups, some of whom cared for someone living in fulltime care. Anxiety at one year was predicted by caring for a more dependent person; caregiver subjective burden; and baseline anxiety. Factors not predicting anxiety levels were: caregiver age, gender, relationship to the person cared for; ADL, Instrumental ADL (IADL), behavioural problems and use of formal support of the person with dementia; and an unvalidated measure of coping described as “management of meaning”. The content of only one of the six coping scale items: “How often do you remind yourself that others are worse off?” was reported, so it was not possible to classify the type of coping strategy although this item would appear to be a type of emotion-focussed coping.

Summary:

There is Grade C evidence (evidence from single studies) that: caring for someone who was more dependent; confrontative coping strategies; caregiver subjective burden and baseline anxiety predict anxiety a year later.

There is Grade C evidence that: neuroticism; confrontative coping strategies and more hassles caused by the cognitive impairment of the person receiving care predicted anxiety six months later.

There is Grade C evidence that higher levels of caregiver education and younger caregiver age predict anxiety eight weeks later.

There is Grade C evidence that anxiety is *not* predicted by: caregiver hassles relating to the degree of ADL or behaviour impairment of the person receiving care,

interactions with nursing home staff or practical problems with visiting six months later; caregiver gender, marital status, number of roles undertaken (employment, mother), years they had been caregiving, social support, the age and ADL scores of the person with dementia eight weeks later; and the coping strategies of accepting responsibility, discrepancy in social support, distancing, and self-controlling coping at six months or a year; and receipt of formal support for the person with dementia or “management of meaning” coping at a year, as all these factors were reported in Level 4 or single Level 1 studies.

There is Grade D evidence for the level of behavioural problems exhibited by the person with dementia and the coping strategy escape-avoidance because the evidence is inconsistent.

2.2.2.3 Cross-Sectional Studies Investigating Covariates Of Anxiety Levels

Twenty-one cross-sectional studies reporting covariates of levels of anxiety symptoms were found.

2.2.2.3.1 Studies Comparing Cg With Other Groups

Three studies compared levels of anxiety in co-resident spousal CG with healthy controls. Two reported that anxiety scores were significantly higher in caregivers (Bauer et al. 2000; Quayhagen 1997). These included a study comparing CG recruited from a UK memory clinic to healthy matched controls recruited for previous research (Bauer et al. 2000); and a USA study (Quayhagen 1997) comparing spousal CG and healthy controls, recruited from the ADA and community agencies. The third (Shaw et al. 1997) found that American spousal caregivers recruited from clinical sources and community support groups were more anxious than controls, but this was not true of Chinese CG recruited for a large-scale epidemiological research program compared with healthy controls from the same survey.

Three further studies compared mean levels of anxiety in CG with reference normal values on the SCL-90R (Stephens et al. 1991) and the BSI (Anthony-Bergstone et al. 1988; Neundorfer 1991). These included two studies which found higher anxiety scores in the caregivers; these involved caregivers for people in care homes or in the community, recruited through nursing homes, ADA and previous contact with a respite care program (Stephens et al. 1991), and co-resident spousal CG recruited mainly from a hospital research registry (Neundorfer 1991). A third study (Anthony-Bergstone et al. 1988) found higher rates of anxiety in female, but not male primary CG recruited in the USA to a caregiver training program. In addition, one study (Crespo et al. 2005) found that primary CG who had been caring for at least six months had higher anxiety levels than caregivers of people who were cognitively intact.

Summary:

There is Grade B evidence that CG have higher anxiety levels than those reported for healthy controls and normal reference values, from Level 1 and 2 studies.

There is Grade C evidence that caregivers for people with dementia are more anxious than caregivers for people who are cognitively intact as this has been demonstrated in a Level 2 study.

2.2.2.3.2 Factors Associated With Anxiety Levels

2.2.2.3.2.1 Caregiver stress and morbidity

Caregivers who experienced more burden had higher anxiety levels in three Level 2 studies of: primary CG recruited to a caregiver training program (Anthony-Bergstone et al. 1988); CG who looked after a parent recruited through Alzheimer disease clinics, newspaper advertisements and ADA newsletters (Parks & Pilisuk 1991); and consecutive CG attending fifteen Italian geriatric clinics (Marvardi 2005; Rinaldi et al. 2005). A fourth Level 2 study reported two multivariate cross-sectional analyses conducted three months apart, in spousal CG of people attending a UK memory clinic

(Vedhara et al. 2000). Higher anxiety scores were associated with the number of caregiving hassles in the last month and the number of caregiver life events in the last three months, but each in only one of the two analyses. The number of caregiving difficulties, which is one subscale of the Burden Interview (the other scale, indicating associated distress, was not included) did not correlate with anxiety in either analysis.

Anxiety scores have also been correlated in studies previously discussed with: more hassles relating to the morbidity of the person with dementia in caregivers of people receiving residential care (Stephens et al. 1991); higher depression levels and poorer physical health in Italian female co-resident CG recruited from a dementia out-patient clinic (Sansoni et al. 2004); and poor physical health in CG of people living at home and in institutional care, recruited through the ADA, local newspaper advertisements and carer group newsletters (Winslow 1997). No relationship was found between anxiety scores and heart rate reactivity to stressful situations in CG aged fifty and over, recruited from the local ADA, carer resource and counselling centres (Knight & McCallum 1998).

Summary:

There is Grade B evidence that more caregiver anxiety was associated with higher levels of caregiver burden and physical health problems as these findings were replicated in Level 2 studies.

There is Grade C evidence that caregiver anxiety was associated with more hassles related to the degree of morbidity of the person receiving care and higher caregiver depression levels, as these associations were found in single Level 2 studies.

There is Grade C evidence that heart rate reactivity to stressful situations was not related to anxiety as this was reported in one Level 3 study.

There is Grade D evidence regarding the relationship of more caregiving hassles in the last month and life events in the last three months to anxiety, because the evidence is inconsistent.

2.2.2.3.2.2 Caregiver coping

Five studies report the association between coping strategies and anxiety in CG. Two were Level 2 studies both of which recruited spouses of people with dementia. In the first they were recruited from a hospital research registry (Neundorfer 1991); in the second, which conducted separate analyses at three time points (0, 6 and 12 months) of a longitudinal study, they were recruited from a UK memory clinic (Vedhara et al. 2001). Both reported correlations of anxiety levels with the eight subscales of the WCCL (see Figure 1.1, page 34) on univariate analysis. More use of *confrontative coping* and *escape avoidance* were the only factors that were correlated with greater anxiety in all four of these analyses (all $p < 0.001$). Using more of the coping style *positive reappraisal* was the only factor *not* to be correlated with anxiety at all four time points. Both studies used factors derived from the WCCL subscales by principal components analyses in multivariate analyses, and *confrontative coping* and *escape avoidance* were the only coping styles represented in the factors associated with anxiety in the analyses of both studies.

In a third study (Level 3), CG were recruited from clinical sources and community support groups, and a large-scale epidemiological research program in Shanghai (Shaw et al. 1997). The authors derived four factors from the WCCL subscores by principal axis factoring. These were: behavioural confronting (a combination of *planful problem solving* and *accepting responsibility*); behavioural distancing (most closely resembling *distancing*); cognitive confronting (coping that was predominantly *confrontative* and emotion-focussed in approach); and cognitive distancing (resembling *seeking social support*). In American caregivers, more use of cognitive confronting was the only factor significantly correlated ($p > 0.4$) with anxiety levels; none of the factors were

associated with anxiety in the Chinese caregivers. A fourth study (Parks & Pilisuk 1991) used subscales derived by factor analysis of CG responses to questions about how they coped with specific caregiving situations in adult child CG recruited through AD clinics, newspaper advertisements and ADA newsletters. The scales were: *objectifying* (planning, problem-focussed coping); *fantasy* (wishfulness, emotion-focussed) coping; *withdrawal* (behavioural disengagement, denial); and *internalising* (problem-focused style involving detachment). Only more use of *fantasy* coping correlated with anxiety.

In the fifth study (Proctor et al. 2002) which used the Miller behavioural style scale, more use of monitoring coping (tending to monitor for threatening information in stressful situations) was significantly associated with anxiety in CG recruited through UK day services on multivariate analysis; and blunting coping (tending to avoid information) was not.

Summary:

There was Grade B evidence that *confrontative* and *escape-avoidance* coping are associated with higher anxiety levels, as these associations were consistently reported by two Level 2 studies.

Positive reappraisal was consistently *not* associated with anxiety levels in two Level 2 studies (Grade B).

There was Grade C evidence that more use of *monitoring coping* and *fantasy coping* were associated with caregiver anxiety.

There was Grade C evidence that blunting, objectifying and internalising coping were *not* associated with caregiver anxiety.

Evidence was inconsistent (Grade D) for the strategies of accepting responsibility, distancing, self-controlling coping, planful problem solving, seeking social support; withdrawal coping; cognitive confronting, behavioural confronting, cognitive distancing and behavioural distancing.

2.2.2.3.2.3 Caregiver strengths

Reporting more positive aspects of caregiving (including feeling useful, appreciated, and satisfied with caregiving), and greater religiosity were associated with *less* anxiety in the REACH (Resources for Enhancing Alzheimer's Caregiver's Health) study (Roff et al. 2004). REACH recruitment criteria were that CG had been caring at least six months; were providing at least four hours care a day; to people with Mini-Mental State Examination (MMSE) scores of less than twenty-four, and at least one impairment in ADL or two impairments in IADL. At one of the four recruitment sites the person with dementia exhibiting at least three behavioural problems was a further inclusion criteria. Greater self-esteem and self-concept were associated with less anxiety in spousal CG of people attending a memory clinic (Vedhara et al. 2000). Among adult child CG recruited through AD clinics, newspaper advertisements and ADA newsletters, greater mastery (having an internal locus of control) in women only, and more informal (friend and family) support in men only were associated with less anxiety (Parks & Pilisuk 1991). Knowing more about biomedical aspects of dementia, but not knowledge about caring and coping with a person with dementia or health and welfare issues related to dementia care, was associated with *greater* caregiver anxiety on multivariate analysis (Proctor et al. 2002).

Summary:

There was Grade C evidence that more positive aspects of caregiving; greater religiosity; and greater self-esteem and self-concept are associated with *less* caregiver anxiety.

There was Grade C evidence that more knowledge about biomedical aspects of dementia was associated with *higher* anxiety levels.

There was Grade C evidence that more knowledge about caring and coping with a person with dementia and health and welfare issues related to dementia care were *not* associated with anxiety levels.

There was inconsistent evidence for caregiver mastery and having informal support (Grade D).

2.2.2.3.2.4 Abuse by caregivers

Studies involving CG have demonstrated that many will report committing abusive acts towards the person they are caring for in research studies. Higher levels of caregiver anxiety were associated with caregiver abusive behaviours towards the person they cared for with dementia in two studies that used unvalidated measures of abusive behaviour. Among spousal caregivers recruited from a research centre, the ADA and community agencies, in dyads where either the caregiver alone or both the caregiver and person with dementia had been reported as abusive in previous qualitative interviews, caregivers were more anxious than those from dyads in which neither partner or only the person with dementia was abusive (Quayhagen 1997). Compton (1997) asked caregivers of people referred to a Community Mental Health Team in Northern Ireland whether they had ever physically or verbally abused the person with dementia (which they defined). About a third of CG reported some verbal or physical abusive acts, and these CG reported higher levels of anxiety symptoms.

Summary:

There was Grade C evidence for an association between abusive behaviours towards a person with dementia and more caregiver anxiety, as this association was reported in a Level 2 and a Level 4 study.

There was Grade C evidence that caregivers from dyads where the person with dementia was abusive were *not* more anxious than those who reported that the person they cared for was not abusive.

2.2.2.3.2.5 Caregiver demographic factors

Three Level 2 studies (Croog et al. 2001; Neundorfer 1991; Parks & Pilisuk 1991) reported no association between caregiver age and levels of anxiety. These included two studies involving spouses of people with dementia, recruited from a hospital research registry (Neundorfer 1991) and a clinic for registration for a drug trial (Croog et al. 2001) respectively and a study of adult child CG, recruited through AD clinics, newspaper advertisements and ADA newsletters (Parks & Pilisuk 1991).

Findings for the relationship of anxiety to caregiver gender are inconsistent. Three Level 2 studies, which included spouses (Neundorfer 1991), adult children (Parks & Pilisuk 1991) and primary CG of people attending UK day services (Proctor et al. 2002), reported no association on multivariate analyses; husband caregivers were more anxious than wife CG attending a dementia drug trial recruitment clinic in one Level 2 study (Croog et al. 2001); while three studies (two Level 4 and one Level 3) of CG recruited from a variety of clinical and community sources (Hooker et al. 2000; Quayhagen 1997; Thompson et al. 2004) all reported that wife caregivers were more anxious than husbands. Neither the relationship of the caregiver to the person with dementia (spouse, child, etc) (which is likely to be confounded by age) (Proctor et al. 2002) (in a Level 2 study) nor, in the REACH study, the caregiver's socioeconomic status (Roff et al. 2004) (in a Level 3 study) were associated with caregiver anxiety.

Findings regarding the relationship of caregiver ethnicity to their anxiety levels are also inconsistent. In the REACH study (Level 3), anxiety levels in the Latin American female caregivers were not significantly different to those in White Americans, and did not differ with levels of acculturation (degree of adaptation to a new culture) (Coon et al. 2004); while African-American caregivers had lower levels of anxiety than White American caregivers (Haley et al. 2004; Roff et al. 2004) and were less likely to use

anxiolytic medication (Burgio et al. 2003). There were no differences between African and non-African Americans in a second Level 3 study (Knight et al. 2000; Knight & McCallum 1998) involving over 150 CG aged 50+ recruited from the local ADA, caregiver resource and counselling centres. Compared with White Americans, Korean and Korean American caregivers were reported to have higher levels of anxiety, in a Level 3 study (Youn et al. 1999). This study included Korean CG recruited from Korean senior centres, a telephone hotline for the elderly and the Korean Gerontological Research Society; Korean-American CG recruited from Korean language newspapers and resource centres in the USA; and White American CG recruited for the study discussed above (Knight et al. 2000). Among over 150 spouse CG who were from San Diego and Shanghai, Chinese caregivers reported less anxiety than White American CG (Shaw et al. 1997).

Duration of caregiving was not correlated with anxiety scores in primary CG of people attending UK day services (Proctor et al. 2002) or Italian female co-resident CG recruited from a dementia out-patient clinic (Sansoni et al. 2004), although a longer duration of dementia (Proctor et al. 2002) and more hours spent caregiving each week (Sansoni et al. 2004) were associated with less caregiver anxiety.

Summary:

There is Grade B evidence that there is *no* association between anxiety levels and caregiver age or duration of caregiving, as both findings have been replicated in Level 2 studies.

There is Grade C evidence that a longer duration of dementia and more hours spent caregiving each week are associated with less caregiver anxiety, as both were reported from single Level 2 studies.

There is Grade C evidence that there is no association between the relationship between the caregiver and person with dementia (spouse, child, etc) or caregiver

socioeconomic status and caregiver anxiety, as these are findings from individual Level 2 and 3 studies respectively.

Evidence for the relationship of CG anxiety to caregiver ethnicity and gender is inconsistent (Grade D).

2.2.2.3.2.6 Factors relating to the person with dementia

Three Level 2 studies (Croog et al. 2001; Proctor et al. 2002; Sansoni et al. 2004) found that there was no relationship between anxiety and level of cognitive impairment of the person receiving care. One (Croog et al. 2001) used the Patient Problem Scale in spouses of people with dementia attending a USA clinic for drug trial registration. The Mini Mental State Examination (MMSE) was used to measure cognition in primary CG of people attending UK day services (Croog et al. 2001); and Italian female co-resident CG recruited from a dementia out-patient clinic (Sansoni et al. 2004) respectively. Two of these studies also reported the relationship between ADL scores of the person receiving care and CG anxiety (Croog et al. 2001; Proctor et al. 2002), and both found no association.

Two Level 2 studies found no association between the number of behavioural problems of the person with dementia and caregiver anxiety, on univariate analysis in primary CG of people attending UK day services (Proctor et al. 2002) and multivariate analysis in co-resident spousal CG recruited mainly from a hospital research registry (Neundorfer 1991) respectively. A Level 3 study undertaken as part of the REACH study did find that CG were more anxious if the person they cared for had more behavioural problems on univariate analysis (Roff et al. 2004). Among spouses of people with dementia attending a clinic for registration for a drug trial (Croog et al. 2001), emotional lability was significantly associated with caregiver anxiety, while destructive behaviour was not. Only one of the cross-sectional studies reported the relationship of any socio-demographic measures relating to the person with dementia receiving care and caregiver anxiety levels. This study found no difference in anxiety levels between CG for people

with dementia living at home recruited from a previous study and CG who visited the person they cared for in a nursing home at least once a week (Stephens et al. 1991).

Summary:

There is Grade B evidence that the level of cognitive and ADL impairments experienced by the person with dementia are *not* related to caregiver anxiety as there are consistent Level 2 studies showing no such associations.

There is Grade C evidence that greater emotional lability is related to higher levels of caregiver anxiety, as this is demonstrated in a single Level 2 study.

There is Grade C evidence that caregiver anxiety is *not* related to the level of destructive behaviour exhibited by the person with dementia or to whether the person cared for lived in a care home, as these are findings from single Level 2 studies.

There is inconsistent evidence regarding the relationship between caregiver anxiety and behaviour problems exhibited by the person with dementia (two small Level 2 studies showed no association and one large Level 3 study showed that there was a positive association) so the evidence Grade is D.

Table 2.2 Studies reporting correlates of anxiety levels in dementia caregivers

Study	Anxiety measure	No. CG (controls)	Factors associated with ↑ anxiety scores
Level one studies			
Stephens (1991)	SCL-90-R	66	More hassles related to cognitive and overall morbidity of the person with dementia
Vedhara (2001)	SPSS	50	Neuroticism; Escape avoidance and confrontative coping
Level two studies			
Anthony-Bergstone (1988)	BSI	184	More caregiver burden
Compton (1997)	GHQ 28	38	More CG abusive behaviours
Croog (2001)	WBS	199	Caring for someone with more emotional lability; Being a husband vs wife caregiver
Marvardi (2005)	BSI	419	More CG burden
Neundorfer (1991)	BSI	60	Confrontative, accepting responsibility or escape-avoidance coping
Parks (1991)	SCL-90	176	More caregiver burden; Fantasy coping
Proctor (2002)	HADS	50	↑ caregiving duration, biomedical knowledge of dementia; Monitoring coping
Sansoni (2004)	STAI	34	↑hours spent caregiving; More CG depression and physical health problems
Vedhara (2000)	SPSS	50	More CG hassles, recent life events, neuroticism; confrontative or escape-avoidance coping; seeking social support; lower self-esteem/ self-concept
Level three studies			
Bauer (2000)	SPSS	49 (67)	Decreased CG immune response
Coon (2004)	STAI-10	420	No factors identified
Crespo (2005)	HADS	66 (42)	No factors identified

Haley (2004)	STAI-10	720	Caucasian vs African American ethnicity CG
Hooker (2000)	STAI-20	88 (87)	Female CG
Knight (1998)	STAI-20	154	No factors identified
Knight (2000)		169	
Roff (2004)	STAI	618	Caring for someone with ↑ behavioural problems; White vs African American CG; Reporting less positive aspects of caregiving and religiosity
Shaw (1997)	BSI	151 (159)	White vs Chinese ethnicity; no other factors reported for whole sample
Thompson (2004)	KSQ	61	Female CG
Youn (1999)	STAI-10	69	Korean /Korean American vs White CG ethnicity
Level four studies			
Chang (2001)	BSI	81	More CG education; Younger CG; Caring for someone with more behavioural problems
Quayhagen (1997)	BSI	50 (17)	Female CG; More CG abusive behaviours
Winslow (1997)	SCL-90 (4 items)	452	More dependent CR; CG subjective burden, baseline anxiety; worse physical health

2.2.3 Treatment studies

2.2.3.1 Study Quality

All twenty-three treatment studies included had methodological limitations and none fulfilled criteria for Level 1 evidence. I found thirteen Level 2 studies (eleven of which were RCTs); and ten Level 4 studies. Only one reported anxiety as the primary outcome (Akkerman & Ostwald 2004); only two undertook any power calculation (Hebert et al. 2003; Moniz-Cook et al. 1998), neither based on anxiety.

Only five ((Akkerman & Ostwald 2004; Gendron et al. 1996; Hebert et al. 2003; King & Brassington 1997; Mohide et al. 1990) had inclusion criteria to select those who were more anxious, so most CG in the studies probably did not have clinically significant anxiety. All studies reported mean change on at least one of nine self or interviewer rated anxiety measures. Adequate psychometric properties have been reported for eight of these scales: the Spielberger Trait Anxiety measure (STAI) (Oei et al. 1990); the HADS (Bjelland et al. 2002); the Brief Symptom Inventory (BSI) (Derogatis 1993), the Symptom Checklist (SCL) (Derogatis et al. 1973); the Profile of Mood States (POMS) (Kuboki et al. 1993) the Beck Anxiety Inventory (BAI) (Osman et al. 1997); the Taylor Manifest Anxiety Scale (TMAS) (Kendall 1954) and the Hamilton Anxiety Scale (HAS) (Maier et al. 1988). As discussed previously, concerns have been expressed about use of the GHQ-28 anxiety subscale to measure anxiety (see section 2.2.2.1, page 63). I will discuss the Level 2 studies below. See Table 2.3 (page 86), Table 2.4 (page 88) and Table 2.5 (page 89) for more details of these and Level 4 studies.

2.2.3.2 Group CBT Including Coping Skill Training

Three RCTs compared group CBT with waiting list (Akkerman & Ostwald 2004) or support group (Gendron et al. 1996; Hebert et al. 2003). Only Akkerman and Ostwald (2004) found a significant reduction in anxiety, in the only study for which anxiety was

the primary outcome measure. They recruited CG through print, radio, the internet and community presentations, excluding those demonstrating “insufficient anxiety or interference with daily activities” (not defined). Scores on both anxiety measures were significantly lower one week post-intervention in the group receiving a program of treatment that involved didactic skills training to address the physical, cognitive and behavioural components of anxiety, by teaching emotion-focussed coping strategies. During the initial session, caregivers were instructed in the strategy of mindfulness meditation, the importance of remaining focussed on the present moment and using diaphragmatic breathing exercises as a focal point to decrease physiological based anxiety. The second session focussed on the use of Progressive Muscle Relaxation. Caregivers were taught to identify physical tension in various muscle groups and learned strategies to reduce their physiological tension. The third session instructed caregivers in the use of guided imagery/visualization to create their own imaginal place (Akkerman 2006, personal communication).

Hebert (2003) recruited CG reporting moderate or severe caregiver burden, who had been caring at least six months for someone with at least one behavioural problem. There was no difference in anxiety levels between groups immediately after the intervention which promoted use of problem-solving and the emotion-focussed strategies of positive reappraisal and seeking emotional support. Gendron (1996) recruited co-resident spouse primary CG, who wanted help in coping with caregiving, through health professionals, community service agencies and the Alzheimer Society. There was no difference in anxiety scores immediately, three or six months after an intervention that involved reducing dysfunctional and promoting problem-focussed coping strategy use (see section 1.5.3.5, page 47).

Summary

- There is inconsistent (Grade D) evidence for group CBT, and the only intervention that demonstrated a positive effect was also the only one that included teaching emotion-focussed coping as its main component.

2.2.3.3 Behavioural Management Techniques (BMT)

There were three RCTs of BMT. The first (Bourgeois et al. 2002) compared two intervention groups of co-resident physically well spousal CG, caring for people with moderate to severe AD with behavioural problems. One attended a CBT based workshop in which the caregivers were taught problem solving coping skills and relaxation, the second a workshop to learn BMT skills (based on antecedent—behaviour—consequence relationships). Both groups then received ten in-home reinforcement sessions. The control was a caregiver support group and then visits for support only. The groups did not differ in anxiety levels immediately, three or six months post-intervention. Burgio et al. (2003) included co-resident CG providing 4 hours care/ day to people with mild dementia, at least 1 ADL impairment and 3 behavioural problems. They found no significant difference in anxiety scores between the group receiving a workshop then eight in home sessions and two phone calls involving BMT as well as problem-solving and cognitive restructuring CBT techniques and controls, immediately after the six month intervention period.

Chang (1999) recruited CG with access to a video and telephone, whose cared for someone who had problems dressing or eating and MMSE scores less than 21. They compared an eight week video intervention which modelled appropriate caregiver behaviour, reinforced positive behaviour by the person with dementia and informed about general caregiving problems, reinforced by weekly phone calls from nurses, conducted with homebound caregivers without face to face contact; with attention only

phone calls, and found no significant difference between the groups during, immediately and four weeks post-intervention.

Summary

There is Grade B evidence not to use 8-10 BMT sessions as consistent Level 2 studies showed lack of efficacy immediately and up to six months. Two studies also taught problem-solving coping skills in a CBT format and one also included relaxation, but the BMT interventions with these additional components were not effective for anxiety.

2.2.3.4 Provision Of Information Technology (IT) Support For Caregivers

An RCT of caregiver IT support by Mahoney et al (2003) (see Burgio et al (2003) above for inclusion criteria) involved weekly automated “conversations” about problems suggesting coping strategies; and a voicemail link to nurse and automated distraction calls for the person with dementia. Overall, anxiety scores did not differ between the groups although they did decrease in caregivers with low mastery.

Summary

There is Grade C evidence not to use IT support delivering a problem-focussed coping intervention for CG immediately and at six month follow-up, as there is only one study.

2.2.3.5 Exercise Therapy

Two Level 2 studies by the same group investigated exercise therapy (Castro et al. 2002; King & Brassington 1997). Both included CG who were aged over 50 and physically well. In the first, a pilot study, Castro (2002) only included people who reported at least moderate stress. King and Brassington (1997) only included CG providing at least ten hours of care per week.

There is Grade B not to use exercise therapy for anxiety as there is evidence that it is ineffective immediately post-intervention.

2.2.3.6 Providing Additional Professional Support For CG

An RCT (Mohide et al. 1990) compared regular visits from caregiver support nurses for six months, including psycho-education, problem-solving targeting behaviour problems, weekly respite and a monthly caregiver self-help group; with conventional community nursing services. Participants were co-resident CG for people with moderate or severe dementia, who screened positive for mental health problems and agreed to nursing services for the person they cared for. There was no significant difference in anxiety scores between the groups after receiving three or six months of these services. By contrast, Woods et al. (2003) did find reduced anxiety in CG of people after receiving 8 months of Admiral Nursing (a nursing service that works specifically with caregivers of people with dementia) compared with community mental health services.

Summary

There is Grade D evidence for provision of additional caregiver support immediately after receiving six to eight months of the intervention.

2.2.3.7 Respite Care

In an RCT, Grant et al (2003) compared ten days of in-home respite over 2 weeks by trained staff with passive observation in co-resident spousal CG receiving less than eight hours respite a week. They found no between-group difference in anxiety levels at one month. Secondly a cohort study of low-income CG qualifying for a USA grant scheme (Cox 1997) found no difference in anxiety levels between those who used the scheme for six months and those who did not.

Summary

There is Grade B evidence *not* to use respite from consistent Level 2 studies, immediately or at one month after receiving this over two or six months.

2.2.3.8 Interventions Investigated In Level 4 Studies Only

Two Level 4 studies reported interventions involving relaxation or yoga. Hosaka et al. (2003) found mean anxiety scores on the General Health Questionnaire (GHQ) anxiety subscale were decreased immediately after the fifth session compared with baseline, but no significant change was found on the other anxiety measure used. Waelde et al. (2004) reported that anxiety scores were lower a month after completion of six sessions of manualised yoga, compared with baseline in twelve female CG providing 4 hours care a day to CRs scoring less than 24 on the MMSE. The programme included group yoga practice followed by a half hour discussion about applying the techniques in stressful caregiving. The GR is therefore C for using yoga and relaxation to treat anxiety as there are consistent Level 4 studies.

Group psychotherapy; full time care for the person with dementia; and current statutory UK service provision have only been investigated in Level 4 studies and were awarded a Grade of evidence of D because results for anxiety were inconsistent or unreplicated.

Table 2.3 Psychological intervention studies with dementia caregivers

Study (Level)	*RCT	Intervention	N	Control	N	Time post- intervention	Anxiety measure	Outcome
Cognitive behavioural therapy (CBT)								
Hebert (2b*)		15 x 2hr/ week: cognitive appraisal, coping strategies taught & practiced	60	Support group	56	Immediate	STAI	No difference
Akkerman (2b* /4 at 6 weeks)		9 weekly CBT groups, including teaching skills eg relaxation	18	Waiting list	17	1 week; 6 weeks for intervention	HAS BAI	Significantly ↓ anxiety in intervention group
Gendron (2b*)		8 week x 90 minute CBT group:	17	Support group	18	Immediate, 3 & 6 months	SCL	No difference
Wilkins (4)		8x 90 minute psychoeducation and CBT and resource information	11	No control	0	Immediate 1 month	BAI	No significant decrease post intervention
Behavioural management techniques (BMT) +/- Cognitive therapy techniques								
Bourgeois (2b*)		Group 1: problem solving & relaxation; 2: BMT then 10 in-home sessions	18 x2	Information workshop	15	Immediate 3 & 6 months	STAI-20	No difference

Burgio (2b*)	Workshop then 8 in-home BMT sessions	61	Support	57	Immediate	STAI-10	No difference
Chang (2b*)	BMT on video and nurse phone support for 8 weeks	34	Phone support	31	Immediate 4 weeks	BSI	No difference
Mahoney (2b*)	12-month computerised intervention	51	Information only	49	Immediate 6 months	STAI	No difference
Group counselling							
Lazarus (4)	10 psychotherapy groups	4	Refusals	3	Immediate	SCL	No difference
Groups involving relaxation/ yoga							
Hosaka (4)	5x90min weekly group including psychoeducation, relaxation training and discussion sessions	20	No control		Immediate	GHQ-30 and POMS	Significant decrease in anxiety on GHQ but not POMS
Waelde (4)	6 weekly sessions manualised yoga meditation; discuss application	12	No control		1 month	STAI	Significant decrease in anxiety

Table 2.4 Other therapies for dementia caregivers

Study (Level;*=RCT)	Intervention	n	Control	n	Time post- intervention	Anxiety measure	Anxiety outcome
Exercise therapy							
Castro (2b*)	12 month exercise training program	45	nutritional control	40	immediate	TMAS	No improvement
King (2b*)	4 month supervised home based moderate intensity physical activity	12	Wait list	12	immediate	TMAS	No difference
Additional professional support for <i>caregiver</i> including behavioural management and coping skills							
Mohide (2b*)	Regular visits from trained Caregiver support nurse for 6 months	22	Usual community nursing care	20	Immediate	STAI	No difference
Woods (2b)	Admiral nursing service, that works primarily with caregiver	43	Usual care	61	immediate	GHQ-28 subscale	Significant ↓ with intervention
Moniz-Cook (4)	Home based intervention for 6-12 hrs over 4-14 weeks	15	Information; month interview	6 10	3 & 15 months	HADS	No differences

Table 2.5 Interventions with the person with dementia to reduce caregiver anxiety

Study (Level;*=RCT)	Intervention	n	Control	n	Post- intervention follow-up	anxiety measure	Change in CG anxiety scores
Services for the person with dementia							
Richards (4)	Treatment in: (1) memory clinic (2) CMHT (3) day hospital	35,34 22	No control		immediate	HADS	Increased in day hospital group; no other change
Respite							
Cox (2b)	CG using in-home and residential respite by trained workers for 6 months	123	access to respite but (1) stopped using it < 6 months (2) never used it	55 50	immediate	BSI	No difference between users and non-users.
Grant (2b*)	10 days in-house respite by trained staff	32	Passive observation	23	1 month	HAS + BSI	No difference between groups

Milan (4)	volunteer befriending, in-home respite;	14	no control		immediate	STAI	Significant reduction in anxiety levels
Care home for person with dementia							
Matsuda (4)	Care home	41	(1) used facilities as respite (2)at home	18 44	6 months	GHQ-60	anxiety decreased in institutionalised group
Pot (4)	Care home admission within the past year	25	no control		immediately 1 year	SCL-90-R	no significant change in anxiety
Schulz (4)	person with dementia placed in fulltime care during RCT 18 month follow-up period	180	No control		12 weeks; 1 year in 41 who were depressed	STAI	no change at 12 weeks; decreased anxiety at 1 year

2.3 Discussion

Perhaps my most striking finding in this systematic review is the lack of evidence regarding the associates as well as the treatment of anxiety in CG. I found only two Level 1 studies which investigated determinants of anxiety levels in CG and as they investigated different putative covariates we found no Grade A evidence. Similarly no determinants of anxiety caseness were investigated in more than one study. There were no treatment studies that fulfilled criteria for Level 1 evidence.

2.3.1 Prevalence studies

Although the prevalence studies reported rates of anxiety ranging from 3.7% to 76.5%, when I considered their methodology, I found that about a quarter of CG included experienced clinically significant anxiety in the only two prospective studies using a valid measure of anxiety (Coope et al. 1995; Mahoney et al. 2005), both of which took place in the UK. The only factor demonstrated to predict anxiety disorders in a longitudinal study was past psychiatric history in the caregiver (Russo et al. 1995).

2.3.2 Anxiety levels

There was good (Grade B) evidence from cross-sectional studies that anxiety levels are related to *caregiver burden; using escape-avoidance and confrontative coping; and poorer caregiver physical health*. I also found good evidence for a lack of association between caregiver anxiety and: degree of cognitive and ADL impairments exhibited by the person with dementia; caregiver age, the coping strategy of *positive reappraisal*; and duration of caregiving. There was a long list of preliminary findings (Grade C) for factors associated with anxiety levels for which further evidence is needed but no good (Grade A or B) evidence about what factors *predict* anxiety levels from longitudinal studies or regarding factors associated with or predicting anxiety caseness.

My findings from cross-sectional studies indicate that caregiver coping style may be an important correlate of anxiety, but this has not replicated in good quality longitudinal

studies. As all of the five studies that reported coping also included depression as an outcome, I rated the evidence for this association using CEBM guidelines. There was Grade B evidence (from two Level 2 studies (Neundorfer 1991; Vedhara et al. 2001)) that escape-avoidance was associated with depression, but there was conflicting evidence from these studies (Grade D) for confrontative coping. There was no evidence that either monitoring (Proctor et al. 2002) or fantasy coping (Parks & Pilisuk 1991), both associated with anxiety (Grade C) were also associated with depression. So there are some similarities with coping styles associated with anxiety, but there are also important differences.

The finding that caregiver burden and poorer caregiver physical health are among factors for which there is good evidence for a correlation with anxiety levels is unsurprising and both are also associated with an increased risk of depression (Schulz et al. 1995). Burden is a multifaceted concept including subjective and objective measures of caregiving stress. The only study which measured caregiver burden and coping only used one of the Burden Interview subscales (number of caregiving hassles), which limits its interpretation (Vedhara et al. 2000). Nonetheless, as this was the only study in which caregiver burden was not associated with anxiety this might suggest that coping mediates the relationship between burden and anxiety in CG, that is CG who experience high burden are more anxious if they use ineffective coping strategies.

2.3.3 Treatment studies

No treatment study demonstrated sufficient power to detect a difference in anxiety levels. The only RCT to report a significant reduction in anxiety was also the only study in which the intervention was specifically targeted at anxiety; it involved CBT which primarily taught emotion-focussed coping, and relaxation (Akkerman & Ostwald 2004). Conversely, a second study focussing on problem-solving techniques and avoiding dysfunctional coping strategies (Gendron et al. 1996) did not demonstrate efficacy.

Three further studies found that BMT that also incorporated problem-solving coping alone (Burgio et al. 2003) or in conjunction with relaxation (Bourgeois et al. 2002) or teaching emotion-focussed coping (Hebert et al. 2003) was not effective, nor was an IT based problem-solving intervention (Mahoney et al. 2003). Perhaps these small studies lacked power to detect a true effect.

I also found preliminary (Grade C) evidence that caregiver interventions including yoga and relaxation may be helpful in reducing CG anxiety (Hosaka & Sugiyama 2003; Waelde et al. 2004). This type of intervention might be viewed as teaching emotion-focussed coping strategy, but as it is delivered in a very different way and usually by physical or yoga therapists rather than psychologists I classified them separately. The finding that anxiety management techniques may help in this group of caregivers is consistent with a hypothesis that caregiver anxiety may be mediated by the caregiver's coping strategies rather than resulting directly from caregiving. Relaxation techniques are an accepted treatment for anxiety symptoms, while evidence for yoga treatment of anxiety is promising but currently inconclusive (Kirkwood et al. 2005).

There is Grade B evidence that exercise therapy, BMT and respite do not reduce anxiety (Bourgeois et al. 2002; Burgio et al. 2003; Chang 1999), even though these interventions have demonstrated efficacy for outcomes such as burden and depression (Selwood et al. 2007; Sorensen et al. 2002). It is notable that only the single study of CBT specifically targeting anxiety, for example by inclusion of relaxation training, was effective at reducing it (Akkerman & Ostwald 2004). Specific strategies may be required to reduce anxiety and we cannot presume treatments that reduce depression or burden will also reduce anxiety. Some of the interventions focussed on reducing contact with the person with dementia, for example use of respite, but caregivers may want to cope with caring and this preliminary evidence suggests strategies to help CGs cope with caring demands may be more effective.

2.4 Limitations

I sought unpublished work by contacting five experts in the field of caregiver mental health, but this method for finding unpublished work is not exhaustive. My review is inevitably biased towards studies that had been published, and perhaps consequently also towards findings of positive associations and intervention effects. There is a tension between use of inclusion criteria for systematic reviews that are well defined to ensure studies are sufficiently homogenous to be comparable, yet inclusive of all relevant studies. As the literature in the area of CG anxiety is currently limited, I used broad inclusion criteria, for example no definition for caregiver was specified, and studies of all but the lowest level of validity were included. Not all the studies used a valid measure of anxiety (see pages 63 and 80), and many of the scales used to measure associates with anxiety were also not validated (as reported in the text); for others (e.g. WCCL) psychometric properties have not been reported in older people.

I classified the studies depending on the prevailing methods used in the interventions, but many were heterogeneous, so there is some overlap between groups. Lack of conclusive evidence of efficacy does not mean inefficacy and so I cannot conclude that any of the interventions studied were definitely ineffective. Co-morbidity, for example with depression, may have affected outcome.

2.5 Conclusions

Clinically significant anxiety effects about a quarter of CG and is more common than in control populations. I found no good evidence about what factors might be associated with clinically significant anxiety, or what factors may predict either anxiety levels or clinically significant anxiety from longitudinal studies. Dysfunctional coping

(specifically *confrontative* and *escape avoidance coping*), *caregiver burden* and *poorer caregiver physical health* were the only factors associated with higher anxiety levels for which there was good evidence from cross-sectional studies. The only type of intervention reported as effective, at the lowest CEBM Grade of evidence, was caregiver groups involving yoga and relaxation, and the only RCT to report a significant reduction in anxiety was also the only one to include relaxation and emotion-focussed coping strategies specifically targeted at anxiety and in an adequately powered study. None of the studies investigated the impact of psychological interventions that involved teaching coping strategies on an individual basis. These findings suggest that further analysis of the role of coping in predicting subsequent anxiety may be particularly helpful as this is a potential target for interventions.

I hypothesised from these results that burden mediates the relationship between coping style and anxiety and depression, and identified the need for a cohort study to test this hypothesis. In the next chapters I will discuss how I designed and carried out such a study for this thesis.

3 AIMS AND HYPOTHESES

In chapter two, I concluded that there is a lack of evidence regarding factors that predict anxiety in CG. I found the most valid evidence (Grade B evidence from cross-sectional studies) for: caregiver burden, dysfunctional coping strategies and worse caregiver physical health. The only psychological intervention that was successful at reducing CG anxiety involved teaching emotion-focussed coping strategies. In chapter one, I found consistent evidence for a relationship between fewer emotion-focussed and more dysfunctional strategies and depression from cross-sectional studies and preliminary evidence the same strategies predicted depression from longitudinal studies. There was also good evidence that an intervention that promoted emotion-focussed and problem-focussed and discouraged dysfunctional coping was efficacious at reducing depression levels. From these findings, I have hypothesised that caregiver coping strategies mediated the relationship between caregiver burden and subsequent anxiety and depression.

3.1 Mediators and moderators

A moderator variable is one that influences the strength of a relationship between two other variables, and a mediator variable is one that explains the relationship between the two other variables. With regards to the relation between caregiver burden and anxiety, gender might be a moderator variable, if the relation between caregiver burden and anxiety were stronger for female caregivers and less strong for male caregivers. I am basing my hypothesis on Lazarus and Folkman's Transactional model of Coping (Lazarus 1966) which states that coping style explains why there is a relation between burden and anxiety, and therefore is a mediator variable.

3.2 Main aim

To investigate whether dysfunctional, emotion-focussed and problem-focussed coping strategies will mediate a relationship between caregiver burden at Time 1 (T1) and anxiety symptoms a year later (T2).

3.3 Main hypothesis

In CG, the relationship between more burden at T1 and more anxiety a year later will be mediated by using more dysfunctional coping strategies, and less emotion-focussed and problem-focussed coping strategies at T1.

3.4 Secondary Hypotheses

In CG, the relationship between more burden at T1 and more anxiety at the same time point will be mediated by using more dysfunctional coping strategies, and less emotion-focussed and problem-focussed coping strategies.

In CG, the relationship between more burden at T1 and more depression at the same time point and a year later will be mediated by using more dysfunctional coping strategies, and less emotion-focussed and problem-focussed coping strategies at T1.

3.5 Other potential mediators and confounders

Table 3.1 (page 99) illustrates the factors for which I reported finding a significant relationship with anxiety or inconsistent evidence for such an association in Chapter 2 and compares this to factors I intend to measure as potential mediators and confounders. All the factors were measured in the current study with the exception of those that I considered to be very similar to other factors included (detailed in Table 3.1, page 99), and three further factors that were excluded due to time and logistical constraints. These

were: CG abuse towards the person with dementia; CG knowledge about dementia, and CG ethnicity. For the latter, care recipient (CR) ethnicity was included as a proxy measure.

Table 3.1 Comparison of evidence base with correlates measured in this study

Factor significantly related to anxiety level or caseness	Measured in this study?
Grade B evidence	
CG coping strategies	yes
CG physical health problems	yes
Caregiver burden	yes
Grade C evidence	
Previous or current depression or anxiety	yes
CG age, gender, level of education and if living with the person with dementia	yes
Worse relationship reported with the person with dementia	yes
Greater dependency/ ADL impairment in person with dementia	yes
Greater emotional lability in person with dementia	yes
More CG knowledge about dementia	X
CG Neuroticism	X similar to anxiety
CG Hassles	X similar to burden/ life events
Positive aspects of caregiving; self-esteem and self-concept	X similar to emotion-focussed coping
Abusive behaviours towards a person with dementia	X
Factors for which evidence from review was inconsistent (Grade D)	
Level of behavioural problems in person with dementia	yes

CG Life events	yes
Informal support	yes
Mastery	X similar to emotion-focussed coping
CG ethnicity	X CR ethnicity measured

4 METHODS

My study was conducted as part of the **London and South-East Region Alzheimer's** disease study (the **LaSER-AD** study) (Livingston et al. 2005; Mahoney et al. 2005). This is a large cohort study, set up in 2002 to measure changes in illness and wellbeing in a representative sample of people with AD living in the community and their caregivers. I have been working with the study group since 2003 and was a member of the team interviewing caregivers at six month and subsequent follow up cohorts. With supervision, I designed the current study. This involved searching the literature, reading and rating all the papers for the systematic reviews, and deciding on the research question. I implemented and analysed data for the current study as part of the 18 month and 30 month interviews. I conducted approximately 20-30 of the carer interviews personally. I discussed the organization and meaning of the findings with my supervisors and at presentations to develop my thoughts before writing this thesis.

In this chapter, I will first describe the setting and recruitment for the main study, in order to explain how the sample for my study was derived. I will then describe the method for the current study.

4.1 The LASER-AD study

4.1.1 Setting

At baseline, participants were contacted through local psychiatric services (including Community Mental Health Teams, inpatient and long stay wards and a memory clinic), the Admiral Nursing Service, the Alzheimer Society and managers of nursing and residential care homes.

4.1.2 Inclusion and exclusion criteria

Dyads were included if:

- (a) The caregiver was a reliable and cooperative informant who was knowledgeable about the care recipient (CR) and spent a minimum of four hours a week in direct contact with them. This criteria was applied at baseline, and the caregivers were included subsequent to this even if the amount of care they gave had decreased below this level (provided that they still gave substantial care and were in regular contact with the CR), in order to provide complete follow-up data for the cohort. At Time 1 (T1) (18 months after initial recruitment of the cohort) only seven of the caregivers reported providing less than four hours care per week. Caregivers were only included if they were able to give informed consent. They could be spouses, relatives, friends or neighbours of the CR. For the main study, a professional caregiver was interviewed where no CG met our criteria, but these dyads are not included in this study. I only included dyads in the longitudinal analysis if the same caregiver was interviewed at T1 and Time 2 (T2).
- (b) The CR was aged fifty or over, had a diagnosis of dementia according to DSM-IV criteria (American Psychiatric Association 1994) and met NINCDS-ADRDA criteria for probable AD (McKhann et al. 1984), whatever the age of onset of AD and the treatment status. There was no upper limit for MMSE score. Instead, the investigators only included CR whose MMSE scores were below that expected for their age and socio-educational status, and who had evidence of cognitive decline.

Caregivers were excluded if they were unable to understand English to a degree that would interfere with, or prevent the assessment. Exclusion criteria for the CR were:

- (a) Vascular dementia, as defined by Haschinski Ischemic Score criteria (Rosen *et al*, 1980)

- (b) Other significant neurological disease (e.g. Dementia with Lewy body, Parkinson's disease, Huntington's disease, Normal Pressure Hydrocephalus, sequelae of brain surgery, brain trauma)
- (c) History of other severe and enduring mental illness
- (d) Endocrine or metabolic disorders possibly causing dementia (e.g. hypothyroidism, B12 deficiency)
- (e) Psychotic episodes requiring hospitalisation or neuroleptic treatment for more than two weeks during the last ten years that were not associated with AD.
- (f) Alcohol or drug abuse according to DSM-IV revised interim version during the last 10 years
- (g) The CR was unable to comply with the study assessment, either due to another disease or inability to understand English that would interfere with, or prevent the participation/conductance of the tests.

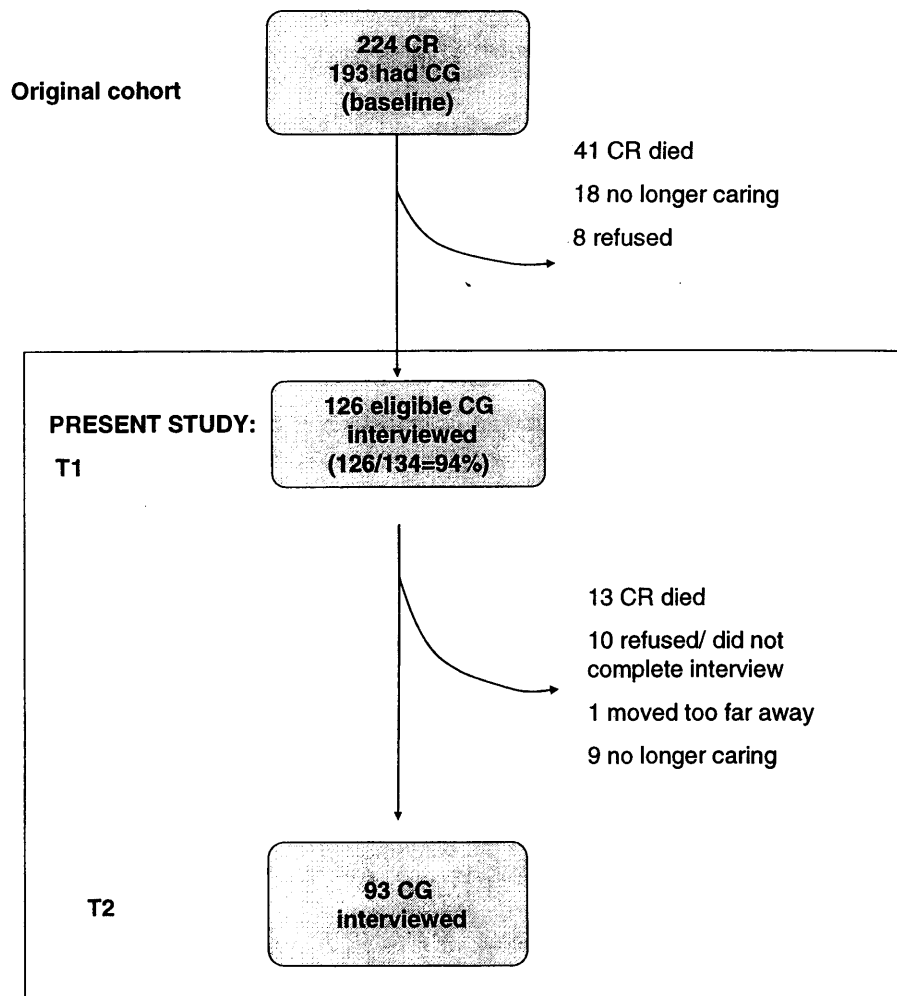
4.1.3 Recruitment method

Recruitment was purposeful to ensure that the sample was representative of people with dementia in terms of dementia severity, gender and care setting. Fratiglioni (1998) reported that 20% of people with AD living in the community have mild disease, 45% moderate disease and 35% severe disease; CR were recruited to reflect this distribution of impairment. CR were considered to have mild AD when MMSE > 20, moderate AD when $MMSE \leq 20$ and ≥ 10 , and severe AD when $MMSE < 10$. Selection methods also ensured that 60-70% of the included CR were female. This gender proportion was applied for the three groups of severity level. Patients were also stratified for living settings: 65% were community-based and 35% living in twenty-four hour care. This stratification for living setting was undertaken independently of gender and disease

severity because people who are severely demented are more likely to live in institutions.

4.1.4 Participants

Please refer to (Figure 4.1) for a summary of the cohort described in the LASER-AD study, and how this relates to participants included in the current study. Two hundred and twenty four CR were originally interviewed for the LASER-AD study, of whom 193 had a CG who was interviewed, while for the remainder (n=31) a CG meeting our criteria could not be identified. Those for whom a CG was not identified were more likely to be: living in a care home (27 (87.1%) vs 46 (23.8%); $\chi^2=45.8$ (p<0.001)) and to have a more severe dementia: 2 (6.5%) had mild, 13 (41.9%) had moderate and 16 (51.6%) had severe dementia, compared with those for whom a family CG was identified, of whom 64 (33.2%) had mild, 79 (40.9%) had moderate and 50 (25.9%) had severe dementia; $\chi^2=12.5$ (p=0.002). This might be expected as those in care homes were probably more unwell, but because of care provided in the home, less likely to have a caregiver visiting and provided care to them for at least four hours a week. There was no statistical difference between the groups in the proportion of caregivers who were caring for a man ((16.1%) vs 59(30.6%); $\chi^2=2.1$ (p=0.15), although there was a trend towards CG being less likely to be identified for female CR, perhaps because women have a longer life expectancy so are more likely to be available to care for a male partner with dementia. As the CR recruited were representative of people with dementia living in the community, we judged that the CG recruited were also representative at baseline of people providing four or more hours of care to someone with dementia.

Figure 4.1 Number of participants in original cohort, T1 and T2

4.2 Current Study

A major finding at baseline was a higher than expected prevalence of clinically significant anxiety in the CG. This lead me to explore in the literature why this might be. My finding that coping strategies and burden were two of the few factors for which there was good evidence of an association with anxiety (see Chapter 2) led to the formulation of the hypotheses and design of this study (see Chapter 3). I used data from two time points. T1 data was collected as part of the 18 month follow-up, and T2 data as part of the 30 month follow-up (a year later) of this baseline LASER-AD cohort.

4.2.1 Participants at Time 1

At 18 months, the CR from 41 of the initially recruited 193 dyads were deceased, and in 18 dyads the CR no longer had a CG with whom they were in regular contact. Therefore 134 of the CG interviewed at baseline were eligible for interview at T1 (18 months later), of whom nine were not available for interview, because they refused (n=8) or moved away (n=1), and 125(93.3%) were reinterviewed. In addition, one CG was identified for a CR who did not have an eligible family caregiver at baseline, so in total 126 CG were interviewed at T1.

CG who were reinterviewed at T1 (n=126) did not differ from those originally recruited to the study who were not reinterviewed (n=68) in terms of their age (63.0(14.0) vs 65.9(13.8); $t=1.4$, $p=0.17$); the proportion who were male (39(31.0%) vs 23(33.8%); $\chi^2=0.061$, $p=0.80$), or the proportion that were caring for a male CR (37(29.4%) vs 22(32.4%); $\chi^2=0.072$, $p=0.79$). The CG who were originally recruited but not interviewed were caring for people who were on average more cognitively impaired (mean MMSE score 12.5(8.4) vs 17.1(7.8); $t=3.9$, $p<0.001$) and living in twenty-four hour care (31(45.6%) vs 16(12.7%); $\chi^2=24.3$, $p<0.001$) at baseline, and they were also less likely to be the spouse of the CR (0(0%) vs 54(42.9%); $\chi^2=38.3$, $p<0.001$). This is

probably because those who had more severe dementia were more likely to have died, and because spousal CG were more likely to be in regular contact with the CR eighteen months later, even if the CR was now in a care home. Overall, of the CG interviewed at T1, 38(30.2%) were caring for someone with mild dementia; 44(34.9%) for someone with moderate dementia and 44(34.9%) for someone with severe dementia. Baseline HADS scores were available for 98/126 (77.8%) and 55/68 (80.9%) of those originally recruited who were and were not interviewed at T1. There was no significant difference in anxiety scores (7.2(4.1) vs 7.8(4.8); $t=-0.83$, $p=0.41$) or depression scores (4.8(3.9) vs 5.6(4.0); $t=-1.2$, $p=0.25$) between these groups. As the proportion lost to follow up was very small, this cohort is likely to be representative of CG who have been caring for at least eighteen months.

4.2.2 Participants at Time 2

Ninety-three (73.8%) of family caregivers interviewed at T1 were re-interviewed a year later. 31 caregivers were not re-interviewed - because the CR died ($n=13$), the caregiver refused ($n=8$), the caregiver did not complete the interview ($n=2$), they had moved too far away ($n=1$) or they were no longer caring ($n=9$). Therefore the response rate for CG who remained eligible for the study was 93/117 (79.5%). Those not re-interviewed were more likely to be caring for someone with greater neuropsychiatric and ADL problems. There was also a non-significant trend towards them being more anxious at T1, and this was accounted for by a high rate of baseline anxiety in those who refused to be re-interviewed (six of the eight caregivers who refused the second assessment were anxiety cases). Those who were not reinterviewed also tended to report using more dysfunctional coping strategies (see Table 4.1).

Table 4.1 Caregivers interviewed at T1 and T2 follow-up

Factor		Mean (%) in those reinterviewed (n=93)	Mean (%) in those NOT reinterviewed (n=33)	χ^2/t	p
CG	Female	59(63.4)	23(69.7)	$\chi^2=0.52$	0.42
	Age	63.9(14.8)	65.0(11.7)	t=0.38	0.70
	Spouse of CR	42(45.2)	12(36.4)	$\chi^2=0.77$	0.38
	Lives with CR	51(54.8)	11(33.3)	$\chi^2=4.5$	0.034
	Burden score	26.8(14.1)	30.0(15.3)	t=1.0	0.31
	Anxiety score	5.7(4.0)	7.8(5.5)	t=2.3	0.024
	Dysfunctional COPE score	15.6(4.1)	17.5(4.9)	WMU=1109	0.036
	Emotion- focussed COPE score	19.4(5.1)	19.4(5.9)	t=0.05	0.96
	Problem- focussed COPE score	11.1(4.1)	12.9(5.1)	t=2.0	0.051
CR	MMSE	14.6(8.9)	11.8(9.1)	t=-1.5	0.13
	NPI	17.8(14.8)	26.1(18.0)	t=2.6	0.01
	ADL-ADCS	33.9(21.4)	21.6(18.0)	t=-2.9	0.004
	In 24 hour care	23(24.7)	14(42.4)	$\chi^2=3.7$	0.055

4.3 Ethics Committee approval

Approval for the study was obtained from ethical committees for the three regions in which the study was conducted (Camden and Islington; Haringey, Barnet and Enfield; and North Essex Mental Health Trusts). Participants gave written, informed consent.

Where the CR did not have capacity, the interviewer asked the CG whether they thought the CR would have agreed to participate if they could, and terminated the interview if the interviewee became distressed or appeared not to want to continue.

4.4 Data collection

I was a member of a team of trained researchers, who were from medical, nursing or psychology backgrounds. We collected information about the following factors at T1. Coping, anxiety and depression were also measured at T2. Interviews with the CR and CG were conducted separately and in private.

4.4.1 Caregiver interview

4.4.1.1 Sociodemographic Data

The interviewer recorded the age and gender of the caregiver; whether they were living with the CR; their relationship to the CR, using the categories: spouse/partner and other informal caregiver; and caregiver marital status, recorded as: married or cohabiting; and single, separated, divorced or widowed. They asked caregivers how many hours per day on average (worked out over a usual week period and divided by 7) they personally supervised or spent time in the company of the CR.

4.4.1.2 Anxiety And Depression Measure

I searched for an instrument to measure anxiety which would fulfil the requirements that: (1) it had been previously administered to CG and found to be acceptable; (2) it was reliable and valid for use in older and younger adults, as CG would span these age groups; a requirement for this was that it did not include somatic items which can be misleading in older subjects; (3) there was an accepted cut-off point for defining

caseness for which adequate sensitivity and specificity had been demonstrated in a community sample; (4) it was reasonably quick to administer and (5) provided a measure of anxiety symptom severity.

I reviewed instruments employed in studies from my systematic review to measure anxiety in CG. The Spielberger State-Trait Inventory (STAI) was used most frequently (in 19/56 studies); this is also the most widely used self-report anxiety measure across all populations. I excluded this as a potential scale however, because it is not recommended for use in older people due to the high number of somatic items included (Kvaal et al. 2001). Of other instruments that have been used previously in CG, I concluded that the HADS best met the above criteria for the scale. A further advantage of using the HADS was its use previously in the LASER-AD cohort, enabling comparisons to be made with anxiety levels at baseline.

4.4.1.3 The Hospital Anxiety And Depression Scale (HADS)

The HADS (Zigmond & Snaith 1983) assesses how the respondent has been feeling within the past week; it consists of two seven-item subscales, with each item scored 0-3, generating scores for generalised anxiety (0-21) and depression (0-21) (see Appendix D). It takes no more than fifteen minutes to complete. The HADS does not include somatic items. In a large study designed to assess use of the HADS across age groups ($n = 6165$), good test-retest reliability was reported; the dimensional structure and reliability of the HADS was stable across medical settings and age groups, and the correlations between HADS scores and age were small (Spinhoven et al. 1997).

Bjelland (2002) reviewed the psychometric properties of the HADS. The instrument performed well in assessing the symptom severity and caseness of anxiety disorders and depression in somatic, psychiatric and primary care patients and in the general population. It was reported to demonstrate a two factor structure (measuring anxiety and depression respectively). Cronbach's alpha coefficients of internal consistency were

reported in fifteen studies and varied from .68 to .93 (mean .83) for the anxiety scale, and from .67 to .90 (mean .82) for the depression scale. Twenty-one studies reported the Pearson correlation coefficient between the HADS anxiety scale (HADS-A) and the HADS depression scale (HADS-D), and a mean value of .56 was reported, demonstrating discriminant validity. With regard to concurrent validity, five studies reported good correlations ($r=0.64 - 0.81$) between the STAI and the HADS anxiety subscale, and six studies reported good correlations ($r=0.62-0.73$) between the BDI and depression subscale. In 24 studies reporting case finding abilities of the scale, optimal balance between sensitivity and specificity was achieved most frequently at a cut-off score of 8/9 for both HADS-A and HADS-D giving sensitivities and specificities for both subscales in the range 0.8-0.9.

4.4.1.4 Coping Measure

I required an instrument to measure coping that was: (1) acceptable; (2) reasonably quick to administer; and (3) had acceptable psychometric properties, and (4) valid subscales measuring clinically relevant aspects of coping, that separated helpful from unhelpful and problem-focussed from emotion-focussed strategies.

4.4.1.4.1 The Coping Orientations to Problems Experienced scale (COPE)

Carver and colleagues developed the original COPE using a theoretical framework, drawing on Folkman and Lazarus' model, their own model of behavioural self-regulation and previous research findings. They derived fifteen subscales, each with four items. They tested this instrument on 978 undergraduates (Carver et al. 1989). The scales were not highly intercorrelated ($p < 0.7$ in all cases) in this population. Although correlations were not strong, the scales did correlate in meaningful ways, for example *denial*, *behavioural disengagement*, *self-distraction*, *venting* and *alcohol use* (all dysfunctional coping strategies) correlated together. Internal consistencies for the subscales were acceptable (behavioural disengagement alone fell below 0.6). Test-retest

reliability was also acceptable six weeks later in 116 students, and eight weeks later in 89 students. Convergent validity was demonstrated by the finding that certain subscales correlated as predicted with measures including: optimism, locus of control, hardiness, type A and anxious personality traits. They also found that correlation with personality traits was not high ($p < 0.4$), nor were the COPE scales strongly correlated with the social desirability scale used ($p < 0.3$), demonstrating discriminant validity. Clark et al. (1995) also reported adequate convergent and discriminant validity by investigating relevant correlations with subscales from two other coping measures, the Coping Strategy Indicator and the WCCL, as well as with a variety of external criteria, including hassles and uplifts, physical symptoms, satisfaction with life, positive affectivity and negative affectivity.

4.4.1.4.2 **The Brief COPE**

I used the Brief COPE, a self-report questionnaire. Respondents are asked to score 28 possible ways of coping from 1 (not doing it at all) to 4 (doing it a lot). These comprise fourteen subscales (Figure 4.2, page 114), thirteen of which were derived from the original COPE. As the Brief COPE has only two items per scale as opposed to four in the original scale, items were selected for inclusion according to their clarity and high loading on the relevant factor in the psychometric analyses for the original COPE. Two of the original COPE scales were omitted as they had been found to be redundant. They changed the item “Focussing on and venting emotions” to venting, and in so doing removed an item that appeared to relate too closely to experiencing distress. They also added the item of self-blame, as this was a coping style that had been found in other research to be dysfunctional as it was a predictor of poor adjustment (Carver 1997). The Brief COPE has been used previously to measure coping in a group of older people which included CG (Crespo et al. 2005).

Psychometric properties are reported from a study of 168 people recovering from Hurricane Andrew. They reported a similar factor structure to the original instrument, and good internal reliability of the abbreviated scales across three administrations of the scale (three, six and twelve months post-hurricane) (Carver, 1997). This is the only example I found of psychometric properties for a coping scale being reported in a sample of people of different ages, and who had experienced significant and unexpected trauma, as opposed to, for example, undergraduates undertaking an examination. The scales demonstrated internal consistency values of 0.5-0.9.

Carver describes the subscales of the original COPE in terms of whether they are predominantly dysfunctional, problem-focussed or emotion-focussed (Carver et al. 1989), but they do not actually report use of these divisions as subscales. Coolidge and colleagues (2000) did use the instrument successfully in this way in a study involving a convenience sample of 100 older adults and 132 younger adults. They found that older anxious adults used more problem-focussed strategies than non-anxious older adults, while younger anxious adults used more dysfunctional coping strategies than non-anxious younger adults interviewed. Their classification of the coping strategies was the same as discussed by Carver (1989), with the single exception the Carver described denial as emotion-focussed while Coolidge classified it as dysfunctional. I used the subscales employed by Coolidge et al (2000) as denial is likely to be a dysfunctional response to caring for someone with a chronic condition such as dementia, and denial correlated with other dysfunctional scales in psychometric testing of the COPE (Carver et al. 1989).

Figure 4.2 The Brief COPE

<p>Emotion-focussed strategies</p> <p>acceptance (accepting the reality that it has happened/ learning to live with it)</p> <p>emotional support (getting emotional support/comfort and understanding)</p> <p>humour (making jokes about it/ making fun of the situation)</p> <p>positive reframing (trying to see it in a different light, make it seem more positive/ look for something good in it)</p> <p>religion (finding comfort in religious or spiritual beliefs/ praying or meditating)</p>
<p>Problem-focussed strategies</p> <p>active coping (concentrating my efforts on doing something about the situation I'm in/ taking action to try to make it better)</p> <p>instrumental support (getting help and advice from other people/ trying to get advice or help from others about what to do)</p> <p>planning (trying to come up with a strategy about what to do/ thinking hard about what steps to take)</p>
<p>Dysfunctional coping strategies</p> <p>behavioural disengagement (giving up trying to deal with it/ the attempt to cope)</p> <p>denial (saying to myself "this isn't real" /refusing to believe that it has happened)</p> <p>self-distraction (turning to work or other activities to take my mind off things/ doing something to think about it less)</p> <p>self-blame (criticising myself/ blaming myself for things that happened)</p> <p>substance use (using alcohol or other drugs to make myself feel better/ to help me get through it)</p> <p>venting (saying things to let unpleasant feelings escape/ expressing negative feelings)</p>

4.4.1.5 Life Events

I measured life events because an association with CG anxiety has been reported (Vedhara et al. 2001) although results are inconsistent (see Table 3.1, page 99). Brown & Harris (1989) emphasised the importance of considering the meaning of life events, specifically whether they are independent or associated with a pre-existing condition, and the contextual threat of the event to the individual. In this study, an instrument is required that (1) is relatively brief and easy to administer, and (2) distinguishes life events that are serious and threatening and that are independent of caregiving. I used the SRRS (Holmes & Rahe 1967), the most frequently used inventory. This consists of a list of 43 life events derived empirically from clinical experience. In development of the measure, *marriage* was arbitrarily awarded an impact value of 500 by the researchers. They then asked 394 subjects to rate the likely impact of numerous life events, whether positive or negative in relation to marriage. From their results they derived a value for each life event, ranging from *death of a spouse*, which was judged to be likely to have the greatest impact and given a value of 100, to *minor violation of the law*, which was awarded an impact value of eleven. Marriage was awarded an impact value of 50 in the final scale. They reported high consensus between people of different gender, age, marital status, social class, ethnicity and religion concerning the order and magnitude of events ($r \geq .82$ for all correlations). The scale asks about life events experienced over the preceding six months. Higher scores on the SRRS have been associated with greater likelihood of relapse from depression in adults prescribed fluoxetine (Reimherr et al. 2001) and worse overall health ratings as assessed by the Duke-UNC Health Profile (Blake & Vandiver 1988), indicating convergent validity.

In order to meet the second requirement of the measure, I used a panel approach similar to that used by Brown and Harris (1989) to rate each of the 43 events prior to collecting data. With one of my supervisors who is experienced in life event research (MO) I decided which of these life events represented a serious threat and which were

independent of caregiving using criteria previously employed by Waite and colleagues (2004), that is whether they were likely to have a significant negative impact on the person persisting for one week or more after the event, and whether the event was such that it could not have been precipitated by the individual. Brugha and colleagues (1985) reported a list of twelve events which had a moderate or marked long term threat which they called the List of Threatening Experiences (LTE), and we used this instrument as a guide. My other supervisor (GL) reviewed our findings and differences were resolved by consensus. At T1 I entered into the analysis: total score on the SRRS, the presence of at least one severe and threatening life event; and the presence or absence of at least one severe, threatening and independent life event.

4.4.1.6 Caregiver Burden

The term “caregiver burden” describes the subjective and objective stresses that arise due to providing care. The Zarit Burden scale (Zarit et al. 1980), a 22-item self-report questionnaire, is the most consistently used measure of caregiver burden. It has a Likert response format, and caregivers are asked the extent to which they agree that each statement regarding the impact of caregiving applies to them, from 0 (never) to 4 (nearly always). Total scores range from 0 to 88, with higher scores indicating greater burden.

High internal consistency ($\alpha=.92$) has been reported in a large sample of primary CG (Hebert et al. 2000). Construct validity has been demonstrated through significant correlations in CG with more depressed mood measured using the BDI; fewer perceived uplifts of caregiving and more behaviour problems of the CR (Pinquart & Sorensen 2003b).

4.4.1.7 Health Perception And Quality Of Life Relating To Physical Health

The Short Form-36 (SF-36) is the most frequently measure of health perception and quality of life relating to health. It was developed for the Medical Outcomes Study, and

has been tested and validated extensively in general adult (Brazier et al. 1992) and elderly (Brazier et al. 1996) populations. Two twelve item scales have been developed from the SF-36: the Short Form-12 (SF-12) and the Health Status Questionnaire (HSQ-12).

The HSQ-12 (Radosevich & Pruitt 1995) has eight subscales: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. It has been adapted for use with older subjects (Bowling & Windsor 1997). In the Islington Study psychometric properties for the HSQ-12 and SF-12 instruments were similar and acceptable. The completion rate was 94.5% for the HSQ-12, and only 2.7% found it “not at all acceptable”. Discriminant validity of the HSQ-12 was demonstrated by the scale’s ability to distinguish between people with self-reported health problems and those without; those who sought help from health and social services and those who did not; and those with ADL limitation and those without. In 135 people who were asked to complete the measure again eighteen months later, it was also sensitive to change (Pettit et al. 2001).

I selected three physical health domains of the HSQ-12: *health perception*, *role physical* and *physical functioning*, all used previously in CG research (Mahoney et al. 2005). These were selected because other domains, for example quality of life relating to mental health were judged to overlap to an unacceptable degree with other measures included (e.g. the HADS) while physical functioning of the CG was not covered adequately by the other tests included and was found to be a significant factor relating to CG anxiety in my systematic review. For *health perception*, caregivers were asked to

rate their health on a Likert scale from 1 (excellent) to 5 (poor). For *physical functioning*, they were asked about how their health limited activities such as climbing stairs, a higher score indicating fewer physical limitations. For *role physical*, they were asked how their physical health problems limited them in their daily activities, and asked to score this on a five point Likert scale, from “limited a little” to “a great deal”. Convergent validity has been demonstrated for these domains in the Islington study: *role-physical* scores were lower in people with ADL limitations, and people with uncorrected visual or hearing impairments; *physical functioning* scores were lower in people with uncorrected hearing impairments or ADL limitations; and those with uncorrected visual impairments had lower *health perception* scores (Pettit et al. 2001).

4.4.1.8 Quality Of Relationship

This was measured using a single item taken from the Quality of Life - Alzheimer’s Disease scale (QoL-AD), which was designed for use with the CG as well as the CR (Logsdon et al, 1999). The caregivers were asked to rate the quality of their relationship with the CR on a 4-point scale, from 1 (poor) to 4 (excellent). This has been used previously as a measure of CR-CG relationship quality (Mahoney et al. 2005). I entered this information into the analysis as a dichotomous variable: whether or not the relationship was reported by the CG as “good or excellent” or not.

4.4.1.9 Past Psychiatric History

Caregivers were asked whether they had ever had contact with a professional for emotional problems.

4.4.1.10 Informal Support

Caregivers were asked how many people they were able to talk to currently about things that were private or personal, and the total number of people they reported was recorded. This measure forms part of the Close Persons Questionnaire (Stansfeld & Marmot 1992),

with items on work colleagues omitted. It has been used previously in this format to measure relationship quality between CG and CR (Murray et al. 1997).

4.4.2 Care Recipient interview

4.4.2.1 Socio-Demographic Factors

Ethnicity (White British or other) and type of accommodation of the CR was recorded. Type of accommodation was analysed as a dichotomous variable: living independently (in their own home or in supported accommodation), or living in a setting with 24 hour care (care home or hospital).

4.4.2.2 Mini Mental State Examination (MMSE)

This is a widely used measure of cognitive impairment (Folstein et al. 1975). The MMSE covers six areas: (1) orientation, (2) registration, (3) attention and calculation, (4) recall, (5) language, and (6) ability to copy a figure. Criterion validity has been demonstrated by a high level of correlation with the clock drawing test and the Cambridge Cognitive Examination (CAMCOG) ($r = .73$ and $r = .93$ respectively; both $p < 0.001$) in 114 psychogeriatric outpatients (Heinik et al. 2003). Test-retest reliability estimates reported in cognitively intact individuals using short test-retest intervals of less than 6 months ranged from .80 to .95 (Tombaugh & McIntyre 1992). Stability of scores over five years was assessed in 160 people with a physician confirmed diagnosis of no cognitive impairment according to DSM-III-R criteria at both time points. Scores did not change significantly (Tombaugh 2005). The MMSE is not sensitive for detecting mild dementia, and late in the course of AD the test has a “floor effect” (Cummings et al. 2002).

4.4.2.3 The Alzheimer’s Disease Assessment Scale-Cognition (ADAS-COG)

This is a more sensitive scale than the MMSE for measuring cognitive function, that includes more items assessing short-term memory (Rosen et al. 1984). It is the cognition scale most frequently used in drug trials because it is sensitive to change. In a

multicentre clinical drug trial involving 440 patients with AD, good internal consistency ($r > .80$) and test-retest reliability ($r = .93$) were reported, and factor analysis supported its validity (Weyer et al. 1997). Concurrent validity has been demonstrated by significant correlations with the MMSE ($r = -0.85$) and CAMCOG-R ($r = -0.84$) in 40 UK participants in a pan-European study (Verhey et al. 2004). It demonstrated 100% sensitivity and specificity for distinguishing between thirty-six patients with AD and 44 healthy controls (Ihl et al. 2000).

4.4.2.4 The Alzheimer's Disease Co-Operative Study Inventory - Activities Of Daily Living Scale (ADCS-ADL)

The 23-item ADCS-ADL scale is completed by the caregiver. Higher scores indicate less impaired ADL functioning. Six of the items cover basic ADL: eating, walking, toileting, bathing, grooming (each scored 0-3) and dressing (scored 0-7); the remaining items are IADL: using the telephone (scored 0-5); watching television, holding a conversation, clearing the dishes, managing personal belongings, obtaining beverages, selecting clothes, disposal of garbage, keeping up with current events, keeping appointments, writing, carrying out hobbies, ability to be left alone (each scored 0-3); making a meal or snack, physical performance, travel outside home, shopping, use of household appliances (scored 0-4) and reading (scored 0-2). Total possible scores range from 0 to 78.

The scale was used in a drug trial involving 659 patients with mild to moderate AD (Galasko et al. 2004). Good test-retest reliability was demonstrated by comparing baseline and 4-week data for total scores in the placebo group ($r = 0.91$, $p < 0.001$). A significant correlation was found between change in ADCS-ADL and ADAS-COG scores from baseline to 5 months ($r = -0.24$, $p < .0001$). Changes in Clinician's Interview Based Impression of Change (CIBIC) -plus scores, a measure of global functioning, were also significantly associated with changes in ADCS-ADL in all treatment groups (placebo, $r = -0.36$, $P < .0001$; treatment group, $r = -0.31$, $p < .0001$). There were weak

correlations between ADCS-ADL and Neuropsychiatric Inventory scores ($r=0.17$ and $p<.0001$). Overall, changes in the ADAS-COG accounted for only 4% to 9% of the variance in the ADL change scores, and the CIBIC-plus accounted for only 7% to 16%, clearly demonstrating that ADL change was largely independent of measured cognitive and clinical global change, and therefore establishing divergent validity.

4.4.2.5 **The Neuropsychiatric Inventory**

I used the Neuropsychiatric Inventory (NPI) to measure neuropsychiatric symptoms including behavioural problems, for which there was inconsistent evidence from previous studies of a relationship with CG anxiety; I also wanted to specifically measure CR emotional lability, as there was preliminary evidence that these were specifically associated with CG anxiety levels (see Table 3.1, page 99). was developed to assess psychopathology in dementia patients (Cummings et al. 1994). It evaluates twelve neuropsychiatric disturbances common in dementia: delusions, hallucinations, agitation, dysphoria, anxiety, apathy, irritability, euphoria, disinhibition, aberrant motor behavior, night-time behavior disturbances, and appetite and eating abnormalities. The NPI uses a screening strategy to minimise administration time, examining and scoring only those behavioural domains with positive responses to screening questions. The caregiver is asked to rate each one by frequency (score 1-4) and severity (score of 1-3) or as absent (score 0), with a maximum global score of 144. It takes about ten minutes to complete. Cummings and colleagues (1994) tested the psychometric properties of the NPI in older people without psychopathology, and in people with dementia attending outpatients, and reported mean scores of 0.43 and 8.25 respectively. Face validity was found to be satisfactory using a panel of appropriate experts, and concurrent validity was demonstrated by significant correlations between relevant NPI subscales and the Hamilton Depression Rating Scale and relevant subscales of the Behavioral Pathology in Alzheimer's Disease Scale (BEHAVE-AD). Excellent reliability in terms of internal

consistency, inter-rater reliability (agreement in over 90% of ratings) and test-retest reliability (a second interview within three weeks) was demonstrated (Cummings et al. 1994). The NPI is sensitive to treatment effects and has demonstrated the amelioration of behavioural symptoms in AD by cholinergic agents (Cummings 1997).

In addition to including the total score in our analysis, I also included the proportion of participants scoring at least 4 on the irritability subscale in my analyses, as this neuropsychiatric factor has been specifically associated with anxiety in CG (Table 3.1, page 99). This cut-off point has been used previously to denote clinically significant irritability (Schneider et al. 2001).

4.5 Power Calculation

In order to detect a moderate (0.4 or above) correlation (with no correlation as the alternate hypothesis) between coping and anxiety scores at a significance level of 0.01 and power of 90%, I calculated that a minimum of 87 caregivers would be required, using software from the University of California website (<http://ebook.stat.ucla.edu/calculators/powercalc/>). The sample size was thus clearly adequate even allowing for refusals and dropouts.

We also analysed data from the first twenty-five participants at T1 to determine whether this number of dyads would be sufficient for analyses planned with the outcome measure anxiety caseness. Mean dysfunctional subscales scores were 18.6(SD=4.5) for anxiety cases (n=5) and 14.1(SD=2.2) for non-anxiety cases (n=20). These results indicate that for a power of 80% and a significance level of 0.01, a minimum of 21 caregivers who were anxiety cases would be required to detect a significant difference in dysfunctional COPE scores between anxious and non-anxious caregivers. Presuming

a prevalence of anxiety of 23.5% (Mahoney et al., in press), we would therefore need to interview at least 90 caregivers.

4.6 Statistical analysis

Two-tailed tests were used throughout. The significance level was $p < 0.01$ for univariate analyses because of the high number of comparisons, and $p < 0.05$ for multivariate tests. For univariate tests, a normal distribution was assumed where the skewness statistic was less than twice the standard error for skewness. I used SPSS version 12.0 (SPSS inc 1999) and AMOS (Arbuckle 2003) to analyse the data.

4.6.1 Cross-sectional analyses

I investigated the relationship between anxiety score and coping strategy subscale scores using linear regression as I was interested in relative scores on each of the subscales. I used Spearman or Pearson correlation coefficients, independent t-tests or Whitney Mann-U tests as appropriate to determine the univariate relationship of anxiety score to all potential mediators and confounders of the relationship between coping, burden and anxiety studied. To test my hypothesis that coping strategies mediated the relationship between caregiver burden and anxiety score, using the criteria identified by Baron and Kenny (1986) to define mediation, I investigated the correlation between coping and burden scores. I then used stepwise linear regression with anxiety score as the dependent variable. I entered burden score on step one, coping subscale scores on step two, all factors that approached significance on univariate analysis ($p < 0.1$) on step 3, and HADS depression score on step four. Missing values (25, 21 and 1 values respectively) were replaced with the series mean for the variables hours spent caring, physical functioning and total life events.

I repeated this analysis to determine what factors were associated with anxiety caseness on univariate analysis, using chi-squared, independent t-tests or Whitney Mann-U tests

as appropriate. I then undertook a stepwise logistic regression entering factors as for the linear regression above to determine whether the same factors also predicted having clinically significant anxiety. Finally I repeated the anxiety score analyses outlined above with depression score as the dependent variable.

4.6.2 Longitudinal analyses

I investigated the relationship between T2 anxiety score and T1 and T2 coping strategy subscale scores using linear regression as above. I used Spearman or Pearson correlation coefficients, independent t-tests or Whitney Mann-U tests as appropriate to determine the univariate relationship of anxiety score at T2 to all potential mediators and confounders studied at T1. I repeated the correlation between T1 coping and burden scores, including only those followed up at T2. I then conducted a stepwise linear regression. I entered burden score on step one, T1 coping subscale scores on step two, baseline anxiety score on step three, T2 coping subscale scores from T2 on step four, and all the other factors studied that approached significance ($p < 0.1$) on univariate analysis on step five (Table 6.2, page 147). I repeated these analyses with anxiety caseness and depression score as dependent variables. In a *post hoc* modification due to the lower than expected levels of depression caseness detected I did not use depression caseness as a dependent variable, and due to the low power to detect an association with depression score, included overall psychological morbidity (total HADS score) as an additional dependent variable.

Because I have used variables that were anticipated to correlate significantly with each other (e.g. burden and anxiety), collinearity was a potential confounding factor in this study. Collinearity is a situation where there is close to a near perfect linear relationship among some or all of the independent variables in a regression model. This might be caused by a very high correlation among two independent variables, or between the sum of a group of variables and another value. Collinearity decreases power and makes

interpretation more difficult. I used structural equation modelling for confirmation of the model that emerged from these analyses for anxiety score (my primary outcome measure), in order to ensure that the positive findings were not resulting from collinearity.

Structural equation modelling is a hybrid statistical technique that encompasses aspects of factor analysis, path analysis and regression. It encourages confirmatory, rather than exploratory, modelling, and therefore it is suited to theory testing, rather than theory development. I have used it to test my theory, generated through the earlier exploratory analyses.

In order to obtain the most parsimonious model I used the accepted criterion that associations between variables were removed from the saturated model (a model in which all possible associations were included) if the rise in χ^2 for the model (which tests the null hypothesis that the model could have occurred by chance) was smaller than the critical value for that association. I reported the Normed Fit Index (NFI; a measure from 0 to 1 (perfect fit) of the extent to which the model fits the data); χ^2 test for the final model, and standardised regression estimates for each association. $\text{NFI} \geq 0.9$ (Bentler & Bonett 1980) is generally accepted as evidence of a well fitting model.

5 CROSS-SECTIONAL STUDY RESULTS

(see published paper, Appendix E)

The mean and standard deviations (sd) for anxiety and depression scores of the sample interviewed at T1 (n=126) were 6.2 (sd=4.5) and 4.2 (sd=3.8) respectively. Forty (31.7%) of participants were anxiety cases on the HADS of whom 19 (47.5%) were also depression cases. There were 24 (19.0%) depression cases at T1.

5.1 Factors associated with anxiety score

Anxiety score was associated on univariate analysis with higher caregiver burden, health perception and role and physical functioning scores (Table 5.1, page 128). Anxiety score was also significantly related to using relatively more dysfunctional ($t=6.1$; $p<0.001$) and less emotion-focussed coping strategies ($t=-2.4$, $p=0.016$) but not with problem-focussed coping strategy scores ($t=1.4$, $p=0.14$).

Anxiety score was predicted on linear regression in step one by burden score ($t=6.0$; $p<0.001$), and this explained 23.0% of the variance in anxiety score. On step two the predictors were burden score ($t=3.5$; $p=0.001$), higher dysfunctional ($t=5.0$; $p<0.001$) and lower emotion-focussed ($t=-2.1$; $p=0.041$) coping strategy scores. Coping strategies explained an additional 14.1% of the anxiety score variance. On step three (once all factors from Table 5.1 (page 128) approaching significance were added) the predictors remained burden score ($t=2.7$; $p=0.009$), higher dysfunctional ($t=4.1$; $p<0.001$) and lower emotion-focussed ($t=-3.0$; $p=0.003$) coping strategy scores. On step four when depression score was added, the predictors were: depression score ($t=8.3$, $p<0.001$); and dysfunctional ($t=3.1$; $p=0.003$) and emotion-focussed coping strategy scores ($t=-2.2$; $p=0.028$) (Table 5.2, page 130); the final model explained 68.8% of the variance in anxiety score. Dysfunctional ($r=0.50$, $p<0.001$) and emotion-focussed ($r=0.28$, $p=0.002$)

coping scores were also correlated with caregiver burden. Therefore, using relatively more dysfunctional and less emotion-focussed coping partially mediated the relationship between burden and anxiety scores cross-sectionally, and together with depression score they were the only significant factors in the final model which fully mediated this relationship.

Table 5.1 Factors associated with anxiety score (T1)

Factor		r	Mean(sd)/mean(sd))	MW U	p
CG	Male/female		6.2(4.9)/6.3(4.4)	1729	0.70
	Age	0.087			0.33
	Living/ not living with CR		7.0(4.9)/5.5(4.1)	1670	0.12
	Married or cohabiting or not		6.1(4.4)/6.6(5.1)	1185	0.81
	Hours spent caring	0.20			0.048
CR in 24 hour care/ living independently			6.0(4.2)/6.3(4.7)	1578	0.81
CR ethnicity White British/ not			6.1(4.5)/8.4(4.8)	289	0.17
Spouse/partner			7.3(4.7)/5.5(4.3)	1492	0.025
Relationship with CR “good/excellent”/not			5.9(4.2)/7.4(5.5)	1147	0.26
Life events	Total score	0.21			0.02
	serious threat		7.3(4.8)/5.3(4.1)	1451	0.015
	Serious threat, independent		7.9(4.9)/5.8(4.4)	989	0.044
Zarit burden score total		0.41			<0.001
No. people CG can talk to		-0.061			0.50
Consult for emotional problems yes/no			8.0(5.3)/5.5(4.1)	1126	0.013
HSQ scores	Health perception	-0.31			<0.001
	Physical functioning	-0.35			<0.001
	Role physical	-0.31			<0.001

CR	ADAS-Cog total score	0.032			0.72
Morbidity	MMSE	-0.003			0.97
	ACDS-ADL	-0.047			0.60
	NPI Total score	0.12			0.18
	NPI irritability score 4+		7.9(5.1)/5.9(4.3)	857	0.064

Key to tables:

MWU = Mann-Whitney U statistic

r = Spearman correlation coefficient

Table 5.2 Linear regression of factors predicting anxiety score (T1)

	Factor	t	P
Step 1 $R^2=0.230$	Caregiver burden	6.0	<0.001
Step 2 $R^2=0.371$	Caregiver burden	3.5	0.001
	Dysfunctional coping T1	5.0	<0.001
	Emotion-focused coping T1	-2.1	0.041
	Problem-focused coping T1	0.12	0.91
Step 3 $R^2=0.489$	Caregiver burden	2.7	0.009
	Dysfunctional coping T1	4.1	<0.001
	Emotion-focused coping T1	3.0	0.003
	Problem-focused coping T1	0.83	0.41
	Hours spent caring	0.78	0.44
	Caring for a spouse	-0.80	0.43
	Life event score	1.1	0.26
	Severe life event	-0.46	0.64
	Independent, severe life event	0.72	0.47
	Health perception	0.079	0.94
	Role physical	-1.4	0.16
	Physical functioning	-1.2	0.25
	Irritability score	-0.89	0.38
	Ever consulted profession for emotional problems?	1.6	0.12
Step 4 $R^2=0.688$	Caregiver burden	1.9	0.067
	Dysfunctional coping T1	3.1	0.003
	Emotion-focused coping T1	-2.2	0.028

	Depression score	8.3	<0.001
	Problem-focused coping T1	0.78	0.45
	Hours spent caring	-0.19	0.85
	Caring for a spouse	-0.52	0.61
	Life event score	1.7	0.087
	Severe life event	-0.34	0.73
	Independent, severe life event	-0.11	0.91
	Health perception	0.92	0.36
	Role physical	-1.2	0.23
	Physical functioning	0.55	0.58
	Irritability score	-1.5	0.14
	Consulted profession for emotional problems?	1.3	0.19

5.2 Factors associated with anxiety caseness

Anxious caregivers reported more use of dysfunctional coping strategies and less use of the other types of strategy (Figure 5.1, page 133). When the proportion of each strategy used was considered, anxious caregivers were relatively more likely to use dysfunctional (Wald=15.1, $p<0.001$) and there was a statistically non-significant trend towards being less likely to use emotion-focussed coping strategies (Wald=1.5, $p=0.23$) than those who were not anxiety cases (Figure 5.2, page 134). Anxious CG did not differ from non-anxious caregivers in their proportional use of problem-focussed (Wald=0.010, $p=0.92$) coping strategies.

More total life events and higher burden score were significantly associated with anxiety caseness on univariate analysis (Table 5.3, page 135). Being an anxiety case was predicted on logistic regression (Table 5.4, page 137) in step one by burden score (Wald 12.8, OR 1.1, $p<0.001$); in step two by burden score (Wald 4.1, OR 1.0, $p=0.042$) and use of dysfunctional coping strategies (Wald=7.3, OR=1.3, $p=0.001$); and in step three by dysfunctional coping strategies (Wald=9.0, OR=1.3, $p=0.003$). On step four, anxiety caseness was predicted by: dysfunctional coping strategies (Wald=7.3, OR=1.3, $p=0.007$) and depression caseness (Wald=12.4, OR=15.3, $p<0.001$). Hence dysfunctional coping strategies also mediated the cross-sectional relationship between burden and anxiety caseness, and together with depression caseness was the only significant factor in the final model which fully mediated the relationship between caregiver burden and experiencing clinically significant anxiety.

Figure 5.1 Coping strategy use reported by anxious and non-anxious caregivers

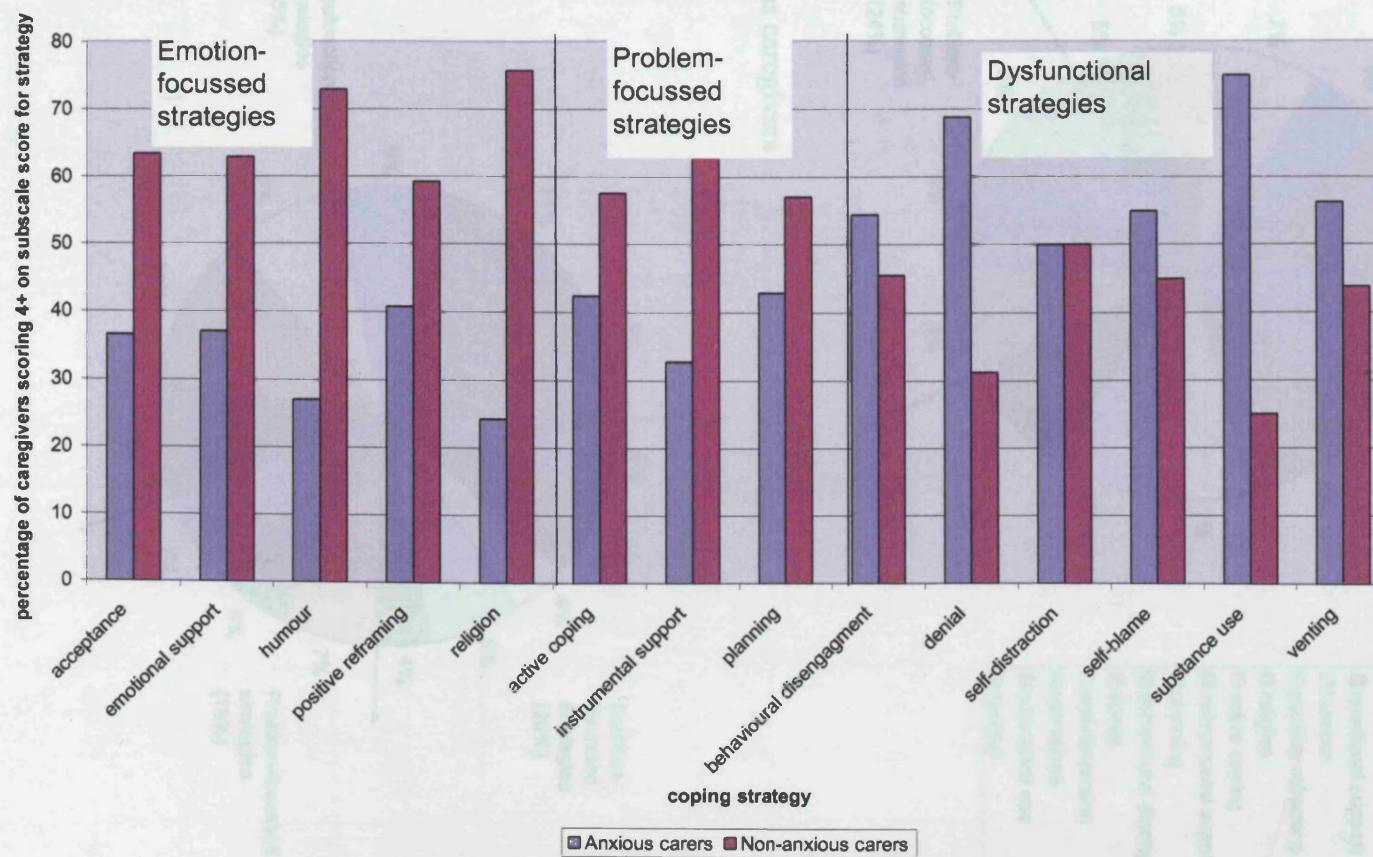


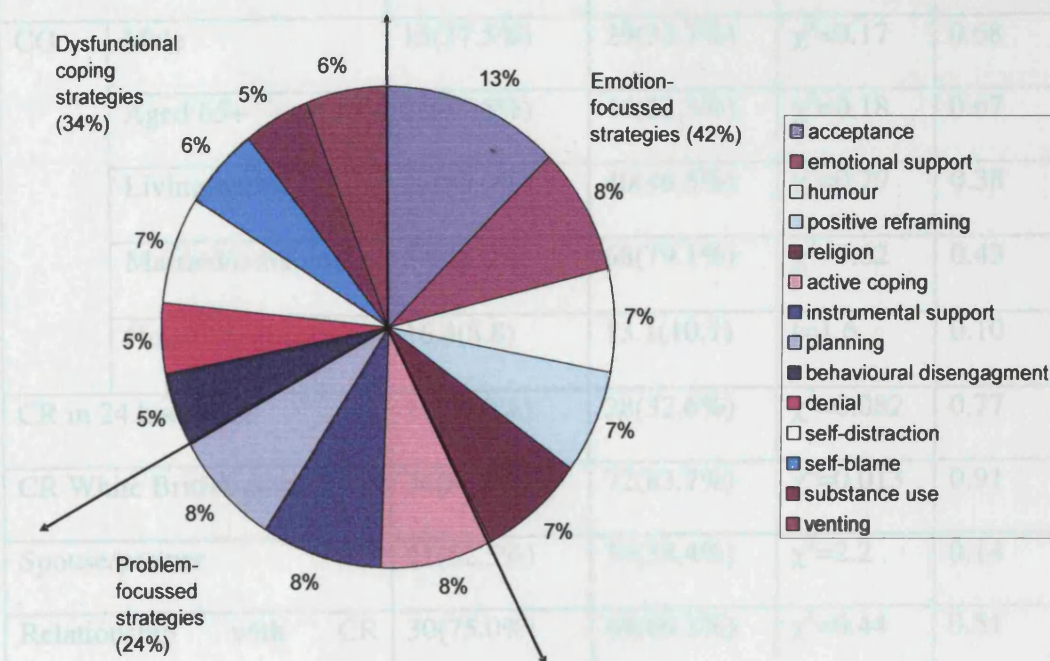
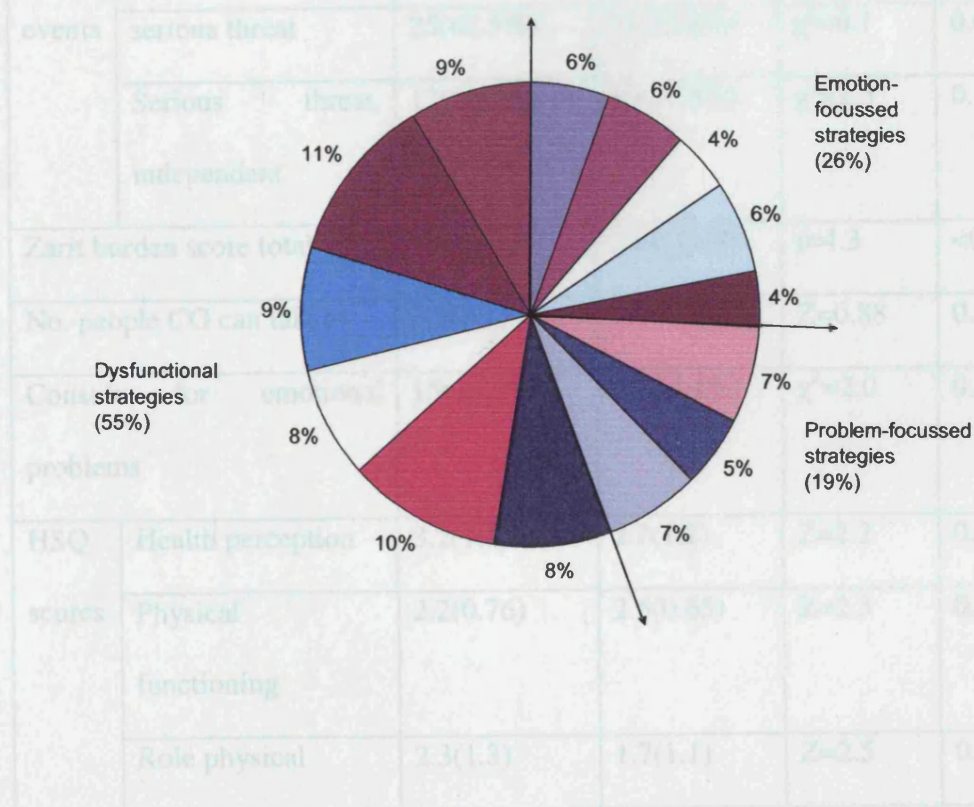
Figure 5.2 Proportional use of coping strategies by caregivers**(a) Non-anxious caregivers****(b) anxious caregivers**

Table 5.3 Factors associated with anxiety caseness (T1)

		Anxiety case(n=40)	Not case(n=86)	χ^2/t	p
CG	Male	15(37.5%)	29(33.7%)	$\chi^2=0.17$	0.68
	Aged 65+	23(57.5%)	46(53.5%)	$\chi^2=0.18$	0.67
	Living with CR	22(55.0%)	40(46.5%)	$\chi^2=0.79$	0.38
	Married/cohabiting	34(85.0%)	68(79.1%)	$\chi^2=0.62$	0.43
	Hours spent caring	16.4(8.8)	13.1(10.1)	t=1.6	0.10
CR in 24 hour care		12(30.0%)	28(32.6%)	$\chi^2=0.082$	0.77
CR White British ethnicity		34(82.9%)	72(83.7%)	$\chi^2=0.013$	0.91
Spouse/partner		21(52.5%)	33(38.4%)	$\chi^2=2.2$	0.14
Relationship with CR “good/excellent”		30(75.0%)	69(80.2%)	$\chi^2=0.44$	0.51
Life events	Total score	85.5(75.8)	50.6(55.4)	Z=2.8	0.006
	serious threat	25(62.5%)	33(38.8%)	$\chi^2=6.1$	0.013
	Serious threat, independent	12(30.0%)	15(17.6%)	$\chi^2=2.5$	0.12
Zarit burden score total		35.2(15.0)	24.0(12.8)	t=4.3	<0.001
No. people CG can talk to		3.3(2.1)	3.7(2.5)	Z=0.88	0.38
Consult for emotional problems		15(36.6%)	21(24.4%)	$\chi^2=2.0$	0.16
HSQ scores	Health perception	3.2(1.1)	2.7(1.2)	Z=2.2	0.030
	Physical functioning	2.2(0.76)	2.5(0.65)	Z=2.3	0.024
	Role physical	2.3(1.3)	1.7(1.1)	Z=2.5	0.013

CR morbi dity scale scores	ADAS-Cog	40.1(20.0)	40.5(24.7)	$t=0.11$	0.92
	MMSE	13.6(8.7)	14.0(9.3)	$t=0.20$	0.85
	ACDS-ADL	28.1(19.3)	31.8(22.0)	$t=0.93$	0.36
	NPI total	22.7(15.8)	18.7(16.0)	$Z=1.6$	0.12
	NPI irritability 4+	10(25.0%)	12(14.0%)	$\chi^2=2.3$	0.13

Table 5.4 Logistic regression of factors predicting anxiety caseness (T1)

	Factor	Wald	OR (CI)	P
Step 1	Caregiver burden	12.8	1.1(1.0-1.1)	<0.001
Step 2	Caregiver burden	4.1	1.0(1.0-1.1)	0.042
	Dysfunctional coping T1	11.5	1.3(1.1-1.5)	0.001
	Emotion-focused coping T1	0.78	0.95(0.85-1.1)	0.38
	Problem-focused coping T1	0.51	0.95(0.82-1.1)	0.48
Step 3	Caregiver burden	3.0	1.0(1.0-1.1)	0.84
	Dysfunctional coping T1	9.0	1.3(1.1-1.5)	0.003
	Emotion-focused coping T1	1.1	0.94(0.83-1.1)	0.29
	Problem-focused coping T1	0.61	0.93(0.78-1.1)	0.43
	Life event score	2.6	1.0(1.0-1.0)	0.10
	Severe life event	0.019	0.92(0.29-3.0)	0.89
	Health perception	0.27	1.0(0.98-1.0)	0.61
	Role physical	0.75	0.99(0.97-1.0)	0.39
	Physical functioning	0.29	0.99(0.97-1.0)	0.59
Step 4	Caregiver burden	2.8	1.0(0.99-1.1)	0.95
	Dysfunctional coping T1	7.3	1.3(1.1-1.5)	0.007
	Emotion-focused coping T1	0.35	0.96(0.85-1.1)	0.56
	Problem-focused coping T1	1.1	0.90(0.74-1.1)	0.29
	Depression case	12.4	15.3(3.4-69.8)	<0.001
	Life event score	3.3	1.0(1.0-1.0)	0.071
	Severe life event	0.069	0.84(0.23-3.0)	0.79
	Health perception	0.79	1.0(0.99-1.0)	0.37
	Role physical	0.61	0.99(0.97-1.0)	0.44
	Physical functioning	0.13	1.0(0.98-1.0)	0.72

5.3 Factors associated with depression score

The following factors were significantly associated with depression score on univariate analysis (Table 5.5, page 139): the caregiver being older, living with and being the spouse of the CR, spending more hours caring; reporting more caregiver burden; and higher health perception, role physical and physical functioning HSQ scores. Depression score was significantly related to using relatively more dysfunctional ($t=4.4$; $p<0.001$), but not emotion-focussed ($t=-0.91$, $p=0.37$) or problem-focussed ($t=0.25$, $p=0.81$) coping strategy scores. On linear regression (Table 5.6, page 141), factors associated with caregiver depression score were: caregiver burden on step one ($t=5.1$; $p<0.001$) which explained 17.8% of depression score variance. Caregiver burden ($t=3.6$, $p<0.001$) and higher dysfunctional coping strategy score ($t=3.3$, $p=0.001$) were significant factors on step two, in which coping strategies explained an additional 7.1% of depression score variance. Emotion-focussed ($t=-2.0$, $p=0.044$), dysfunctional coping strategy ($t=2.9$, $p=0.005$) and physical functioning scores ($t=-2.6$, $p=0.010$) were the significant factors on step three after all factors approaching significance on univariate analysis (Table 5.5, page 139) were entered; and physical functioning ($t=-2.3$, $p=0.026$) and anxiety score ($t=7.9$, $p<0.001$) were the only significant factors on step four after adding anxiety score into the equation. The final model explained 68.3% of the variance in depression score. The analysis was not repeated with depression caseness as the dependent variable due to the low number of cases in the sample ($n=24$).

Table 5.5 Factors associated with depression score (T1)

Factor that depression score relationship reported for		r	Mean(sd)/mean (sd)	MWU	p
CG	Male/female		4.6(3.9)/3.9(3.7)	4995	0.27
	Age	0.26			0.003
	Living/ not living with CR		5.2(3.8)/3.3(3.5)	1325	0.001
	Married/cohabiting or not		4.3(3.8)/3.8(3.7)	1121	0.52
	Hours spent caring	0.41			<0.001
CR in 24 hour care/ living independently			3.8(3.9)/4.3(3.7)	1121	0.52
CR ethnicity White British/ not			4.0(3.7)/7.1(3.3)	199	0.020
Spouse/partner or not			5.8(3.9)/3.0(3.3)	1047	<0.001
Relationship with CR "good/excellent"			3.8(3.6)/5.4(4.3)	1082	0.13
Life events	Total score	0.13			0.14
	serious threat		4.9(3.8)/3.5(3.7)	1436	0.011
	Serious threat, independent		5.7(4.1)/3.7(3.6)	902	0.011
Zarit burden score total		0.41			<0.001
No. people CG can talk to		-0.087			0.34
Consult for emotional problems yes/no			5.1(4.3)/3.7(3.5)	1294	0.12
HSQ	Health perception	-0.47			<0.001

scores	Physical functioning	-0.52			<0.001
	Role physical	-0.48			<0.001
CR morbidity scale scores	ADAS-Cog	0.013			0.89
	MMSE	0.001			0.99
	ACDS-ADL	-0.041			0.65
	NPI Total score	0.14			0.13
	NPI irritability score 4+		5.9(4.5)/3.8(3.5)	818	0.035

Table 5.6 Linear regression of factors predicting depression score (T1)

	Factor	t	P
Step 1 ($R^2=0.178$)	Caregiver burden	5.1	<0.001
Step 2 $R^2=0.249$	Caregiver burden	3.6	<0.001
	Dysfunctional coping T1	3.3	0.001
	Emotion-focused coping T1	-0.47	0.64
	Problem-focused coping T1	-1.1	0.27
Step 3 $R^2=0.494$	Caregiver burden	1.7	0.091
	Dysfunctional coping T1	2.9	0.005
	Emotion-focused coping T1	-2.0	0.044
	Problem-focused coping T1	0.28	0.78
	CG age	-1.5	0.14
	Living with CR	0.88	0.38
	Hours spent caring	1.7	0.089
	CR ethnicity	-0.11	0.92
	Caring for a spouse	0.45	0.65
	Severe life event	-0.77	0.45
	Independent, severe life event	1.4	0.16
	Health perception	-1.1	0.27
	Role physical	-0.57	0.57
	Physical functioning	-2.6	0.010
	Irritability score	0.31	0.76
Step 4 $R^2=0.683$	Caregiver burden	0.45	0.66
	Dysfunctional coping T1	0.079	0.94
	Emotion-focused coping T1	-0.27	0.79

	Problem-focused coping T1	0.44	0.66
	CG age	-0.61	0.54
	Living with CR	0.61	0.54
	Hours spent caring	1.3	0.20
	CR ethnicity	-0.34	0.73
	Caring for a spouse	0.58	0.57
	Severe life event	-0.93	0.35
	Independent, severe life event	1.1	0.28
	Health perception	-1.1	0.28
	Role physical	0.18	0.85
	Physical functioning	-2.3	0.026
	Irritability score	1.1	0.27
	Anxiety score	7.9	<0.001

6 RESULTS FROM LONGITUDINAL STUDY

6.1 Changes in anxiety and coping scores

6.1.1 Anxiety

Mean (sd) anxiety scores for the participants interviewed at both T1 and T2 (n=93) were 6.0 (4.4) at T1 and 6.2 (4.4) at T2 (paired $t = -0.77$, $p = 0.44$). Mean depression scores were 3.9 (3.4) at T1 and 4.1 (3.5) at T2 (paired Wilcoxon signed rank statistic (Z) = -1.2, $p = 0.23$). 24 (25.8%) of the caregivers interviewed at both time points were anxiety cases at T1, of whom 18 (75.0%) were still cases at T2. Thirteen CG newly fulfilled criteria for caseness at T2, so in total, 31 (33.3%) caregivers were anxiety cases at T2.

6.1.2 Depression

Fifteen (16.1%) of the caregivers were depression cases at T1 of whom 11 (73.3%) were still cases at T2. Eight CG newly fulfilled criteria for caseness at T2, so in total, 19 (20.4%) caregivers were depression cases at T2.

6.1.3 Coping

Coping subscale scores all increased but not significantly so, although the increase in use of problem-focussed strategies approached significance. Mean scores at T1 and T2 were: 11.1 (4.1) and 11.8 (4.3) ($t = -2.1$, $p = 0.041$) for problem-focussed; 19.4 (5.1) and 20.0 (5.1) ($t = -1.2$, $p = 0.22$) for emotion-focussed; and 15.6 (4.0) and 16.1 (4.2) ($Z = -0.84$, $p = 0.40$) for dysfunctional coping strategies. Correlations between T1 and T2 scores were significant for dysfunctional ($r = 0.63$, $p < 0.001$), problem-focussed ($r = 0.71$, $p < 0.001$) and emotion-focussed ($r = 0.51$, $p < 0.001$) strategies.

6.2 Anxiety score and coping

Anxiety score at T2 was associated with: using relatively fewer emotion-focussed, and more problem-focussed and dysfunctional coping at T1, but only using relatively more dysfunctional coping at T2 (Table 6.1, page 146). I repeated the T1 cross-sectional analysis using only those caregivers who were reinterviewed at T2, and found that use of relatively more dysfunctional coping strategies ($t=3.9$, $p<0.001$) but neither emotion-focussed ($t=-0.82$, $p=0.42$) nor problem-focussed ($t=1.1$, $p=0.26$) at T2 were associated with anxiety score at T1 in this cohort.

The T1 factors studied that were significantly associated with anxiety score at T2 on univariate analysis were burden score and self-rated health perception (Table 6.2, page 147). Pearson's correlation coefficients were significant for the relationship of caregiver burden score to: T1 dysfunctional ($r=0.58$; $p<0.001$); emotion-focussed ($r=0.34$; $p=0.001$) and problem-focussed ($r=0.46$, $p<0.001$) coping strategies. On linear regression (see Table 6.3, page 150 for factors added to the equation at each step), caregiver burden was a significant predictor of T2 anxiety score ($t=3.1$, $p=0.002$) on step one and explained 10.0% of its variance. Using more problem-focussed strategies ($t=2.2$; $p=0.028$) was the only predictor on step two, where addition of coping strategies to the equation explained an additional 12.3% of T2 anxiety score variance. T1 anxiety score ($t=10.5$; $p<0.0005$), using fewer emotion-focussed ($t=-2.0$; $p=0.046$) and more problem-focussed strategies at T1 ($t=2.3$; $p=0.023$) were the only significant predictors on step three; T1 anxiety score ($t=9.2$; $p<0.0005$) and using fewer emotion-focussed strategies at T1 ($t=-0.13$; $p=0.036$) were the predictors on step four, where T2 coping strategy scores were added. They explained only an additional 0.32% of anxiety score variance. In the final model, which explained 74.3% of T2 anxiety score variance and fully mediated the relationship between T1 burden and T2 anxiety scores, T1 anxiety score ($t=8.8$; $p<0.0005$), using relatively fewer emotion-focussed strategies ($t=-2.3$;

$p=0.023$) and more problem-focussed strategies at T1 ($t=2.2$; $p=0.034$) and higher health perception ($t=-2.8$; $p=0.007$) were the only significant predictors.

Finally, I explored the relationship between T1 anxiety score and T2 coping strategy scores to confirm direction of causality. Higher anxiety score significantly predicted using relatively more dysfunctional coping strategies a year later ($t=6.3$, $P<0.001$) but was not related to subsequent emotion-focussed ($t=-0.44$, $p=0.66$) or problem-focussed ($t=1.1$, $p=0.29$) coping strategy use.

6.3 Anxiety caseness and coping

Anxiety caseness at T2 was also associated with using relatively fewer emotion-focussed, and more problem-focussed and dysfunctional coping at T1 but only using more dysfunctional coping at T2 (Table 6.1, page 146). Burden score was the only T1 factor associated with being an anxiety case at T2 on univariate analysis (Table 6.4, page 152).

On step one of the logistic regression analysis with anxiety caseness as the dependent variable, caregiver burden predicted anxiety caseness at T2 (see Table 6.5, page 154 for factors added to the equation at each step). On step two there were no predictors. On step three using fewer emotion-focussed and more problem-focussed strategies at T1, and T1 anxiety caseness were significant factors. On step four only using fewer emotion-focussed strategies and T1 anxiety caseness were significant factors. In the final model which fully mediated the relationship between T1 burden and T2 anxiety caseness, using fewer emotion-focussed and more problem-focussed strategies, being an anxiety case and consulting a professional about emotional problems at T1; and using more dysfunctional coping strategies at T2 were the only significant factors.

Table 6.1 The relationship of coping scores to anxiety and depression

	Anxiety score T2		Anxiety caseness T2		Depression score T2	
	t	p	Wald	p	t	p
T1 emotion-focussed coping	-2.1	0.039	4.8	0.028	-1.01	0.31
T1 dysfunctional coping	2.8	0.007	9.9	0.002	2.2	0.027
T1 problem-focussed coping	2.5	0.016	1.9	0.017	1.0	0.30
T2 emotion-focussed coping	-0.56	0.58	0.72	0.40	-0.93	0.35
T2 dysfunctional coping	4.9	<0.001	11.4	0.001	3.8	<0.001
T2 problem-focussed coping	1.1	0.28	0.66	0.42	0.86	0.39

Table 6.2 Factors at T1 and association with anxiety and depression score (T2)

Factor studied		n	Anxiety score			Depression score		
			Mean (sd)	t or r	p	Mean (sd)	MWU or r	p
CG gender	Male	34	5.6(4.0)	0.91	0.37	4.1(2.7)	932	0.57
	Female	59	6.5(4.7)			4.1(3.8)		
CG age		93		0.59	0.57		0.26	0.011
CR ethnicity White British?	yes	90	9.7(3.1)	1.4	0.17	4.0(3.4)	87	0.29
	no	3	6.1(4.5)			6.0(3.6)		
Living with CR	yes	51	6.3(4.5)	0.38	0.70	4.6(3.6)	864.5	0.11
	no	42	6.0(4.5)			3.5(3.2)		
Carer married/ cohabiting	yes	76	5.9(4.5)	1.1	0.28	4.6(2.9)	531	0.025
	no	17	7.2(4.1)			4.0(3.5)		
Carer level of education	O Level or below	52	6.4(4.6)	1.0	0.31	4.60(3.7)	659.5	0.16

	Post 16 education	31	5.4(4.0)			3.32(2.8)		
CG hours spent caring		78		0.14	0.17		0.41	<0.001
CR in 24 hour care	yes	22	7.2(4.5)	1.3	0.21	3.9(3.2)	746	0.75
	no	71	5.8(4.4)			4.2(3.5)		
CR spouse/ partner of carer	yes	42	6.7(4.3)	1.0	0.31	4.9(3.3)	752	0.013
	no	51	5.7(4.6)			3.4(3.4)		
Relationship with CR “good/excellent”	yes	74	6.0(4.6)	0.62	0.54	3.9(3.4)	597	0.31
	no	19	6.7(4.2)			4.8(3.5)		
Carer ever had consult for mental health problems	yes	25	7.9(4.4)	2.3	0.022	5.4(3.8)	595	0.032
	no	67	5.5(4.4)			3.6(3.2)		
No. confidants for personal/ private matters		91		-0.043	0.69		-0.099	0.35
Life event score (in last 6 months)		92		0.20	0.057		0.10	0.32
Serious, threatening life event	yes	43	6.9(4.8)	1.4	0.15	5.0(3.8)	778	0.030
	no	49	5.5(4.3)			3.2(2.8)		

Serious, independent life event	Yes	17	7.71(5.2)	1.6	0.11	5.8(3.9)	433	0.038
	No	75	5.79(4.3)			3.7(3.2)		
Zarit burden score		93		0.34	0.001		0.32	0.002
Carer physical health	Health perception	93		-0.34	0.001		-0.41	<0.001
	Physical functioning	93		-0.26	0.013		-0.36	<0.001
	Role physical	93		-0.25	0.018		-0.31	0.002
MMSE		93		-0.19	0.075		-0.043	0.69
ACDS-ADL		93		-0.18	0.094		-0.068	0.52
NPI Total score		93		0.14	0.17		0.19	0.063
NPI irritability score 4+	Yes	13	7.85(5.2)	-1.46	0.15	6.4(4.5)	337	0.041
	No	80	5.19(1.4)			3.7(3.1)		
ADAS-Cog		93		0.20	0.055		0.047	0.66

Table 6.3 Linear regression of factors predicting anxiety score (T2)

	R squared	Factor	Standard-ised Beta	t	P
Step 1	0.100	Caregiver burden	0.316	3.122	0.002
Step 2	0.223	Caregiver burden	0.122	1.057	0.293
		Dysfunctional coping T1	0.254	1.962	0.053
		Emotion-focused coping T1	-0.256	-1.984	0.051
		Problem-focused coping T1	0.324	2.238	0.028
Step 3	0.665	Caregiver burden	-0.037	-0.476	0.635
		Dysfunctional coping T1	-0.010	-0.115	0.909
		Emotion-focused coping T1	-0.174	-2.026	0.046
		Problem-focused coping T1	0.223	2.315	0.023
		Anxiety score T1	0.776	10.526	<0.0005
Step 4	0.668	Caregiver burden	-0.045	-0.556	0.580
		Dysfunctional coping T1	-0.027	-0.279	0.781
		Emotion-focused coping T1	-0.199	-0.127	0.036
		Problem-focused coping T1	0.237	1.877	0.064
		Anxiety score T1	0.755	9.159	<0.0005
		Dysfunctional coping T2	0.042	0.432	0.667
		Emotion-focused coping T2	0.050	0.586	0.559

		Problem-focused coping T2	-0.018	-0.174	0.862
Step 5	0.743	Caregiver burden	-0.100	-1.260	0.212
		Dysfunctional coping T1	-0.014	-0.143	0.887
		Emotion-focused coping T1	-0.210	-2.325	0.023
		Problem-focused coping T1	0.279	2.159	0.034
		Anxiety score T1	0.746	8.794	<0.0005
		Dysfunctional coping T2	-0.047	-0.450	0.654
		Emotion-focused coping T2	0.048	0.582	0.562
		Problem-focused coping T2	0.030	0.293	0.770
		Health perception score	-0.262	-2.769	0.007
		Consultation for emotional problems	0.087	1.343	0.183
		Total life event score	-0.073	-1.059	0.293
		Physical functioning score	0.031	0.345	0.731
		Role physical score	0.040	0.382	0.704
		ADAS-Cog total score	0.155	0.680	0.499
		ADCS-ADL total score	-0.056	-0.491	0.625
		MMSE score	0.046	0.205	0.838

Table 6.4 Factors at T1 and their association with anxiety caseness (T2)

Factor at T1		Anxiety case T2 (n=31)	Not anxiety case T2 (n=64)	χ^2 /t	p
Caregiver demographic factors *n=79	Male	9(29.0%)	26(40.6%)	$\chi^2=1.2$	0.27
	Aged 65+	17(54.8%)	34(53.1%)	$\chi^2=0.025$	0.88
	Living with CR	17(54.8%)	34(53.1%)	$\chi^2=0.025$	0.88
	Married/cohabiting	25(80.6%)	53(82.8%)	$\chi^2=0.067$	0.80
	Hours spent caring*	16.1(9.5)	14.0(9.6)	Z=0.87	0.38
CR in 24 hour care		11(35.5%)	13(20.3%)	$\chi^2=2.5$	0.11
CR ethnicity White British		30(93.8%)	89(94.7%)	$\chi^2=0.39$	0.84
Spouse/partner		16(51.6%)	26(40.6%)	$\chi^2=1.0$	0.31
Relationship with CR “good/excellent”		23(74.2%)	53(82.8%)	$\chi^2=0.97$	0.33
Caregiver ever had consult for mental health		13(43.3%)	13(20.3%)	$\chi^2=5.4$	0.020
No. people CG can talk to		3.6(2.4)	3.6(2.4)	Z=-0.071	0.94
Life events (in last 6	Total score	72.9(62.8)	55.0(60.1)	Z=1.3	0.19
	serious threat	19(63.3)	26(40.6)	$\chi^2=4.2$	0.040
	Serious threat,	7(23.3%)	11(17.2%)	$\chi^2=0.50$	0.48

months)	independent				
Zarit burden score total		32.7(15.8)	23.7(12.2)	t=3.1	0.003
Carer physical health (HSQ)	Health perception	50.8(28.2)	65.4(27.9)	t=2.4	0.019
	Physical functioning	62.4(37.8)	81.3(28.7)	t=2.5	0.018
	Role physical	65.2(38.3)	77.3(30.9)	t=1.7	0.10
CR Morbidity	ADAS-Cog total score	39.3(22.4)	35.7(21.6)	t=0.76	0.45
	MMSE	13.8(9.5)	15.1(8.6)	t=0.65	0.51
	ACDS-ADL	30.3(19.8)	35.4(21.9)	t=1.1	0.28
	NPI Total score	16.1(14.3)	20.8(15.3)	t=1.5	0.15
	NPI irritability score 4+	7(22.6%)	6(9.4%)	$\chi^2=3.1$	0.079

Table 6.5 Logistic regression of factors predicting anxiety caseness (T2)

	Factor	OR	CI	P
Step 1	Caregiver burden	1.0	1.0-1.1	0.014
Step 2	Caregiver burden	1.0	0.97-1.0	0.54
	Dysfunctional coping T1	1.2	0.99-1.4	0.072
	Emotion-focused coping T1	0.89	0.78-1.0	0.089
	Problem-focused coping T1	1.2	0.98-1.4	0.082
Step 3	Caregiver burden	1.0	0.95-1.0	0.96
	Dysfunctional coping T1	1.1	0.91-1.3	0.38
	Emotion-focused coping T1	0.85	0.73-0.99	0.032
	Problem-focused coping T1	1.3	1.0-1.5	0.029
	Anxiety case T1	11.4	3.1-41.4	<0.001
Step 4	Caregiver burden	0.99	0.94-1.0	0.57
	Emotion-focussed coping T1	0.84	0.71-0.99	0.036
	Dysfunctional coping T1	1.0	0.87-1.3	0.63
	Problem-focused coping T1	1.2	0.95-1.6	0.12
	Anxiety case T1	9.4	2.5-34.9	0.001
	Dysfunctional coping T2	1.2	0.96-1.4	0.13
	Emotion-focused coping T2	0.99	0.86-1.1	0.88
	Problem-focused coping T2	1.0	0.84-1.3	0.81
Step 5	Caregiver burden	0.96	0.91-1.0	0.26
	Emotion-focussed coping T1	0.78	0.63-0.96	0.018
	Dysfunctional coping T1	0.94	0.76-1.2	0.57
	Problem-focused coping T1	1.5	1.0-2.1	0.034
	Anxiety case T1	10.1	2.2-45.5	0.003

	Dysfunctional coping T2	1.2	1.0-1.5	0.043
	Emotion-focused coping T2	1.0	0.89-1.2	0.64
	Problem-focused coping T2	0.96	0.77-1.2	0.75
	Irritability score	1.4	0.21-9.0	0.75
	Severe life events	2.7	0.67-11.0	0.16
	Physical functioning score	0.98	0.96-1.0	0.19
	Health perception score	1.0	0.97-1.0	0.92
	Consult for emotional problems	6.6	1.4-29.9	0.015

6.4 Structural Equation Model: anxiety, burden and coping

I entered coping strategy, burden and anxiety scores into a model in order to explore my primary hypothesis that coping strategies would mediate the relationship between T1 caregiver burden and T2 anxiety score. I used anxiety score rather than caseness as AMOS-based structural equation modelling is not recommended for dichotomous variables (Byrne 2006). Figure 6.1 (page 158) demonstrates the “best fit model” for these factors, which results from the process outline in the method whereby connections between variables in a saturated model (where all variables are connected to each other) are removed one by one from the least to the most significant, until the point where the resulting model is significantly less good at explaining the data, defined by a rise in χ^2 statistic by more than the critical ratio. χ^2 for the model obtained by this process was 17.3 (df=9, p=0.57); this indicates the null hypothesis, that the model fits the data was not disproved (because p>0.05). The normed fit index was 0.96, indicating that the model is a good representation of the data.

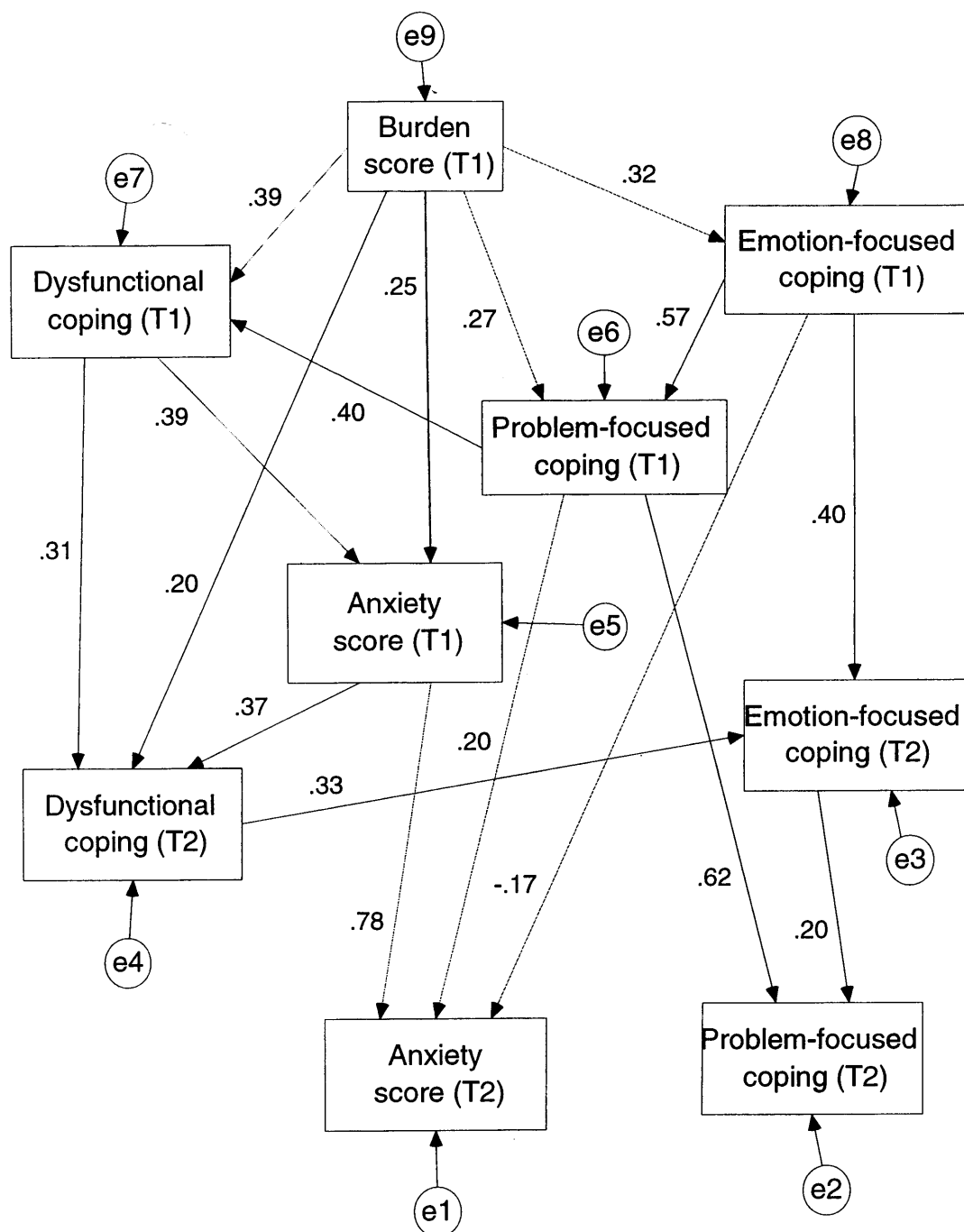
Latent error variables (e1 to e9) are included in Figure 6.1. These are required for all models tested in AMOS, because the software package is often used to test models that include latent variables. Latent variables are those that cannot be directly observed or measured. If, for example, I had included a variable of ‘general coping ability’, a latent variable estimated from different subscales of the COPE in the model, the subscales would have been an approximation to the concept ‘general coping ability’, so mathematically, it would also have been necessary to include a variable (of unknown or approximated value) for the difference between the actual concept and measured scales. This variable is called the latent error. Because I included only directly observed (measured) and no latent variables, the latent errors were all set to zero.

Figure 6.1 displays standardised regression coefficients, which indicate the relationship between variables. For example, the standardised regression coefficient for the relationship

between Burden score and Dysfunctional coping (T1) is 0.39. This means that for every 1 point increase in burden score, after standardising to allow for the different range of possible scores on the two scales, dysfunctional coping score would increase by 0.39 point. The analysis confirmed findings from the SPSS exploratory analyses that the relationship between T2 anxiety score and burden is mediated by T1 anxiety score (regression coefficient = 0.78), using fewer emotion-focussed (regression coefficient = -0.17) and more problem-focussed (regression coefficient = 0.20) coping strategies.

Figure 6.1 Model for relationship of coping strategies, burden and anxiety score

(numbers by arrows represent standardised regression coefficients; e= latent error)



6.5 Depression and coping

T2 depression score was associated with spending more time caring and reporting higher burden and scoring for worse physical health on all three HSQ measures at T1 (Table 6.2, page 147); and with using relatively more dysfunctional coping strategies at T1 and T2 (Table 6.1, page 147). On step one of a linear regression with depression score as the dependent variable (Table 6.6, page 160), caregiver burden was a significant predictor of T2 anxiety score ($t=2.5$, $p=0.015$) and explained 10.8% of the variance in depression score. On step two T1 coping strategies were added to the equation, and explained an additional 3.3% of the variance in depression score; there were no significant predictors. On steps three and four only T1 depression score ($t=8.9$; $p<0.001$ and $t=8.6$; $p<0.001$ respectively) predicted depression score at T2. In the final model which fully mediated the relationship between T1 burden and T2 depression score and predicted 65.6% of the variance, depression score at T1 ($t=6.6$, $p<0.001$) and having previously consulted a professional about mental health ($t=2.5$, $p=0.016$) were the only significant factors. Thus the hypothesis that coping mediated the relationship between burden and depression score a year later was not proved.

Table 6.6 Linear regression of factors predicting depression score (T2)

	Factor	t	P
Step 1 $R^2=0.108$	Caregiver burden	3.3	0.002
Step 2 $R^2=0.141$	Caregiver burden	1.9	0.058
	Dysfunctional coping T1	1.4	0.18
	Emotion-focused coping T1	-0.99	0.32
	Problem-focused coping T1	0.67	0.51
Step 3 $R^2=0.559$	Caregiver burden	0.71	0.48
	Dysfunctional coping T1	0.25	0.80
	Emotion-focused coping T1	-1.7	0.094
	Problem-focused coping T1	1.4	0.17
	Depression score T1	8.9	<0.001
Step 4 $R^2=0.569$	Caregiver burden	0.57	0.57
	Dysfunctional coping T1	0.42	0.68
	Emotion-focused coping T1	-2.0	0.053
	Problem-focused coping T1	0.71	0.48
	Depression score T1	8.6	<0.001
	Dysfunctional coping T2	-0.43	0.67
	Problem-focused coping T2	0.054	0.59
	Emotion-focused coping T2	1.1	0.28
Step 5 $R^2=0.656$	Caregiver burden	0.32	0.75
	Dysfunctional coping T1	-0.56	0.58
	Emotion-focused coping T1	-1.8	0.083
	Problem-focused coping T1	0.72	0.47

	Depression score T1	6.6	<0.001
	Dysfunctional coping T2	0.33	0.75
	Problem-focused coping T2	-0.025	0.98
	Emotion-focused coping T2	1.5	0.15
	CG age	1.6	0.11
	CG married?	-1.1	0.26
	Hours spent caring	0.44	0.66
	Spouse of CR	-0.49	0.63
	Severe life event	1.1	0.26
	Independent severe life event	0.079	0.94
	Consulted professional for emotional problem?	2.5	0.016
	Health perception score	-0.8	0.42
	Physical functional score	1.0	0.30
	Role physical score	-0.13	0.89
	Irritability score	1.5	0.13
	NPI total score	0.31	0.76

6.6 Overall psychological morbidity and coping

The linear regression analysis was repeated using total HADS score as the dependent variable, and including factors that approached a significant association with anxiety or depression score on univariate analysis in step five (Table 6.7, page 162). Burden was a significant predictor on step one ($t=3.3$, $p=0.002$), and in the final model the only significant predictors were T1 emotion-focussed coping score ($t=-2.2$, $p=0.034$), T1 total HADS score ($t=8.0$, $p<0.001$); and ever having consulted a professional for emotional problems ($t=2.2$, $p=0.034$).

Table 6.7 Linear regression of factors predicting psychological morbidity at T2

	Factor	t	P
Step 1 $R^2=0.345$	Caregiver burden	3.4	0.001
Step 2 $R^2=0.455$	Caregiver burden	1.6	0.12
	Dysfunctional coping T1	1.8	0.069
	Emotion-focused coping T1	-1.6	0.097
	Problem-focused coping T1	1.7	0.098
Step 3 $R^2=0.822$	Caregiver burden	-0.056	0.96
	Dysfunctional coping T1	-0.059	0.95
	Emotion-focused coping T1	-2.2	0.030
	Problem-focused coping T1	2.2	0.029
	Total HADS score T1	11.0	<0.001
Step 4 $R^2=0.826$	Caregiver burden	-0.13	0.90
	Dysfunctional coping T1	-0.006	1.0
	Emotion-focused coping T1	-2.4	0.017
	Problem-focused coping T1	1.6	0.12
	Total HADS score T1	10.0	<0.001
	Dysfunctional coping T2	-0.21	0.84
	Problem-focused coping T2	0.19	0.85
	Emotion-focused coping T2	1.1	0.28
Step 5 $R^2=0.869$	Caregiver burden	-0.51	0.61
	Dysfunctional coping T1	-0.61	0.54
	Emotion-focused coping T1	-2.2	0.034
	Problem-focused coping T1	1.6	0.12

	Total HADS score T1	8.0	<0.001
	Dysfunctional coping T2	0.13	0.90
	Problem-focused coping T2	-0.042	0.97
	Emotion-focused coping T2	1.2	0.24
	CG age	1.2	0.25
	CG married?	-0.77	0.44
	Hours spent caring	0.27	0.79
	Spouse of CR	-0.87	0.39
	Severe life event	0.53	0.60
	Independent severe life event	0.17	0.86
	Consulted professional for emotional problem?	2.2	0.034
	Health perception score	-2.0	0.051
	Physical functional score	0.66	0.51
	Role physical score	0.096	0.92
	Irritability score	1.2	0.24
	NPI total score	0.18	0.86
	Total life event score	-0.86	0.39
	ADAS-Cog score	0.094	0.93
	ADCS-ADL score	-0.17	0.86
	MMSE score	-0.18	0.86

7 DISCUSSION

This is the first longitudinal study to examine the role of coping in predicting anxiety and depression in caregivers selected to be representative of those caring for people with dementia living in the community, rather than caregivers recruited from only clinical sources. It is also the first to study the extent to which CG use emotion-focussed, problem-focussed and dysfunctional coping and to consider them in relation to each other. At the start of my study, nearly a third of CG reported clinically significant levels of anxiety, while just under a fifth had clinically significant levels of depression. Mean scores on coping strategy scales increased slightly between the first and second follow-ups, as would be expected if CG are gradually learning and acquiring different ways to cope. The increase in problem-focussed strategies approached significance, perhaps indicating that these are the types of strategies people are most likely to adopt, either on the advice of health professionals and others or by their own initiative, as new problems occur. However, use of the three types of coping strategy did not change significantly over the year of the study and scores at the two time points were highly correlated for each subscale, demonstrating that use of types of coping strategies remains fairly stable over time without intervention, as reported previously (Powers et al. 2002).

7.1 Anxiety

7.1.1 Cross-Sectional Findings

The first and second hypotheses were supported by the results, that using relatively more dysfunctional, and less emotion-focussed coping, partially mediated the relationship between burden and anxiety scores cross-sectionally. Taken together with depression score they were the only significant factors in the final model which fully mediated this relationship. Similarly, dysfunctional coping strategies mediated the relationship

between burden and anxiety caseness (as opposed to scores), and, together with depression caseness, was the only significant factor in the final model which fully mediated the relationship between caregiver burden and experiencing clinically significant anxiety.

Contrary to the third hypothesis, problem-focussed coping was not a mediator of the relationship between either burden and anxiety score or caseness cross-sectionally.

7.1.2 Longitudinal Findings

Reporting fewer emotion-focussed and more problem-focussed coping strategies, higher anxiety score, and having a more negative self-perception of their overall health at baseline, mediated the relationship between baseline caregiver burden score and anxiety score at follow-up a year later. Similarly, using fewer emotion-focussed and more problem-focussed coping strategies, being an anxiety case, and the caregiver ever having consulted a professional about emotional problems at baseline, and greater use of dysfunctional coping strategies at follow-up, predicted being an anxiety case at follow-up. Analysis using structural equation modelling confirmed that anxiety score and using fewer emotion-focussed and more problem-focussed coping strategies at baseline, mediated the relationship between baseline burden score and anxiety score at follow-up.

Considering my main hypotheses, the prediction that use of emotion-focussed coping strategies would mediate the relationship between burden and anxiety a year later was therefore upheld, but I found the opposite of the relationship I expected with regard to problem-focussed strategies, i.e. that their use in response to burden was related to increased anxiety score a year later. My third hypothesis, that using more dysfunctional coping strategies mediated the relationship between burden and anxiety score (or caseness) a year later was not upheld.

7.1.3 Interpretation of findings

Caregivers experiencing greater burden reported more use of all three types of coping strategy. Those that used relatively more problem-focussed strategies were more anxious a year later, indicating that these strategies did not protect against the impact of greater burden on psychological wellbeing in the long term. Those that responded by using more emotion-focussed strategies, however were less anxious a year later, suggesting that use of these strategies is protective. It is unsurprising that adding coping strategy use a year later to regression equations that already included initial measures of coping explained little additional variance in anxiety score, as coping scores at both time points were highly correlated. The finding that initial emotion-focussed and problem-focussed coping scores predicted anxiety score and caseness a year later better than coping styles measured concurrently with these outcomes supports my hypothesis regarding the direction of causality of the relationship between coping and anxiety, i.e. that emotion-focussed and problem-focussed coping strategies cause an increase or decrease in anxiety, rather than anxiety provoking these coping strategies. This is further reinforced by the finding that at follow-up emotion-focussed and problem-focussed coping scores were not predicted by initial anxiety score. Less use of emotion-focussed strategies and greater use of problem-focussed strategies also mediated of the relationship between initial caregiver burden score and clinically significant levels of anxiety a year later (i.e. anxiety caseness) on logistic regression. This suggests that coping strategies determine both levels of anxiety and the presence of anxiety disorders in CG.

Using relatively more dysfunctional coping strategies was associated with higher anxiety scores cross-sectionally for each time point. There was also a clear association between using relatively more dysfunctional coping strategies initially and anxiety score a year later, but this was no longer significant when initial anxiety score and all other factors were taken into account. This indicates that caregivers who used more

dysfunctional strategies in response to burden were more anxious initially and most remained more anxious a year later. In contrast, those who used dysfunctional coping strategies but were not anxious by the start of the study were no more likely to have developed anxiety a year later. Anxiety score and caseness were both predicted better by dysfunctional coping scores measured concurrently than those measured a year before, and there was a stronger relationship on post hoc analysis between initial anxiety score and dysfunctional coping a year later than the converse. Thus the hypothesised direction of causality for this relationship was not supported. These findings suggest that those caregivers who were more anxious tended to use more dysfunctional coping strategies subsequently.

7.2 Depression

As reported in this cohort prior to my study (Mahoney et al. 2005), CG reported more anxiety than depressive symptoms. Depression scores were on average two points lower than anxiety scores at both time points, and relatively few caregivers had clinically significant levels of depression. This is consistent with findings from epidemiologically representative studies of the general population, but not previous prevalence studies in CG that have found similar rates of anxiety and depression. Perhaps this is because the LASER-AD study is the first study of anxiety and depression in CG that aimed to recruit a sample that was representative of people with dementia and those caring for them in the community, or because the focus on depression in CG in the earlier literature has led to it being identified and managed better. A possible alternative explanation would be that the HADS case finding abilities are either less specific for anxiety or less sensitive for depression, but this is not supported by the literature (Bjelland et al. 2002).

7.2.1 Cross-sectional and longitudinal findings

In the cross-sectional analysis, using more emotion-focussed and less dysfunctional coping strategies and reporting worse physical functioning mediated the relationship between burden and depression score once potential confounders other than anxiety score were considered. Once anxiety score at baseline was included, only the CG reporting more anxiety and worse physical functioning were predictive factors in the final regression model that mediated the relationship between burden and depression scores.

The only significant predictors in the final model that mediated the relationship between caregiver burden and depression scores a year later were: the CG reporting more depression or ever having consulted a professional about emotional problems at baseline. Baseline use of fewer emotion-focussed strategies approached significance. Therefore none of the hypotheses that coping style would mediate the relationship between burden and depression cross-sectionally or a year later were upheld.

7.2.2 Interpretation of findings

Depression score was associated with using relatively more dysfunctional coping strategies in both cross-sectional analyses, but neither concurrent nor previous coping strategy use mediated the relationship between initial burden score and depression score a year later. It is possible that the study was underpowered (a Type II error) to detect this relationship, because depression scores were lower than those for anxiety in the population studied. Using less emotion-focussed coping approached significance in the final model, and so in a larger study it is possible that this may have been shown to be a mediator. This hypothesis was supported by the finding that emotion-focussed coping was also an important mediator of the impact of carer burden on overall psychological morbidity a year later. Alternative explanations would be that coping is an important mediator for anxiety, but other factors determine whether a CG experiencing high levels

of burden becomes depressed. Past history of emotional problems, for example, was an important predictor in the current study.

All of the factors predicting morbidity outcomes in multivariate analyses were CG factors, including coping, physical health, past history of emotional problems, and burden reported, and neither anxiety nor depression was related to CR factors. This suggests that CG psychological morbidity is related more to how caregiving stresses are managed rather than the nature of the stressors. Perhaps this is because it is difficult to solve many of the problems in severe dementia, such as those caused by increasing dependency, so how CG cope with these difficulties is critical.

7.3 Comparison with findings from other recent studies

7.3.1 Anxiety and coping

7.3.1.1 Cross-Sectional Findings

Previous studies investigating the relationship of coping to anxiety have all examined anxiety as a continuous variable (anxiety score) rather than the presence or absence of caseness, and most have been of cross-sectional design (see Chapter 2). The strongest evidence was that more use of dysfunctional coping strategies was associated with higher anxiety levels, and this is consistent with my findings (see section 5.1). This study also found that dysfunctional coping strategies predicted anxiety caseness (see section 5.2). No previous authors have explored the hypothesis that coping strategies mediate the relationship between caregiver burden and anxiety.

The relationship of emotion-focussed strategies to anxiety in previous cross-sectional studies has been unclear. *Positive reappraisal* was consistently *not* associated with anxiety levels in two Level 2 studies (Neundorfer 1991; Vedhara et al. 2001) (Grade B), while evidence was inconsistent for *accepting responsibility* in the same surveys. My

finding that more use of emotion-focussed strategies (including positive reappraisal) was associated with lower anxiety scores cross-sectionally may be different to rather than inconsistent with these few previous results because positive reappraisal is only one of the subscales included in the COPE. These two previous studies were small ($n=50$ (Neundorfer 1991) and $n=60$ (Vedhara et al. 2001)), and therefore could well have been underpowered. The same two studies are also the only two previous published studies to have explored the relationship of problem-focussed coping strategies to anxiety. They reported inconsistent results ((Neundorfer 1991; Vedhara et al. 2001); see section 1.5.3.1, page 40), while I found in my study that use of problem-focussed coping strategies was not associated with anxiety score or caseness on cross-sectional analysis.

7.3.1.2 Cohort Studies

Only two cohort studies have previously investigated the relationship of CG coping to anxiety scores (Vedhara et al. 2001; Winslow 1997), and both have methodological limitations. Vedhara and colleagues (2001) reported results from a prospective cohort study that measured neither caregiver burden nor CG physical health perception, both of which I have found to be significantly associated with anxiety score a year later, nor did they include baseline anxiety in their analyses. In fact, only coping strategy scores and neuroticism were included in their multivariate analyses. Furthermore, the sample was small ($n=50$) and not epidemiologically representative. The second study by Winslow (1997) only fulfilled CEBM criteria for a Level 4 study and included a single measure of coping, classifiable as emotion-focussed coping. This is an important limitation as most caregivers cope in a variety of different ways, and their relative use of one strategy compared with others is important.

Vedhara (2001) found that more use of a dysfunctional coping strategy (confrontative coping) predicted anxiety six and twelve months later, and a second dysfunctional strategy (escape-avoidance) predicted anxiety six months but not twelve months later. I

found that using relatively more dysfunctional coping was associated with anxiety a year later when coping strategies alone were considered; this relationship between dysfunctional coping and anxiety score narrowly missed significance when burden was added, and was not significant once initial anxiety score was added to the equation. As Vedhara and colleagues included neither burden nor baseline anxiety in their analyses their findings are not in conflict with my study, and may have been confounded by these factors.

Emotion-focussed and problem-focussed strategies did not predict anxiety in these two previous cohort studies (Vedhara et al. 2001; Winslow 1997), but I found that both using relatively more problem-focussed and less emotion-focussed coping strategies were mediating factors in the relationship between burden and anxiety score and caseness a year later. Neither of these previous studies considered relative use of different coping strategies, entering only one and a few coping strategies that were significant on univariate tests into their multivariate analyses, respectively. Therefore they did not control for response bias (some people tending to rate overall use of coping higher than others) nor, as burden was not measured in either study, did they control for the stressors the caregivers were required to cope with. It is also possible that because they were clinical samples, the strategies used to cope by caregivers in their study were different to the CG we recruited from the community. It is conceivable that less effective coping, with use of fewer helpful emotion-focussed and more dysfunctional coping strategies, might have contributed to higher levels of stress, and an increased likelihood of the CR being referred to secondary care, and hence having sufficient power to detect a relationship between anxiety and more dysfunctional coping, but not less emotion-focussed coping.

7.3.2 Depression and coping

7.3.2.1 Cross-Sectional Studies

There was a significant association between using relatively more dysfunctional coping and depression in univariate cross-sectional analyses, but they did not mediate the relationship between burden and depression cross-sectionally or longitudinally, after controlling for potential confounders. Neither problem-focussed nor emotion-focussed coping strategies were significantly associated with depression scores. This is consistent with previous findings that dysfunctional coping strategies are associated with increased depression in cross-sectional studies (Ashley & Kleinpeter 2006; Haley et al. 1996; Mausbach et al. 2006b; Neundorfer 1991; Vedhara et al. 2001). Interestingly there is evidence from previous cross-sectional studies of a relationship between emotion-focussed strategies and less depression but not less anxiety, while I found this relationship was significant for anxiety but not depression. Those previous studies exploring the relationship of emotion-focussed strategies to anxiety were smaller than my study ($n=50-60$) (Neundorfer 1991; Vedhara et al. 2000), while those exploring this relationship with depression were larger ($n=107-197$) (Ashley & Kleinpeter 2006; Haley et al. 1996; Mausbach et al. 2006b). This would therefore support my previous interpretation that the failure to clearly demonstrate a relationship between emotion-focussed coping and depression may be because my study lacked the power to detect a true relationship between these variables. Only two other authors (Neundorfer 1991; Vedhara et al. 2001) have reported the correlation of depression score with coping scales containing only problem-solving items. In both, correlations were generally (as in this study) positive, lower than for anxiety scores, and not statistically significant.

7.3.2.2 Cohort Studies

Only two longitudinal studies have investigated the relationship of coping to subsequent depression in CG. Goode and colleagues (1998) conducted the largest of these three studies ($n=122$). They employed an approach coping scale that included logical analysis,

seeking guidance and support and taking problem-solving action; but also positive reappraisal (which is considered by others to be an emotion-focussed strategy) as well as a measure of avoidance coping. Approach, but not avoidance coping, mediated an effect between primary stressors (e.g. patient self-care and behavioral problems) and decreased depression a year later. In a smaller study, Vedhara et al (2001) reported that neither problem-focussed nor emotion-focussed coping strategies significantly predicted depression six or twelve months later, while results for dysfunctional coping strategies were inconsistent. Together with my finding that use of emotion-focussed coping approached significance in the final model of the multivariate analysis for depression score, this could support a hypothesis that there is a longitudinal relationship between emotion-focussed coping and subsequent depression which my study and the smaller study by Vedhara lacked the power to detect. This is, however, a speculative hypothesis not least because problem-focussed strategies were also included in the approach scale.

7.4 Clinical implications

Previous authors have found that it is possible to change the types of coping strategies CG use (Chiverton & Caine 1989; Lavoie et al. 2005). Lavoie et al (2005) interviewed 30 CG in a qualitative study before and after a psychoeducational group. They found that participants learned coping strategies, with reframing playing a more important role than problem-solving or seeking social support. This finding, together with the evidence from my study suggests that future interventions to reduce anxiety in CG could usefully focus on modifying the psychological coping strategies caregivers use. These seemed to be more important determinants of psychiatric morbidity than all other factors including CR previous psychiatric symptoms and hours of care provided. This study provides a rationale for a pilot RCT of a psychological therapy for anxiety, aimed at promoting emotion-focussed and reducing dysfunctional coping strategy use, which was associated

with greater anxiety immediately that persisted. Such a study could then form the basis of a large RCT, based on the guidelines outlined in the Medical Research Council Framework for development and evaluation of RCTs (Medical Research Council 2000). A rational intervention could draw on the techniques used by previous authors to promote acceptance, positive reappraisal, seeking emotional support and mindfulness (Akkerman & Ostwald 2004; Gallagher-Thompson et al. 2003), as well as other emotion-focussed strategies the use of which has not yet been formally tested, such as humour. A caregiver group have produced an audio resource that encourages CG to draw on humour to cope with caring (Glasgow Carers Panel 2006) and they reported circumstantial evidence for its effectiveness at the 2006 Royal College of Psychiatrists' Annual General Meeting. Outside the CG literature, some focussed psychological therapies include teaching of emotion-focussed coping skills such as acceptance and mindfulness (a concept which originated in Buddhist meditation). These include Acceptance and Commitment Therapy (Hayes et al. 2006), Rational Emotive Therapy (Haaga & Davison 1993) and Dialectical Behavioural Therapy (Linehan 2000); they are sometimes called "third wave psychological therapies" indicating their evolution from the more problem-based approaches of earlier CBT programmes. Acceptance and Commitment Therapy, for example, teaches mindfulness and acceptance skills and then explores their use in practical exercises. It was developed from research that found a relationship between experiential avoidance (a concept very similar to avoidant coping) and anxiety and depression, and aims to replace avoidant with acceptance strategies. Acceptance and Commitment Therapy is becoming increasingly established as a treatment for anxiety and affective disorders in the USA, but the evidence base for its effectiveness is currently small, and there are no RCTs. Its use has never been described in dementia CG (Lopez 1999; Orsillo et al. 2006), but the theoretical basis described for Acceptance and Commitment Therapy suggests it may act by increasing emotion-

focussed coping and decreasing dysfunctional coping, and Acceptance and Commitment Therapy techniques might usefully inform a future coping intervention for CG.

Interestingly, two recent prospective studies in other populations have also found that using emotion-focussed rather than other types of coping protects people from psychological distress. Pakenham (2005) interviewed 155 caregivers for people with Multiple Sclerosis. Positive reframing (emotion-focussed) coping was associated with less, and practical assistance (problem-focussed) coping with more, depression and anxiety three months later. In a second longitudinal study by Carver and colleagues (1993) that interviewed 59 breast cancer patients one day pre-surgery, ten days post-surgery, and at three, six and twelve month follow-ups, acceptance and the use of humor (emotion-focussed strategies) predicted lower distress, while the dysfunctional strategies of denial and disengagement predicted more distress. This suggests that the beneficial effects of emotion-focussed coping and deleterious effects of dysfunctional coping might be wider still.

Coping strategies were not predictive of depression a year later in the current study. Although I found some differences between the impact of coping on anxiety and depression in previous studies, similarities were far more common. Previous studies have reported good evidence for the effectiveness of an intervention that sought to increase use of emotion-focussed and decrease use of dysfunctional strategies in the treatment of depression (Coon et al. 2003). I have hypothesised that my study was underpowered to detect a true relationship between these coping styles and depression, because the depression scores were lower and therefore a larger sample size would have been required to detect a relationship between coping and depression of a similar magnitude as that between coping and anxiety; my findings that the same coping styles predicted overall psychological morbidity would support this hypothesis. If this is correct, then psychological interventions targeting emotion-focussed and dysfunctional

coping strategies may also help alleviate caregiver depression. As caregiver psychiatric morbidity is associated with CR institutionalisation (Gaugler et al. 2003) there may be economic as well as health benefits to such an intervention. On the other hand, this study was fairly large, suggesting that if levels of depression in the CG population are comparable to those in the study, a coping intervention would have a smaller effect size for depression than anxiety, even if my hypothesis that the current study was underpowered were true. This study indicates that coping strategy use impacted significantly on anxiety and overall psychological morbidity, while the hypothesised relationship with depression was not demonstrated.

My results do not support the use of psychological interventions based on teaching problem-focussed strategies to treat CG anxiety or depression. How the anxious and depressed CG in this study were evaluating situations and whether they were already selecting appropriate problem-focussed strategies is not known. My findings might explain why interventions to treat psychological morbidity in CG based on promoting problem-based coping alone have not demonstrated effectiveness (Gendron et al. 1996; Morris et al. 1992; Roberts et al. 1999). Many CG have access to fact sheets, internet or other sources of basic written advice about coping, so it is possible that many of those taking part in this study would already have access to didactic coping advice. This advice generally combines practical, problem-focussed strategies about accessing help and managing difficult behaviours, with more emotion-focussed strategies such as making time for oneself and seeking social support (e.g. Alzheimer Society 2006). Perhaps problem-focussed strategies are more easy to adopt after reading about them, and once this has occurred there are no additional benefits to knowing more, while CG need support to adopt emotion-focussed coping strategies. This study suggests that further interventions for caregivers should not focus on teaching problem-focussed coping alone.

7.5 Methodological considerations and limitations

7.5.1 Design

Logical analytic structure with use of both exploratory and confirmatory analyses to test the main hypothesis is, I believe a strength of the study design. I used a high level of significance ($p < 0.01$) for univariate tests, but the conventional level ($p < 0.05$) for multivariate tests, all of which were hypothesis driven.

7.5.2 Study population

Our purposive recruitment method sought to ensure that the population of people with dementia, and therefore their caregivers, was representative of the community population of people with dementia in terms of gender, disease severity and care setting. However, people who agree to participate in research may differ systematically from those who do not, for example they may be more willing to seek help from services.

To consider other methodological limitations, I assessed my study against CEBM criteria (see page 58) assessing cohort studies.

7.5.3 Objective outcome measures

The CEBM states that a good cohort study will measure exposures and outcomes in the same (preferably blinded), objective way in all study participants. The main measures in my study (caregiver burden, coping strategies and anxiety and depression) were all in a self-report format, so the interviewers should not have been able to influence them directly, although as they were in the room during instrument completion and CG were permitted to ask questions to clarify items, interviewer bias is a theoretical possibility.

7.5.4 Length and completeness of follow-up

According to the CEBM, cohort studies should carry out a sufficiently long and complete follow-up of patients. The follow-up period of one year was demonstrated to be sufficient to observe changes in coping, anxiety and depression scores in CG in similar studies (e.g. Vedhara et al. 2001). The response rate for the study was 79.5% when caregivers who were eligible for follow-up were considered and this approaches the cut point defined by CEBM for a good cohort study of 80%. Death of the CR was the most common reason preventing follow up (in 10.3% of the initial cohort). Those caregivers who were not re-interviewed had higher anxiety scores, used more dysfunctional coping strategies and cared for people who had higher levels of dependency and neuropsychiatric symptoms, but there were few refusals (n=10) suggesting that the results are still applicable.

7.5.5 Properties of main outcome measures

All the measures included had previously demonstrated reliability and validity in these populations and settings. The measure of anxiety and depression, the HADS, was selected in a systematic way to ensure that predetermined requirements for the measure were met. The Zarit Burden Inventory is the most commonly used measure of caregiver burden.

7.5.5.1 The difficulties of measuring coping

Employing meaningful categories of coping strategies is critically important if results are to be clinically applicable, and this study has benefited from a well validated measure of coping, developed with the purpose of overcoming problems identified in the WCCL, the instrument that has been used most commonly in CG coping research to date (see section 4.3.1). CG were asked about how they coped with stresses arising from caregiving. This is the method employed most frequently in the caregiver coping literature, but it is open to criticism. Two recent reviews have commented that measuring coping according to more specific stressors (e.g. wandering) ensures greater

homogeneity of the situations considered by respondents and therefore is a more valid method (Gottlieb & Wolfe 2002; Kneebone & Martin 2003). Specifying the stressor does not, however, ensure homogeneity in terms of the meaning or stressfulness of the event to the CG, a requirement which may be better served by the current method of asking caregivers to consider the most troublesome problems and stresses of caregiving for themselves. It is also impractical where CG report a wide variety of stressors.

I measured the relative proportions of emotion-focussed, problem-focussed and dysfunctional coping strategies used. An analytic strategy that measured relative coping was supported by the literature (Fleishman et al. 2003), but did mean that total coping effort was not factored into the analysis, and this may have been significantly associated with anxiety.

Classifying coping responses to caring stresses, which vary for individual caregivers depending on the nature of the stressor and between caregivers is a complicated process, and whilst the COPE was the measure which I found to be most clinically relevant and valid, the extent to which people's answers on coping strategy measures relate to how they actually manage caring situations is debatable (Kneebone & Martin 2003). Some coping strategies that have been the target of previous intervention studies are not included in the COPE, for example increasing pleasant activities which give enjoyment, and assertiveness that enables caregivers to avoid passive-aggressive forms of communication. It would have been helpful for the application of these results to have measured these elements of coping in the study.

7.5.6 Confounders

The CEBM states that cohort studies should control appropriately for known confounders. Most of the factors that have been associated with anxiety in my systematic review or for which evidence of an association was conflicting or

inconsistent were measured, with the exceptions of: CG ethnicity; mastery, hassles, neuroticism, positive aspects of caring, abusive behaviours towards the CR and knowledge about dementia. The reasons for this have been discussed earlier (see section 3.5, page 97). The resulting list of factors was comprehensive, but the strategy for variable selection could have missed some factors that have previously been associated with depression or overall psychological morbidity but not specifically with anxiety. Anxious and depressed caregivers may be more likely to report the coping strategies they used negatively, and this 'mood bias' could potentially have confounded the results.

7.5.7 Alternative study designs

The sample size was sufficient to investigate my primary hypothesis that coping mediated the relationship between burden and anxiety a year later. There were a small number of people with clinically significant depression and mean depression scores were lower than anxiety scores. A larger study might have provided power to detect a clinically significant mediating effect of coping strategy scores on the relationship between burden and depression scores, and would have allowed me to use the lower level of significance for all analyses and thus increased the confidence with which results can be viewed. A much larger sample would have enabled me to determine the relationship of coping strategies to new onset of clinically significant anxiety and depression.

Because caregivers were recruited 18 months before T1, all caregivers had been caring at least 18 months and many had probably been caring for several years longer. Recruiting caregivers of people newly diagnosed with dementia would have enabled me to chart coping strategies used by people at different stages of caring, although due to the insidious onset of AD caregivers would still have varied considerably in the amount of time they had been providing care. Caregivers were not reinterviewed after the death

of a CR, but former CG also often need support, so exploration of coping strategies used by those who have stopped caregiving would also be a useful avenue for future research.

Using a series of Likert scales (the format of the COPE) to measure the complicated construct of coping could be viewed as simplistic. Qualitative research, for example using focus groups with family caregivers could have provided valuable additional information about how CG cope. Such a study could have included participants selected from the main study purposively to ensure a spectrum of different coping styles and sociodemographic groups were represented. I investigated what coping strategies CG reported using but not whether or not they thought they were helpful or not. In focus groups, the types of strategy that CG found subjectively useful, how they learnt and selected strategies and the acceptability to CG of possible interventions could also have been explored.

Another alternative approach would have been to design a pilot, as discussed above (see page 174) for the first CG coping intervention study demonstrating adequate power to detect a clinically significant change in anxiety scores. By measuring change in use of coping strategies post intervention I could have identified which aspects of the intervention (i.e. those targeting problem-focussed, emotion-focussed or dysfunctional coping) had been helpful. While this empirical alternative might have been successful, numerous different coping interventions have been designed and implemented with mixed success, but the inevitable heterogeneity of psychological interventions has prevented researchers from determining their active component. I think that this thesis provides a clear theoretical base from which to design the first RCT of a coping intervention targeting both anxiety and depression in CG.

8 FURTHER WORK

The findings of this thesis have informed two further protocols for research. The first seeks to determine whether the model I developed regarding the relationship of caregiver burden, coping strategies and psychological distress might be extended to predict abusive behaviours occurring within the CG-CR dyad (see page 183, section 8.1). I have recently commenced this study, funded by a three year Medical Research Council Fellowship in Health Services Research. Secondly, my results have also contributed to the development of a protocol for a study to develop a rational intervention package targeting coping strategies to reduce psychological stress in CG.

8.1 Is abusive behaviour a consequence of caregiver distress?

In previous research, a quarter of caregivers of elders have been willing to report actions towards CRs that would be defined as abusive (Beach et al. 2005), although they may not be aware their behaviours could be seen in this light. Compton and colleagues (1997) reported a high prevalence (37%) of caregiver abusive behaviours in the only study (n=38) so far to measure distress and abusive behaviours towards the people they care for in CG referred to community psychiatric services. In chapter 2, I reported preliminary evidence from two studies (Compton et al. 1997; Quayhagen 1997) that both found that caregiver abusive behaviours towards their CR were associated with higher CG anxiety, and such behaviours have also been associated with CG depression (Paveza et al. 1992). Prevention of elder abuse is difficult as we do not know what leads some caregivers to behave abusively towards people with dementia while other caregivers in similar circumstances manage without recourse to abuse. The House of Commons Health Select Committee Report on elder abuse (2004) devotes only a few lines of their sixty page report to abuse by family caregivers, and concludes that “there

was no sound research evidence to underpin the theory that elder abuse frequently results from [family] caregiver stress". They consequently did not make recommendations based on family caregiver stress reduction.

In this new study, I will use the structural equation modelling methods I have learnt during preparation of the current thesis to explore the relationship between abusive behaviours and CG coping, burden and distress. I intend to use the HADS as a measure of anxiety and the Modified Conflict Tactics Scale (Beach et al. 2005) to measure CG reports of verbal and physically abusive behaviours, in 220 CG of consecutive people with dementia referred to five CMHTs in Inner and Outer London and Essex. I predict that coping strategies employed, specifically using relatively fewer emotion-focussed strategies may also mediate a hypothesised relationship between caregiver burden and abusive behaviours. I commenced recruitment for this new study in January 2007.

8.2 Developing a coping-based intervention for CG

In this thesis, I have concluded that no intervention can be recommended to reduce CG anxiety from the current evidence base (see page 80, section 2.2.3) although I did find some preliminary evidence for an intervention that taught emotion-focussed coping strategies. Most interventions involving coping that were successful at treating depression included promotion of emotion-focussed strategies alone or in conjunction with problem-focussed strategies, while the most conclusive evidence found for training programme that included promotion of emotion-focussed and problem-focussed and discouragement of dysfunctional coping strategies. As change in use of coping strategies was not measured in any of these studies and most were heterogeneous interventions, it is difficult to determine whether either of these or different treatments were responsible for the reduction in depression scores (see page 36 section 1.5). My study has indicated that emotion-focussed may be the active component of these treatments, and paves the

way for the development of a coping intervention clearly informed by the coping literature for the first time in this group. Identifying the active component of these treatments is important because CG are probably more likely to engage in a briefer therapy, and shorter therapies are also more likely to demonstrate economic benefits.

The recent proposal by Layard (2006) that increasing availability of CBT for people with anxiety and depression in Britain could pay for itself by reducing the numbers of people on incapacity benefit was widely reported in the media. The cost-effectiveness calculations for this proposal presumed that most of the therapy would be delivered by recently qualified clinical psychologists or other mental health professionals (nurses, Occupational Therapists) who had undertaken one or two years additional part time study in CBT, who would work under the supervision of senior practitioners. In most of the studies I have identified which reported effective psychological interventions in CG, the therapies were also carried out by highly skilled psychology and medical practitioners, who in some cases were involved in evaluating them. I think that a logical next step is to determine whether a psychological intervention package for CG, developed from existing interventions and informed by this study, would be cost-effective for routine use in the British healthcare system. This is possible if such an intervention increased the capacity of CG to continue caring at home, and therefore delayed or prevented entry of the CR to a twenty-four hour care facility, which is usually cheaper than community care. It is more likely that economic benefits would be demonstrable if the therapy was effective when delivered by staff with a similar level of training to that outlined in the Layard proposal.

9 CONCLUSIONS

Caregivers who used relatively more emotion-focussed coping strategies in response to caregiver burden were protected from developing clinically significant anxiety a year later, while those using problem-focussed strategies were not. Caregivers who used relatively more dysfunctional strategies in response to burden were more anxious initially and most remained more anxious a year later, but those who used dysfunctional coping strategies but were not anxious when first interviewed were no more likely to have developed anxiety a year later. I did not prove my hypothesis that coping strategy use mediated the relationship between depression and burden, although the relationship between using relatively more emotion-focussed strategies and depression score a year later approached significance, suggesting that my study may have been underpowered to detect this relationship.

A randomised controlled trial of a psychological intervention package to increase emotion focussed and decrease dysfunctional coping would be a rational intervention to reduce anxiety in CG. There are several examples in the literature of interventions that have included components targeting these strategies, and my results suggest these may have been the components determining their effectiveness. There are however currently no randomised controlled trials which include anxiety as a primary outcome measure and demonstrate sufficient power to detect a clinically significant result. A rational next step would be to develop an intervention package to reduce and prevent anxiety and depression in CG and to determine whether its use routinely in the National Health Service would be acceptable, effective and economically viable.

10 REFERENCES

- Aguero-Torres, H., Fratiglioni, L., & Winblad, B. 1998, "Natural history of Alzheimer's disease and other dementias: Review of the literature in the light of the findings from the Kungsholmen Project", *International Journal of Geriatric Psychiatry*, vol. 13, no. 11, pp. 755-766.
- Akkerman, R. 2006.
Ref Type: Personal Communication
- Akkerman, R. & Ostwald, S. 2004, "Reducing anxiety in Alzheimer's disease family caregivers: effectiveness of a nine-week cognitive behavioral intervention", *American Journal of Alzheimer's disease and other dementias*, vol. 19, no. 2, pp. 117-123.
- Almberg, B., Grafstrom, M., & Winblad, B. 1997, "Major strain and coping strategies as reported by family members who care for aged demented relatives", *Journal of Advanced Nursing*, vol. 26, no. 4, pp. 683-691.
- Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, I. S., Bryson, H., de Girolamo, G., De Graaf, R., Demyttenaere, K., Gasquet, I., Haro, J. M., Katz, S. J., Kessler, R. C., Kovess, V., Lepine, J. R., Ormel, J., Polidori, G., Russo, L. J., Vilagut, G., Almansa, J., Arbabzadeh-Bouchez, S., Autonell, J., Bernal, M., Buist-Bouwman, M. A., Codony, M., Domingo-Salvany, A., Ferrer, M., Joo, S. S., Martinez-Alonso, M., Matschinger, H., Mazzi, F., Morgan, Z., Morosini, R., Palacin, C., Romera, B., Taub, N., & Vollebergh, W. A. M. 2004, "Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project", *Acta Psychiatrica Scandinavica*, vol. 109, pp. 21-27.
- Alzheimer Society. Alzheimer's Society website . 2006.
Ref Type: Electronic Citation
- American Psychiatric Association 1994, *Diagnostic and Statistical Manual of Mental Disorders (4th edition)*. American Psychiatric Association, Washington DC.
- Anderson, A. Anxiety-Panic History. Internet . 2006.
Ref Type: Electronic Citation
- Andrews, G., Issakidis, C., Sanderson, K., Corry, J., & Lapsley, H. 2004, "Utilising survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders", *British Journal of Psychiatry*, vol. 184, no. 6, pp. 526-533.
- Anthony-Bergstone, C. R., Zarit, S. H., & Gatz, M. 1988, "Symptoms of psychological distress among caregivers of dementia patients", *Psychology and Aging*, vol. 3, no. 3, pp. 245-248.
- Arbuckle, J. L. 2003, *Amos 5.0 Update to the Amos User's Guide*. Smallwaters Corporation, Chicago IL.
- Aschbacher, K., Patterson, T. L., von Kanel, R., Dimsdale, J. E., Mills, P. J., Adler, K. A., Ancoli-Israel, S., & Grant, I. 2005, "Coping processes and hemostatic reactivity to acute stress in dementia caregivers", *Psychosomatic Medicine*, vol. 67, no. 6, pp. 964-971.
- Ashley, N. R. & Kleinpeter, C. H. 2006, "Gender differences in coping strategies of spousal dementia caregivers", *Journal of Human Behavior in the Social Environment*, vol. 6, no. 2, pp. 29-46.
- Baron, R. M. & Kenny, D. A. 1986, "The Moderator Mediator Variable Distinction in Social Psychological-Research - Conceptual, Strategic, and Statistical Considerations", *Journal of Personality and Social Psychology*, vol. 51, no. 6, pp. 1173-1182.

Bauer, M. E., Vedhara, K., Perks, P., Wilcock, G., Lightman, S. L., & Shanks, N. 2000, "Chronic Stress in caregivers of dementia patients is associated with reduced lymphocyte sensitivity to glucocorticoids", *Journal of Neuroimmunology*, vol. 103, pp. 84-92.

Bayley, J. 1998, *Iris Abacus*, London.

Beach, S. R., Schulz, R., Williamson, G. M., Miller, L. S., Weiner, M. F., & Lance, C. E. 2005, "Risk factors for potentially harmful informal caregiver behavior", *Journal of the American Geriatrics Society*, vol. 53, no. 2, pp. 255-261.

Beekman, A. T. F., Bremmer, M. A., Deeg, D. J. H., van Balkom, A. J. L. M., Smit, J. H., De Beurs, E., van Dyck, R., & van Tilburg, W. 1998, "Anxiety disorders in later life: A report from the longitudinal aging study Amsterdam", *International Journal of Geriatric Psychiatry*, vol. 13, no. 10, pp. 717-726.

Beekman, A. T. F., Deeg, D. J. H., van Tilburg, T., Smit, J. H., Hooijer, C., & Van Tilburg, W. 1995, "Major and minor depression in later life: A study of prevalence and risk factors", *Journal of Affective Disorders*, vol. 36, no. 1-2, pp. 65-75.

Bentler, P. M. & Bonett, D. G. 1980, "Significance Tests and Goodness of Fit in the Analysis of Covariance-Structures", *Psychological Bulletin*, vol. 88, no. 3, pp. 588-606.

Bertrand, R. M., Fredman, L., & Saczynski, J. 2006, "Are all caregivers created equal? Stress in caregivers to adults with and without dementia", *Journal of Aging and Health*, vol. 18, no. 4, pp. 534-551.

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. 2002, "The validity of the Hospital Anxiety and Depression Scale: An updated literature review", *Journal of Psychosomatic Research*, vol. 52, no. 2, pp. 69-77.

Blake, R. L. & Vandiver, T. L. 1988, "The association of health with stressful life changes, social supports, and coping", *Family Practice Research Journal*, vol. 7, no. 4, pp. 205-218.

Blennow, K., de Leon, M. J., & Zetterberg, H. 2006, "Alzheimer's disease", *Lancet*, vol. 368, no. 9533, pp. 387-403.

Bourgeois, M. S., Schultz, R., & Burgio, L. D. 2002, "Skills training for spouses of patients with Alzheimer's Disease: outcomes of an intervention study", *Journal of Clinical Geropsychology*, vol. 8, no. 1, pp. 53-73.

Bowling, A. & Windsor, J. 1997, "Discriminative power of the health status questionnaire 12 in relation to age, sex, and longstanding illness: findings from a survey of households in Great Britain", *Journal of Epidemiology and Community Health*, vol. 51, no. 5, pp. 564-573.

Boyle, M. H. 1998, "Guidelines for evaluating prevalence studies", *Evidence-Based Mental Health*, vol. 1, no. 2, pp. 37-39.

Brazier, J. E., Harper, R., Jones, N. M. B., O'cathain, A., Thomas, K. J., Usherwood, T., & Westlake, L. 1992, "Validating the SF-36 Health Survey Questionnaire - New Outcome Measure for Primary Care", *British Medical Journal*, vol. 305, no. 6846, pp. 160-164.

Brazier, J. E., Walters, S. J., Nicholl, J. P., & Kohler, B. 1996, "Using the SF-36 and Euroqol on an elderly population", *Quality of Life Research*, vol. 5, no. 2, pp. 195-204.

Brodsky, H., Green, A., & Koschera, A. 2003, "Meta-Analysis of Psychosocial Interventions for Caregivers of People with Dementia", *Journal of the American Geriatrics Society*, vol. 51, no. 5, pp. 657-664.

Brown, G. W. & Harris, T. O. 1989, *Life events and illness* Unwin Hyman, London.

- Brown, J. E., King, M. T., Butow, P. N., Dunn, S. M., & Coates, A. S. 2000, "Patterns over time in quality of life, coping and psychological adjustment in late stage melanoma patients: An application of multilevel models", *Quality of Life Research*, vol. 9, no. 1, pp. 75-85.
- Brugha, T., Bebbington, P., Tennant, C., & Hurry, J. 1985, "The List of Threatening Experiences - A Subset of 12 Life Event Categories with Considerable Long-Term Contextual Threat", *Psychological Medicine*, vol. 15, no. 1, pp. 189-194.
- Buist-Bouwman, M. A., De Graaf, R., Vollebergh, W. A. M., Alonso, J., Bruffaerts, R., & Ormel, J. 2006, "Functional disability of mental disorders and comparison with physical disorders: a study among the general population of six European countries", *Acta Psychiatrica Scandinavica*, vol. 113, no. 6, pp. 492-500.
- Burgio, L., Stevens, A., Guy, D., Roth, D. L., & Haley, W. E. 2003, "Impact of two psychosocial interventions on white and african american family caregivers of individuals with dementia", *Gerontologist*, vol. 43, no. 4, pp. 568-579.
- Byrne, B. 2006, *Structural equation modelling using AMOS*.
- Carers UK 2002, *Without us? Calculating the value of carers' support*, Carers UK.
- Carver, C. S. 1997, "You want to measure coping but your protocol's too long: Consider the brief COPE", *International Journal of Behavioral Medicine*, vol. 4, no. 1, pp. 92-100.
- Carver, C. S., Pozo, C., Harris, S. D., Noriega, V., Scheier, M. F., Robinson, D. S., Ketcham, A. S., Moffat, F. L., & Clark, K. C. 1993, "How Coping Mediates the Effect of Optimism on Distress - A Study of Women with Early-Stage Breast-Cancer", *Journal of Personality and Social Psychology*, vol. 65, no. 2, pp. 375-390.
- Carver, C. S. & Scheier, M. E. 1994, "Situational Coping and Coping Dispositions in A Stressful Transaction", *Journal of Personality and Social Psychology*, vol. 66, no. 1, pp. 184-195.
- Carver, C. S., Scheier, M. F., & Weintraub, J. K. 1989, "Assessing Coping Strategies - A Theoretically Based Approach", *Journal of Personality and Social Psychology*, vol. 56, no. 2, pp. 267-283.
- Castro, C. M., Wilcox, S., O-Sullivan, P., Baumann, K., & King, A. C. 2002, "An exercise program for women who are caring for relatives with dementia", *Psychosomatic Medicine*, vol. 64, no. 3, pp. 458-468.
- Centre of Evidence Based Medicine. Levels of Evidence and Grades of Recommendation. Centre of Evidence Based Medicine website . 2006.
Ref Type: Electronic Citation
- Chang, B. L. 1999, "Cognitive-behavioural intervention for homebound caregivers of persons with dementia", *Nursing Research*, vol. 48, no. 3, pp. 173-182.
- Chang, B. L., Brecht, M. L., & Carter, P. A. 2001, "Predictors of social support and caregiver outcomes", *Women and Health*, vol. 33, no. 1-2, pp. 39-61.
- Chiverton, P. & Caine, E. D. 1989, "Education to Assist Spouses in Coping with Alzheimers Disease - A Controlled Trial", *Journal of the American Geriatrics Society*, vol. 37, no. 7, pp. 593-598.
- Clark, K. K., Bormann, C. A., Cropanzano, R. S., & James, K. 1995, "Validation Evidence for 3 Coping Measures", *Journal of Personality Assessment*, vol. 65, no. 3, pp. 434-455.
- Clipp, E. C. & George, L. K. 1993, "Dementia and Cancer - A Comparison of Spouse Caregivers", *Gerontologist*, vol. 33, no. 4, pp. 534-541.

Cohen, C. I., Magai, C., Yaffee, R., & Walcott-Brown, L. 2006, "The Prevalence of Anxiety and Associated Factors in a Multiracial Sample of Older Adults", *Psychiatric Services*, vol. 57, no. 12, pp. 1719-1725.

Compton, S. A., Flanagan, P., & Gregg, W. 1997, "Elder abuse in people with dementia in Northern Ireland: prevalence and predictors in cases referred to a psychiatry of old age service", *International Journal of Geriatric Psychiatry*, vol. 12, no. 6, pp. 632-635.

Conway, K. P., Compton, W., Stinson, F. S., & Grant, B. F. 2006, "Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the national epidemiologic survey on alcohol and related conditions", *Journal of Clinical Psychiatry*, vol. 67, no. 2, pp. 247-257.

Coolidge, F. L., Segal, D. L., Hook, J. N., & Stewart, S. 2000, "Personality disorders and coping among anxious older adults", *Journal of Anxiety Disorders*, vol. 14, no. 2, pp. 157-172.

Coon, D. W., Rupert, M., Solano, N., Mausbach, B., Kraemer, H., Argu, I. T., Haley, W. E., & Thompson, L. W. 2004, "Wellbeing, appraisal and coping in Latina and Caucasian female dementia caregivers: findings from the REACH study", *Aging and Mental Health*, vol. 8, no. 4, pp. 330-345.

Coon, D. W., Thompson, L., Steffen, A., Sorocco, K., & Gallagher-Thompson, D. 2003, "Anger and depression management: Psychoeducational skill training interventions for women caregivers of a relative with dementia", *Gerontologist*, vol. 43, no. 5, pp. 678-689.

Coope, B., Ballard, C., Saad, K., Patel, A., Benthams, P., Bannister, C., Graham, C., & Wilcock, G. 1995, "The prevalence of depression in the carers of dementia sufferers", *International Journal of Geriatric Psychiatry*, vol. 10, no. 3, pp. 237-242.

Cox, C. 1997, "Findings from a statewide program of respite care: a comparison of service users, stoppers, and nonusers", *Gerontologist*, vol. 37, no. 4, pp. 511-517.

Crespo, M., Lopez, J., & Zarit, S. H. 2005, "Depression and anxiety in primary caregivers: a comparative study of caregivers of demented and nondemented older persons", *International Journal of Geriatric Psychiatry*, vol. 20, pp. 591-592.

Croog, S. H., Sudilovsky, A., Burleson, J. A., & Baume, R. M. 2001, "Vulnerability of husband and wife caregivers of Alzheimer disease patients to caregiving stressors", *Alzheimer Disease and Associated Disorders*, vol. 15, no. 4, pp. 201-210.

Cuijpers, P. 2005, "Depressive disorders in caregivers of dementia patients: A systematic review", *Aging and Mental Health*, vol. 9, no. 4, pp. 325-330.

Cummings, J. L. 1997, "The Neuropsychiatric Inventory: assessing psychopathology in dementia patients", *Neurology*, vol. 48, no. 5, pp. 10S-116.

Cummings, J. L., Frank, J. C., Cherry, D., Kohatsu, N. D., Kemp, B., Hewett, L., & Mittman, B. 2002, "Guidelines for managing Alzheimer's disease: Part I. Assessment", *American Family Physician*, vol. 65, no. 11, pp. 2263-2272.

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. 1994, "The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia", *Neurology*, vol. 44, no. 12, pp. 2308-2314.

Department of Health. The Carers' (Recognition and Services) Act. 1995.
Ref Type: Statute

Department of Health 1999a, *A National Strategy for Carers*, The Stationery Office, London.

Department of Health 1999b, *National service framework for mental health: modern standards and service models*, The Stationery Office, London.

Department of Health. The Carers and Disabled Children Act. 2000.
Ref Type: Statute

Department of Health 2001, *National Service Framework for Older People*, The Stationery Office, London.

Department of Health. Carers (Equal Opportunities) Act. 2004.
Ref Type: Statute

Department of Health. The Mental Capacity Act. 2005.
Ref Type: Statute

Derogatis, L. R. 1993, *BSI Brief Symptom Inventory: Administration, Scoring and Procedures Manual* National Computer Systems, Minneapolis.

Derogatis, L. R., Lipman, R. S., & Covi, L. 1973, "SCL-90: an outpatient psychiatric rating scale-preliminary report", *Psychopharmacological Bulletin*, vol. 9, no. 1, pp. 13-28.

Ducharme, F., Levesque, L., Giroux, F., & Lachance, L. 2005, "Follow-up of an intervention program for caregivers of a relative with dementia living in a long-term care setting: Are there any persistent and delayed effects?", *Aging & Mental Health*, vol. 9, no. 5, pp. 461-469.

Dura, J. R., Stukenberg, K. W., & Kiecolt-Glaser, J. K. 1991, "Anxiety and depressive disorders in adult children caring for demented parents", *Psychology and Aging*, vol. 6, no. 3, pp. 467-473.

Fergusson, D. M., Horwood, L. J., & Lynskey, M. T. 1996, "Childhood sexual abuse and psychiatric disorder in young adulthood .2. Psychiatric outcomes of childhood sexual abuse", *Journal of the American Academy of Child and Adolescent Psychiatry*, vol. 35, no. 10, pp. 1365-1374.

Ferri, C. P., Prince, M., Brayne, C., Brodaty, H., Fratiglioni, L., Ganguli, M., Hall, K., Hasegawa, K., Hendrie, H., & Huang, Y. 2005, "Global prevalence of dementia: a Delphi consensus study", *Lancet*, vol. 366, no. 9503, pp. 2112-2117.

Flaskerud, J. H., Carter, P. A., & Lee, P. 2000, "Distressing emotions in female caregivers of people with AIDS, age-related dementias, and advanced-stage cancers", *Perspectives in Psychiatric Care*, vol. 36, no. 4, pp. 121-130.

Fleishman, J. A., Sherbourne, C. D., Cleary, P. D., Wu, A. W., Crystal, S., & Hays, R. D. 2003, "Patterns of coping among persons with HIV infection: Configurations, correlates, and change", *American Journal of Community Psychology*, vol. 32, no. 1-2, pp. 187-204.

Folkman, S. & Lazarus, R. S. 1980, "An Analysis of Coping in A Middle-Aged Community Sample", *Journal of Health and Social Behavior*, vol. 21, no. 3, pp. 219-239.

Folkman, S. & Lazarus, R. S. 1988, *The Ways of Coping Questionnaire* Consulting Psychologists' Press, Palo Alto, California.

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*, vol. 12, no. 3, pp. 189-198.

Fratiglioni, L. 1998, "Epidemiology," in *Health Economics of Dementia*, Wimo A et al., eds., John Wiley & Sons Ltd, USA.

Galasko, D., Kershaw, P. R., Schneider, L., Zhu, Y., & Tariot, P. N. 2004, "Galantamine Maintains Ability to Perform Activities of Daily Living in Patients with Alzheimer's Disease", *Journal of the American Geriatrics Society*, vol. 52, no. 7, pp. 1070-1076.

Gallagher, T. J., Wagenfeld, M. O., Baro, F., & Haepers, K. 1994, "Sense of Coherence, Coping and Caregiver Role Overload", *Social Science & Medicine*, vol. 39, no. 12, pp. 1615-1622.

Gallagher-Thompson, D., Arean, P., Rivera, P., & Thompson, L. W. 2001, "A psychoeducational intervention to reduce distress in hispanic family caregivers: Results of a pilot study", *Clinical Gerontologist*, vol. 23, no. 1-2, pp. 17-32.

Gallagher-Thompson, D., Coon, D. W., Solano, N., Ambler, C., Rabinowitz, Y., & Thompson, L. W. 2003, "Change in indices of distress among Latino and Anglo female caregivers of elderly relatives with dementia: Site-specific results from the REACH national collaborative study", *Gerontologist*, vol. 43, no. 4, pp. 580-591.

Gatz, M., Reynolds, C. A., Fratiglioni, L., Johansson, B., Mortimer, J. A., Berg, S., Fiske, A., & Pedersen, N. L. 2006, "Role of genes and environments for explaining Alzheimer disease", *Archives of General Psychiatry*, vol. 63, no. 2, pp. 168-174.

Gaugler, J. E., Kane, R. L., Kane, R. A., Clay, T., & Newcomer, R. 2003, "Caregiving and Institutionalization of Cognitively Impaired Older People: Utilizing Dynamic Predictors of Change", *Gerontologist*, vol. 43, no. 2, pp. 219-229.

Gelder, M., Lopez-Ibor, J. J., & Andreasen, N. 2001, "New Oxford Textbook of Psychiatry," 1 edn, Oxford University Press.

Gendron, C., Poitras, L., & Dastoor, D. P. 1996, "Cognitive-behavioural group intervention for spouse caregivers: Findings and clinical considerations", *Clinical Gerontologist*, vol. 17, no. 1, pp. 3-19.

Glasgow Carers Panel 2006, *Caring is no joke but you can still have a laugh!*

Goode, K. T., Haley, W. E., Roth, D. L., & Ford, G. R. 1998, "Predicting longitudinal changes in caregiver physical and mental health: A stress process model", *Health Psychology*, vol. 17, no. 2, pp. 190-198.

Gottlieb, B. H. & Gignac, M. A. M. 1996, "Content and domain specificity of coping among family caregivers of persons with dementia", *Journal of Aging Studies*, vol. 10, no. 2, pp. 137-155.

Gottlieb, B. H. & Wolfe, J. 2002, "Coping with family caregiving to persons with dementia: a critical review", *Aging & Mental Health*, vol. 6, no. 4, pp. 325-342.

Graham, C., Ballard, C., & Sham, P. 1997, "Carers' knowledge of dementia, their coping strategies and morbidity", *International Journal of Geriatric Psychiatry*, vol. 12, no. 9, pp. 931-936.

Grant, I., McKibbin, C. L., Taylor, M. J., Mills, P., Dimsdale, J., Zielger, M., & Patterson, T. L. 2003, "In-home respite intervention reduces plasma epinephrine in stressed Alzheimer caregivers", *American Journal of Geriatric Psychiatry*, vol. 11, no. 1, pp. 62-72.

Haaga, D. A. F. & Davison, G. C. 1993, "An Appraisal of Rational-Emotive Therapy", *Journal of Consulting and Clinical Psychology*, vol. 61, no. 2, pp. 215-220.

Haley, W. E., Gitlin, L., & Wisniewski, R. 2004, "Well-being, appraisal, and coping in African-American and Caucasian dementia caregivers: findings from the REACH study", *Aging and Mental Health*, vol. 8, no. 4, pp. 316-329.

Haley, W. E., Roth, D. L., Coletton, M. I., Ford, G. R., West, C. A. C., Collins, R. P., & Isobe, T. L. 1996, "Appraisal, coping, and social support as mediators of well-being in black and white family caregivers of patients with Alzheimer's disease", *Journal of Consulting and Clinical Psychology*, vol. 64, no. 1, pp. 121-129.

Hayes, S. C., Luoma, J. B., Bond, F. W., Masuda, A., & Lillis, J. 2006, "Acceptance and commitment therapy: Model, processes and outcomes", *Behaviour Research and Therapy*, vol. 44, no. 1, pp. 1-25.

- Hebert, R., Bravo, G., & Preville, M. 2000, "Reliability, validity and reference values of the Zarit Burden Interview for assessing informal caregivers of community-dwelling older persons with dementia", *Canadian Journal on Aging*, vol. 19, no. 4, pp. 494-507.
- Hebert, R., Levesque, L., Vezina, J., Lavoie, J. P., Ducharme, F., Gendron, C., Preville, M., Voyer, L., & Dubois, M. F. 2003, "Efficacy of a psychoeducative group program for caregivers of demented persons living at home: a randomised controlled trial", *Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*, vol. 58, no. 1, p. S58-S67.
- Heinik, J., Solomesh, I., Bleich, A., & Berkman, P. 2003, "Are the clock-drawing test and the MMSE combined interchangeable with CAMCOG as a dementia evaluation instrument in a specialized outpatient setting?", *Journal of Geriatric Psychiatry and Neurology*, vol. 16, no. 2, pp. 74-79.
- Hepburn, K. W., Tornatore, J., Center, B., & Ostwald, S. W. 2001, "Dementia Family Caregiver Training: Affecting Beliefs About Caregiving and Caregiver Outcomes", *Journal of the American Geriatrics Society*, vol. 49, no. 4, pp. 450-457.
- Hinrichsen, G. A. & Niederehe, G. 1994, "Dementia Management Strategies and Adjustment of Family Members of Older Patients", *Gerontologist*, vol. 34, no. 1, pp. 95-102.
- Holmes, T. H. & Rahe, R. H. 1967, "Social Readjustment Rating Scale", *Journal of Psychosomatic Research*, vol. 11, no. 2, pp. 213-218.
- Hooker, K., Manoogian, O. D. M., Monahan, D. J., Frazier, L. D., & Shifren, K. 2000, "Does type of disease matter? Gender differences among Alzheimer's and Parkinson's disease spouse caregivers", *Gerontologist*, vol. 40, no. 5, pp. 568-573.
- Hosaka, T. & Sugiyama, Y. 2003, "Structure intervention in family caregivers of the demented elderly and changes in their immune function", *Psychiatry and Clinical neurosciences*, vol. 57, no. 2, pp. 147-151.
- House of Commons Health Select Committee 2004, *Elder Abuse 2*.
- Ihl, R., Brinkmeyer, J., Janner, M., & Kerdar, M. S. 2000, "A comparison of ADAS and EEG in the discrimination of patients with dementia of the Alzheimer type from healthy controls", *Neuropsychobiology*, vol. 41, no. 2, pp. 102-107.
- Johnson, J. G., Cohen, P., Gould, M. S., Kasen, S., Brown, J., & Brook, J. S. 2002, "Childhood adversities, interpersonal difficulties, and risk for suicide attempts during late adolescence and early adulthood", *Archives of General Psychiatry*, vol. 59, no. 8, pp. 741-749.
- Kantojarvi, L., Veijola, J., Laksy, K., Jokelainen, J., Herva, A., Karvonen, J. T., Kokkonen, P., Jarvelin, M. R., & Joukamaa, M. 2006, "Co-occurrence of personality disorders with mood, anxiety, and substance use disorders in a young adult population", *Journal of Personality Disorders*, vol. 20, no. 1, pp. 102-112.
- Kapczinski, F., Lima, M. S., Souza, J. S., Cunha, A., & Schmitt, R. 2006, "Antidepressants for generalized anxiety disorder", *The Cochrane Database of Systematic Reviews* no. 2.
- Katona, C., Livingston, G., Cooper, C., Ames, D., Brodaty, H., & Chiu, E. 2007, "International Psychogeriatric Association Consensus Statement on Defining and Measuring Treatment Benefits in Dementia", *International Psychogeriatrics*.
- Kaye, W. H., Bulik, C. M., Thornton, L., Barbarich, N., & Masters, K. 2004, "Comorbidity of anxiety disorders with anorexia and bulimia nervosa", *American Journal of Psychiatry*, vol. 161, no. 12, pp. 2215-2221.
- Keely, B. & Clarke, M. 2002, *Carers Speak Out: Report on findings and recommendations*, The Princess Royal Trust for Carers.

- Kendall, E. 1954, "The Validity of Taylor Manifest Anxiety Scale", *Journal of Consulting Psychology*, vol. 18, no. 6, pp. 429-432.
- Kendler, K. S. 1995, "Adversity, Stress and Psychopathology - A Psychiatric Genetic Perspective", *International Journal of Methods in Psychiatric Research*, vol. 5, no. 3, pp. 163-170.
- Kessler, R. C., Davis, C. G., & Kendler, K. S. 1997, "Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey", *Psychological Medicine*, vol. 27, no. 5, pp. 1101-1119.
- King, A. C. & Brassington, G. 1997, "Enhancing physical and psychological functioning in older family caregivers: The role of regular physical activity", *Annals of behavioral medicine*, vol. 19, pp. 91-100.
- Kirkwood, G., Rampes, H., Tuffrey, V., Richardson, J., Pilkington, K., & Ramaratnam, S. 2005, "Yoga for anxiety: a systematic review of the research evidence * Commentary", *British Journal of Sports Medicine*, vol. 39, no. 12, pp. 884-891.
- Kneebone, I. I. & Martin, P. R. 2003, "Coping and caregivers of people with dementia", *British Journal of Health Psychology*, vol. 8, pp. 1-17.
- Knight, B. G. & McCallum, T. J. 1998, "Heart rate reactivity and depression in African-American and white dementia caregivers: reporting bias or positive coping?", *Aging and Mental Health*, vol. 2, no. 3, pp. 212-221.
- Knight, B. G., Silverstein, M., McCallum, T. J., & Fox, L. S. 2000, "A sociocultural stress and coping model for mental health outcomes among African American caregivers in Southern California", *Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*, vol. 55, no. 3, pp. 142-150.
- Koeter, M. W. J. 1992, "Validity of the Ghq and Scl Anxiety and Depression Scales - A Comparative-Study", *Journal of Affective Disorders*, vol. 24, no. 4, pp. 271-279.
- Kolanowski, A. M., Fick, D., Waller, J. L., & Shea, D. 2004, "Spouses of persons with dementia: their healthcare problems, utilization, and costs", *Research in Nursing and Health*, vol. 27, no. 5, pp. 296-306.
- Krueger, R. F. 1999, "The Structure of Common Mental Disorders", *Archives of General Psychiatry*, vol. 56, no. 10, pp. 921-926.
- Kuboki, T., Nomura, S., Wada, M., Akabayashi, A., Nagataki, M., Suematsu, H., Yokoyama, K., & Araki, S. 1993, "Multidimensional Assessment of Mental State in Occupational-Health Care - Combined Application of 3 Questionnaires - Tokyo-University Egogram (Teg), Time Structuring Scale (Tss), and Profile of Mood States (Poms)", *Environmental Research*, vol. 61, no. 2, pp. 285-298.
- Kukull, W. A., Higdon, R., Bowen, J. D., McCormick, W. C., Teri, L., Schellenberg, G. D., van Belle, G., Jolley, L., & Larson, E. B. 2002, "Dementia and Alzheimer Disease Incidence: A Prospective Cohort Study", *Archives of Neurology*, vol. 59, no. 11, pp. 1737-1746.
- Kvaal, K., Macijauskiene, J., Engedal, K., & Laake, K. 2001, "High prevalence of anxiety symptoms in hospitalized geriatric patients", *International Journal of Geriatric Psychiatry*, vol. 16, no. 7, pp. 690-693.
- Lavoie, J. P., Ducharme, F., Levesque, L., Hebert, R., Vezina, J., Gendron, C., Preville, M., St Laurent, C., & Voyer, L. 2005, "Understanding the outcomes of a psycho-educational group intervention for caregivers of persons with dementia living at home: A process evaluation", *Aging & Mental Health*, vol. 9, no. 1, pp. 25-34.
- Layard, R. 2006, *The Depression Report: a new deal for anxiety and depression*, The London School of Economics and Political Science, London.

- Lazarus, R. S. 1966, *Psychological stress and the coping process* McGraw-Hill, New York.
- Lazarus, R. S. & Folkman, S. 1984, "Stress, appraisal and coping", *New York, Springer*.
- Lee, W. E., Wadsworth, M. E. J., & Hotopf, A. 2006, "The protective role of trait anxiety: a longitudinal cohort study", *Psychological Medicine*, vol. 36, no. 3, pp. 345-351.
- Levesque, L., Gendron, C., Vezina, J., Hebert, R., Ducharme, F., Lavoie, J. P., Gendron, M., Voyer, L., & Preville, M. 2002, "The process of a group intervention for caregivers of demented persons living at home: conceptual framework, components, and characteristics", *Aging & Mental Health*, vol. 6, no. 3, pp. 239-247.
- Liddell, M. B., Lovestone, S., & Owen, M. J. 2001, "Genetic risk of Alzheimer's disease: advising relatives", *British Journal of Psychiatry*, vol. 178, pp. 7-11.
- Linehan, M. M. 2000, "The empirical basis of dialectical behavior therapy: Development of new treatments versus evaluation of existing treatments", *Clinical Psychology-Science and Practice*, vol. 7, no. 1, pp. 113-119.
- Livingston, G., Mahoney, R., Regan, C., & Katona, C. 2005, "The Caregivers for Alzheimer's disease Problems Scale (CAPS): development of a new scale within the LASER-AD study", *Age and Ageing*, vol. 34, no. 3, pp. 287-290.
- Livingston, G., Manela, M., & Katona, C. 1996, "Depression and other psychiatric morbidity in carers of elderly people living at home", *British Medical Journal*, vol. 312, no. 7024, pp. 153-156.
- Lopez, F. J. C. 1999, "Acceptance and Commitment Therapy (ACT) in panic disorder with agoraphobia: a case study", *Psicothema*, vol. 11, no. 1, pp. 1-12.
- Mahoney, D. F., Tarlow, B. J., & Jones, R. N. 2003, "Effects of an automated telephone support system on caregiver burden and anxiety: findings from the REACH for TLC intervention study", *Gerontologist*, vol. 43, no. 4, pp. 556-567.
- Mahoney, R., Regan, C., Katona, C., & Livingston, G. 2005, "Anxiety and depression in family caregivers of people with Alzheimer's disease - the LASER-AD study", *American Journal of Geriatric Psychiatry*, vol. 13, no. 9, pp. 795-801.
- Maier, W., Buller, R., Philipp, M., & Heuser, I. 1988, "The Hamilton Anxiety Scale - Reliability, Validity and Sensitivity to Change in Anxiety and Depressive-Disorders", *Journal of Affective Disorders*, vol. 14, no. 1, pp. 61-68.
- Marriott, A., Donaldson, C., Tarrier, N., & Burns, A. 2000, "Effectiveness of cognitive-behavioural family intervention in reducing the burden of care in carers of patients with Alzheimer's disease", *British Journal of Psychiatry*, vol. 176, pp. 557-562.
- Marvardi, M. 2005, "The caregiver burden inventory in evaluating the burden of caregivers of elderly demented patients: results from a multicenter study", *Aging Clinical and Experimental Research*, vol. 17, pp. 46-53.
- Mausbach, B. T., Coon, D., Cardenas, V., & Thompson, L. W. 2006a, "Religious Coping among Caucasian and Latina Dementia Caregivers", *Journal of Mental Health and Aging*, vol. 9, no. 2, pp. 97-110.
- Mausbach, B. T., Aschbacher, K., Patterson, T. L., Ancoli-Israel, S., von Kanel, R., Mills, P. J., Dimsdale, J. E., & Grant, I. 2006b, "Avoidant Coping Partially Mediates the Relationship Between Patient Problem Behaviors and Depressive Symptoms in Spousal Alzheimer Caregivers", *American Journal of Geriatric Psychiatry*, vol. 14, no. 4, pp. 299-306.
- McClendon, M. J., Smyth, K. A., & Neundorfer, M. M. 2004, "Survival of persons with Alzheimer's disease: Caregiver coping matters", *Gerontologist*, vol. 44, no. 4, pp. 508-519.

McKee, K. J., Whittick, J. E., Ballinger, B. B., Gilhooly, M. M. L., Gordon, D. S., Mutch, W. J., & Philp, I. 1997, "Coping in family supporters of elderly people with dementia", *British Journal of Clinical Psychology*, vol. 36, pp. 323-340.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. 1984, "Clinical Diagnosis of Alzheimers Disease - Report of the NINCDS-ADRDA Work Group Under the Auspices of Department Of Health And Human Services Task Force on Alzheimers Disease", *Neurology*, vol. 34, no. 7, pp. 939-944.

Medical Research Council 2000, *A framework for the development and evaluation of randomised controlled trials for complex interventions to improve health*, MRC, London.

Mindgarten website. Ways of Coping Questionnaire.
<http://www.mindgarden.com/products/wayss.htm> . 2006.
 Ref Type: Electronic Citation

Mitte, K. 2005, "Meta-analysis of cognitive-behavioral treatments for generalized anxiety disorder: A comparison with pharmacotherapy", *Psychological Bulletin*, vol. 131, no. 5, pp. 785-795.

Mitte, K., Noack, P., Steil, R., & Hautzinger, M. 2005, "A meta-analytic review of the efficacy of drug treatment in generalized anxiety disorder", *Journal of Clinical Psychopharmacology*, vol. 25, no. 2, pp. 141-150.

Mohide, E. A., Pringle, D. M., Streiner, D. L., Gilbert, J. R., Muir, G., & Tew, M. 1990, "A randomized trial of family caregiver support in the home management of dementia", *Journal of the American Geriatric Society*, vol. 38, pp. 446-454.

Moniz-Cook, E., Agar, S., Gibson, G., Win, T., & Wang, M. 1998, "A preliminary study of the effects of early intervention with people with dementia and their families in a memory clinic", *Aging and Mental Health*, vol. 2, no. 3, pp. 199-211.

Morano, C. L. 2003, "Appraisal and coping: Moderators or mediators of stress in Alzheimer's disease caregivers?", *Social Work Research*, vol. 27, no. 2, pp. 116-128.

Morris, R. G., Woods, R. T., Davies, K. S., & Berry, J. 1992, "The use of a coping strategy focused support group for carers of dementia sufferers", *Counselling Psychology Quarterly*, vol. 5, no. 4, pp. 337-348.

Murray, J. M., Manela, M. V., Shuttleworth, A., & Livingston, G. A. 1997, "Caring for an older spouse with a psychiatric illness", *Aging & Mental Health*, vol. 1, no. 3, pp. 256-260.

National Institute for Clinical Excellence (NICE) 2004, *Management of anxiety (panic disorder, with or without agoraphobia, and generalised anxiety disorder) in adults in primary, secondary and community care* 22.

Neundorfer, M. M. 1991, "Coping and health outcomes in spouse caregivers of persons with dementia", *Nursing Research*, vol. 40, no. 5, pp. 260-265.

Noyes, R., Clarkson, C., Crowe, R. R., Yates, W. R., & Mcchesney, C. M. 1987, "A Family Study of Generalized Anxiety Disorder", *American Journal of Psychiatry*, vol. 144, no. 8, pp. 1019-1024.

Oei, T. P. S., Evans, L., & Crook, G. M. 1990, "Utility and Validity of the Stai with Anxiety Disorder Patients", *British Journal of Clinical Psychology*, vol. 29, pp. 429-432.

Orsillo, S. M., Roemer, E., Block-Lerner, J., LeJeune, C., & Herbert, J. D. 2006, "ACT with Anxiety Disorders," in *A practical guide to acceptance and commitment therapy*, S. C. Haynes & K. D. Stroschal, eds., Springer science and business media, New York, USA, pp. 103-132.

- Ory, M. G., Hoffman, R. R., Yee, J. L., Tennstedt, S., & Schulz, R. 1999, "Prevalence and impact of caregiving: A detailed comparison between dementia and nondementia caregivers", *Gerontologist*, vol. 39, no. 2, pp. 177-185.
- Osman, A., Kopper, B. A., Barrios, F. X., Osman, J. R., & Wade, T. 1997, "The Beck Anxiety Inventory: Reexamination of factor structure in psychometric properties", *Journal of Clinical Psychology*, vol. 53, no. 1, pp. 7-14.
- Pakenham, K. I. 2005, "Relations between coping and positive and negative outcomes in carers of persons with multiple sclerosis (MS)", *Journal of Clinical Psychology in Medical Settings*, vol. 12, no. 1, pp. 25-38.
- Parks, S. H. & Pilisuk, M. 1991, "Caregiver burden: gender and the psychosocial costs of caregiving", *The American Journal of Orthopsychiatry*, vol. 61, pp. 501-509.
- Paveza, G. J., Cohen, D., Eisdorfer, C., Freels, S., Semla, T., Ashford, J. W., Gorelick, P., Hirschman, R., Luchins, D., & Levy, P. 1992, "Severe Family Violence and Alzheimers-Disease - Prevalence and Risk-Factors", *Gerontologist*, vol. 32, no. 4, pp. 493-497.
- Pett, M. A., Caserta, M. S., Hutton, A. P., & Lund, D. A. 1988, "Intergenerational Conflict - Middle-Aged Women Caring for Demented Older Relatives", *American Journal of Orthopsychiatry*, vol. 58, no. 3, pp. 405-417.
- Pettit, T., Livingston, G., Manela, M., Kitchen, G., Katona, C., & Bowling, A. 2001, "Validation and normative data of health status measures in older people: the Islington study", *International Journal of Geriatric Psychiatry*, vol. 16, no. 11, pp. 1061-1070.
- Pinquart, M. & Sorensen, S. 2003a, "Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis", *Psychology and Aging*, vol. 18, no. 2, pp. 250-267.
- Pinquart, M. & Sorensen, S. 2006, "Helping caregivers of persons with dementia: which interventions work and how large are their effects?", *International Psychogeriatrics* pp. 1-19.
- Pinquart, M. & Sorensen, S. 2003b, "Associations of Stressors and Uplifts of Caregiving With Caregiver Burden and Depressive Mood: A Meta-Analysis", *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, vol. 58, no. 2, pp. 112-128.
- Powers, D. V., Gallagher-Thompson, D., & Kraemer, H. C. 2002, "Coping and depression in Alzheimer's caregivers: Longitudinal evidence of stability", *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, vol. 57, no. 3, pp. 205-211.
- Pratt, C., Schmall, V., & Wright, S. 1985, "Burden, Coping and Health - Family Caregivers to Community-Dwelling and Institutionalized Dementia Patients", *Gerontologist*, vol. 25, p. 149.
- Proctor, R., Martin, C., & Hewison, J. 2002, "When a little knowledge is a dangerous thing...: A study of carers' knowledge about dementia, preferred coping style and psychological distress.", *International Journal of Geriatric Psychiatry*, vol. 17, no. 12, pp. 1133-1139.
- Pruchno, R. A. & Resch, N. L. 1989, "Mental-Health of Caregiving Spouses - Coping As Mediator, Moderator, Or Main Effect", *Psychology and Aging*, vol. 4, no. 4, pp. 454-463.
- Quayhagen, M. 1997, "Coping with dementia: family caregiver burnout and abuse", *Journal of Mental Health and Aging*, vol. 3, no. 3, pp. 357-364.
- Rabinowitz, Y. G., Mausbach, B. T., Coon, D. W., Depp, C., Thompson, L. W., & Gallagher-Thompson, D. 2006, "The moderating effect of self-efficacy on intervention response in women family caregivers of older adults with dementia", *American Journal of Geriatric Psychiatry*, vol. 14, no. 8, pp. 642-649.
- Radosevich, D. & Pruitt, M. 1995, *Twelve-Item Health Status Questionnaire: HSQ-12 Version 2.0*. Bloomington, Health Outcomes Institute.

- Rasmusson, D. X., Brandt, J., Steele, C., Hedreen, J. C., Troncoso, J. C., & Folstein, M. F. 1996, "Accuracy of clinical diagnosis of Alzheimer disease and clinical features of patients with non-Alzheimer disease neuropathology", *Alzheimer Disease & Associated Disorders*, vol. 10, no. 4, pp. 180-188.
- Reimherr, S. W., Strong, R. E., Marchant, B. K., Hedges, D. W., & Wender, P. H. 2001, "Factors affecting return of symptoms 1 year after treatment in a 62-week controlled study of fluoxetine in major depression", *Journal of Clinical Psychiatry*, vol. 62, no. 22, pp. 16-23.
- Rinaldi, P., Spazzafumo, L., Mastriforti, R., Mattioli, P., Marvardi, M., Polidori, M. C., Cherubini, A., & Abate, G. 2005, "Predictors of high level of burden and distress in caregivers of demented patients: results of an Italian multicenter study", *International Journal of Geriatric Psychiatry*, vol. 20, no. 2, pp. 168-174.
- Rinne, T., de Kloet, E. R., Wouters, L., Goekoop, J. G., Derijk, R. H., & van den Brink, W. 2002, "Hyperresponsiveness of hypothalamic-pituitary-adrenal axis to combined dexamethasone/corticotropin-releasing hormone challenge in female borderline personality disorder subjects with a history of sustained childhood abuse", *Biological Psychiatry*, vol. 52, no. 11, pp. 1102-1112.
- Roberts, J., Browne, G., Milne, C., Spooner, L., Gafni, A., Drummond-Young, M., LeGris, J., Watt, S., LeClair, K., Beaumont, L., & Roberts, J. 1999, "Problem-solving counseling for caregivers of the cognitively impaired: effective for whom?", *Nursing Research*, vol. 48, no. 3, pp. 162-172.
- Roff, L. L., Burgio, L. D., Gitlin, L., Nichols, L., Chaplin, W., & Hardin, J. M. 2004, "Positive aspects of Alzheimer's caregiving: the role of race", *Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*, vol. 59, no. 4, pp. 185-190.
- Romero, B. & Wenz, M. 2001, "Self-maintenance therapy in Alzheimer's disease", *Neuropsychological Rehabilitation*, vol. 11, no. 3/4, pp. 333-355.
- Rose, S. K., Strauss, M. E., Neundorfer, M. M., Smyth, K. A., & Stuckey, J. C. 1997, "The relationship of self-restraint and distress to coping among spouses caring for persons with Alzheimer's disease", *Journal of Applied Gerontology*, vol. 16, no. 1, pp. 91-103.
- Rose-Rego, S. K., Strauss, M. E., & Smyth, K. A. 1998, "Differences in the perceived well-being of wives and husbands caring for persons with Alzheimer's disease", *Gerontologist*, vol. 38, no. 2, pp. 224-230.
- Rosen, W. G., Mohs, R. C., & Davis, K. L. 1984, "A new rating scale for Alzheimer's disease", *American Journal of Psychiatry*, vol. 141, no. 11, pp. 1356-1364.
- Roth, A. & Fonagy, P. 1996, *What works for whom? A critical review of Psychotherapy Research* The Guilford Press, New York.
- Russo, J., Vitaliano, P. P., Brewer, D. D., Katon, W., & Becker, J. 1995, "Psychiatric disorders in spouse caregivers of care recipients with Alzheimer's disease and matched controls: a diathesis-stress model of psychopathology", *Journal of Abnormal Psychology*, vol. 104, no. 1, pp. 197-204.
- Saad, K., Hartman, J., Ballard, C., Kurian, M., Graham, C., & Wilcock, G. 1995, "Coping by the Carers of Dementia Sufferers", *Age and Ageing*, vol. 24, no. 6, pp. 495-498.
- Sansoni, J., Vellone, E., & Piras, G. 2004, "Anxiety and depression in community-dwelling, Italian Alzheimer's disease caregivers", *International Journal of Nursing Practice*, vol. 10, no. 2, pp. 93-100.
- Sareen, J., Cox, B. J., Clara, I., & Asmundson, G. J. G. 2005a, "The relationship between anxiety disorders and physical disorders in the US National Comorbidity Survey", *Depression and Anxiety*, vol. 21, no. 4, pp. 193-202.

- Sareen, J., Cox, B. J., Afifi, T. O., de Graaf, R., Asmundson, G. J. G., ten Have, M., & Stein, M. B. 2005b, "Anxiety Disorders and Risk for Suicidal Ideation and Suicide Attempts: A Population-Based Longitudinal Study of Adults", *Archives of General Psychiatry*, vol. 62, no. 11, pp. 1249-1257.
- Schmitz, N. & Kruse, J. 2002, "The relationship between mental disorders and medical service utilization in a representative community sample", *Social Psychiatry and Psychiatric Epidemiology*, vol. 37, no. 8, pp. 380-386.
- Schneider, L. S., Tariot, P. N., Lyketsos, C. G., Dagerman, K. S., Davis, K. L., Davis, S., Hsiao, J. K., Jeste, D. V., Katz, I. R., Olin, J. T., Pollock, B. G., Rabins, P. V., Rosenheck, R. A., Small, G. W., Lebowitz, B., & Lieberman, J. A. 2001, "National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) - Alzheimer disease trial methodology", *American Journal of Geriatric Psychiatry*, vol. 9, no. 4, pp. 346-360.
- 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 AMSTEL study", *International Journal of Geriatric Psychiatry*, vol. 18, no. 11, pp. 994-1001.
- Schulz, R. & Beach, S. R. 1999, "Caregiving as a risk factor for mortality - The caregiver health effects study", *Journal of the American Medical Association*, vol. 282, no. 23, pp. 2215-2219.
- Schulz, R., O'Brien, T., & Bookwala, J. 1995, "Psychiatric and physical morbidity effects of dementia caregiving: prevalence, correlates, and causes", *Gerontologist*, vol. 35, no. 6, pp. 771-791.
- Schuermans, J., Comijs, H. C., Beekman, A. T. F., De Beurs, E., Deeg, D. J. H., Emmelkamp, P. M. G., & van Dyck, R. 2005, "The outcome of anxiety disorders in older people at 6-year follow-up: results from the Longitudinal Aging Study Amsterdam", *Acta Psychiatrica Scandinavica*, vol. 111, no. 6, pp. 420-428.
- Schuermans, J., Comijs, H., Emmelkamp, P. M. G., Gundy, C. M. M., Weijnen, I., van den Hout, M., & van Dyck, R. 2006, "A Randomized, Controlled Trial of the Effectiveness of Cognitive-Behavioral Therapy and Sertraline versus a Waitlist Control Group for Anxiety Disorders in Older Adults", *American Journal of Geriatric Psychiatry*, vol. 14, no. 3, pp. 255-263.
- Selwood, A. et al. Systematic review of the effect of psychological interventions on family caregivers of people with dementia. *Journal of Affective Disorders* . 2007.
Ref Type: In Press
- Shaw, W. S., Patterson, T. L., Semple, S. J., Grant, I., Yu, E. S. H., Zhang, M. Y., He, Y., & Wu, W. Y. 1997, "A cross-cultural validation of coping strategies and their associations with caregiving distress", *Gerontologist*, vol. 37, no. 4, pp. 490-504.
- Silver, R. C., Holman, E. A., McIntosh, D. N., Poulin, M., & Gil-Rivas, V. 2002, "Nationwide longitudinal study of psychological responses to September 11", *Journal of the American Medical Association*, vol. 288, no. 10, pp. 1235-1244.
- Singleton, G., Bumpstead, R., O'Brien, T., Lee, A., & Meltzer, H. 2001, *Psychiatric morbidity among adults living in private households*, TSO, London.
- Singleton, G., Maung, N. A., Cowie, A., Sparks, J., Bumpstead, R., & Meltzer, H. 2002, *Mental Health of Carers*, Office of National Statistics.
- Sorensen, S., Pinquart, M., & Duberstein, P. 2002, "How Effective Are Interventions With Caregivers? An Updated Meta-Analysis", *Gerontologist*, vol. 42, no. 3, pp. 356-372.
- Spinhoven, P., Ormel, J., Sloekers, P. P. A., Kempen, G. I. J. M., Speckens, A. E. M., & VanHemert, A. M. 1997, "A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects", *Psychological Medicine*, vol. 27, no. 2, pp. 363-370.

SPSS inc 1999, *SPSS Base 10.0 for Windows User's Guide* SPSS inc, Chicago, IL.

Stansfeld, S. & Marmot, M. 1992, "Deriving A Survey Measure of Social Support - the Reliability and Validity of the Close Persons Questionnaire", *Social Science & Medicine*, vol. 35, no. 8, pp. 1027-1035.

Steffen, A. M. 2000, "Anger management for dementia caregivers: A preliminary study using video and telephone interventions", *Behaviour Therapy*, vol. 31, no. 2, pp. 281-299.

Stephens, M. A., Ogrocki, P. K., & Kinney, J. M. 1991, "Sources of stress for family caregivers of institutionalized dementia patients", *Journal of Applied Gerontology*, vol. 10, no. 3, pp. 328-342.

Stevens, T., Livingston G, Kitchen, G., Manela, M., Walker, Z., & Katona, C. 2002, "Islington study of dementia subtypes in the community", *British Journal of Psychiatry*, vol. 180, no. 3, pp. 270-276.

Stolley, J. M., Buckwalter, K. C., & Koenig, H. G. 1999, "Prayer and religious coping for caregivers of persons with Alzheimer's disease and related disorders", *American Journal of Alzheimer's Disease(R) and Other Dementias*, vol. 14, no. 3, pp. 181-191.

Sutcliffe, C. & Lerner, S. 1988, "Counselling carers of the elderly at home: a preliminary study", *Br.J.Clin.Psychol.*, vol. 27 (Pt 2), pp. 177-178.

Tarlow, B. A. & Mahoney, D. F. 2000, "The cost of recruiting Alzheimer's disease caregivers for research", *Journal of Aging and Health*, vol. 12, no. 4, pp. 490-510.

Thompson, R. L., Lewis, S. L., Murphy, M. R., Hale, J. M., Blackwell, P. H., Acton, G. J., Clough, D. H., Patrick, G. J., & Bonner, P. N. 2004, "Are there Sex Differences in Emotional and Biological Responses in Spousal Caregivers of Patients with Alzheimer's Disease?", *Biological Research For Nursing*, vol. 5, no. 4, pp. 319-330.

Tombaugh, T. N. & McIntyre, N. J. 1992, "The Mini-Mental-State-Examination - A Comprehensive Review", *Journal of the American Geriatrics Society*, vol. 40, no. 9, pp. 922-935.

Tombaugh, T. N. 2005, "Test-retest reliable coefficients and 5-year change scores for the MMSE and 3MS", *Archives of Clinical Neuropsychology*, vol. 20, no. 4, pp. 485-503.

van Balkom, A. J. L. M., Beekman, A. T. F., De Beurs, E., Deeg, D. J. H., van Dyck, R., & van Tilburg, W. 2000, "Comorbidity of the anxiety disorders in a community-based older population in The Netherlands", *Acta Psychiatrica Scandinavica*, vol. 101, no. 1, pp. 37-45.

van der Linden, G. H., Stein, D. J., & van Balkom, A. J. L. M. 2000, "The efficacy of the selective serotonin reuptake inhibitors for social anxiety disorder (social phobia): a meta-analysis of randomized controlled trials", *International Clinical Psychopharmacology*, vol. 15, p. S15-S23.

Vedhara, K., Shanks, N., Anderson, S., & Lightman, S. L. 2000, "The role of stressors and psychosocial variables in the stress process: a study of chronic caregiver stress", *Psychosomatic Medicine*, vol. 62, pp. 374-385.

Vedhara, K., Shanks, N., Wilcock, G., & Lightman, S. L. 2001, "Correlates and predictors of self-reported psychological and physical morbidity in chronic caregiver stress", *Journal of Health Psychology*, vol. 6, no. 1, pp. 101-119.

Verhey, F. R., Houx, P., van Lang, N., Huppert, F., Stoppe, G., Saerens, J., Bohm, P., de Vreese, L., Nordlund, A., Dedeyn, P. P., Neri, M., Pena-Casanova, J., Wallin, A., Bollen, E., Middelkoop, H., Nargeot, M. C., Puel, M., Fleischmann, U. M., & Jolles, J. 2004, "Cross-national comparison and validation of the Alzheimer's Disease Assessment Scale: results from the European Harmonization Project for Instruments in Dementia (EURO-HARPID)", *International Journal of Geriatric Psychiatry*, vol. 19, no. 1, pp. 41-50.

- Vitaliano, P. P., Russo, J., Young, H. M., Teri, L., & et al 1991, "Predictors of burden in spouse caregivers of individuals with Alzheimer's disease.", *Psychology and Aging*, vol. 6, no. 3, pp. 392-402.
- Waelde, L. C., Thompson, L., & Gallagher-Thompson, D. 2004, "A pilot study of a yoga and meditation intervention for dementia caregiver stress", *Journal of Clinical Psychology*, vol. 60, no. 6, pp. 677-687.
- Waghorn, G., Chant, D., White, P., & Whiteford, H. 2005, "Disability, employment and work performance among people with ICD-10 anxiety disorders", *Australian and New Zealand Journal of Psychiatry*, vol. 39, no. 1-2, pp. 55-66.
- Waite, A., Bebbington, P., Skelton-Robinson, M., & Orrell, M. 2004, "Social factors and depression in carers of people with dementia", *International Journal of Geriatric Psychiatry*, vol. 19, no. 6, pp. 582-587.
- Wancata, J., Musalek, M., Alexandrowicz, R., & Krautgartner, M. 2003, "Number of dementia sufferers in Europe between the years 2000 and 2050", *European Psychiatry*, vol. 18, no. 6, pp. 306-313.
- Weyer, G., Erzigkeit, H., Kanowski RI, & Dietrich, H. 1997, "Alzheimer's Disease Assessment Scale: reliability and validity in a multicenter clinical trial.", *International Psychogeriatrics*, vol. 9, no. 2, pp. 123-138.
- Wheller, L. 2006, "Caring and carers," in *Focus on Health*, Office of National Statistics, pp. 151-163.
- Williamson, G. M. & Schulz, R. 1993, "Coping with Specific Stressors in Alzheimers-Disease Caregiving", *Gerontologist*, vol. 33, no. 6, pp. 747-755.
- Wilson, R. S., Krueger, K. R., Arnold, S. E., Barnes, L. L., de Leon, C. F. M., Bienias, J. L., & Bennett, D. A. 2006, "Childhood adversity and psychosocial adjustment in old age", *American Journal of Geriatric Psychiatry*, vol. 14, no. 4, pp. 307-315.
- Winslow, B. W. 1997, "Effects of formal supports on stress outcomes in family caregivers of Alzheimer's patients", *Research in Nursing and Health*, vol. 20, no. 1, pp. 27-37.
- Woods, R. T., Willis, W., Higginson, I. J., Hobbins, J., & Whitby, M. 2003, "Support in the community for people with dementia and their carers: a comparative outcome study of specialist mental health service interventions", *International Journal of Geriatric Psychiatry*, vol. 18, no. 4, pp. 298-307.
- World Health Organisation 1992, *The ICD-10 Classification of Mental and Behavioural Disorder* World Health Organisation, Geneva.
- World Health Organisation 2003, *World Health Report 2003 - Shaping the future* Geneva.
- Wright, L. K. 1994, "Alzheimers-Disease Afflicted Spouses Who Remain at Home - Can Human Dialectics Explain the Findings", *Social Science & Medicine*, vol. 38, no. 8, pp. 1037-1046.
- Youn, G., Knight, B. G., Jeong, H. S., & Benton, D. 1999, "Differences in familism values and caregiving outcomes among Korean, Korean American, and White American dementia caregivers", *Psychology and Aging*, vol. 14, no. 3, pp. 355-364.
- Zarit, S. H., Reever, K. E., & Bachpeterson, J. 1980, "Relatives of the Impaired Elderly - Correlates of Feelings of Burden", *Gerontologist*, vol. 20, no. 6, pp. 649-655.
- Zigmond, A. S. & Snaith, R. P. 1983, "The Hospital Anxiety and Depression Scale", *Acta Psychiatrica Scandinavica*, vol. 67, no. 6, pp. 361-370.

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**London and South East Region Alzheimer's Disease
(Laser-AD) Study**

MPhil Proposal

**Development of a model to predict anxiety and depression in caregivers of people with
Alzheimer's Disease**

Claudia Cooper

September 2004

Supervised by Dr Gill Livingston and Professor Martin Orrell

1. Introduction

It is now well established that caring for someone with dementia is stressful and adversely affects mental and physical health (Pinquart & Soerensen, 2003). It is less clear whether caregivers of people with dementia (CGPD) are more likely to experience psychiatric morbidity meeting diagnostic criteria, and if so, which disorders are most associated with caregiving.

Several large studies have investigated factors determining the development of anxiety disorders in the general adult and older people populations. Studies examining predictors of anxiety in caregivers of people with dementia have used smaller sample sizes, and no study has yet included measures of life events and coping styles as well as other important putative factors. Caregivers of people with dementia tend to be older people as they frequently care for a spouse, but many people with dementia are cared for by their off spring who are therefore of a younger generation. In this study I will investigate predictors of anxiety in caregivers, and compare this with current evidence for predictors of anxiety in the general population of younger and older adults. I will seek to determine whether causation of anxiety in caregivers of people with dementia is qualitatively different from the general population, for example whether certain coping styles have a proportionally greater impact, or whether caregivers have greater morbidity because they have more of some causative stressors.

Prevalence of anxiety in older people

Current evidence suggests that anxiety disorders are less frequent in older people than in the younger adult population (Beekman et al, 1998). Prevalence rates reported for obsessive compulsive disorder and panic disorder are consistently low. Beekman et al (1998) reviewed seven studies and found that rates for OCD were between 0.2% - 1.5% and for panic disorder 0.04%-0.3%. Rates of phobic disorder and generalised anxiety disorder show more variation. Manela et al (1996) found that phobic disorders were the most common subclassification of anxiety disorder in older people, but that the phobic disorder was usually not associated with depression or debilitating anxiety. In their community sample of older people, 15% had an anxiety disorder, and 12% had phobic disorder. Beekman et al. (1998) found rates of phobic disorder in eight studies varied from 0.6% to over 10%.

Reported prevalences of generalised anxiety disorder in older adults also vary considerably. The Epidemiologic Catchment Area study reported a one year prevalence of 2.2% (Robins & Regier, 1991). In the Amsterdam study of the elderly (AMSTEL) (Schoevers et al., 2003), 4051 community living older people (65+) were interviewed, of whom 3.2% (n=128) fulfilled diagnostic criteria for generalised anxiety disorder. Allsup & Gosney (2002) interviewed 695 people presenting at primary care for influenza injections; using the Hospital anxiety and depression scale, they found a similar rate of anxiety caseness (using a 7/8 cut-off point) of 4% (n=28). Beekman et al (1998) interviewed 3107 people aged 55-85. They found an overall prevalence of anxiety disorders of 10.2% (n=137), of whom 7.3% (n=76) had generalised anxiety disorder.

Prevalence of anxiety in younger adults

The largest recent study of anxiety disorder prevalence was conducted in the USA by the National Institute on Alcohol Abuse and Alcoholism in 2001-2002 (Grant et al, 2004). They undertook a nationally representative face-to-face survey of 43093 respondents, who were 18 years and older. The prevalence of any current independent anxiety disorder was 11.08%, representing 23.0 million US adults. Other studies have reported lower prevalences. Merikangas et al (2002) undertook a 15 year prospective cohort study of 4547 participants aged 19-20 years from Zurich, Switzerland. They were interviewed every three years, between 1979 and 1993. Levels of anxiety increased over time, and by 1993, 2.9% met DSM-III-R criteria for generalised

anxiety or panic disorder. By this point, the cohort were aged 34-35 years, so it is likely that some cases of generalised anxiety disorder were yet to develop.

Prevalence of anxiety in CGPD

In the largest study so far of anxiety disorders in caregivers, the clinical LASER-AD study group recently reported a prevalence of 23.5% (n=36) for anxiety in caregivers of an epidemiologically representative group of people with dementia using the Hospital anxiety and depression scale (HADS), among 153 informal caregivers (Maidment et al., in press). Two other groups have interviewed smaller groups of CGPD using the HADS, and reported similar findings. Clare et al. (2002) interviewed carers of people attending a memory clinic. Only 13 caregivers were interviewed, of whom 4 (31%) and 3 (23%) were cases for anxiety at the two study time points. Proctor et al. (2002) in their study of fifty CGPD, report a mean HADS anxiety score of 8.7 (sd 4.0) which is even higher than that found by Maidment et al. (in press). By contrast, Dura et al. (1991) found that only 10% of 72 adult children caring for parents with dementia met DSM-III-R criteria for an anxiety disorder. This lesser proportion might be because spousal caregivers seem to be more likely to experience caregiver-related anxiety than adult children, and that this relates to their own fears about ageing (Wulschleger et al., 1996) or because adult children are less likely to be co-resident than spouses (Maidment et al., in press). It might also be that the HADS detected some cases that would not have met DSM-III-R criteria for anxiety disorder. Other studies in this area have reported anxiety symptoms rather than diagnoses, making interpretation difficult (e.g. Gallagher et al, 1989; Neundorfer, 1991).

Correlates of anxiety in older people

In the AMSTEL study (Schoevers et al., 2003), in which 4051 community living older people (65+) were interviewed, female gender, being married, having a past history of anxiety or depression, cognitive decline, suffering from chronic disease and being more disabled were associated with anxiety. Beekman et al (1998) studied risk factors for anxiety in older age using a vulnerability stress model. Regression analyses were carried out for men and women, and for younger, middle and oldest older people separately, although they report that risk factors varied very little with age and gender. Having a family history of anxiety disorder and functional limitations were predictive for anxiety disorders in men (OR 4.47 (1.71-11.6) and 7.73 (2.80-21.4) respectively). Receiving less emotional support was predictive of anxiety in women but not in men. Experiencing severe events in the second world war was significantly associated with anxiety disorders in the middle age group. Risk factors identified as predictive for the whole sample in logistic regression were female sex, a smaller contact network, recent losses in the family, chronic physical illness, lower level of education, extreme experiences in World War 2 and an external locus of control.

Coolidge et al (2000) examined the relationship between anxiety, personality disorder and coping strategies in 28 anxious older adults (55+), 100 non-anxious older adults and 132 anxious younger adults. Measures used included the COPE. Prevalence of generalised anxiety disorder was similar in younger and older adults. Anxious older adults were more likely to have an anxious or dependent personality disorder, and used different coping strategies to non-anxious older adults.

These results indicate that certain demographic factors, particularly female sex and lower educational level, a smaller social network, and a history of psychiatric illness and physical and cognitive decline are associated with anxiety in older adults. Intrapsychic factors are less studied; those that have been investigated, that is having an external locus of control, personality traits and coping strategies have all been implicated in the pathogenesis of anxiety.

Correlates of anxiety in younger adults

Merikangas et al (2002) found that anxiety was 1.5-2 times more common in women, and this is a finding common to other studies. The study replicated other findings that there is considerable comorbidity between anxiety and depression; 24% of people who originally had anxiety alone, and 21% of people who had depression alone, developed comorbid anxiety and depression. Grant et al (2004) found that 18% of people in the general population with a current substance use disorder, and 33% of those who sought treatment for alcohol problems, had an anxiety disorder, compared with 11.08% of the general population. Substance use clearly has an important relationship with anxiety disorders, which is probably of two directional causality.

Smari et al (1997) assessed the coping styles (using the COPE) and anxiety and depression (using the HADS) of 283 adults (aged 18-69) registering at an unemployment service. An avoidant coping style, and also, in women, focus on emotion, was significantly related to anxiety and depression. Hughes et al (1999) found that avoidant and self-vigilant coping correlated with levels of anxiety in a postal survey of 112 members (16-70) of a self-help group for people with agoraphobia and panic sufferers.

Correlates of anxiety in CGPD

The finding that nearly 1 in 4 caregivers for people with dementia have clinically significant levels of anxiety has potentially important implications for the health of the caregiver and the person with dementia. It has been found that caregiver wellbeing is even more important than dementia severity in determining whether an older person with dementia is able to live in the community (Morris et al., 1988). Previous studies have mostly investigated factors which predict caregiver burden, or non-specific psychological morbidity. They have found that caregiver psychiatric morbidity is related to the care recipient's neuropsychiatric symptoms, rather than level of cognitive impairment (e.g. Eagles et al., 1987). Other factors which have been implicated in greater caregiver burden or non-specific psychological morbidity include being a female caregiver, caring for a spouse, having a poor relationship with the care-recipient (CR), and lacking social support (Gilleard, 1998; Pinquart & Soerensen, 2003). Vedhara et al. (2000) suggest that use of heterogeneous outcome measures limits the interpretation of such studies.

Relatively few studies have specifically examined the factors that predict anxiety disorders in CGPD. Proctor et al. (2002) found no association between caregiver gender, relationship to care recipient, caring duration, or care recipient cognition, behaviour or physical functioning and caregiver anxiety (as measured by HADS) on regression analysis. Shorter duration of the dementia, having more knowledge about dementia and a tendency to use a monitoring coping style were the only factors that were significantly predictive of anxiety. Graham et al. (1997) also found that caregiver anxiety was associated with greater caregiver knowledge of dementia.

1.4 Life events

These are sudden life changes which can be desirable or undesirable. They have been defined as "objective occurrences of sufficient magnitude to bring about change in the usual activities of most individuals who experience them" (Perkins, 1982). Life events have been associated with increased risk of anxiety, depression (Finlay-Jones & Brown, 1981) and deliberate self-harm, and with abdominal pain leading to the removal of a healthy appendix (Creed, 1981).

Measurement of life events

Holmes and Rahe (1967) were the first to study life events quantitatively; they developed the Social Readjustment Rating Scale; this is an inventory of over 40 classes of life event,

classified according to how stressful they are. Use of inventories to record life events have been criticised. Brugha et al. (1985) found that 17.5% of life events reported by a random sample of 310 people from the general population of Camberwell and 74 psychiatric outpatients, using the Bedford College semi-structured interview for life events, were not covered by a standard life events inventory.

Despite the possible disadvantages, inventories are a quick and cheap way of recording life events. Holmes and Rahe (1967) made no distinction between positive and negative life events in their scale. Subsequent studies have categorised life events to take some account of their meaning - e.g. desirable versus undesirable; controlled versus uncontrolled (Brugha et al., 1985). Brugha et al. (1985) report a list of 12 events which had a moderate or marked long term threat, and 15 events which had a mild or no long term threat. Waite et al (2003) subdivided reported life events as being threatening if they were judged likely to have a severely negative impact on the individual lasting for at least a week after the event.

Life events in CGPD

A few studies have investigated the life events in CGPD. Caregivers do not appear to experience more life events than non-caregivers (Owen et al., 2002; Reed et al., 1990; Russo and Vitaliano, 1995), but they may experience fewer positive events (Owens et al., 2002), or appraise events more negatively (Reed et al., 1990). Russo and Vitaliano (1995) found that caregivers were more likely to report changes in the health of their spouse, the relationship with their spouse health, or the way people treated them.

Vedhara et al. (2000) are the only group to have studied the association of life events with anxiety in CGPD. They found that more life events (measured by the Geriatric Social Readjustment Scale) and daily hassles predicted anxiety, depression and generalised stress. Interestingly, caregiver burden predicted generalised stress, but not anxiety or depression, once life events were taken into account.

Other authors have examined the relationship between life events and burden or depression in CGPD. Russo and Vitaliano (1995) measured life events, caregiver burden and social supports in 175 spouse CGPD and 92 age and gender-matched controls. The measure of life events used was the Psychiatric Epidemiological Research Interview (PERI) life events scale.

The authors distinguished between life events that were associated with caregiving, for example reduction in work or recreation opportunities, and those that were not. They judged that life events that were present in caregivers and non-caregivers to a similar degree were unassociated with caregiving. Of these, serious family arguments and trouble with social security predicted more caregiver burden, and moving to a retirement home less burden, after controlling for demographic variables, objective primary stressors, and social support. This study suggests that even life events which are unrelated to caregiving can increase burden; this might be because people who are already stressed by caregiving may have fewer resources to cope with extrinsic stressors.

Owen et al. (2002) measured life events, depression and quality of life in 197 family caregivers for people with dementia, recruited through a memory clinic, and 218 non-caregivers recruited through community outreach programs. The Louisville Older persons event schedule (LOPES) was used to measure life events. Caregiver depression and decreased life satisfaction were both associated with primary caregiving stressors and associated life events, but not unassociated life events.

Waite et al. (2004) interviewed 72 CGPD using the Bedford College Life Events and Difficulties Schedule and the Geriatric Depression Scale. The authors rated the life events included in the schedule, and only included life events judged to be independent of caregiving and to be threatening. They determined that depression in carers was predicted by depression in the care recipient, and with living with the person with dementia. Contrary to the study hypothesis,

they found no association between life events and carer depression. The finding that living with a person with dementia who was depressed predicted caregiver depression is contrary to the finding of the LASER-AD study. This might be due to the different measures of depression used: the GDS, used by Waite et al. (2004) has a lower specificity for depression than the HADS, and therefore some caregivers who screened positive for depression could have been adjusting to life events rather than actually depressed.

These studies therefore give conflicting results. Owen et al (2002) found that only associated life events were important in determining depression and life satisfaction in caregivers. Russo and Vitilano (1995) reported that unassociated life events did predict burden. Waite et al. (2004) also found no association between depression and unassociated life events. In the only study to specifically examine caregiver anxiety, the number of life events was a significantly predictive factor.

1.3 Coping styles

The role of coping styles in predicting caregiver anxiety has been studied by several authors. Proctor et al. (2002), in the study described above, divided the coping styles of participants into those who tend to monitor for threat relevant information during stressful situations (a monitoring style), and those who avoid information which might be distressing (a blunting style). People who used a monitoring coping style were more anxious and also more knowledgeable about dementia. They conclude that these people may have been more anxious to start with, but it is also possible that their tendency to seek out information and not necessarily social support could have a causal relationship to anxiety disorders.

Other studies have compared emotion-focussed and problem-focussed coping strategies. Emotion-focussed strategies aim to lessen emotional distress, and can include use of avoidance, minimisation, distancing, selective attention, positive comparisons and wresting positive value from negative events. Problem-focussed strategies would involve defining the problem, weighing the benefits and disadvantages of possible solutions, choosing a potential solution and acting upon it. Research findings suggest that CGPD who use problem-solving and acceptance styles of coping are less likely to be distressed or depressed, report lower caregiver burden and physical health problems, and higher life satisfaction (Kneebone & Martin, 2003). They are also less likely to request institutionalisation of their dependent (Markiewicz et al., 1997).

Neundorfer (1991) interviewed sixty caregivers for people with dementia. Measures included the Brief Symptom Inventory depression and anxiety dimensions. Emotion-focussed coping styles, including escape-avoidance, confrontative coping and accepting responsibility, was found to predict greater anxiety, depression, and poorer physical health. Vedhara et al. (2000) interviewed fifty spousal caregivers of people with dementia, and a control group of 67 non-caregivers. Subscales of the Savage Personality Screening Scale were used to measure anxiety and depression. Coping styles associated with anxiety were escape/avoidance, confrontative and self-controlling coping; these were different to the coping styles which predicted depression and non-specific stress. Winslow (1997) investigated the coping styles of 452 caregivers of people with dementia. A measure of anxiety was included, derived mainly from the Hopkins Symptom Checklist, for which psychometric data is not described. Coping style had no effect on likelihood of suffering from anxiety.

Measuring Coping Styles

Numerous measures have been developed to evaluate coping strategies quantitatively. These include the Ways of Coping (Folkman & Lazarus, 1985), the COPE inventory (Carver et al., 1989), and the Coping Inventory for Stressful Situations (McWilliams et al., 2003). These instruments generally consist of a number of subscales which measure the extent to which

participants engage in various different coping strategies, both adaptive and maladaptive. In some, composite scales are used to measure what the prevalent coping styles are that underlie the pattern of coping strategies used. For example, in the Coping Inventory for Stressful Situations, respondents are scored for three general coping styles, which are task-oriented, emotion-oriented and avoidance-oriented coping (McWilliams et al., 2003). Folkman & Lazarus (1980) divided the subscales of the 'Ways of Coping' into problem-focussed and emotion-focussed strategies. DiBartolo and Soeken (2003) suggest that it is more meaningful to report mean subscale score as a proportion of mean total score, as this better reflects the prevailing coping strategies used.

This study uses the brief COPE, which has been developed from the original COPE (Carver, 1997). Internal reliability and a clear factor structure have been demonstrated (Carver, 1997). The scales scores participants on the extent to which they use 14 different coping strategies. No study has yet reported grouping these scores to give a clearer indication of the prevalent coping style.

1.5 Conclusion

Factors which have previously been associated with anxiety in this group are a shorter time since diagnosis of the dementia, and the caregiver reporting more knowledge about dementia, having more daily hassles or life events, and using certain coping styles, including emotion-focussed and monitoring coping styles. Recent studies suggest that anxiety disorders might be more common in caregivers of people with dementia than previously realised, and in the light of this knowledge, the determinants of this anxiety need to be re-examined. It is suggested that life events and coping styles might both be important in the aetiology of caregiver anxiety, no study has yet examined both factors together to determine their relative contributions.

2. Aim

The aim of this MPhil is to conduct the most comprehensive study so far of anxiety disorders in CGPD, including the role of caregiver and care recipient demographic, social and illness characteristics, and the type and quality of their relationship, as well as intrinsic factors such as coping strategies, extrinsic factors (for example life events and care recipient behaviour), and social support. It is hoped that this knowledge might then inform approaches to addressing anxiety disorders in caregivers.

Primary Hypothesis

- Caregivers who have experience at least one negative and threatening life event in the past year will be more likely to score positive for an anxiety disorder on the HADS.

Secondary Hypotheses

- The likelihood of a caregiver who has experienced at least one negative life event having an anxiety disorder will be mediated by their use of coping styles; whether they live with the care recipient; employment, physical health, and past psychiatric history; the quality of their relationship with the care recipient; care recipient behavioural problems, depression, ADL functioning and cognition.
- Previous caregiver anxiety at 1 year follow-up will predict current anxiety.
- The HADS is a specific screening instrument for depression and anxiety in caregivers of people with dementia.

Power Calculation

Waite et al. (2004) found that 48.6% (n=35) of caregivers of people with dementia experienced at least one independent and severely threatening life event in the preceding six months, using the Bedford Life events and difficulties schedule. Therefore, it is anticipated that in this study approximately half the participants in our group will experience such an event. A sample size of 71 in each group would be sufficient to detect a difference of 20% in the proportion of people experiencing anxiety disorders, at 80% power and 5% significance.

3. Method

This investigation is part of the LASER Ad study, a longitudinal research project including 224 people with Alzheimer's disease and their caregivers. The study commenced in 2003, and baseline and six month follow-up cycles have already been completed. 18-month follow up of the cohort began in February 2004.

3.1 Sample Characteristics

The cohort were recruited purposefully at baseline, to reflect the proportion of people with AD in the community who have mild, moderate and severe cognitive impairment (Fratiglioni 1998).

Inclusion criteria at baseline were:

1. A standardised diagnosis of dementia (American Psychiatric Association 1994).
2. Fulfilment of criteria for possible or probable AD (McKhann et al 1984).
3. Aged over 55 years
4. Living in London and the Southeast region (LASER) - either North London (inner city and suburban areas) or Essex (semi-rural and new town).
5. Having a caregiver who spent a minimum of 4 hours a week caring for them.

Exclusion criteria were:

1. Vascular dementia.
2. Other significant neurological disease such as Parkinson's disease, any enduring mental illness (including: psychotic episodes requiring hospitalisation or neuroleptic treatment for more than 2 weeks during the last 10 years not associated with AD), endocrine or metabolic disorders possibly causing dementia, or alcohol or drug abuse.
3. Being unable to comply with the study assessment, either due to another disease or inability to understand the national language, which would interfere with participation in the study.

3.2 Study Centres

The people with AD and their carers were recruited from three centres: Camden and Islington, Barnet, Haringey and Enfield; and Essex (Harlow and Epping). These centres are a cross-section of urban, suburban and semi-rural areas and therefore should be generalisable to the United Kingdom as a whole.

3.3 Procedures

Caregivers that have already taken part in the project will be approached in writing enclosing an information sheet about the 18-month follow-up. In all cases, caregivers will be asked to consent to be interviewed and for their relative to be approached before any interviews took place. People with AD will be given the information sheet at the time of interview and asked to give written informed consent if they are able. Those people with AD who cannot give informed consent will also be asked for consent. If they are not able to communicate their choice but appear distressed by the interview, the interview will be stopped. Interviews with the people with AD and their carers will be carried out by trained interviewers at a place of their choice i.e. the participants' home, the carer's homes, day hospital, nursing home etc.

3.4 Assessment

The interviews with the care recipients and caregivers will take place in private, usually simultaneously. The interview takes about 1.5 hours; the following data will be collected:

3.5 Demographic data

Care recipient: age, gender, ethnicity and domicile.

Caregiver: age, gender, relationship to CR, employment status, marital status and number of

children under 18 years living with them.

3.6 Caregiver data

The number of people with whom the caregiver has a confiding relationship will be recorded as a measure of social support. Caregiver past psychiatric history and psychiatric medication will be recorded. In addition the following instruments will be completed:

The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). This does not include somatic items (which can be misleading in older subjects) and has been validated throughout the age range and in all settings to identify clinically significant anxiety and depression (Mykleton et al., 2001). The 14-item HADS assesses how the person has been feeling within the past week; it consists of two seven-item subscales, each score 0-3, which generate scores for generalised anxiety and depression (0-21). A score of 8-10 implies borderline cases; and scores of 11 are considered cases. We used scores of 11 to define 'caseness' in our analysis.

The Zarit Burden scale for caregiver burden (Zarit et al 1980).

Three domains of the Health Status Questionnaire (HSQ-12) to measure physical functioning: health perception, physical functioning and role physical (whether health interferes with daily living) (Radosevich & Pruitt, 1995; Pettit et al., 2001).

Caregivers were asked to rate the quality of their relationship with the CR on a 4-point scale, where 1= poor, 2= fair, 3= good, and 4= excellent. This is part of the Quality of Life for patients with Alzheimer's Disease (QoL-AD) (Lodgson et al, 1999).

The Brief COPE. This is a self-report questionnaire with 14 scales describing different coping strategies, with two items per scale. Psychometric properties have been described (Carver, 1997). Each of the 14 subscales will be evaluated by three clinicians, to determine whether they reflect a prevailing task-orientated, emotion-orientated or avoidance-orientated coping style. Total score on each of these subscales will be obtained by summing the individual scales scores.

The Social Readjustment Rating Scale (Holmes & Rahe, 1967) to measure life events. This lists 43 positive and negative life events, and for each a value between 1 and 100. Hence a total score indicating the impact of life events on the caregiver's life over the previous year can be calculated. The life events will be judged for whether they are independent and threatening, using the method devised by Waite et al. (2004), in which a panel of three assessors will rate the events according to whether they were likely to have a significant negative impact on the person persisting for one week or more after the event, and whether the event was such that it could not have been precipitated by the individual.

Caregivers who screen positive on the HADS will be interviewed using a structured interview designed to determine whether they meet ICD-10 criteria for a mild, moderate or severe depressive disorder; panic disorder, phobic disorder or generalised anxiety disorder.

3.7 Care recipient data

The following scales will be completed:

For cognition: the Alzheimer's Disease Assessment Scale-cognition (ADAS-cog) (Mohs et al 1983) and the Severe Impairment Battery (SIB) (Saxton et al 1993, Schmitt et al 1997).

Activities of daily living will be assessed by the Alzheimer's Disease Co-operative Study inventory - activities of daily living (ADCS-ADL) (Galasko et al 1997) and the Modified D-test (Ferm 1974).

BPSD will be evaluated using the Neuropsychiatric Inventory (NPI) (Cummings 1997).

The patient will be assessed globally by the Clinical interview-based impression, (CIBIC-+) (Knopman et al 1994).

The Quality of Life for patients with AD (QoL-AD) (Logsdon et al 1999). This has been specially designed for patient with Alzheimer's disease. It is completed by the caregiver and the care recipient independently, and a weighted mean is calculated.

Depressive illness will be rated using the Cornell Scale for Depression in Dementia (CSDD). (Alexopoulos et al., 1988). A score of 8 indicates depression.

Current medications will also be recorded.

Service use and cost-related data will be collected using the Client Service Receipt Inventory (CSRI) (Beecham & Knapp 1992).

3.8 Statistics

SPSS 11.5 will be used for data entry and analysis. The proportion of participants who are cases for anxiety on the HADS will be calculated. As the data is non-parametric, I will use Mann Whitney-U or Chi-square analyses to identify factors associated with anxiety in caregivers. The independent predictors of anxiety caseness (including odds ratios, OR and 95% confidence intervals, CI) will then be identified by forward logistic regression analysis. The following dependent variables will be entered into the analysis: caregiver age; gender; marital status; carer living with the CR; relationship to the CR; perceived quality of the relationship to the CR; employment; presence of children; physical health; past psychiatric history; total life event score, and total score for negative, positive and neutral life events; scores on the 14 subscales of the Brief COPE; Zarit burden scale score; CR at home or in 24-hour care, CR gender, cognition (MMSE), each neuropsychiatric symptom and total NPI score, ADL functioning, CR depression (CSDD), psychotropic medications.

4. Time line

Projected completion dates for key stages of project:

Write systematic literature review: what causes anxiety in caregivers of people with dementia?
December 2004

Assist research team in undertaking interviews/ data collection and entry
January 2005

Analyse data
April 2005

Write up MPhil
August 2006

5. References

- Alexopoulos, G.S, Abrams, R.C, Young, R.C, Shamoian, C.A. Cornell Scale for Depression in Dementia. *Biological Psychiatry*, 1988; 23: 271-284.
- Allsup SJ & Gosney MA (2002) Anxiety depression in an older research population and their impact on clinical outcomes in a randomised controlled trial. *Postgraduate Medical Journal* 78(925):674-678.
- American Psychiatric Association (1994), Diagnostic and statistical manual of Mental Disorders (4th edition). Washington DC: American Psychiatric Association
- Antonovsky A. (1987) Unravelling the mystery of health. San Francisco: Jossey-Bass.
- Atienza AA, Stephens MAP, Townsend AL. Dispositional optimism, role-specific stress, and the well-being of adult daughter caregivers *Research on Aging*, Mar 2002, vol. 24, no. 2, p. 193-217,
- Beecham, J. & Knapp, M. (1992) Costing psychiatric interventions. [Chapter] Thornicroft, Graham (Ed); Brewin, Chris R. (Ed); et al. *Measuring mental health needs*. (pp. 163-183). viii, 328pp
- Beekman ATF, Bremmer MA, Deeg DJH, van Balkom AJLM, Smit JH, de Beurs E, van Dyck R, van Tilburg W (1998) Anxiety disorders in later life: a report from the longitudinal aging study Amsterdam. *International Journal of Geriatric Psychiatry*, 13, 717-726.
- Boss P, Wayne C, Horbal J, Mortimer J. (1990) Predictors of depression in caregivers of dementia patients: Boundary ambiguity and mastery. 29(3)245-254.
- Brugha T, Bebbington P, Tennant C, Hurry J. (1985) The list of threatening experiences: a subset of 12 life event categories with considerable long-term contextual threat. *Psychological Medicine*, 15, 189-194.
- Clark PC. (2002) Effects of individual and family hardiness on caregiver depression and fatigue. *Research in Nursing & Health*, 25(1)37-48,
- Carver C 1997 You want to measure coping but your protocol's too long: consider the brief COPE *International Journal of Behavioral Medicine* 4(1), 92-100
- Clare L, Wilson BA, Carter G, Breen K, Berrios GE, Hodges JR. Depression and anxiety in memory clinic attenders and their carers: implications for evaluating the effectiveness of cognitive rehabilitation interventions. *International Journal of Geriatric Psychiatry*;2002;17(10):962-967.
- Coolidge FL, Segal DL, Hook JN, Stewart S. (2000) Personality disorders and coping among anxious older adults. *Journal of anxiety disorders* 14(2):157-172.
- Creed F 1981 Life events and appendicectomy *Lancet* i 1381-5
- Cummings, J.L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D.A., Gornbein, J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology*, 1994; 44: 2308-14.
- DiBartolo MC, Soeken KL. (2003) Appraisal, Coping, Hardiness, and Self-Perceived Health in Community-Dwelling Spouse Caregivers of Persons with Dementia. *Research in Nursing & Health*, 26(6):445-458
- Dura JR, Stukenberg KW, Kiecolt-Glaser JK. Anxiety and depressive disorders in adult children caring for demented parents. *Psychology and Ageing* 1991;6(3):467-473

- Eagles, J.M., Craig, A., Rawlinson, F., Restall, D.B., Beattie, J.A.G., Besson, J.A.O. The psychological well-being of supporters of the demented elderly. *British Journal of Psychiatry*, 1987; 150: 293-298.
- Ferm L. 1974. Behavioural activities in demented geriatric patients. *Gerontol Clin* 16: 185-194.
- Finlay-Jones R. & Brown, GW (1981) Types of stressful life event and the onset of anxiety and depressive disorders *Psychological medicine* 11, 803-15
- Folkman S & Lazarus RS. (1985) If it changes it must be a process: study of emotion and coping during three stages of a college examination. *Journal of personality and social psychology*, 49, 739-747
- Fortinsky RH, Kercher K, Burant CJ (2002) Measurement and correlates of family caregiver self-efficacy for managing dementia. *Aging and Mental Health*; 6(2):153-160.
- Fratiglioni, L. Epidemiology. In *Health Economics of Dementia*. Eds. Wimo A, Jonsson B, Karisson G., Winblad, B. *John Wiley & Sons Ltd, USA*, 1998.
- Galasko, D., Edland, S., Morris, J., Clark, C., Mohs, R., Koss, E. An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. *Alzheimer's Disease and Associated Disorders*, 1997; 11: 33-39.
- Gallagher D, Wrabetz A, Lovett S, Del Maestro S, Rose J (1989) Depression and other negative effects in family caregivers In: *Alzheimer's Disease Treatment and family stress: directions for research*, Light E, Debowitz B eds; National Institute for Mental Health Washington DC; 89-159.
- Gallagher TJ, Wagenfeld MO, Baro F, Haepers K. (1994) Sense of coherence, coping and caregiver role overload. *Social Science & Medicine*, 39(12):1615-1622.
- Gilleard, C. Carers. In *Seminars in Old Age*. Eds. Butler, R., Pitt, B. *Gaskell, London*, 1998.
- Graham C, Ballard C, Sham P. Carers' knowledge of dementia, their coping strategies and morbidity. *International Journal of Geriatric Psychiatry*; 1997: 12(9):931-936
- Grant BF, Stinson FS, Dawson DA, Chou SP, et al. (2004) Prevalence and Co-occurrence of Substance Use Disorders and Independent Mood and Anxiety Disorders: Results From the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*. Chicago: 61(8); 807
- Holmes, TH & Rahe, RH (1967) The social readjustment scale *Journal of Psychosomatic Research* 11, 213-217
- Hughes I, Budd R, Greenaway S (1999) Coping with anxiety and panic: a factor analytic study. *British Journal of Clinical Psychology* 38(3):295-304.
- Kneebone II, Martin PR. Coping and caregivers of people with dementia. 2003;8:1-17
- Lazarus RS & Folkman S *Stress, appraisal and coping*. 1984; New York: Springer.
- Knopman DS, Knapp MJ, Gracon SI, Davis CS. The Clinician Interview-Based Impression (CIBI) : a clinician's global change rating scale in Alzheimer's disease. *Neurology* 1994; 44: 2315-2321.

- Lawton, M. Powell, Morton H. Kleban, Miriam Moss, Michael Rovine, and Allen Glicksman. 1989. "Measuring Caregiver Appraisal." *Journal of Gerontology: Psychological Sciences* 44:P61-P71.
- Livingston G, Manela M, and Katona C. (1996) Depression and other psychiatric morbidity in carers of elderly people living at home *BMJ*; 312: 153 - 156.
- Lodgson, R.G., Gibbons, L.E., McCurry, S.M., Teri, L. Quality of Life in Alzheimer's Disease: Patient and Caregiver Reports. *Journal of Mental Health & Aging*, 1999; 5, 21-32.
- Maidment R, Regan C, Katona C, Livingston G. Anxiety and depressive disorders in family caregivers of people with Alzheimer's Disease - the LASER-AD study (in press)
- Manela M, Katona C, Livingston G (1996) How common are the anxiety disorders in old age? *International Journal of Geriatric Psychiatry*; 11:65-70.
- Markiewicz D, Reis M, Gold DP. An exploration of attachment styles and personality traits in caregiving for dementia patients. *Int J Aging Hum Dev*; 1997; 45(2):111-132.
- Merikangas KR, Zhang H, Avenevoli S, Acaryya S, Neuenschwander M, Angst J. (2003) Longitudinal trajectories of depression and anxiety in a prospective community study. *60(10)*993-999
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., Stadlan, E.M. Clinical diagnosis of Alzheimer's disease: report of the NINADS-ADRDA Work Group under the auspices of Department of Health and Human services task force on Alzheimer's disease. *Neurology*, 1984; 34, 939-944.
- McWilliams LA, Cox BJ, Enns MW. (2003) Use of the Coping Inventory for Stressful Situations in a clinically depressed sample: Factor structure, personality correlates, and prediction of distress. *Journal of Clinical Psychology*, 59(4)423-437.
- Mohs RC, Rosen WG, Davis KL The Alzheimer's Disease Assessment Scale: an instrument for assessing treatment efficacy *Psychopharm bulletin* 19, s448-450 1983
- Morris, L.W., Morris, R.G., Britton, P.G. The relationship between marital intimacy, perceived strain and depression in spouse caregivers of dementia sufferers. *The British Journal of Medical Psychology*, 1988; 61, 231-236.
- Mykletun, A., Stordal, E., Dahl, A.A. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *British Journal of Psychiatry*, 2001; 179: 540-544.
- Neundorfer MM. Coping and Health Outcomes in spouse caregivers of persons with dementia. *Nursing Research* 1991, 40 (5) 260-265
- Nunley BL. (2002) Stress, hardiness, and psychological distress of elderly spousal caregivers of persons with dementia. *Dissertation Abstracts International: Section B: The Sciences & Engineering*, 63(2B)742
- Owen JE, Roth DL, Stevens AB McCarty HJ, Clay OJ, Wadley VG, Goode KT, Haley WE Association of life events and psychological distress in family caregivers of dementia patients *Aging and Mental Health* 2002; 6(1):62-71

- Perkins, DV (1982) The assessment of stress using life event scales. In: L. Goldberger & S Breznitz (eds) *Handbook of stress: theoretical and clinical aspects* p. 321
- Pettit, T., Livingston, G., Manela, M., Kitchen, G., Katona, C., Bowling, A. Validation and normative data of health status measures in older people: the Islington study. *International Journal of Geriatric Psychiatry*, 2001; 16: 1061-1070.
- Pinquart, M. & Soerensen, S. (2003) Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. *Psychology & Aging*, 18(2), 250-267
- Proctor R, Martin C, Hewison J. When a little knowledge is a dangerous thing....A study of carers' knowledge about dementia, preferred coping style and psychological distress. *International Journal of Geriatric Psychiatry*;2002;17(12):1133-1139.
- Radosevich, D., Pruitt, M. Twelve-Item Health Status Questionnaire: HSQ-12 Version 2.0. *Health Outcomes Institute, Bloomington*, 1995.
- Reed BR, Stone AA, Neale JM. Effects of caring for a demented relative on elders' life events and appraisals. *The Gerontologist*: 1990; 30(2):200-205.
- Rennemark M & Hagberg B (1997) Sense of coherence among the elderly in relation to their perceived life history in an Eriksonian perspective. *Aging & Mental Health*;1(3):221-229.
- Robins LN & Regier DA (1991) *Psychiatric disorders in America*. New York: Free Press.
- Russo J, Vitaliano PP, Life Events as Correlates of Burden in Spouse Caregivers of Persons with Alzheimer's Disease *Experimental Aging Research* 1995; 21:273-294
- Saxton J, McGonigle KL, Swihart AA, Boller F. *The Severe Impairment Battery*. Bury St. Edmunds, UK: Thames Valley Test Company, 1993.
- Schmitt, FA.; Ashford, W; Ernesto, C; Saxton, J; Schneider, LS.; Clark, CM.; Ferris, S H.; Mackell, JA.; Schafer, K; Thal, L J.; *Alzheimer Disease and Associated Disorders*. "The Severe Impairment Battery: Concurrent Validity and the Assessment of Longitudinal Change in Alzheimer's Disease." Vol. 11, Suppl. 2, S51-S56. (1997)
- Schoevers RA, Beekman ATF, Deeg DJH, 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 AMSTEL study. *International Journal of Geriatric Psychiatry*, 18:994-1001.
- Siegel, K, Anderman SJ, Schrimshaw EW. Religion and coping with health-related stress. *Psychology & Health*, 2001, vol. 16, no. 6, p. 631-653
- Smari J, Arason E, Hafsteinsson H, Ingimarsson S. (1997) Unemployment, coping and psychological distress. *Scandinavian Journal of Psychology*, 38(2)151-156.
- Vedhara K, Shanks N, Wilcock G, Lightman SL. Correlates and predictors of self-reported psychological and physical morbidity in chronic caregiver stress. *Journal of Health Psychology*;2000;6(1):101-119.
- Waite A, Bebbington P, Skelton-Robinson M, Orrell M. Social factors and depression in carers of people with dementia *International Journal of Geriatric Psychiatry* 2004;19:581-587
- Winslow BW. Effects of formal support on stress outcomes in family caregivers of Alzheimer's patients. *Research in Nursing and Health*, 1997: 20,27-37

Wulschleger KS, Lund DA, Caserta MS, Wright SD. Anxiety about aging: a neglected dimension of caregivers' experiences. *Journal of Gerontological Social Work*: 1996; 26(3/4):3-18.

Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. *Gerontologist*. 1980 Dec;20(6):649-55

Zigmond, A.S. and Snaith, R.P. The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, 1983; 67: 361-370.



Epidemiological Study Protocol

Title: A longitudinal study in patients with memory difficulties

Clinical study ID: Study no **99782**

Phase of development: Phase III

Indication: Alzheimer's disease

Sponsor: International Clinical Research H. Lundbeck A/S Ottiliavej 9
K-2500 Copenhagen-Valby, Denmark Telephone no.: Fax no.:

Study director: Brigitte Roch, H. Lundbeck A/S

Issue date: 08 January 2002

This clinical study protocol is the property of H. Lundbeck A/S and is a confidential document. It is not to be copied or distributed to other parties without prior written authorisation from H. Lundbeck A/S.

Clinical Study Protocol Approval and Authorisation

Study title: **A longitudinal study in patients with memory difficulties**

Epidemiological study ID:
Study no

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Main principal investigator:

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Summary and Assessment Plan

TITLE A longitudinal study in patients with memory difficulties

SUMMARY

OBJECTIVE

The overall objective of the present study is to assess the feasibility of a memantine phase IIIB outcome study that will examine quality-of-life, resource utilisation and caregiver burden as well as clinical domains in patients with Alzheimer's disease.

The secondary objectives are:

1.
Correlating clinical data and Quality-of-life and thereby translating clinical efficacy as traditionally assessed in clinical trials into patient's benefit,
2.
Collecting health economic data and determining which factors influence the costs of illness,
3.
Selecting outcome indicators appropriate for this population
4.
To model possible memantine-associated clinical changes against those occurring in response to disease progression or to current treatments

DESIGN

Epidemiological study of a population of patients with Alzheimer's disease with a follow-up at 6 months

CENTRE ?

Two centres, in the greater London catchment areas

POPULATION ?

Patients with Alzheimer's disease of all severity level

ASSESSMENTS

At baseline and at 6 months: ?

Clinical scales:

MMSE, CIBIC-+, ADAS-cog, SIB, ADCS-ADL, Modified D-test, Rating Scale for Geriatric Patients (BGP), NPI, Cornell scale for depression ?

Quality-of-life scales:

Patient: HSQ-12, QoL-AD Caregiver: HSQ-12 ?

Resource Use:

Patient: CSRI

Caregiver: specific questionnaire

TOTAL DURATION OF THE STUDY

18 months data collection

Executive Summary

Alzheimer's' disease is a neurodegenerative disorder resulting in progressing dementia and death. It is of growing burden for health authorities because of its increasing frequency as the population is ageing .

Specific treatments are currently available. Their efficacy has been assessed on cognition but the problem still remains on its translation into patient's daily life and Quality-of-life. This difficulty partly arises from an inadequate knowledge regarding the validity of the clinical instruments in assessing the patients' and caregivers' daily life and burden and in correlating this with the disease severity and the disease progression.

The present study will be a longitudinal study conducted with Alzheimer's disease patients of all severity levels with a baseline assessment and a second assessment at 6 months.

It will be used to assess the feasibility of a memantine phase IIIB outcomes study.

It will also aim to correlate clinical data and Quality-of-life, thereby translating clinical benefit, as traditionally assessed in clinical trials, into patient's benefit assessment.

It will give information for selecting outcome indicators (clinical instruments, Quality-of-life instruments and resource utilisation) most appropriate for this population.

Finally it will collect health economic data on Alzheimer's disease at all levelsof severity.

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Abbreviations

AChEIs:	Acetyl-choline Esterase Inhibitors
ADAS-cog:	Alzheimer's Disease Assesment Scale, cognitive subscale
ADCS-ADL:	Alzheimer's Disease Co-operative Study - Activities of Daily Living
BGP:	Rating Scale for Geriatric Patients (Beurteilungsskala für Geriatrische Patienten)
CIBIC +:	Clinician Interview-Based Impression of Change with caregiver input
CSRI:	Client Service Receipt Interview
DLB:	Dementia with Lewy Bodies
DSM-IV:	Diagnosis and Statistical Manual; 4 th edition, interim revision
HIS:	Haschinski Ischemic Score
HSQ-12:	12 items health status questionnaire - version 2.0
MMSE:	Mini Mental State Examination
NINCDS-ADRDA:	National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association
NMDA:	N-Methyl-D-Aspartate (a synthetic amino acid with activating properties on a subtype of CNS glutamate receptors)
NPI:	Neuropsychiatric Inventory
NPH:	Normal Pressure Hydrocephalus
QoL-AD:	Quality of Life-Alzheimer's Disease scale
RUD:	Resource Utilisation in Dementia
SIB:	Severe Impairment Battery
SPSS®:	Statistical Package for the Social Sciences

1 Introduction

Alzheimer's disease is a neurodegenerative disorder with a frequency which increases with age. The initial clinical picture is usually of memory loss. As Alzheimer's disease progresses, patients become increasingly impaired in different cognitive functions (orientation, language, reasoning, integration of information...) in such a way that they progressively lose their autonomy. In the later stages most sufferers can no longer be cared for in their own homes and require transfer to specialised institutions. The emergence of behavioural problems increases the likelihood of transfer to such residential care.

Recently approved treatments have considerably changed the drug management of Alzheimer's disease. They have demonstrated their ability to improve cognition in randomised clinical trials. Nevertheless, it remains difficult to evaluate their benefits in term of patients' everyday life. Evaluation is further complicated by the fact that patients have lost the capacity to report reliably on their symptoms and ability to cope with activities of daily living (ADL), or on the effects of drugs on them. Other possible treatments include vitamin E at high doses. Other treatments such as vasodilators, cerebral oxygenators (ginkgo biloba), antidepressants and antipsychotics are being used without being approved in this specific indication.

Alzheimer's disease is a growing concern to health and social care providers because of the increasing number of affected persons, the cost of caring for them and the emergence of specific and effective but costly pharmacological therapies (acetylcholinesterase inhibitors- AChEIs) that may produce increased expenditure.

2 Rationale:

People with Alzheimer's disease and their caregivers may have an impaired quality of life due to the progressive decline of cognitive functions and the associated behavioural disorders. Although many factors are known to be associated with such impairment, it is not easy to rank them in importance in terms of their impact on patients and caregivers' lives. The difficulty arises partly from the lack of validation of the Quality-of-life scales used in Alzheimer's disease, and more particularly from lack of information concerning their sensitivity to changes in ADL skills. It is also difficult to predict what the consequences of a treatment-related improvement in cognition will be, in terms of patients' global functioning, on patients' and caregiver's daily lives and on disease cost. Despite the recent availability of drugs with significant positive effects on cognitive functioning in Alzheimer's disease, no published study to date tackles these issues adequately.

Memantine is a NMDA antagonist already marketed in some European countries for the treatment of cognitive impairment, Parkinson's disease and spasticity. It is currently being evaluated as a potential treatment in Alzheimer's disease. In order to be able to evaluate the pharmaco-economic impact of memantine on the Alzheimer's disease, it is necessary to have information about which aspects of

Alzheimer's disease symptomatology are the most important and how best to measure change in them. It is also important to determine which scale(s) is/are most suitable to reflect the patient's overall situation. The memantine health economic evaluation will be partly based on health-economic trials. For these future studies we will be able to use the knowledge of Alzheimer's disease issued from the data gathered in the study described here and this will help in designing future trials to perform.

Modelling provides some important results in Alzheimer's disease that cannot be obtained by any other way. In order to have the best chance of reaching adequate and reliable conclusions in forthcoming memantine studies, it is necessary to plan these using data that is up to date and relevant.

The proposed study will address some of these issues.

3 Study Objectives and Design

3.1 Study objectives

The overall objective of the present study is to assess the feasibility of a memantine phase IIIB outcome study that will examine quality-of-life, resource utilisation and caregiver burden (time spent, economic burden, physical burden and psychological burden) as well as cognition, behaviour, psychosis, mood and daily living skills of the patient with Alzheimer's disease.

This overall aim will be achieved by specifically targeting the following objectives:

1. Correlating clinical data and Quality-of-life and thereby translating clinical efficacy as traditionally assessed in clinical trials into patient's benefit,
2. Collecting health economic data and determining which factors will influence the costs of illness,
3. Selecting outcome indicators appropriate for this population:
 - (a) Identifying clinically meaningful discriminative determinant(s) of Quality-of-life in patients with Alzheimer's disease
 - (b) Assessing the suitability and sensitivity to change of some Quality-of-life instruments
 - (c) Examining correlations between clinical instruments, Quality-of-life instruments and resource utilisation

The study will also allow us to model likely recruitment rate to future memantine studies, to calculate optimal study duration, to assess the likely impact of inclusion/exclusion criteria on such recruitment, and to model possible memantine-associated clinical changes against those occurring in response to disease progression or to current treatments.

3.2 Study design

The study design is an epidemiological study with a 6-months following of a cohort of patients with Alzheimer's disease.

Patients will be selected to be representative of the community in terms of gender, severity and living settings. There will be stratification on severity of dementia in order to balance the sample for mild, moderate and severe patients, gender and living status (see § 4.1). Participants will be known to the clinical teams (Essex and Camden and Islington) or will be volunteers (through the local Alzheimer's Society).

There will be a first assessment (baseline) with data collection on the disease, the patient's and caregiver's status, quality-of-life and resource use.

A second assessment at 6 months is planned.

3.3 Rationale for design

The current design allows collection of clinical data at a given point of time in a given population. This is appropriate for the overall objective and for assessing the relationships between scales, determining the best Quality-of-life instrument, and the ability to discriminate between clinical populations. The study will also allow to generate a database that can be used for various purposes (disease modelling, memantine modelling, Alzheimer's disease economic evaluation...).

Having a second assessment 6 months later is necessary to obtain data for:

- the sensitivity to changes of the Quality-of-life scales and other rating instruments
- mapping of the determinant(s) of outcomes and resource utilisation
- modelling of cost effectiveness of memantine based on the natural history of Alzheimer's disease progression.

Study Population

4.1 Population description:

Patients will have dementia (DSM-IV; American Psychiatric Association, 1994) due to Alzheimer's disease (NINCDS-ADRDA) whatever the age of onset of Alzheimer's disease and the treatment status. There is no upper limit for Mini Mental Status Examination (MMSE). The investigator will judge the clinical significance of each individual MMSE in his own clinical opinion, in order to adapt MMSE scores to age and socio-educational level.

Patient's repartition will be balanced regarding the disease severity on MMSE score. Patient will be considered mild when $MMSE > 20$, moderate when $MMSE \leq 20$ and

10, and severe when MMSE < 10. 20% of the included patients will be mild, 45% moderate and 35% will be severe, in order to roughly reflect the Alzheimer's disease population (for review see Fratiglioni, 1998). In addition 60-70% of the included patients will be female. This gender proportion will have to be applied for the three groups of severity level. On the other hand, patients will be balanced regarding their living settings: 65% will have to be community-based and 35% institutionalised. The stratification on living status will be independent of severity and gender, i.e. this proportion of 65%/35% will not be applied to the three groups of severity. This is because people who are severely demented are more likely to live in institutions.

Caregivers are defined by the mean time per week they spend (minimum of 4 hours/week contact) in close contact with the patient (see section 4.2). There is no condition on the nature of the relation they have with the patient (spouse/husband, relatives, neighbours...). One person only be considered the caregiver and this person will be the same throughout the whole study.

4.2 Inclusion criteria

- Age more than or equal to 50 years old at inclusion
- Diagnosis of dementia according to DSM-IV revised interim version
- Diagnosis of probable and possible Alzheimer's disease according to NINCDS-ADRDA criteria
- MMSE score that, in the opinion of the investigator, is below the normal value expected for the age and the socio-educational status,
- Patient has to have a knowledgeable, co-operative and reliable caregiver/informant,
- Caregiver/informant has to spend at least 4 hours a week with the patient to be able to observe the patients ability to cope with the Alzheimer's disease
- Signed Consent of the patient
- Signed Consent of the caregiver
- Stable living conditions.

4.3 Exclusion criteria

- Vascular dementia, as defined by Haschinski Ischemic Score (HIS) criteria (Rosen *et al*, 1980)
- Other significant neurological disease (e.g. Dementia with Lewy body [DLB], Parkinson's disease, Huntington's disease, Normal Pressure Hydrocephalus [NPH], sequelae of brain surgery, brain trauma...)
- History of other severe and enduring mental illness
- Endocrine or metabolic disorders possibly causing dementia (e.g. hypothyroidism, B₁₂ deficiency...)
- Psychotic episodes requiring hospitalisation or neuroleptic treatment for more than 2 weeks during the last 10 years not associated with Alzheimer's disease

- Alcohol/drug abuse according to DSM-IV revised interim version during the last 10 years
- Patient unable to comply with the study assessment, either due to another disease or inability to understand the national language that would interfere with, or prevent the participation/conductance of the tests.

5 Assessments

5.1 Study plan

	1 st assessment	2 nd assessment
Consent Forms (Patient and Carer)	X	
Inclusion / Exclusion Criteria	X	
Social History and Demographics	X	
Medical History	X	
Interview and Relevant Physical Examination	X	X
MMSE	X	X
CIBIC+	X	X
ADAS-Cog	X	X
SIB	X	X
ADCS-ADL inventory	X	X
BGP	X	X
Modified D-test	X	X
NPI	X	X
Cornell Scale for Depression	X	X
Patient Quality-of-life: HSQ-12	X	X
Patient Quality-of-life: QoL-AD	X	X
CSRI amended	X	X
Concomitant Medication	X	X
Caregiver questionnaire	X	X
Caregiver Quality-of-life: HSQ-12	X	X

5.2

5.3 Sociodemographics:

Data on demographics and socioeducational status of the patient will be collected at baseline. Demographics will also be collected at baseline for the caregiver.

5.4 Medical examination and history:

A relevant medical examination (interview and physical exam) and history at inclusion will allow the investigator to insure that the patient fulfils the inclusion

criteria and does not match the exclusion criteria. Patients who have already had a biochemical dementia screen to determine the diagnosis will not require another.

At the 6-month follow-up the patient and the caregiver will be interviewed about the patient's medical conditions. A specific medical examination will be carried out if the interview reveals any significant change since the last visit. This will ensure that any change in the medical status of the patient that could significantly interfere with the Alzheimer's disease assessment has been noted.

5.5 Clinical scales:

All the four main clinical domains of Alzheimer's disease will be assessed.

The global domain will be assessed by the CIBIC-+ (the CIBIC-Plus Interview Guide®, NYU, 1994).

Cognition will be assessed by the ADAS-cog (Mohs *et al*, 1983 and 1988) and the SIB. The SIB has been added to the ADAS-cog in order to evaluate in a more appropriate way the severe patients (Saxton *et al*, 1993; Schmitt *et al*, 1997). All the patients will have to fill both cognitive scales, whatever their severity rating. It will allow us to preserve the possibility to compare the two periods even for patients that would move from moderate to severe throughout the 6 months follow-up.

The functional domain will be assessed by the ADCS-ADL inventory (Galasko D. *et al.*, 1997), the modified D-test and the rating of geriatric patient BGP scale. The ADCS-ADL inventory is a 42-items scale corresponding to the Modified Alzheimer's Disease Co-operative Study - Activities of Daily Living. This questionnaire has to be filled by an experienced physician, nurse or psychologist via an informant interview.

The behavioural dimension will be assessed by the NPI (Cummings *et al.*, 1994).

In addition mood will also be evaluated with the Cornell Scale for Depression.

The condition of use for all the scales, inventories mentioned above will be provided in the specific guidelines added to the CRF.

All the assessments will be repeated at 6 months with all the same scales, except the sociodemographics of both the patient and the caregiver.

5.6 Quality-of-life scales

Patients will be assessed through two distinct Quality-of-life scales: a generic scale and a specific scale. The scales suitable for mild-moderate patients that have been selected are HSQ-12 (Radosevitch *et al*, 1996) and the QoL-AD (Logsdon *et al.*, 1999). The HSQ-12 is a generic scale derived from the SF-36, adapted to older

subjects (Bowling and Windsor, 1997). It has been shown to be suitable for monitoring Quality-of-life in patients with dementia too (Pettit *et al.*, 2001). Using a generic scale in Alzheimer's disease is recommended by the International Working Group for Harmonization of Dementia Drug Guidelines (The 1st International Quality Research in Dementia Conference, 2000). It is also recommended to associate a specific scale to the generic scale when possible even if no scale has been found to be a gold standard in Alzheimer's disease. The QoL-AD scale has been specially designed for patient with Alzheimer's disease (Selai C *et al.*, 2001). All the patients will have to carry out both Quality-of-life scales.

Caregivers will fill in the HSQ-12 Quality-of-life scale too.

The complete Quality-of-life assessment will be repeated at 6 months for both the patient and the caregiver. In case the caregiver and the patient could not come for the 6 months-follow-up visit, an assessment could be performed by a phone call.

The conditions of administration for the two Quality-of-life scales will be provided in the specific guidelines added to the CRF.

5.7 Economic assessment

The socio-economic status of the patient will be assessed at baseline by the English CSRI questionnaire specially amended for older people. The CSRI collects general data (sociodemographics, educational level, on his/her living status, marital status...) on the patient as well as data on medical services consumption, non-medical services, treatments, hospitalisations and their causes ... The same questionnaire but without the sociodemographic part will be filled in at the 6months-follow-up visits too.

Caregiver's resource use consumption is not included in the CSRI. Therefore a socio-economic evaluation of the caregiver has been added through a specific questionnaire. It will focus on the description of the caregiver, the time spent giving care and his/her work status. It will be carried out at baseline. A follow-up questionnaire administered at the 6 months-follow-up visit will allow monitoring any change in these domains.

6 Treatment

There is no study treatment. All treatments are allowed since we cannot interfere with naturalistic management during the follow-up period though any change will be recorded.

7 Statistics

7.1 Sample Size Rationale

A sample size of 220 patients has been calculated based on the known psychometric properties of the HSQ-12 to be able to show a 10% difference (Ware *et al*, 1993) between the three groups of severity level as defined by MMSE score (see section 4.1).

The patient numbers per group will be as follow: 44 patients with mild Alzheimer's disease, 99 patients with moderately severe Alzheimer's disease and 77 patients with severe Alzheimer's disease.

7.2 Statistical Analysis

The statistical software used will be SAS version 6.12 or a more recent version.

Two distinct and independent analyses will be performed:

- at the first assessment, where resources use will be collected retrospectively
- at final assessment for patients who will have comply with the assessment at 6 months. A comparison between both periods will be done and correlated to resource use collected retrospectively.

Interim analysis will be conducted on the first assessment period for the first 100-150 patients.

A descriptive analysis will be done separately for the different populations of AD patients regarding severity. A comparison will be done for all variables between mild, moderate and severe AD. Summary statistics (mean, standard deviation, median, and range) will be presented for continuous variables, counts and percentages will be presented for categorical variables. Comparisons will be made for continuous variables using parametric or non-parametric tests, as appropriate. Qualitative variable will be compared using χ^2 -test or Fisher's exact test.

The data quality will be evaluated through completeness and psychometric evaluation.

Completeness: The completeness of responses to HSQ-12 and QoL-AD will be evaluated in term of:

- % of response completed
- whether or not scale scores could be computed for those with missing data using standardised scoring algorithm

Psychometric evaluation:

All patients, including those who completed only a baseline assessment will be included in this evaluation.

- Item internal consistency: check that items in the same scale are substantially related to the scale score based on other items in that scale
- Item discriminant validity: check that item correlates significantly higher with its scale than competing scale

- Internal consistency: Cronbach's alpha
- Ceiling and floor effect will be evaluated

A plot of the QoL scales output in each other scale will be performed in order to try to extrapolate the expected outcome in using that scale in a sample of memantine treated patients. The relationship between the QoL scales and the other scales will be explored through analysis of variance.

Unless otherwise explicitly stated, all statistical tests will be two-sided and will be carried out at the 5% level of significance for main effects and 10% level of significance for interaction terms.

An analysis plan describing the data sort-out and the planned statistical analyses in more detail will be prepared by the Pharmaco-economics and Epidemiology Department, H. Lundbeck A/S.

7.3 Data Inspection

N/A.

8 Proposed study site

Patients will be recruited from clinical catchment areas in Camden and Islington, W. Essex.

9 Study duration

The expected start date for inclusion is March 2002.

Patients should have completed baseline evaluations within 12 months. The naturalistic 6 months follow up study would require a further 6 months. The clinical part of the study, i.e. 220 observations with the two evaluations, should thus be completed in 18 months.

A first interim analysis is planned after the first 6 months period. It will analyse the baseline assessment for the included patients. A second interim analysis will be performed at 12 months with the total baseline assessments and a part of the follow-up assessments. At last, the final analysis will take place at 18 months.

10 Adverse Events

N/A.

11 Study Closure Considerations

H. Lundbeck A/S reserves the right to terminate the study and/or the study site at any time. The reasons for such action include but are not limited to:

- the required number of patients for the study have been recruited
- the investigator does not comply with the protocol, GCP Guidelines, and/or any contract entered into between the investigator and H. Lundbeck A/S, including affiliates and subsidiaries hereof
- Inadequate recruitment by the investigator.

12 Study Materials

12.1 Study Documents

The following essential documents must be completed before the study can start and will be enclosed in the Trial Master File:

- 1) A protocol, protocol amendment, if appropriate, signature page and/or declaration signed by the Investigator.
- 2) Signed agreements:
 - Secrecy (if not included in Contract)
 - Financial (if not included in Contract)
 - Contract
- 3) A copy of the signed approval favourable opinion from the Ethics Committee, clearly identifying the study by title and number and submission letter.
- 4) The names of members of the independent Ethics Committee, if permitted, and their professional position in the institution or other credentials.
- 5) An approval from or notification to the national health authorities, as appropriate.
- 6) A sample of the Patient Information Sheet and Consent Form approved by the Ethics Committee or Institutional Review Board.
- 7) A copy of the CVs of investigators and authorised persons with signature log will be filed in the sponsor and investigator TMF.

It is the Investigator's responsibility to file amendments and updates for the above documents and any other documents that are essential before, during and after completion of the study, in the Investigator's TMF.

12.2 Case Report Forms

Case Report Forms (CRFs) will be provided in an electronic form for each patient/carer and all data relating to the study will be recorded on these CRFs. The CRFs have to be completed by the investigator or researcher at the time of the patient's visit so that they always reflect the latest observations on the patient participating in the study. In some cases the forms will be filled in on paper in the first instance for subsequent transcribing onto electronic forms.

A copy of the CRF is provided in APPENDIX 7.

Every effort should be made to ensure that the subsequent interviews and ratings are completed by the same person who performed the baseline visit.

The investigator must verify that all data entries in the CRFs are accurate and correct. If certain information is not available, not applicable or unknown, the investigator (or the authorised person in the staff) will enter "N.A", "N.App." or "U" respectively, in the appropriate space.

The monitor will review the CRFs and evaluate them for completeness. He/she will inform the investigator or the authorised persons in the staff for correction. All entries, corrections and alterations are to be made by the responsible Investigator or his/her designee.

12.3 Patient Identification Code

In order to identify the patients during and after the study, the investigator is responsible for keeping a list of patient identification codes.

12.4 Archiving

12.4.1 Investigator Trial Master File

The investigator shall arrange for the retention of the Patient Identification Code and other essential documents in the Investigator File for at least 15 years after the final study report has been signed (see APPENDIX 6). However, documents belonging to the hospital shall be kept for the maximum period of time permitted by the hospital, institution or private practice.

Under no circumstances will the investigator dispose of any study documents before having obtained H. Lundbeck A/S's consent.

If it becomes necessary for H. Lundbeck A/S or the appropriate Regulatory Authority to review any documentation relating to this study, the investigator must permit access to such documents.

Any difficulty in storing original documents should be discussed with the relevant person in Lundbeck prior to the initiation of the study.

12.4.2 Sponsor Trial Master File

All essential documents as defined in generated before, during and after completion of the study will be archived at the Regulatory Central Archive at H. Lundbeck A/S.

13 Ethical Considerations

13.1 Declaration of Helsinki

The study will be conducted in accordance with the Declaration of Helsinki as adopted by the 18th World Medical Assembly 1964 and subsequent amendments: Tokyo (1975), Venice (1983), Hong Kong (1989) and Somerset West, South Africa (1996).

Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

This study will be undertaken only after full approval of the protocol has been obtained from the appropriate IEC and a copy of the approval has been received by H. Lundbeck A/S.

The IEC must be informed of all subsequent protocol amendments and should be asked for its opinion if a re-evaluation of the ethical aspects of the study is necessary.

If applicable, interim reports and/or reviews of the study and its progress will be submitted to the IEC by the investigator at intervals stipulated in their guidelines.

13.2 Consent Form

It is the responsibility of the investigator to consent from the participants. The patient is not to participate in any study-specific procedures before patient's and carer's consents has been obtained (see APPENDIX 1).

Prior to obtaining the Consent Form, the investigator or nurse will explain to potential participants and caregivers the aims, methods, and potential hazards of the study and any discomfort it may entail. In the particular case of Alzheimer's disease, patient may not be able to read the documents, to understand the meaning of the study, of participating to and giving a written consent. If the patient can not give informed consent they will be asked for assent and their caregiver will also be asked for consent. The study itself does not include anything that is potentially hazardous to the participant. If the participant is unco-operative or appears distressed by the study then the investigator will terminate the interview. The recent guidelines issued in April 2001 from the dept of Health regarding consent for research from people with dementia made it clear that people should not be excluded because they were unable to give fully informed consent.

The caregiver should be present during the Consent Form discussion, and will have to co-sign and date the consent form.

If the participant is currently known to any member of the community mental health team then they should be approached through them. If living in a home they should be approached through a carer in the home.

For details of the information provided, please refer to the Patient Information Sheet and Consent Form, which are in APPENDIX 1.

14 Indemnity and Insurance

In the event of study related injury or death, during the present study, insurance of patients, and indemnity of investigators and those of their employees, servants or agents, who have been documented to take part in this study are provided. Insurance and liability will be in accordance with applicable law and ICH Topic E6 Guideline for Good Clinical Practice, January 1997.

15 Regulatory Approval or Notification

This study requires submission of protocol and protocol amendments to the Regulatory Authority for approval or alternatively the Regulatory Authority will receive a notification, in accordance with local requirements.

The study will be conducted in compliance with applicable regulatory requirements. Furthermore, the participation of patients in this study should be notified to the appropriate local data protection agencies, in accordance with EU Directive 95/46/EC and country specific guidelines/laws.

16 Financial Agreement

Before the study is initiated an Investigator Agreement between the investigator or his/her delegate (the UCL Office of Sponsored and Collaboration Research) and H. Lundbeck A/S must be signed.

17 Monitoring

Data monitoring will be done by an electronic instantaneous data management and by a study monitor. The Investigator will make the Case Report Forms available, provide missing or corrected data and validate the Case Report Forms.

Study Monitor will ensure that:

- there are no missing data in the CRF;
- information mentioned in the CRF are coherent.

The above-mentioned procedure does not, by definition, compromise patient confidentiality. Any queries to the data will be resolved electronically.

18 Inspection of the Study

N/A.

19 Reporting and Publication

19.1 Reporting

At the completion of the study, an integrated pharmaco-economic study report will be prepared by the Pharmaco-Economics & Epidemiology Department of H. Lundbeck A/S to the current Pharmaco-economics Guidelines from the ISPOR (International Society for Pharmaco-economics and Outcome Research) (Gagnon *et al*, 1999) and the Guidelines for Economic Evaluation of Pharmaceuticals from the Coordinating Officer for Economic Evaluation of Pharmaceuticals (CCOHTA, 1997).

19.2 Data Ownership

The data generated in this study are the property of H. Lundbeck A/S.

19.3 Publication

The main publication has to be published before any sub-publications. Order of authors has to be established.

Publication of the results by the investigator will be subject to mutual agreement between the investigator and H. Lundbeck A/S. Manuscripts and abstracts must be sent to H. Lundbeck A/S at least one month prior to submission for publication or presentation.

References

The 1st International Quality Research in Dementia Conference was held at the Queen Elizabeth 11 Conference centre on November 19-21st 2000
http://dementia.ion.ucl.ac.uk/harmon/qol_links.html

American Psychiatric Association,: Diagnostic and Statistical Manual of Mental Disorders. APA, Washington DC. 1994.

Bowling A and Windsor J: Discriminative power of the health status questionnaire 12 in relation to age, sex, and longstanding illness: findings from a survey of households in Great Britain. *J Epidemiol Community Health*, 1997. **51**: 564-573

CCOHTA (Canadian Coordinating Office for Health Technology Assessment), Guidelines for Economic Evaluation of Pharmaceuticals. Methods and Guidelines, 1997. Available from: URL: <http://www.ccohta.ca/newweb/pubapp/pubs.asp>,.

Cummings JL et al: The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology*. 1994. **44**:2308-14.

Fratiglioni L: Epidemiology of Alzheimer's disease, in *Health Economics of Dementia*, Ed A. Wimo, B. Jönsson, G. Karlsson and B. Windblad, John Wiley & Sons Ltd, 1998. pp 13-31

Ferm L et al,: Behavioural activities in demented geriatric patients, *Gerontol Clin*, 1974. **16**: 185-194.

Galasko D. et al: Alzheimer's Dis Asso Disord, 1997. **11S2**: S33-S39

Gagnon JP, Dix Smith M, Rindress D, Healey M, Deverka P, Hay J et al. Pharmacoeconomics: Identifying the issues. Proceedings of the Advisory Panel Meeting and Conference on Pharmacoeconomics Issues. Third Annual International Meeting of the International Society for Pharmaco-economics and Outcome Research (ISPOR) 1998 May 27-30; Philadelphia, USA; *Value in Health* 1999; **2**: 67.

Logsdon RG, Gibbons LE, M.S, McCurry SM and Teri L: Quality of Life in Alzheimer's Disease: Patient and Caregiver Reports. *J Mental Health Aging*, 1999. **5**: 21-32

Mohs RC et al: The Alzheimer's disease assessment scale: an instrument for assessing treatment efficacy, *Psychopharmacol Bull*, 1983. **19**: 448-450.

Mohs RC et al: Alzheimer's Disease Assessment Scale (ADAS), *Psychopharmacol Bull*, 1988. **24**: 627-628

Pettit T, Livingston G, Manela M, Kitchen G, Katona C, Bowling A,: Validation and Normative data of Health Status Measures in older people: The Islington Study.

Submitted **Rosen W.G. et al**, 1908: Pathological verification of ischemic score in differentiation of dementias, *Ann Neurol*, 2001. **7**:486-8.

Radosevitch DM, Pruitt M. Twelve-Item Health Status Questionnaire (HSQ-12) Cooperative Validation Project: Comparability Study. Abstracts from the Academy of Health Services Research Annual Meeting; 1996 June 9-11; Atlanta, USA. Available from: URL <http://www.academyhealth.org/abstracts/1996/index.htm>

Saxton J et al: the University of Pittsburgh, o.t.C.S.o.H.E., editor, The Severe Impairment Battery. 1. Suffolk-England: Thames Valley Test Company. 1st edition: 1993. p1-16.

Schmitt FA et al: The severe impairment battery: concurrent validity and the assessment of longitudinal change in Alzheimer's disease. The Alzheimer's Disease Cooperative Study. *Alzheimer Dis Asso Disord*, 1997. **11S2**: S51-S56.

Selai C, Vaughan A, Harvey RJ, Logsdon R.,: Using the QOL-AD in the UK. *Int, J Geriatr Psychiatry*, 2001. **16**:537-538

Ware JE, Snow KK, Kosinski MA and Gandek B: Reliability, Precision, and Data Quality. In: SF-36® Health Survey: Manual and Interpretation Guide, Lincoln, RI: Qualimetric Incorporated, 1993, 2000. p7:1-7:16



**North Central London
Community Research Consortium**

Dr Gill Livingston
A13 Charterhouse Building
Archway Campus
Highgate Hill
London
N19 5NF

8 April 2002
Dr Paul Fox
Assistant Director
Research and Development Unit
3rd Floor, West Wing
St Pancras Hospital
London
NW1 0PE

Phone:
Fax: 0207 530 3235
E-mail: Paul.fox@cichs-tr.nthames.nhs.uk

Dear Dr Livingston

LREC Ref: 1
Title: A Longitudinal Study in People with Memory Difficulties

I am pleased to note that the Local Research Ethics Committee has recommended to the Trust that there are no ethical reasons why your study should not proceed.

Projects are registered with the North London Community Research Consortium if they utilise patients, staff, records, facilities or other resources of Camden Primary Care Trust, Islington Primary Care Trust or the Camden & Islington Mental Health and Social Care Trust. On the basis of the documentation supplied to us, your study has the support of the clinical service manager/assistant locality director of the service in which it will be based.

The Trust notes that funding for this project is still pending. Please note that once a finalised funding contract has been received from Lundbeck a copy should be forwarded to the R&D Unit for their records. This requirement is also set out in the Research Governance Framework of Health and Social Care to ensure that funding bodies agree to have accountability for funding and awards for research studies.

The Mental Health and Social Care Trust therefore grants permission to undertake the research, as stated in the study protocol. This permission is only valid concurrently with the appropriate ethical consideration for this study. This approval is therefore subject to the conditions set out by Camden and Islington Community LREC in their letter of 13 February 2002. Should you fail to adhere to these conditions, then the Trust would consider your approval to undertake research to be invalid.

As part of the implementation of the Department of Health Research Governance Framework for Health and Social Care I am required to bring to your attention your responsibilities under the framework. Appendix A to this letter outlines responsibilities for principal investigators; appendix B for local investigators and other researchers. Principal investigators should bring the responsibilities outlined in appendix B to all those in their research teams.

All research conducted within the Trust which comes under the provisions of the Safety at Work Act 1974. These are also contained in Appendix B to this letter.

The North Central London Community Research Consortium is a partnership between Camden Primary Care Trust, Islington Primary Care Trust, Camden & Islington Mental Health and Social Care Trust and the North Central Thames Primary Care Research Network (NoCTeN).

Further information on the research governance framework for health and social care can be found on the DH web pages at <http://www.nhsetrent.gov.uk/trentrd/resgov/govhome.htm>. Staff working within trusts covered by the research consortium can also find the information on the Trust Intranet.

This approval is subject to your consent for information to be extracted from your project registration form for inclusion in NHS project registration/management databases and, where appropriate, the National Research Register and the UCL Clinical Research Network register.

Except in the case of commercially funded research projects, the following acknowledgement and disclaimer **MUST** appear on all publications arising from your work.

"This work was undertaken with the support of Mental Health and Social Care Trust, who received [insert "funding" or a "proportion of funding"] from the NHS Executive; the views expressed in this publication are those of the authors and not necessarily those of the NHS Executive".

* "a proportion of funding" where the research is also supported by an external funding body;

* "funding" where no external funding has been obtained

This is a requirement of the contract between the Trust and the Consortium in which the Trust receives funding to cover the infrastructure costs associated with performing non-commercial research.

Please make all members of the research team aware of the contents of this approval. I wish you every success with your research.

Yours sincerely,

Dr Paul Fox
Assistant Director of Research and Development

Camden and Islington Community Health Service LOCAL RESEARCH ETHICS COMMITTEE

Research & Development Unit, 3rd Floor, West Wing, St. Pancras Conference Centre

St Pancras Hospital, London NW1 0PE

tel: 020 7530 3376 fax: 020 7530 3236

e-mail: ayse.ali@clcha-tr.nthames.nhs.uk

Chair: Stephanie Ellis Administrator: Ayse Ali

13 February 2002

Dr Gill Livingston
A13 Charterhouse Building
Archway Campus
Highgate Hill
London
N19 5NF

Dear Dr Livingston

LREC Ref: [redacted]

Title: A Longitudinal Study in People with Memory Difficulties

Thank you for your letter dated 4 March 2002 addressing the concerns raised by the committee. I am pleased to inform you that after careful consideration the Local Research Ethics Committee has no ethical objections to your project proceeding. This opinion has also been communicated to the Research and Development Unit of Camden & Islington Mental Health NHS Trust.

PLEASE NOTE THAT THIS OPINION ALONE DOES NOT ENTITLE YOU TO BEGIN RESEARCH.

Camden and Islington Community Health Service LREC considers the ethics of proposed research projects and provides advice to NHS bodies under the auspices of which the research is intended to take place. It is that NHS body which has the responsibility to decide whether or not the project should go ahead, taking into account the ethical advice of the LREC¹. Where these procedures take place on NHS premises or using NHS patients, the researcher must obtain the agreement of local NHS management, who will need to be assured that the researcher holds an appropriate NHS contract, and that indemnity issues have been adequately addressed.

N.B. Camden and Islington Community Health Service LREC is an independent body providing advice to the North Central London Community Research Consortium. A favourable opinion from the LREC and approval from the Trust to commence research on Trust premises or patients are **NOT** one and the same. Trust approval is notified through the Research & Development Unit.

The following conditions apply to this project:

- You must write and inform the Committee of the start date of your project. The Committee (via the Local Research Ethics Committee Administrator or the Chair at the above address) must also receive notification:
 - a) when the study commences
 - b) when the study is complete;
 - c) if it fails to start or is abandoned;
 - d) if the investigator's change and
 - e) if any amendments to the study are made.
- The Committee must receive immediate notification of any adverse or unforeseen circumstances arising out of the project.

¹ Governance Arrangements for NHS Research Ethics Committees, July 2001 (known as G. LREC)

- It is the responsibility of the investigators to ensure that all associated staff, including nursing staff, are informed of research projects and are told that they have the approval of the Ethics Committee and management approval from the body hosting the research.
- The Committee will require a copy of the report on completion of the project and may request details of the progress of the research project periodically (i.e. annually for longer projects).
- If data is to be stored on a computer in such a way as to make it possible to identify individuals, then the project must be registered under the Data Protection Act 1998. Please consult your department data protection officer for advice.
- Failure to adhere to these conditions set out above will result in the invalidation of this letter of no objection.

Please forward any additional information/amendments regarding your study to the Local Research Ethics Committee Administrator or the Chair at the above address.

Yours sincerely

Stephanie Ellis
Chair, LREC

**OPERATING THROUGH THE
WEST ESSEX LOCAL RESEARCH
ETHICS COMMITTEE**

Westgate House, c/o The Princess Alexandra Hospital NHS Trust
Hamstel Road, Harlow, Essex CM20 1QX
Tel: 01279 641884 Answerphone/Fax:
Internal: (69)4917

North Essex NHS
Health Authority



10th April 2002

Professor C Katona
Professor Psychiatry of the Elderly
UCL and Hon Consultant Psychiatrist
Haymeads Day Hospital
Herts & Essex Hospital
Bishops Stortford

Dear Professor Katona

A LONGITUDINAL STUDY IN PATIENTS WITH MEMORY DIFFICULTIES

The Research Ethics Committee considered your project at its meeting on 14th March 2002, and requested certain additional information and amendments to your submission and protocol.

Following consideration of the additional information provided in your undated letter, received here on 2nd April, by the Chairman under delegated powers, he has given ethical approval for your project to proceed.

The following documents were considered by the Committee and/or Chairman:

- ☐ Protocol dated 8th January 2002
- ☐ LREC Application Form dated 29th January 2002
- ☐ Indemnity Certificate
- ☐ Patient information Sheet version 1 dated 10 December 2001
- ☐ Patient Consent Form undated
- ☐ GP Information Sheet version 1 dated 10th December 2001
- ☐ Carer Information Sheet version 1 dated 10th December 2001
- ☐ Caregiver Consent Form undated
- ☐ CV for Professor Katona and Gillian Livingston
- ☐ Professor Katona's undated letter received here on 11th March 2002
- ☐ Professor Katona's undated letter received here on 2nd April 2002.

The Committee specifically confirms that it would expect you to approach both Dr Walker and any other local old age psychiatry consultants necessary in identifying and making the initial approach to suitable patients under their care.

Chairman: Alex Sexton
Chief Executive: Nigel Beverley

PL7274

Whilst giving approval to this project, the Committee is still interested in exactly how the sum of nearly £369,000 is being utilised in this piece of research. They felt that this is important in view of your statement that the refurbishment of the room at St Margaret's hospital appears to have been undertaken from the existing UCL research trust funds. Perhaps you could give us, in due course, further detail and clarification of the proposed budget for this research project.

Whilst this letter gives approval to the ethical aspects of your application, it is the researcher's responsibility to ensure that all other approvals necessary or required are received prior to commencing work on the research.

It is the researcher's responsibility to ensure that the research is carried out in strict accordance with the protocol submitted and that no changes to the protocol are undertaken without the prior approval of this Committee (other than matters of urgency for the safety of the participants).

Should any serious unexpected events occur in connection with your research, these should be reported immediately to the Committee, together with your recommendations as to any changes to the protocol or other action that might be necessary. These reports should be received within 7 days of the incident concerned.

The Committee retains the right to inspect or review your project at any time during the currency of the research.

You should submit a progress report not less than annually (where appropriate). A brief report or Abstract on the final results of the research should be submitted within 3 months of its completion.

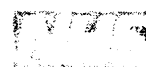
It is confirmed that this Committee operates under ICH-GCP guidelines and in accordance with the Declaration of Helsinki 2000. A list of members in attendance at the meeting in March when your project was considered is attached.

May I wish you every success with your research.

Yours sincerely

Liz Wrighton
Administrator

North Central London Strategic Health Authority



Victory House
170 Tottenham Court Road
London W1T 7HA
Tel: 020 7756 2500
Fax: 020 7756 2510

Chair Marcia Saunders
Chief Executive Christine Outram

29th November 2002

Ginnette Kitchen
Team Manager & Research Nurse
Department of Psychiatry and Behavioural Sciences
Holborn Union Building, Archway Campus
Whittington Hospital, Highgate Hill
London N19 5LW

Dear Ms Kitchen

**147/02 –
Difficulties**

A Longitudinal Study in Patients with Memory

Acting under delegated authority I write to inform you that the Barnet, Enfield & Haringey LREC sub group considered in full the locality issues relating to the above application at the meeting held on 12th November 2002. The issues reviewed were as follows:

- The suitability of the local researcher
- The appropriateness of the local research environment and facilities
- Any specific issues that may relate to this local community

The LREC members on behalf of the LREC consider the locality issues have been adequately addressed and the proposed research can be conducted within the boundary of this Health Authority on the understanding that you will follow the conditions set out below:

- You do not undertake this research in an NHS organisation until the relevant NHS management approval has been granted as set out in the framework for Research Governance in Health and Social Care.
- You do not deviate from, or make changes to, the protocol without prior written approval of the lead LREC (C&I) and notifying this LREC of this approval, except where this is necessary to eliminate immediate hazards to research participants, or when the change involves only logistical or administrative aspects of the research.
- You notify this LREC when you have completed your research, or if you decide to terminate it prematurely.

- You advise your sponsor of any unusual or unexpected results that raise questions about the safety of patients taking part in the research.

It was noted that the patient Information sheet has two addresses at the top and it was suggested that you remove one to avoid confusion.

Please quote LREC number 147/02 on any future correspondence.

Yours sincerely

Christine Hamilton
Barnet, Enfield & Haringey, LREC Co-ordinator

**Royal Free & University College Medical School
UNIVERSITY COLLEGE LONDON**

DEPARTMENT OF MENTAL HEALTH SCIENCES



Juanita Hoe, Research Nurse
Royal Free & University College London Medical School
UCL – Department of Mental Health Sciences
Holborn Union Building - Archway Campus
Highgate Hill, London N19 5LW

Direct Line:

Insert Date

PATIENT INFORMATION SHEET

Dear Insert Name

You have been invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information.

Dr Gill Livingston and Professor Katona run this project from the Whittington hospital.

This study aims to describe the characteristics and difficulties of people with memory problems and how these change over six months. This is in order to know which aspects matter most in people's lives. This information may also help in designing and developing new medicines for these problems.

We are asking for you to participate in this study because we understand that you may have memory problems. If you agree to participate in the study we intend to see you and make a full assessment to see if we think that you might have a medical diagnosis. We are particularly interested in studying people who may have Alzheimer's Disease. This will involve asking you questions about yourself and your symptoms, examining you and taking blood tests if these have not been done already. We would also want to see you again after six months to ask some of the same questions again.

The interviews will be about:

- Personal details (age, education, etc.)
- Memory, feeling, thinking and any difficulties in looking after yourself
- Quality-of-life
- Use of services

The study does not involve any new treatments or affect your current or future treatment.

The time taken for this study will vary but we estimate that the first interview is likely to take about an hour and the second interview about one hour. If you find this tiring the person seeing you can stop and come back again. We will come and visit you at home.

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

The results of this study are expected to be published in relevant conferences and publications. All interviews are confidential and your name will not be disclosed to anyone else. The information collected in the study will be anonymised but may be seen by Lundbeck Pharmaceuticals, the funders of the study. You will not be identified in any report/publication.

All proposals for research using human subjects are reviewed by an Ethics Committee before they can proceed. This proposal was reviewed by Camden and Islington NHS Research Ethics Committee.

Thank you for reading this letter. Please contact a member of the research team at the above address or number if you would like further information.

Yours Sincerely

Juanita Hoe
Clinical Research Nurse

Study Number: _____

CRF No. _____

Centre No. _____

Patient Identification Number for this trial: _____

PATIENT CONSENT FORM

Title: A longitudinal study in people with memory difficulties

Name of Researcher: _____

Please initial box

1. I confirm that I have read and understand the information sheet dated..... for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I agree to take part in the above study

Name of Patient :

Date

Signature

Name of caregiver

Date

Signature

Name of Person taking
consent (if different from
researcher)

Date

Signature

Researcher

Date

Signature

**Royal Free & University College Medical School
UNIVERSITY COLLEGE LONDON**

DEPARTMENT OF MENTAL HEALTH SCIENCES



Juanita Hoe, Research Nurse
Royal Free & University College London Medical School
UCL – Department of Mental Health Sciences
Holborn Union Building - Archway Campus
Highgate Hill, London N19 5LW

Direct Line:

Insert Date

CARER INFORMATION SHEET

DEAR Insert Name

We would like to invite you and insert name to take part in a research project. Before you decide whether to take part, it is important that you understand why the research is being done and what the study will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information.

Dr Gill Livingston and Professor Katona run this project from the Whittington Hospital.

This study aims to describe the characteristics and difficulties of people with memory problems, any change in these problems over six months, and the effects of any changes. This is in order to understand which aspects matter most in people's lives. This information may also help in designing and developing new medications for these problems.

We are asking you to participate in this study because we understand that insert name to whom you provide care, may have memory problems. If you agree to participate in the study we intend to see you and make an assessment of the consequences providing care has on your life. We are particularly interested in studying people who may have Alzheimer's Disease.

The interview will involve asking you questions about insert name and yourself. We would also want to see you again after six months to ask some of the same questions again.

The interviews will be about:

- Demographic details such as your dates of birth and schooling.
- How you feel about you and insert name health and lifestyle.
- Current contact with care services.
- Your impression of the care that insert name requires.

The study does not involve any new treatments or affect insert name current or future treatment.

The time taken for the interview will vary but we estimate that each interview is likely to take approximately an hour. We will come and visit you at home. If either of you find this tiring the person seeing you will be happy to stop and come back at a later date which is convenient to you.

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to take part you are free to withdraw at any time, without giving a reason.

The results of this study are expected to be published in relevant conferences and journals. All interviews are confidential and your name will not be disclosed to anyone else. The information collected will be anonymised but may be seen by Lundbeck Pharmaceuticals, who are funding the study. You will not be identified in any report/publication.

All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Camden and Islington NHS Research Ethics Committee.

Thank you for reading this information sheet. Please contact the research team at the above address or number if you would like any further information. (Please mark written correspondence for the attention of the research team).

Yours Sincerely

Juanita Hoe
Clinical Research Nurse

Study Number:

CRF No. _____

Centre No. _____

Patient Identification Number for this trial: _____

CARER/RELATIVE CONSENT FORM

Title: A longitudinal study in people with memory difficulties

Name of Researcher: _____

Please initial box

4. I confirm that I have read and understand the information sheet dated..... for the above study and have had the opportunity to ask questions.

5. 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.

6. I agree to take part in the above study

_____ Name of Carer:	_____ Date	_____ Signature
_____ Name of Person taking consent (if different from researcher)	_____ Date	_____ Signature
_____ Researcher	_____ Date	_____ Signature

**Royal Free & University College Medical School
UNIVERSITY COLLEGE LONDON**



DEPARTMENT OF MENTAL HEALTH SCIENCES

Juanita Hoe, Research Nurse
Royal Free & University College London Medical School
UCL – Department of Mental Health Sciences
Holborn Union Building - Archway Campus
Highgate Hill, London N19 5LW

Email j.hoe@ucl.ac.uk

Direct Line:

Insert Date

GENERAL PRACTITIONER INFORMATION SHEET

Title: A longitudinal study in people with memory difficulties

Dear Dr *Insert Name*

Insert Name (Dob *insert*) has been invited and consented to take part in a research study. Please let us know if there is anything that is not clear or if you would like more information.

Prof Katona and Juanita Hoe run this project from North Essex Mental Health Partnership Trust .

This study aims to describe the characteristics and difficulties of people with memory problems any change over six months and the effects of any changes. This is in order to know which aspects matter most in people's lives. This information may also help in designing and developing new medicines for these problems.

We are particularly interested in studying people who may have Alzheimer's Disease. We would also want to see your patient again after six months to ask some of the same questions again.

The interviews will be about:

- Personal details (age, relationship, educational level, etc.)
- quality-of-life
- Use of services
- Difficulties your patient's caregiver may experience

The study does **not** involve any new treatments or affect your patient's current or future treatment.

The results of this study are expected to be published in relevant conferences and journals. All interviews are confidential and will not be disclosed to anyone else. The information collected in the study will be anonymised but may be seen by Lundbeck Pharmaceuticals, the funders of the study. Patients will not be identified in any report/publication.

All proposals for research using human subjects are reviewed by the local Ethics Committee before they can proceed

Thank you for reading this. Please contact Prof Katona at the above address or number if you would like further information.

Yours Sincerely

Juanita Hoe
Clinical Research Nurse

The Hospital Anxiety and Depression Scale

Read each item and tick the box next to the reply that comes closest to how you have been feeling in the past week.

A I feel tense or wound up:

Most of the time

From time to time, occasionally

A lot of the time

Not at all

D I still enjoy the things I used to enjoy:

Definitely as much

Only a little

Not quite so much

Hardly at all

A I get a sort of frightened feeling as if something awful is about to happen:

Very definitely and quite badly

A little, but it doesn't worry me

Yes, but not too badly

Not at all

D I can laugh and see the funny side of things:

As much as I always could

Definitely not so much now

Not quite so much now

Not at all

A Worrying thoughts go through my mind:

A great deal of the time	From time to time but not too often
A lot of the time	Only occasionally

D I feel cheerful:

Not at all	Sometimes
Not often	Most of the time

A I can sit at ease and feel relaxed:

Definitely	Not often
Usually	Not at all

D I feel as if I am slowed down:

Nearly all the time	Sometimes
Very often	Not at all

A I get a sort of frightened feeling like 'butterflies' in the stomach:

Not at all	Quite often
Occasionally	Very often

D I have lost interest in my appearance:

Definitely	I may not take quite as much care
I don't take as much care as I should	I take just as much care as ever

A I feel restless as if I have to be on the move:

Very much indeed	Not very much
Quite a lot	Not at all

D I look forward with enjoyment to things:

As much as I ever did	Definitely less than I used to
Rather less than I used to	Hardly at all

A I get sudden feelings of panic:

Very often indeed	Not very often
Quite often	Not at all

D I can enjoy a good book or radio or TV programme:

Often	Not often
Sometimes	Very seldom

The Brief COPE

There are many ways to try to deal with problems. These items ask *what you've been doing to cope* with the problems/ stress of caring for your relative/friend with Alzheimer's Disease. We want to know *how often* you've been doing what the item says. Don't answer on the basis of whether it seems to be working or not – just whether you're doing it or not. Please *tick the box that best applies to you*. There are no right or wrong answers. Please treat each question separately.

How often have you:	I'm not doing this at all	I have been doing this a little bit	I have been doing this a medium amount	I have been doing this a lot
I've been turning to work or other activities to take my mind off things				
I've been concentrating my efforts on doing something about the situation I'm in				
I've been saying to myself "this isn't real"				
I've been using alcohol or other drugs to make myself feel better				
I've been getting emotional support from others				
I've been giving up trying to				

deal with it				
I've been taking action to try to make the situation better				
I've been refusing to believe that it has happened				
I've been saying things to let my unpleasant feelings escape				
I've been getting help and advice from other people				
I've been using alcohol or other drugs to help me get through it				
I've been trying to see it in a different light, to make it seem more positive				
I've been criticising myself				
I've been trying to come up with a strategy about what to do				
I've been getting comfort and understanding from someone				
I've been giving up the attempt to cope				
I've been looking for something good in what is happening				
I've been making jokes about it				
I've been doing something to				

think about it less, such as going to the cinema, watching TV, reading, daydreaming, sleeping or shopping				
I've been accepting the reality of the fact that it has happened				
I've been expressing my negative feelings				
I've been trying to find comfort in my religion or spiritual beliefs				
I've been trying to get advice or help from other people about what to do				
I've been learning to live with it				
I've been thinking hard about what steps to take				
I've been blaming myself for things that happened				
I've been praying or meditating				
I've been making fun of the situation				
I've been smoking to make myself feel better				

LIFE EVENTS (18 months)

Below is a list of life events. Please tick the boxes next to the events that have happened in your life within the last *six months*. Please ignore the events that are not applicable to you.

		<u>Life event</u>
100	<input type="checkbox"/>	Death of a spouse
73	<input type="checkbox"/>	Divorce or marital separation
63	<input type="checkbox"/>	Jail term
63	<input type="checkbox"/>	Death of close family member
53	<input type="checkbox"/>	Personal injury, illness or major change in personal health
50	<input type="checkbox"/>	Marriage
47	<input type="checkbox"/>	Loss of job
45	<input type="checkbox"/>	Moving house
45	<input type="checkbox"/>	Marital reconciliation
45	<input type="checkbox"/>	Retirement
44	<input type="checkbox"/>	Serious illness of family member
40	<input type="checkbox"/>	Pregnancy
39	<input type="checkbox"/>	Sexual difficulties
39	<input type="checkbox"/>	Birth of a new child
39	<input type="checkbox"/>	Change of job
38	<input type="checkbox"/>	Financial problems
37	<input type="checkbox"/>	Death of a close friend
35	<input type="checkbox"/>	Increase in family disharmony
31	<input type="checkbox"/>	High mortgage
30	<input type="checkbox"/>	Legal action over debt
29	<input type="checkbox"/>	Change in work responsibilities
29	<input type="checkbox"/>	Children leaving home
29	<input type="checkbox"/>	Trouble with in-laws
28	<input type="checkbox"/>	Outstanding personal achievement
26	<input type="checkbox"/>	Spouse begins or stops work
26	<input type="checkbox"/>	Children beginning or ending school
25	<input type="checkbox"/>	Change in living conditions
24	<input type="checkbox"/>	Revision of personal habits
23	<input type="checkbox"/>	Trouble with boss
20	<input type="checkbox"/>	Change in work hours or conditions
20	<input type="checkbox"/>	Change in children's school
19	<input type="checkbox"/>	Change in recreation or leisure pursuits
19	<input type="checkbox"/>	Change in church activities
18	<input type="checkbox"/>	Change in social activities
17	<input type="checkbox"/>	Small mortgage or loan
16	<input type="checkbox"/>	Change in sleeping habits
15	<input type="checkbox"/>	Change in contact with family
15	<input type="checkbox"/>	Change in eating habits
13	<input type="checkbox"/>	Holidays
12	<input type="checkbox"/>	Christmas
11	<input type="checkbox"/>	Minor violations of the law

Official use only:

Total Score _____

The List of Threatening Experiences (30 month follow-up)

Please tick any of these that have happened to you within the past six months:

	Tick if has happened
You suffered a serious illness, injury or assault	
A serious illness, injury or assault happened to a close relative (excluding your relative/ friend's memory problems)	
Your parent, child or spouse died	
A close family friend, aunt, cousin, or grandparent died	
You had a separation due to marital difficulties	
You broke off a steady relationship	
You had a serious problem with a close friend, neighbour or relative	
You became unemployed or were seeking work unsuccessfully for more than one month	
You were sacked from your job	
You had a major financial crisis	
You had problems with the police and a court appearance	
Something you valued was stolen or lost	

ZARIT BURDEN INTERVIEW (ZBI)

INSTRUCTIONS: The following is a list of statements, which reflect how people sometimes feel when taking care of another person. After each statement, indicate how often you feel that way; never, rarely, sometimes, quite frequently, or nearly always. There are no right or wrong answers.

1. Do you feel that your relative asks for more help than he/she needs?
 0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

2. Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?
 0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

2. Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?
 0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

4. Do you feel embarrassed over your relative's behaviour?
 0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

5. Do you feel angry when you are around your relative?

0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
6. Do you feel that your relative currently affects your relationship with other family members or friends in a negative way?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
7. Are you afraid what the future holds for your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
8. Do you feel your relative is dependent upon you?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
9. Do you feel strained when you are around your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

10. Do you feel your health has suffered because of your involvement with your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
11. Do you feel that you don't have as much privacy as you would like, because of your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
12. Do you feel that your social life has suffered because you are caring for your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
13. Do you feel uncomfortable about having friends over, because of your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
14. Do you feel that your relative seems to expect you to take care of him/her, as if you were the only one he/she could depend on?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

15. Do you feel that you don't have enough money to care for your relative, in addition to the rest of your expenses?
- 0. Never
 - 1. Rarely
 - 2. Sometimes
 - 3. Quite Frequently
 - 4. Nearly Always
16. Do you feel that you will be unable to take care of your relative much longer?
- 0. Never
 - 1. Rarely
 - 2. Sometimes
 - 3. Quite Frequently
 - 4. Nearly Always
17. Do you feel you have lost control of your life since your relative's illness?
- 0. Never
 - 1. Rarely
 - 2. Sometimes
 - 3. Quite Frequently
 - 4. Nearly Always
18. Do you wish you could just leave the care of your relative to someone else?
- 0. Never
 - 1. Rarely
 - 2. Sometimes
 - 3. Quite Frequently
 - 4. Nearly Always
19. Do you feel uncertain about what to do about your relative?
- 0. Never
 - 1. Rarely
 - 2. Sometimes
 - 3. Quite Frequently
 - 4. Nearly Always

20. Do you feel you should be doing more for your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
21. Do you feel you could do a better job in caring for your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always
22. Overall, how burdened do you feel in caring for your relative?
0. Never
 1. Rarely
 2. Sometimes
 3. Quite Frequently
 4. Nearly Always

For office use only:

TOTAL SCORE _____

PERSONAL STRAIN SCORE (ITEMS 1, 4, 5, 8, 9, 14, 16, 17, 18, 19, 20, 21) _____

ROLE STRAIN SCORE (ITEMS 2, 3, 6, 11, 12, 13)_____

CAREGIVER HSQ-12

1. In general, would you say your health is (circle one number only):

Excellent	1
Very good	2
Good	3
Fair	4
Poor	5

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(Circle one number on each line)

<u>ACTIVITIES</u>	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
2. Lifting or carrying groceries	1	2	3
3. Climbing several flights of stairs	1	2	3
4. Walking several blocks	1	2	3

5. During the **past 4 weeks**, how much difficulty did you have doing your work or other daily regular activities as a result of your physical health? (circle one number only)

Not at all	1
A little bit	2
Some	3
Quite a bit	4
Could not do daily work	5

6. During the **past 4 weeks**, to what extent have you accomplished less than you would like in your work or other daily activities as a result of emotional problems (such as feeling depressed or anxious)? (circle one number)

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

7. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (circle one number)

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

8. How much **bodily** pain have you had during the **past 4 weeks**? (circle one number)

None	1
Very mild	2
Mild	3
Moderate	4
Severe	5
Very severe	6

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks:

(Circle one number on each line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
1. Physical health.	Poor	Fair	Good	Excellent		
2. Energy.	Poor	Fair	Good	Excellent		
3. Mood.						
4. Living situation.						
9. Have you felt calm and peaceful?	1	2	3	4	5	6
10. Did you have a lot of energy?	1	2	3	4	5	6
11. Have you felt downhearted and blue?	1	2	3	4	5	6
12. Have you been a happy person?	1	2	3	4	5	6

10. Life around the house.	Poor	Fair	Good	Excellent
11. Ability to do things for fun.	Poor	Fair	Good	Excellent
12. Money.	Poor	Fair	Good	Excellent
13. Life as a whole.	Poor	Fair	Good	Excellent

Comments: _____

QoL -AD

SECTION 2: CAREGIVER VERSION

1. Physical health.	Poor	Fair	Good	Excellent
2. Energy.	Poor	Fair	Good	Excellent
3. Mood.	Poor	Fair	Good	Excellent
4. Living situation.	Poor	Fair	Good	Excellent
5. Memory.	Poor	Fair	Good	Excellent
6. Family.	Poor	Fair	Good	Excellent
7. Marriage.	Poor	Fair	Good	Excellent
8. Friends.	Poor	Fair	Good	Excellent
9. Self as a whole.	Poor	Fair	Good	Excellent
10. Ability to do chores around the house.	Poor	Fair	Good	Excellent
11. Ability to do things for fun.	Poor	Fair	Good	Excellent
12. Money.	Poor	Fair	Good	Excellent
13. Life as a whole.	Poor	Fair	Good	Excellent

Comments:

ADAS-COG

1. WORD RECALL

"I am going to show you some words, one at a time. Please read each word out loud and try to remember it, because later I will ask you to remember all of the words I have shown you".

The subject reads aloud 10 words, exposed for 2 seconds each. The subject then recalls the words aloud. Three trials of reading and recalling are given...

<u>TRIAL 1</u>			<u>TRIAL 2</u>			<u>TRIAL 3</u>		
	Recalled	Not Recalled		Recalled	Not Recalled		Recalled	Not Recalled
HOME <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	SKIN	<input type="checkbox"/>	<input type="checkbox"/>	RAILROAD	<input type="checkbox"/>	
COIN <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	CHILD	<input type="checkbox"/>	<input type="checkbox"/>	OCEAN	<input type="checkbox"/>	
RAILROAD <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	WHEAT	<input type="checkbox"/>	<input type="checkbox"/>	FLAG	<input type="checkbox"/>	
CHILD <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	LIBRARY	<input type="checkbox"/>	<input type="checkbox"/>	ARMY	<input type="checkbox"/>	
ARMY <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	HOME	<input type="checkbox"/>	<input type="checkbox"/>	WHEAT	<input type="checkbox"/>	
FLAG <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	OCEAN	<input type="checkbox"/>	<input type="checkbox"/>	CHILD	<input type="checkbox"/>	
SKIN <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	RAILROAD	<input type="checkbox"/>	<input type="checkbox"/>	COIN	<input type="checkbox"/>	
LIBRARY <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	FLAG	<input type="checkbox"/>	<input type="checkbox"/>	SKIN	<input type="checkbox"/>	
WHEAT <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	COIN	<input type="checkbox"/>	<input type="checkbox"/>	HOME	<input type="checkbox"/>	

OCEAN ☐ ☐ ☐ ☐ ARMY ☐ ☐ LIBRARY ☐ ☐

Total not recalled ☐ ☐ Total not recalled ☐ ☐ Total not recalled ☐ ☐

Score ☐ ☐ score = mean number of words NOT recalled on 3 trials (max = 10).

2. NAMING OBJECTS AND FINGERS

The subject names 12 randomly presented objects. The subject is asked about each object: **“What is this thing called?”** or **“What is the name of this thing?”**

If the subject does not respond then a prompt should be given, If the subject still does not respond or makes an error, go on to the next object...

OBJECTS	PROMPT	CORRECT	INCORRECT (or not named)
FLOWER	- Grows in the garden	<input type="checkbox"/>	<input type="checkbox"/>
BED	- Used for sleeping	<input type="checkbox"/>	<input type="checkbox"/>
WHISTLE	- Makes a sound when you blow it	<input type="checkbox"/>	<input type="checkbox"/>
PENCIL	- Used for writing	<input type="checkbox"/>	<input type="checkbox"/>
RATTLE	- A baby's toy	<input type="checkbox"/>	<input type="checkbox"/>
MASK	- Hides your face	<input type="checkbox"/>	<input type="checkbox"/>
SCISSORS	- Cuts paper	<input type="checkbox"/>	<input type="checkbox"/>
COMB	- Used on hair	<input type="checkbox"/>	<input type="checkbox"/>
WALLET	- Holds you money	<input type="checkbox"/>	<input type="checkbox"/>
HARMONICA	- A musical instrument	<input type="checkbox"/>	<input type="checkbox"/>
STETHOSCOPE	- Doctor uses it to listen to your heart	<input type="checkbox"/>	<input type="checkbox"/>
TWEEZERS	- Used to pick things up	<input type="checkbox"/>	<input type="checkbox"/>

The subject names the fingers on his/ her dominant hand...

FINGER	CORRECT	INCORRECT (or not named)
THUMB	<input type="checkbox"/>	<input type="checkbox"/>
INDEX	<input type="checkbox"/>	<input type="checkbox"/>
MIDDLE	<input type="checkbox"/>	<input type="checkbox"/>
RING	<input type="checkbox"/>	<input type="checkbox"/>
LITTLE FINGER	<input type="checkbox"/>	<input type="checkbox"/>











Total incorrect ☐ ☐ ☐

Score: 0 = 0-2 items names incorrectly
 1 = 3-5 items names incorrectly
 2 = 6-8 items names incorrectly
 3 = 9-11 items names incorrectly
 4 = 12-14 items names incorrectly
 5 = 15-17 items names incorrectly

Score ☐ ☐ ☐
 (maximum 5)

3. COMMANDS

Ask the subject to carry out the following commands. Each command should be read once. If the subject does not respond or makes an error, the tester should the the entire command one more time. Then go on to the next command...

	CORRECT	INCORRECT (or not named)
Make a <u>fist</u>		
Point to the <u>ceiling</u> and then to the <u>floor</u>		
Line up a pencil, watch, and card, in that order, On a table in front of the subject.		
Put the <u>pencil on top of the card</u> and then <u>put it back</u>		
Put the <u>watch</u> on the <u>other side of the pencil</u> And then <u>turn over the card</u>		
Tap <u>each shoulder twice</u> , with <u>two fingers</u> , Keeping your <u>eyes shut</u>		

Each underlined element represents a single step. Each command is scored as a whole

Score: 0 = all commands correct


1 = 1 command incorrect, 4 commands correct

2 = 2 commands incorrect, 3 commands correct

3 = 3 commands incorrect, 2 commands correct

4 = 4 commands incorrect, 1 command correct

5 = All 5 commands incorrect

Score 
(maximum 5)









4. CONSTRUCTIONAL PRAXIS

Instruct the subject “**On this piece of paper is a shape. Try and draw another one that looks just like this, somewhere on the page**”.


Allow the subject two attempts for each shape, and permit the subject to erase. If the subject cannot reproduce the figure in two attempts, the tester should go onto the next item.

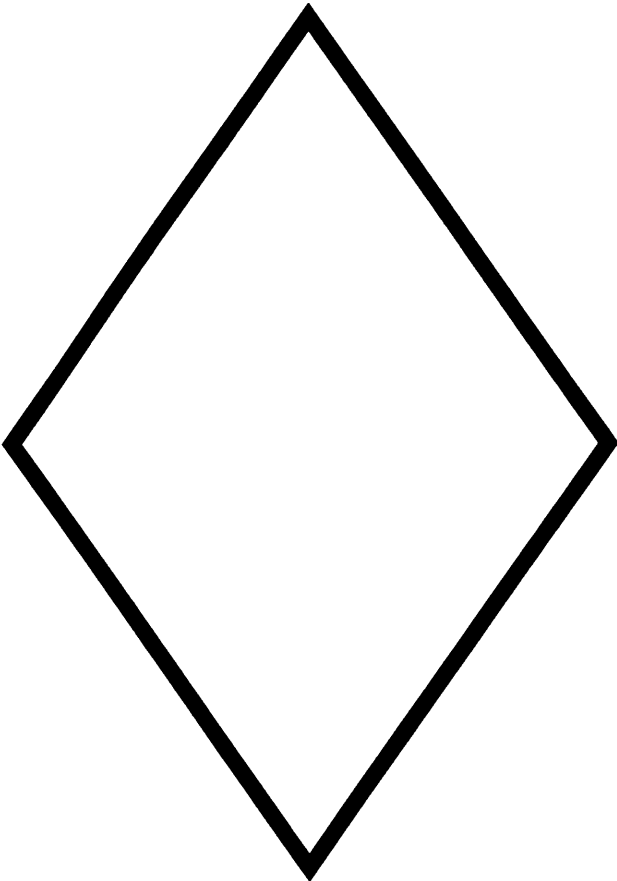
A drawing should be scored as correct if the subject has reproduced all of the essential geometric features of the original. Changes in size do not count as errors. Small gaps between lines do not indicate an error, as long as the shape has been reproduced. Scoring criteria...

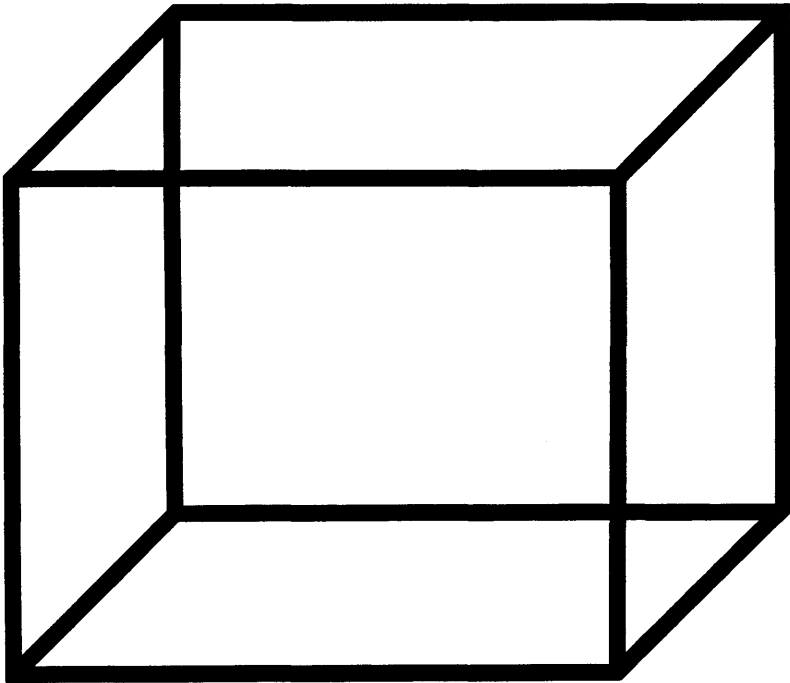
1. **Circle.** A closed curved figure.
2. **Two overlapping rectangles.** Forms must be four sided, and overlap must be similar to presented form.
3. **Diamond.** Figure must be four sided, oriented so that points are at the top and bottom, and the sides are approximately equal length.
4. **Cube.** The form is three-dimensional, with front face in the correct orientation, internal lines drawn correctly between corners. Opposite sides of faces should be approximately parallel.

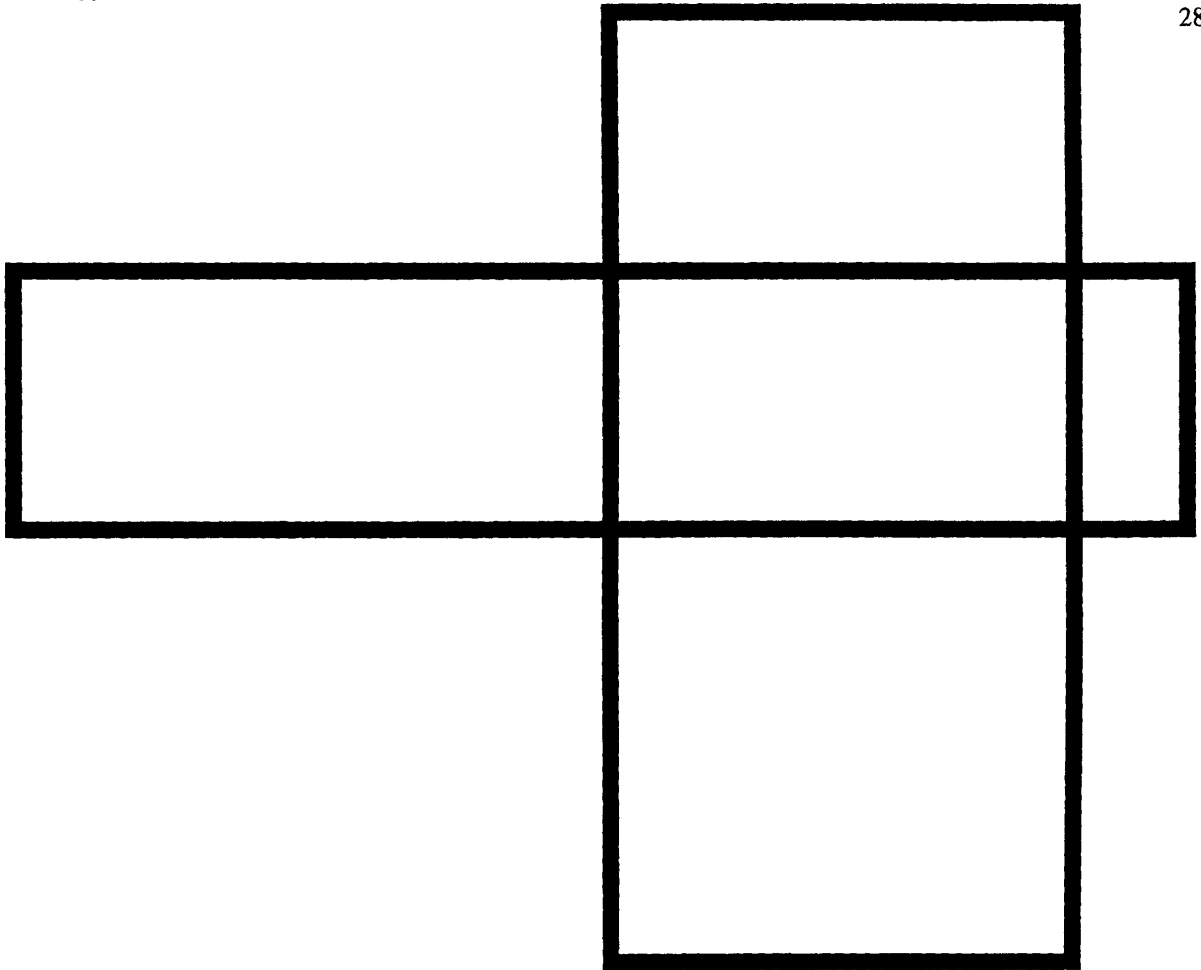
	CORRECT	INCORRECT (or not drawn)
Circle		
Two overlapping rectangles		
Diamond		
Cube		

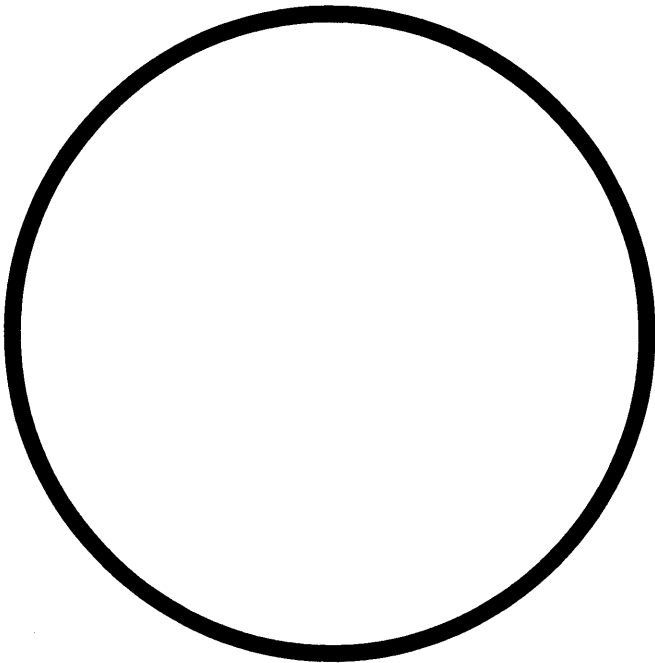
Score: 0 = all 4 drawings correct
 1 = 1 form drawn incorrectly
 2 = 2 forms drawn incorrectly
 3 = 3 forms drawn incorrectly
 4 = 4 forms drawn incorrectly
 5 = No figures drawn, scribbles;
 parts of forms; words instead of forms

Score 
 (maximum 5)



















5. IDEATIONAL PRAXIS

“I want you to pretend that you have written yourself a letter. Take this piece of paper, fold it so that it will fit into the envelope, and then put it into the envelope. Then seal the envelope, address the envelope to yourself, and show me where the stamp goes”.

Indicate each underlined step completed correctly or incorrectly. If the subject forgets part of the task or is having difficulty, the tester should repeat the instruction for the component of the task where they are having difficulty...

	CORRECT	INCORRECT (or not done)
Fold a letter		
Put the letter in an envelope		
Seal the envelope		
Address the envelope		
Indicate where the stamp goes		

Score: 0 = all components performed correctly

1 = failure to perform 1 component

2 = failure to perform 2 components

3 = failure to perform 3 components

4 = failure to perform 4 components

5 = failure to perform 5 components

Score 
(maximum 5)

6. ORIENTATION

Before testing for orientation, the tester should be sure that no clocks, watches or calendars are visible to aid the subject. Indicate each item answered correctly or incorrectly.

	CORRECT	INCORRECT (or not answered)		CORRECT	INCORRECT (or not answered)
Full name	<input type="checkbox"/>	<input type="checkbox"/>	Year	<input type="checkbox"/>	<input type="checkbox"/>
Day	<input type="checkbox"/>	<input type="checkbox"/>	Season	<input type="checkbox"/>	<input type="checkbox"/>
Date	<input type="checkbox"/>	<input type="checkbox"/>	Time of day	<input type="checkbox"/>	<input type="checkbox"/>
Month	<input type="checkbox"/>	<input type="checkbox"/>	Place	<input type="checkbox"/>	<input type="checkbox"/>

Score: **1 point** is given for each incorrect response

Score
(maximum 8)

N.B. Acceptable answers include ± 1 day for the date, naming of upcoming season within 1 week before its onset or name of previous season for 2 weeks after its termination, within 1 hour for the time, and partial name for place. First and last names, day of the week, month and year must be exact.

7. WORD RECOGNITION

Bold are the words shown before. Tick the subject's responses; circles indicate incorrect responses. Note if the subject needs a reminder (Rem) of the test instructions.

<u>TRIAL 1</u>			<u>TRIAL 2</u>			<u>TRIAL 3</u>		
<u>Yes</u>	<u>No</u>	<u>Rem</u>	<u>Yes</u>	<u>No</u>	<u>Rem</u>	<u>Yes</u>	<u>No</u>	<u>Rem</u>
Corn	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	River	<input type="checkbox"/>	<input type="radio"/> //	Plant	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>
Effort	<input type="radio"/>	<input type="checkbox"/> <input type="checkbox"/>	Officer	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	River	<input type="checkbox"/>	<input type="radio"/>
Party	<input type="radio"/>	<input type="checkbox"/> <input type="checkbox"/>	Thought	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Amount	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>
River	<input type="checkbox"/>	<input type="radio"/>	Event	<input type="checkbox"/>	<input type="radio"/>	Event	<input type="checkbox"/>	<input type="radio"/>
Folly	<input type="radio"/>	<input type="checkbox"/> <input type="checkbox"/> //	Queen	<input type="checkbox"/>	<input type="radio"/>	// Queen	<input type="checkbox"/>	
<input type="radio"/>								
Locker	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/> //	Position	<input type="checkbox"/>	<input type="radio"/> //	Industry	<input type="radio"/> //	
<input type="checkbox"/> <input type="checkbox"/>								
Event	<input type="checkbox"/>	<input type="radio"/> //	Camp	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Position	<input type="checkbox"/>	<input type="radio"/>
Queen	<input type="checkbox"/>	<input type="radio"/> //	Fate	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Occasion	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>
Position	<input type="checkbox"/>	<input type="radio"/> //	Golf	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Dove	<input type="checkbox"/>	<input type="radio"/>
Quality	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/> //	Dove	<input type="checkbox"/>	<input type="radio"/> //	Cradle	<input type="radio"/> //	
<input type="checkbox"/> <input type="checkbox"/>								
Sunset	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/> //	Belief	<input type="checkbox"/>	<input type="radio"/> //	Banality	<input type="radio"/> //	
<input type="checkbox"/> <input type="checkbox"/>								
Dove	<input type="checkbox"/>	<input type="radio"/>	Permission	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Singer	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>
Belief	<input type="checkbox"/>	<input type="radio"/>	Umbrella	<input type="checkbox"/>	<input type="radio"/> //	Belief	<input type="checkbox"/>	<input type="radio"/>
Umbrella	<input type="checkbox"/>	<input type="radio"/> //	Hint	<input type="checkbox"/>	<input type="radio"/> //	Umbrella	<input type="checkbox"/>	<input type="radio"/>
Allegory	<input type="radio"/>	<input type="checkbox"/> <input type="checkbox"/>	Missile	<input type="checkbox"/>	<input type="radio"/> //	Hypothesis	<input type="radio"/> //	
<input type="checkbox"/> <input type="checkbox"/>								
Hound	<input type="radio"/>	<input type="checkbox"/> <input type="checkbox"/>	Blister	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Hint	<input type="checkbox"/>	<input type="radio"/>
Idiom	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Concept	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Missile	<input type="checkbox"/>	
<input type="radio"/>								
Hint	<input type="checkbox"/>	<input type="radio"/> //	Proxy	<input type="checkbox"/>	<input type="radio"/> //	Proxy	<input type="checkbox"/>	<input type="radio"/>
Missile	<input type="checkbox"/>	<input type="radio"/> //	Pianist	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Noose	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>
Gem	<input type="radio"/>	<input type="checkbox"/> <input type="checkbox"/>	Lobster	<input type="checkbox"/>	<input type="radio"/> //	Distinction	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>
Proxy	<input type="checkbox"/>	<input type="radio"/> //	Gender	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Lobster	<input type="checkbox"/>	<input type="radio"/>
Lobster	<input type="checkbox"/>	<input type="radio"/> //	Criterion	<input type="checkbox"/>	<input type="radio"/> //	Tank		<input type="radio"/> //
<input type="checkbox"/> <input type="checkbox"/>								
Criterion	<input type="checkbox"/>	<input type="radio"/> //	Bullet	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Criterion	<input type="checkbox"/>	<input type="radio"/>
Deceit	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Intellect	<input type="radio"/> //	<input type="checkbox"/> <input type="checkbox"/>	Decree		<input type="radio"/> //
<input type="checkbox"/> <input type="checkbox"/>								

Total circles ticked Total circles ticked Total circles ticked

Score score = mean number of incorrect responses on 3 trials (max = 12).

Total number of reminders (for scoring item 8)

8. REMEMBERING TEST INSTRUCTIONS

Evaluate the subject's ability to remember the requirements of the word recognition task based upon noting each instance of failure to remember the test instructions.

Score: 0 = Subject never needs extra reminders of instructions

1 = Very mild - forgets once

2 = Mild – must be reminded 2 times

3 = Moderate – must be reminded 3 or 4 times

4 = Moderately severe – must be reminded 5 or 6 times

5 = Severe – must be reminded 7 or more times

Score

9. SPOKEN LANGUAGE ABILITY

Provide a global rating of the quality of speech, i.e., clarity, difficulty in making oneself understood.

Score: 0 = No instance where it is difficult to understand the subject

1 = Very mild - one instance of lack of understandability

2 = Mild – subject has difficulty less than 25% of time

3 = Moderate – subject has difficulty 25-50% of time

4 = Moderately severe – subject has difficulty more than 50% of time

5 = Severe – one or two word utterances; fluent but empty speech; mute

Score

10. WORD-FINDING DIFFICULTY IN SPONTANEOUS

Rate the subject's difficulty in finding desired words, e.g., circumlocutions.

Score: 0 = No evidence of word-finding difficulty in spontaneous speech

1 = Very mild - 1 or 2 instances, not clinically significant

2 = Mild – noticeable circumlocution or synonym substitution

3 = Moderate – loss of words without compensation on occasion

4 = Moderately severe – frequent loss of words without compensation

5 = Severe –nearly total loss of content words; speech sounds empty; 1-2 word utterances

Score

11. COMPREHENSION

Rate the subject's ability to understand speech. Do not include responses to commands.

Score: **0** = No evidence of poor comprehension

1 = Very mild - 1-2 instances of misunderstanding

2 = Mild – 3-5 instances of misunderstanding

3 = Moderate – requires several repetitions and rephrasing

4 = Moderately severe – subject only occasionally responds correctly; e.g., yes/no questions.

5 = Severe – subject rarely responds to questions appropriately; not due to poverty of speech.

Score

12. CONCENTRATION/ DISTRACTIBILITY

Rate the frequency with which the subject is distracted by irrelevant stimuli and/ or must be reoriented to the ongoing task because the subject has lost his/ her train of thought or appears to be caught up in his/ her own thoughts.

Score: **0** = No evidence of poor concentration or distractibility

1 = Very mild - one instance of poor concentration

2 = Mild – 2-3 instances of poor concentration/ distractibility; signs of restlessness and inattentiveness

3 = Moderate – 4-5 instances during interview

4 = Moderately severe – poor concentration/ distractibility throughout much of interview

5 = Severe – Extreme difficulty in concentration and extremely distractible, unable to complete tasks

Score

ADAS-COG SCORE SUMMARY SHEET

			Score
1.	WORD RECALL	(maximum 10)	<input type="text"/> <input type="text"/>
2.	NAMING OBJECTS AND FINGERS	(maximum 5)	<input type="text"/> <input type="text"/>
3.	COMMANDS	(maximum 5)	<input type="text"/> <input type="text"/>
4.	CONSTRUCTIONAL PRAXIS	(maximum 5)	<input type="text"/> <input type="text"/>
5.	IDEATIONAL PRAXIS	(maximum 5)	<input type="text"/> <input type="text"/>
6.	ORIENTATION	(maximum 8)	<input type="text"/> <input type="text"/>
7.	WORD RECOGNITION	(maximum 12)	<input type="text"/> <input type="text"/>
8.	REMEMBERING TEST INSTRUCTIONS	(maximum 5)	<input type="text"/> <input type="text"/>
9.	SPOKEN LANGUAGE ABILITY	(maximum 5)	<input type="text"/> <input type="text"/>
10.	WORD FINDING DIFFICULTY	(maximum 5)	<input type="text"/> <input type="text"/>
11.	COMPREHENSION	(maximum 5)	<input type="text"/> <input type="text"/>
12.	CONCENTRATION/ DISTRACTIBILITY	(maximum 5)	<input type="text"/> <input type="text"/>

Total Score
 (maximum 75)

ADCS-ADL INVENTORY

1. Regarding eating, which best describes patient's usual performance during the past 4 weeks?

- | | |
|---|---|
| Ate without physical help, and used a knife | 3 |
| Used a fork or a spoon, but not a knife, to eat | 2 |
| Used fingers to eat | 1 |
| Usually or always was fed by someone else | 0 |

2. Regarding walking (or getting around with a wheelchair) in the past 4 weeks, which best describes patient's performances?

- | | |
|--|---|
| Mobile outside of home without physical help | 3 |
| Mobile across room without physical help | 2 |
| Transferred from bed to chair without help | 1 |
| Required physical help to walk or transfer | 0 |

3. Regarding bowel and bladder function at the toilet, which best describes patient's usual performance in the past 4 weeks?

- | | |
|--|---|
| Did everything necessary without supervision or help | 3 |
| Needed supervision, but no physical help | 2 |
| Needed physical help, and was usually continent | 1 |
| Needed physical help, and was usually incontinent | 0 |

4. Regarding bathing, in the past 4 weeks, which best describes patient's usual performances?

- | | |
|--|---|
| Bathed without reminding or physical help | 3 |
| No physical help, but needed supervision/reminders to bathe completely | 2 |
| Needed minor physical help (e.g. washing hair) to bathe completely | 1 |
| Needed to be bathed completely | 0 |

7. In the past 4 weeks, did the patient use a telephone?

No

Don't know

5. Regarding grooming, in the past 4 weeks, which best describes patient's optimal performance?

Cleaned and cut fingernails without physical help 3

Brushed and combed hair without physical help 2

Kept face and hands clean without physical help 1

Needed help for grooming of hair, face, hands and fingernails 0

6. Regarding dressing in the past 4 weeks:

6.A. Did patient select his/her first set of clothes for the day?

No 0

Don't know 0

If yes: which best describes his/her usual performance?

Without supervision or help 3

With supervision 2

With physical help 1

6.B. Regarding physical getting dressed, which best describes patient's usual performance in the past 4 weeks?

Dressed completely without supervision or physical help 4

Dressed completely with supervision but without help 3

Needed physical help only for buttons, clasps or shoelaces 2

Dressed without help if clothes needed to fastening or buttoning 1

Always needed help, regardless of the type of clothing 0

6.C. Talk about the content of a program within a day (24 hours) after watching it?

Yes 1

No 0

Don't know 0

7. In the past 4 weeks, did the patient use a telephone?

No	0
----	---

Don't know	0
------------	---

If yes: which best describes patient's highest level of performance?

Made calls after looking up numbers in white or yellow pages, or by dialling directory assistance	5
---	---

Made calls to only well-known numbers, without referring to a directory or list	4
---	---

Made calls to only well-known numbers, by using a directory or list	3
---	---

Answered the phone; did not make calls	2
--	---

Did not answer the phone but spoke when put on the line	1
---	---

8. In the past 4 weeks, did the patient watch television?

No	0
----	---

Don't know	0
------------	---

If yes: ask all following questions:**8.A. Usually select or ask for different programs or his/her favourite show?**

Yes	1
-----	---

No	0
----	---

Don't know	0
------------	---

8.B. Usually talk about the content of a program while watching it?

Yes	1
-----	---

No	0
----	---

Don't know	0
------------	---

8.C. Talk about the content of a program within a day (24 hours) after watching it?

Yes	1
-----	---

No	0
----	---

Don't know	0
------------	---

9. In the past 4 weeks, did the patient ever appear to pay attention to conversation or small talk for at least 5 minutes?

(Note: patient did not need to initiate the conversation)

No	0
Don't know	0

If yes: which best describes his/her usual degree of participation?

Usually said things that were related to the topic	3
Usually said things that were not related to the topic	2
Rarely or never spoke	1

10. Did the patient clear the dishes from the table after a meal or snack?

No	0
Don't know	0

If yes: which best describes his/her usual performance?

Without supervision or help	3
With supervision	2
With physical help	1

11. In the past 4 weeks, did the patient usually manage to find his/her personal belongings at home?

No	0
Don't know	0

If yes: which best describes his/her usual performance?

Without supervision or help	3
With supervision	2
With physical help	1

12. In the past 4 weeks, did the patient obtain a hot or cold beverage for him/herself? (a cold beverage includes a glass of water)

- No 0
- Don't know 0

If yes: which best describes his/her highest level of performance?

- Made a hot beverage, usually without physical help 3
- Made a hot beverage, usually if someone else heated the water 2
- Obtained a cold beverage, usually without physical help 1
- Only when accompanied or supervised, regardless of the trip 2
- Only with physical help, regardless of the trip 1

13. In the past 4 weeks, did the patient make him/herself a meal or a snack at home?

- No 0
- Don't know 0

If yes: which best describes patient's highest level of performance?

- Cooked or microwaved food, with little or no help 4
- Cooked or microwaved food, with extensive help 3
- Mixed or combined food items for a meal or snack, without cooking or microwaving (e.g. made a sandwich) 2
- Obtained food for his/her own, without mixing or cooking it 1

14. In the past 4 weeks, did the patient dispose of garbage or litter in an appropriate place or container at home?

- No 0
- Don't know 0

If yes: which best describes how patient usually performed?

- Without supervision or help 3
- With supervision 2
- With physical help 1

17. In the past 4 weeks, did the patient keep appointments or meetings with other people, such as relatives, a doctor, the hairdresser, etc?

15. In the past 4 weeks, did the patient get around (or travel) outside of his/her home?

No 0

Don't know 0

If yes: which best describes his/her optimal performance?

Alone, went at least 1 mile away from home 4

Alone, but remained within 1 mile of home 3

Only when accompanied or supervised, regardless of the trip 2

Only with physical help, regardless of the trip 1

18. In the past 4 weeks, was the patient ever lift on his/her own?

No 0

16. In the past 4 weeks, did the patient ever go shopping?

No 0

Don't know 0

16.A. Away from home, for 15 minutes or longer, during the day?

If yes: ask all following questions:

16.A. Which one best describes how patient usually selects items?

Without supervision or physical help 3

With some supervision or physical help 2

Not at all or selected mainly random or inappropriate items 1

16.B. Did patient usually pay for items without supervision or physical help?

Yes 1

No 0

Don't know 0

No 0

Don't know 0

17. In the past 4 weeks, did the patient keep appointments or meetings with other people, such as relatives, a doctor, the hairdresser, etc?

No 0
Don't know 0

If yes: which best describes his/her awareness of the meeting ahead on time?

Usually remembered, may have needed written reminders,
e.g. notes, a diary, or calendar 3
Only remembered the appointment after verbal reminders
on the day 2
Usually did not remember, in spite of verbal reminders
on the day 1

18. In the past 4 weeks, was the patient ever left on his/her own ?

No 0
Don't know 0

If yes: ask all following questions?

18.A. Away from home, for 15 minutes or longer, during the day?

Yes 1
No 0
Don't know 0

18.B. At home, for an hour or longer, during the day?

Yes 1
No 0
Don't know 0

18.C. At home, for less than 1 hour, during the day?

Yes 1
No 0
Don't know 0

20. In the past 4 weeks, did patient read a magazine, newspaper or book for

19. In the past 4 weeks, did the patient talk about current events?

(this means events or incidents that occurred during the past month)

No 0

Don't know 0

If yes: ask all following questions:

Did patient talk about events that:

19.A. he/she heard or read about or saw on TV but did not take part in?

Yes 1

No 0

Don't know 0

19.B. he/she took part in outside home involving family, friends or neighbours?

Yes 1

No 0

Don't know 0

19.C. occurred at home that he/she took part in or watched ?

Yes 1

No 0

Don't know 0

Patient's signature or name

1

20. In the past 4 weeks, did patient read a magazine, newspaper or book for more than 5 minutes at a time?

No	0
Don't know	0

If yes: ask all following questions:

Did patient usually:

20.A. Talk about details of what he/she read while or shortly (< than 1 hour) after reading?

Yes	1
No	0
Don't know	0

20.B. Talk about what he/she read 1 hour or longer after reading?

Yes	1
No	0
Don't know	0

21. In the past 4 weeks, did the patient ever write anything down?

(Note: if patient wrote things only after encouragement or with help, the response should still be « yes »)

No	0
Don't know	0

If yes: which best describes the most complicated things that patient wrote?

Letters or long notes that other people understood	3
Short notes or messages that other people understood	2
Patient's signature or name	1

22. In the past 4 weeks, did the patient perform a pastime, hobby or game?

No 0

Don't know 0

If yes: which of the following did patient perform?

(ask about all of the following, tick all that apply)

- | | |
|---|--------------------------|
| card or board games (including bridge, chess, checkers) | <input type="checkbox"/> |
| bingo | <input type="checkbox"/> |
| musical instrument | <input type="checkbox"/> |
| reading | <input type="checkbox"/> |
| tennis | <input type="checkbox"/> |
| crosswords | <input type="checkbox"/> |
| knitting | <input type="checkbox"/> |
| gardening | <input type="checkbox"/> |
| workshop | <input type="checkbox"/> |
| art | <input type="checkbox"/> |
| sewing | <input type="checkbox"/> |
| golf | <input type="checkbox"/> |
| fishing | <input type="checkbox"/> |
| other: specify _____ | <input type="checkbox"/> |

Note: Walking does NOT count as a hobby/pastime for this scaleIf patient performs hobbies/pastime only a **day care**, check here:☐**If yes:** how did patient usually perform his/her most common pastimes?

Without supervision or help 3

With supervision 2

With help 1

23. In the past 4 weeks, did the patient use a household appliance to do chores?

No 0

Don't know 0

If yes: which of the following?

(tick all that apply)

- | | | |
|--|----------------|--------------------------|
| <input type="checkbox"/> 1. does the patient use a | Washer | <input type="checkbox"/> |
| <input type="checkbox"/> 2. does the patient use a | Vacuum | <input type="checkbox"/> |
| <input type="checkbox"/> 3. does the patient use a | Toaster | <input type="checkbox"/> |
| <input type="checkbox"/> 4. does the patient use a | Range | <input type="checkbox"/> |
| <input type="checkbox"/> 5. does the patient use a | Food processor | <input type="checkbox"/> |
| <input type="checkbox"/> 6. does the patient use a | Dryer | <input type="checkbox"/> |
| <input type="checkbox"/> 7. does the patient use a | Dishwasher | <input type="checkbox"/> |
| <input type="checkbox"/> 8. does the patient use a | Toaster oven | <input type="checkbox"/> |
| <input type="checkbox"/> 9. does the patient use a | Other: specify | <input type="checkbox"/> |

If yes: for the most commonly used appliances, which best describes how patient usually used them?

- | | |
|---|----------|
| Without help, operating more than on-off controls if needed | 4 |
| Without help, but operated only on-off controls | 3 |
| With supervision, but no physical help | 2 |
| With physical help | 1 |

NPI-D

A. Delusions

Does the patient have beliefs that you know are not true? For example, insisting that people are trying to harm him/her or steal from him/her. Has he/she said the family members are not who they say they are or that the house is not their home? I'm not asking about mere suspiciousness, I am interested if the patient is convinced that these things are happening to him/her.

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient believe that he/she is in danger – that others are planning to hurt him/her?
- ☐ 2. does the patient believe that others are stealing from him/her?
- ☐ 3. does the patient believe that his/her spouse is having an affair?
- ☐ 4. does the patient believe that unwelcome guests are living in his/her house?
- ☐ 5. does the patient believe that his/her spouse or others are not who they claim to be?
- ☐ 6. does the patient believe that his/her house is not his/her home?
- ☐ 7. does the patient believe that family members plan to abandon him/her?
- ☐ 8. does the patient believe that television or magazine figures are actually present in the home? (does he/she try to talk or interact with them?)
- ☐ 9. does the patient believe any other unusual things that I haven't asked about?

A-Frequency:

- ☐ 1 occasionally – less than once per week
- ☐ 2 often – about once per week
- ☐ 3 frequently – several times per week but less than every day
- ☐ 4 very frequently – once or more per day

B-Severity:

- ☐ 1 mild – delusions present but seem harmless and produce little distress in the patient
- ☐ 2 moderate – delusions are distressing and disruptive
- ☐ 3 marked – delusions are very disruptive and are a major source of behavioural disruption (if PRN medications are prescribed, their use signals that the delusions are of marked severity)

B. Hallucinations

Does the patient have hallucinations such as false visions or voices? Does he/she seem to see, hear or experience things that are not present? By this question we do not mean just mistaken beliefs such as stating that someone who has died is still alive, rather we are asking if the patient actually has abnormal experiences of sounds, or visions.

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient describe hearing voices or act as if he/she hears voices?
- ☐ 2. does the patient talk to people who are not there?
- ☐ 3. does the patient describe seeing things not seen by others or behave as if he/she is seeing things not seen by others (people, animals, lights etc)?
- ☐ 4. does the patient report smelling odours not smelled by others?
- ☐ 5. does the patient describe feeling things on his/her skin or otherwise appear to be feeling things crawling or touching him/her?
- ☐ 6. does the patient describe tastes that are without any known cause?
- ☐ 7. does the patient describe any other unusual sensory experience?

A-Frequency:

- ☐ 1 occasionally – less than once per week
- ☐ 2 often – about once per week
- ☐ 3 frequently – several times per week but less than every day
- ☐ 4 very frequently – once or more per day

B-Severity:

- ☐ 1 mild – hallucinations present but seem harmless and cause little distress for the patient
- ☐ 2 moderate – hallucinations are distressing and are disruptive to the patient
- ☐ 3 marked – hallucinations are very disruptive and are a major source of behavioural disturbance. PRN medications may be required to control them.

C. Agitation/Aggression

Does the patient have periods when he/she refuses to cooperate or won't let people help him/her? Is he/she hard to handle?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient get upset with those trying to care for him/her or resist activities such as bathing or changing clothes?
- ☐ 2. is the patient stubborn, having to have things his/her way?
- ☐ 3. is the patient uncooperative, resistive to help from others?
- ☐ 4. does the patient have any other behaviours that make him/her hard to handle?
- ☐ 5. does the patient shout or curse angrily?
- ☐ 6. does the patient slam doors, kick furniture, throw things?
- ☐ 7. does the patient attempt to hurt or hit others?
- ☐ 8. does the patient have any other aggressive or agitated behaviours?

A-Frequency:

- ☐ 1 occasionally – less than once per week
- ☐ 2 often – about once per week
- ☐ 3 frequently – several times per week but less than every day
- ☐ 4 very frequently – once or more per day

B-Severity:

- ☐ 1 mild – behaviour is disruptive but can be managed with redirection or reassurance
- ☐ 2 moderate – behaviours disruptive and difficult to redirect or control
- ☐ 3 marked – agitation is very disruptive and difficult to redirect or control; there may be a threat of personal harm. Medications are often required

D. Depression/Dysphoria

Does the patient seem sad or depressed? Does he/she say that he/she feels sad or depressed?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient have periods of tearfulness or sobbing that seem to indicate sadness?
- ☐ 2. does the patient say or act as if he/she is sad or in low spirits?
- ☐ 3. does the patient put him/herself down or say that he/she feels like a failure?
- ☐ 4. does the patient say that he/she is a bad person or deserves to be punished?
- ☐ 5. does the patient seem very discouraged or say that he/she has no future?
- ☐ 6. does the patient say he/she is a burden to the family or that the family would be better off without him/her?
- ☐ 7. does the patient express a wish for death or talk about killing him/herself?
- ☐ 8. does the patient show any other signs of depression or sadness?

A-Frequency:

- ☐ 1 occasionally – less than once per week
- ☐ 2 often – about once per week
- ☐ 3 frequently – several times per week but less than every day
- ☐ 4 very frequently – essentially continuously present

B-Severity:

- ☐ 1 mild – depression is present but usually responds to redirection or reassurance
- ☐ 2 moderate – depression is distressing, depressive symptoms are spontaneously voiced by the patient and difficult to alleviate
- ☐ 3 marked – depression is very distressing and a major source of suffering for the patient

E. Anxiety

Is the patient very nervous, worried or frightened for no apparent reason? Does he/she seem very tense or fidgety? Is the patient afraid to be apart from you?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

☐ 1. does the patient say that he/she is worried about planned events?

☐ 2. does the patient have periods of feeling shaky, unable to relax, or feeling excessively tense?

☐ 3. does the patient have periods of (or complain of) shortness of breath, gasping or sighing for no other reason other than nervousness?

☐ 4. does the patient complain of butterflies in his/her stomach, or of racing or pounding of the heart in association with nervousness? (Symptoms not explained by ill health)

☐ 5. does the patient avoid certain places or situations that make him/her more nervous such as riding in the car, meeting with friends, or being in crowds?

☐ 6. does the patient become nervous and upset when separated from you (or his/her caregiver)? (does he/she cling to you to keep from being separated?)

☐ 7. does the patient show any other signs of anxiety?

A-Frequency:

☐ 1 occasionally – less than once per week

☐ 2 often – about once per week

☐ 3 frequently – several times per week but less than every day

☐ 4 very frequently – once or more per day

B-Severity:

☐ 1 mild – anxiety is distressing but usually responds to redirection or reassurance

☐ 2 moderate – anxiety is distressing, anxiety symptoms are spontaneously voiced by the patient and difficult to alleviate

☐ 3 marked – anxiety is very distressing and a major source of suffering for the patient

F. Elation/Euphoria

Does the patient seem to be too cheerful or too happy for no reason? I don't mean the normal happiness that comes from seeing friends, receiving presents, or spending time with family members. I am asking if the patient has a persistent and abnormally good mood or finds humour where others do not.

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

☐ 1. does the patient appear to feel too good or to be too happy, different from his/her usual self?

☐ 2. does the patient find humour and laugh at things that others do not find funny?

☐ 3. does the patient seem to have a childish sense of humour with a tendency to giggle or laugh inappropriately (such as when unfortunate things happens to others)?

☐ 4. does the patient tell jokes or make remarks that have little humour for others but seem funny to him/her?

☐ 5. does he/she play childish pranks such as pinking or playing "keep away" for the fun of it?

☐ 6. does the patient "talk big" or claim to have more abilities or wealth than is true?

☐ 7. does the patient show any other signs of feeling too good or being too happy?

A-Frequency:

☐ 1 occasionally – less than once per week

☐ 2 often – about once per week

☐ 3 frequently – several times per week but less than every day

☐ 4 very frequently – essentially continuously present

B-Severity:

☐ 1 mild – elation is notable to friends and family but is not disruptive

☐ 2 moderate – elation is notably abnormal

☐ 3 marked – elation is very pronounced, patient is euphoric and finds nearly everything
to be humorous

G. Apathy/Indifference

Has the patient lost interest in the world around him/her? Has he/she lost interest in doing things or lack motivation for starting new activities? Is he/she more difficult to engage in conversation or in doing chores? Is the patient apathetic or indifferent?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient seem less spontaneous and less active than usual?
- ☐ 2. is the patient less likely to initiate a conversation?
- ☐ 3. is the patient less affectionate or lacking in emotions when compared to his/her usual self?
- ☐ 4. does the patient contribute less to household chores?
- ☐ 5. does the patient seem less interested in the activities and plans of others?
- ☐ 6. has the patient lost interest in friends and family members?
- ☐ 7. is the patient less enthusiastic about his/her usual interests?
- ☐ 8. does the patient show any other signs that she doesn't care about doing new things?

A-Frequency:

- ☐ 1 occasionally – less than once per week
- ☐ 2 often – about once per week
- ☐ 3 frequently – several times per week but less than every day
- ☐ 4 very frequently – nearly always present

B-Severity:

- ☐ 1 mild – apathy is notable but produces little interference with daily routines; only mildly different from patient's usual behaviour; patient responds to suggestion to engage in activities
- ☐ 2 moderate – apathy is very evident; may be overcome by the caregiver with coaxing and encouragement; responds spontaneously only to powerful events such as visits from close relatives or family members
- ☐ 3 marked – apathy is very evident and usually fails to respond to any encouragement or external events

H. Disinhibition

Does the patient seem to act impulsively without thinking? Does he/she do or say things that are not usually done or said in public? Does he/she do things that are embarrassing to you or others?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

☐ 1. does the patient act impulsively without appearing to consider the consequences?

☐ 2. does the patient talk to total strangers as if he/she knew them?

☐ 3. does the patient say things to people that are insensitive or hurt their feelings?

☐ 4. does the patient say crude things or make sexual remarks that they would not usually have said?

☐ 5. does the patient talk openly about very personal or private matters not usually discussed in public?

☐ 6. does the patient take liberties or touch or hug others in a way that is out of character for him/her?

☐ 7. does the patient show any other signs of loss of control of his/her impulses?

A-Frequency:

☐1 occasionally – less than once per week

☐2 often – about once per week

☐3 frequently – several times per week but less than every day

☐4 very frequently – essentially continuously present

B-Severity:

☐1 mild – disinhibition is notable but usually responds to redirection and guidance

☐2 moderate – disinhibition is very evident and difficult to overcome by the caregiver

☐3 marked – disinhibition usually fails to respond to any intervention by the caregiver and is a source of embarrassment or social distress

I. Irritability/Lability

Does the patient get irritated and easily disturbed? Are his/her moods very changeable? Is he/she abnormally impatient? We do not mean frustration over memory loss or inability to perform usual tasks; we are interested to know if the patient has abnormal irritability, impatience, or rapid emotional changes different from his/her usual self.

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

☐ 1. does the patient have a bad temper, flying "off the handle" easily over little things?

☐ 2. does the patient rapidly change moods from one to another, being fine one minute and angry the next?

☐ 3. does the patient have sudden flashes of anger?

☐ 4. is the patient impatient, having trouble coping with delays or waiting for planned activities?

☐ 5. is the patient cranky and irritable?

☐ 6. is the patient argumentative and difficult to get along with?

☐ 7. does the patient show any other signs of irritability?

A-Frequency:

☐1 occasionally – less than once per week

☐2 often – about once per week

☐3 frequently – several times per week but less than every day

☐4 very frequently – essentially continuously present

B-Severity:

☐1 mild – irritability or lability is notable but usually responds to redirection and reassurance

☐2 moderate – irritability and lability are very evident and difficult to overcome by the caregiver

☐3 marked – irritability and lability are very evident, they usually fail to respond to any intervention by the caregiver, and they are a major sources of distress

J. Aberrant motor behaviour

Does the patient pace, do things over and over such as opening closets or drawers, or repeatedly pick at things or wind string or threads?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient pace around the house without any apparent purpose?
- ☐ 2. does the patient rummage around opening and unpacking drawers or closets?
- ☐ 3. does the patient repeatedly put on and take off clothing?
- ☐ 4. does the patient have repetitive activities or "habits" that he/she performs over and over?
- ☐ 5. does the patient engage in repetitive activities such as handling buttons, picking, wrapping string, etc.?
- ☐ 6. does the patient fidget excessively, seem unable to sit still, or bounce his/her feet or tap his/her fingers a lot?
- ☐ 7. does the patient do any other activities over and over?

A-Frequency:

- ☐1 occasionally – less than once per week
- ☐2 often – about once per week
- ☐3 frequently – several times per week but less than every day
- ☐4 very frequently – essentially continuously present

B-Severity:

- ☐1 mild – abnormal motor activity is notable but produces little interference with daily routines
- ☐2 moderate – abnormal motor activity is very evident; can be overcome by the caregiver
- ☐3 marked – abnormal motor activity is very evident, it usually fails to respond to any intervention by the caregiver and is a major source of distress

K. Sleep

Does the patient have difficulty sleeping (do not count as present if the patient simply gets up once or twice per night only to go to the bathroom and falls back asleep immediately)? Is he/she up at night? Does he/she wander at night, get dressed or disturb your sleep?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

- ☐ 1. does the patient have difficulty falling asleep?
- ☐ 2. does the patient get up during the night (do not count if the patient simply gets up once or twice per night only to go to the bathroom and falls back asleep immediately)?
- ☐ 3. does the patient wander, pace or get involved in inappropriate activities at night?
- ☐ 4. does the patient awaken you during the night?
- ☐ 5. does the patient awaken during the night, dress and plan to go out, thinking that it is morning and time to start the day?
- ☐ 6. does the patient awaken too early in the morning (earlier than was his/her habit)?
- ☐ 7. does the patient sleep excessively during the day?
- ☐ 8. does the patient have any other night-time behaviours that bother you that we haven't talked about?

A-Frequency:

- ☐1 occasionally – less than once per week
- ☐2 often – about once per week
- ☐3 frequently – several times per week but less than every day
- ☐4 very frequently – once or more per day

B-Severity:

- ☐1 mild – night-time behaviours occur but they are not particularly disruptive
- ☐2 moderate – night-time behaviours occur and disturb the patient and the sleep of the caregiver; more than one type of night-time behaviour may be present
- ☐3 marked – night-time behaviours occur; several types of night-time behaviour may be present; the patient is very distressed during the night and the caregiver's sleep is markedly disturbed

L. Appetite and eating disorders

Has he/she had any change in appetite, weight, or eating habits (count as NA if the patient is incapacitated and has to be fed)? Has there been any change in type of food he/she prefers?

☐ not applicable ☐ no (proceed to next screening question) ☐ yes (proceed to subquestions)

☐ 1. has he/she had a loss of appetite?

☐ 2. has he/she had an increase in appetite?

☐ 3. has he/she had a loss of weight?

☐ 4. has he/she gained weight?

☐ 5. has he/she had a change in eating behaviour such as putting too much food in his/her mouth at once?

☐ 6. has he/she had a change in the kind of food he/she likes such as eating too many sweets or other specific types of food?

☐ 7. has he/she developed eating behaviours such as eating exactly the same types of food each day or eating the food in exactly the same order?

☐ 8. Have there been any other changes in appetite or eating that I haven't asked about?

A-Frequency:

☐1 occasionally – less than once per week

☐2 often – about once per week

☐3 frequently – several times per week but less than every day

☐4 very frequently – once or more per day

B-Severity:

☐1 mild – changes in appetite or eating are present but have not led to changes in weight and are not disturbing

☐2 moderate – changes in appetite or eating are present and cause minor fluctuations in weight

☐3 marked – obvious changes in appetite or eating are present and cause fluctuations in weight, are embarrassing, or otherwise disturb the patient

NPI-D

Item	N.Ap [†]	Absent [†]	Frequency*	Severity*	F*S
Delusion	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Hallucination	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Agitation	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Depression/dysphoria	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Anxiety	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Euphoria/elation	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Apathy/indifference	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Disinhibition	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Irritability/lability	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Aberrant motor behaviour	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Night-time behaviour	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]
Appetite/Eating change	<input type="checkbox"/>	<input type="checkbox"/>	1 2 3 4	1 2 3	[][]

[†] Please tick when relevant; then do not complete the following corresponding numbered items (frequency, severity, F*S, and distress).

* Please circle the right answer; one answer only by domain.

MINI-MENTAL STATE EXAMINATION

Total score: _____ /30

1.1.1.1 Orientation:

What is the – year season date day month ?

5 _

Where are we now? – country city/county town/borough road/street
number/name of facility

5 _

1.1.1.2 Registration:

Ask the patient to repeat and then remember the following three objects:

APPLE TABLE PENNY (allocate one second to say each word and then ask the patient to name all three objects after you have said them.) Give one point for each correct answer given. Make sure that you have repeated them until the patient has clearly heard. Do not prompt any answers. Count the trials and record number of attempts.

3 _

Attention and calculation:

Ask the patient to begin with 100 hundred and count backwards removing 7 from the total each time and stop after 5 answers i.e. 93, 86, 79, 72, 65.

Score one point for each correct answer. It is fine to repeat the instruction whilst the patient is completing the task.

If the patient refuses to perform this task, ask them to spell the word **WORLD** backwards i.e. **DLROW**. Record the patient's spelling _____

5 _

Recall:

Ask the patient to recall the three items that they were previously asked to remember (see registration section). Give one point for each correct answer given. Do not prompt any answers. **APPLE TABLE PENNY**

3 _

1.1.1.3 Language:

Naming:

Show the patient a **pencil** and then a **wristwatch** and ask the patient to name them. Do not prompt and do not accept descriptions e.g. a writer or a time-teller. Score one point for each correct answer.

2 _

Repetition:

Speak slowly and clearly and ask the patient to repeat the following saying,

"no ifs ands or buts"

1 _

Three stage command:

Ask the patient to listen carefully and then to follow the following task. "Please take this paper in your **right hand**....**fold it in half**.....and then **place it on the table**. Score one point for each correct performance. Once the task has commenced do not prompt.

3 _

Reading:

Show the patient the second sheet and ask them to read the top line (close your eyes) and follow the task. Score 1 point only if they complete both instructions.

1 _

Writing:

Ask the patient to write any sentence they like on the second sheet. Score only if the sentence makes grammatical sense.

1 _

Copying:

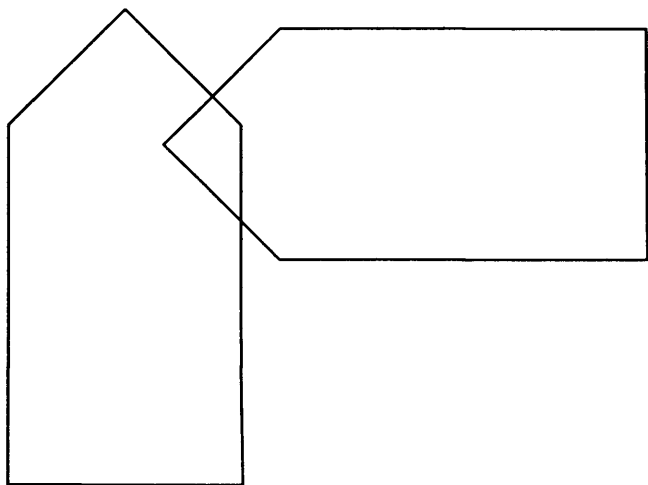
Ask the patient to copy the intersecting pentagon design on the second page.

1 _

CLOSE YOUR EYES

Please write a sentence below:

Please copy the diagram below:



Word Count =3,930 excluding abstract, tables/figures and references

Coping strategies as predictors of anxiety and depression in carers of people with Alzheimer's disease: The LASER-AD longitudinal study

Running title: Coping and anxiety and depression in dementia carers

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Background: There have been few longitudinal studies investigating the impact of coping on psychological morbidity in Care Givers of people with dementia (CG), and those have conflicting or unreplicated findings. Anxiety is relatively neglected in this group. **Methods:** 126 people with Alzheimer's disease and their family carers were recruited, of whom 95(75.4%) were re-interviewed a year later. Sampling was designed to ensure that the participants were representative of people living in the UK with Alzheimer's disease in terms of dementia severity, gender and care setting. We used the Hospital Anxiety and Depression Scale to measure carer anxiety, and Brief COPE to measure coping strategies, and explored our hypothesis that the relationship between carer burden and anxiety and depression is mediated by coping style. **Results:** Using fewer emotion-focussed strategies and more problem-focussed strategies (but not dysfunctional strategies) mediated the relationship between carer burden and anxiety a year later, after controlling for potential confounders. Using fewer emotion focussed strategies also predicted higher psychological morbidity in general.

Conclusion: Carers who used more emotion-focussed coping strategies in response to carer burden were protected from developing higher anxiety levels a year later, while those using problem-focussed strategies were not. Most current psychological interventions are based on problem-solving coping strategies, but our results suggest that a psychological intervention package to encourage emotion-focussed coping may be a rational approach to reduce anxiety in dementia carers. Studies are needed to test such interventions.

Introduction

The number of people with dementia is projected to double every 20 years until 2040 and the number of family carers will therefore also rise (Ferri et al. 2005). Caring for people with dementia is stressful and can have important negative consequences, including psychiatric morbidity (Pinquart & Sorensen, 2003; Schulz et al., 1995) which is in turn associated with care recipient (CR) institutionalisation (Morris et al., 1988). Similar prevalence rates have been reported for clinically significant anxiety (10-35%) and depression (10-34%) in Care Givers of people with dementia (CG) (Coope et al. 1995; Dura et al 1991; Mahoney et al. 2005; Neundorfer 1991; Russo et al. 1995; Vitaliano et al. 1991), but most carer mental health literature has focused on depression and overall psychiatric morbidity, and little is known about factors predicting CG anxiety.

Life events (Kessler et al., 1997) and coping strategies (Silver et al., 2002) are known to predict affective illnesses in the general population, but have been considered less in carers, as researchers have focussed on the stresses of caring and the illness of the CR. Coping strategies are behavioural and psychological efforts employed to overcome, tolerate or reduce the impact of stressful events, in this case the stress of caring for someone with dementia. Problem-solving strategies are efforts to change the stressful circumstances, whereas emotion-focused coping strategies involve efforts to regulate the emotional consequences of the stressor. The literature is complicated by the tendency of some instruments to group helpful (acceptance, humour, religion, positive reframing) and non-helpful (venting, denial) emotion-focussed strategies together. Carver et al (1989) separated these, employing the term 'emotion-focussed' for helpful emotion-focussed strategies alone, and 'dysfunctional' for strategies that are generally accepted as being unhelpful.

In our cross-sectional study from baseline data of the LASER-AD cohort, dysfunctional coping was strongly associated with clinically significant anxiety, whereas, after confounders and mediators were taken into account emotion-focussed and problem-focussed coping were not (Cooper et al. 2006a) . Other cross-sectional studies in this area have reported inconsistent results; finding the use of problem-based coping

strategies to be unrelated to or associated with higher or decreased rates of CG psychological morbidity including anxiety (Morano et al., 2003; Vedhara et al., 2001; Hinrichsen et al., 1994; Neundorfer et al., 1991; Mckee et al. 1997; Pruchno & Resch 1989). Studies using scales that include problem-focussed and emotion-focussed coping strategies (Haley et al. 1996; Almberg et al, 1997) or emotion-focussed items alone (Gallagher et al. 1994; Saad et al. 1995) have by contrast reported more favourable CG psychological outcomes. The only two studies to explore the relationship of CG anxiety to emotion-focussed coping strategies were small, probably underpowered, and did not report a significant relationship (Neundorfer, 1991; Vedhara et al., 2001). Dysfunctional coping strategies have been consistently associated with adverse caregiver outcomes in cross-sectional studies, including increased depression (Haley et al. 1996; Mausbach et al. 2006; Neundorfer, 1991) and anxiety (Neundorfer MM 1991; Vedhara et al., 2001). Many of these studies included CG recruited from clinical or convenience samples, and omitted potentially important confounders. Unlike our study, none used accepted subscales to measure emotion-focussed, problem-focussed and dysfunctional strategies separately. This may explain why the results of these studies differ from ours.

Coping strategies are potentially a target for interventions to relieve distress in CG, but before expending resources to develop these it is important to determine which, if any, coping styles protect from or predict subsequent CG morbidity. This requires evidence from longitudinal studies and there are few in this area. Goode and colleagues (1998) found that a coping scale that included problem-focussed and emotion-focussed strategies mediated an effect between primary stressors and decreased depression a year later. Vitaliano and colleagues (1991) found that only emotion-focussed strategies and not problem-based strategies studied predicted subsequent caregiver burden 15-18 months later, but in a second study the emotion-focussed strategy of "management of meaning" was not associated with anxiety a year later (Winslow 1997). A small longitudinal study which used a non- standardised measure of anxiety and depression found that dysfunctional coping strategies predicted greater anxiety, depression and self-

perceived stress, but emotion-focussed and problem-focussed strategies did not six months and a year later (Vedhara et al. 2001). In summary, while there is both a lack of and conflicting evidence in the existing literature regarding the impact of all three types of coping strategy on CG anxiety and depression longitudinally, several studies show a relationship between coping style and carer outcome.

We therefore hypothesised that carer coping styles mediate the relationship between carer burden and anxiety a year later. In order to test this hypothesis, we carried out a prospective follow-up of the cohort from our cross-sectional study. Our specific hypotheses were that use of (1) more dysfunctional (unhelpful emotion-focussed) coping strategies (2) fewer problem-focussed strategies (3) fewer (helpful) emotion-focussed strategies would mediate a relationship between carer burden at baseline and anxiety score a year later.

Method

Participants

The current study is part of a longitudinal study of people with Alzheimer's disease and their carers (and draws on data from the 18 and 30 month follow-up of participants from inner-city, suburban, semi-rural, and new town areas in London and South-East Region of England (**LASER-AD**) (Livingston et al. 2004; Regan et al. 2005). Recruitment was initially purposeful to ensure that the sample was representative in terms of dementia severity, gender and care setting (Fratiglioni, 1998). Participants were contacted through local psychiatric services, the voluntary sector and nursing and residential care homes. Inclusion criteria comprised having a CR with DSM-IV diagnoses of dementia (American Psychiatric Association 1994) and a diagnosis of AD using standardised criteria (McKhann et al. 1984) and a carer who spent at least four hours a week caring for the CR.

We originally interviewed 224 CR and their carers, of whom 193 had a family carer (baseline). 126 of these family carers were included in our study at Time 1 (T1). Of those not included, 41 had cared for someone who had subsequently died between baseline

and T1, 18 were no longer caring and 8 refused. 95(75.4%) were re-interviewed a year later at Time 2 (T2). Reasons for non-participation at T2 by those interviewed at T1 were: 13 cared for someone who had died since T1, 8 refused, one moved too far away and 9 were no longer caring.

Data collection

Local Research Ethics Committees for the areas in which the study was conducted gave approval. After complete description of the study to the subjects, written informed consent was obtained. Where the CR did not have capacity to consent, we asked carers whether they thought the CR would have agreed to participate if they could. We only proceeded where the carer was happy for us to do so and the CR assented and we terminated the interview if the interviewee became distressed or appeared not to want to continue. Trained researchers collected information about the following factors, selected because they had previously been associated with carer anxiety in our systematic review of the correlates of anxiety in CG (Cooper et al., 2006b).

Carer data

We collected socio-demographic data: age, gender, relationship to CR, marital status, level of education, and hours spent caring; whether they had ever seen a professional for emotional problems (as a measure of previous mental health problems). As a measure of perceived instrumental and emotional support, we asked about the number of friends of family who they could talk to about matters that were very personal or private. This measure forms part of the Close Persons Questionnaire (Stansfeld & Marmot 1992), with items on work colleagues omitted. In addition carers completed:

Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith 1983) . This instrument has previously been used for CG. It does not include somatic items (which can be misleading in older subjects) and has been validated throughout the age range and in all settings to identify clinically significant anxiety and depression (Bjelland et al. 2002). It assesses how the person has been feeling within the past week; it consists of

two seven-item subscales, each scored 0-3, which generate scores for generalised anxiety and depression (0-21). A score of ≥ 8 implies caseness; we used this cut-off as it is reported to achieve optimal balance between sensitivity and specificity for clinically significant anxiety (Bjelland et al, 2002).

Brief COPE (Coping Orientations to Problems Experienced scale) (see Figure 1). This is a self-report questionnaire with fourteen subscales describing different coping strategies, (two items per scale) with satisfactory psychometric properties (Carver 1997). It has been used previously to measure coping in CG (Crespo et al., 2005). Carers were asked to score each strategy from 1 (not doing it at all) to 4 (doing it a lot). We used three subscales of the COPE (Coolidge et al. 2000): problem-focussed, emotion-focussed and dysfunctional coping.

The Social Readjustment Rating Scale (Holmes & Rahe 1967) was used to measure life events. This lists 43 positive and negative life events, and gives a value between 1 and 100 for each. A total score indicating the impact of these events on the carer's life over the previous 6 months was calculated. This measure sums all events, and does not distinguish positive from negative events. A consensus panel of three of the authors (CC, GL, MO) agreed which of these were negative life events representing a *serious* threat as defined by Brugha et al (1985), that is whether they were likely to have a significant negative impact on the person persisting for one week or more after the event.

The Zarit Burden scale (Zarit et al. 1980) for carer burden, a 22-item self-report questionnaire, is the most consistently used measure of carer burden. It has a high internal consistency and construct validity (Hebert et al. 2003). "Carer burden" encompasses the physical, psychological, social, and financial demands of caring for someone.

The Health Status Questionnaire (HSQ-12) is a quality of life instrument. Three of its domains measure physical health: health perception, role physical and physical functioning (Pettit et al. 2001; Radosevich & Pruitt 1995). For health perception, carers were asked to rate their health on a Likert scale. For physical functioning, they were asked about how their health limited activities such as climbing stairs, a higher score

indicating fewer physical limitations. For role physical, people were asked how their physical health problems limited them in their daily activities, and asked to score this on a five point Likert scale.

Quality of Life - Alzheimer's disease (QoL-AD) (Lodgson et al. 1996). One item from the QoL-AD was used where carers rated the quality of their current relationship with the CR on a 4-point scale, from 1(poor) to 4(excellent).

Care Recipient data

We recorded whether the CR was living independently (in their own home or in supported accommodation) or in an institutional setting (care home or hospital). We used the Mini Mental State Examination (MMSE) (Folstein, et al 1975) and the Alzheimer's Disease Assessment Scale-Cognition (ADAS-Cog) (Rosen et al., 1984) to measure cognition; the Alzheimer's Disease Co-operative Study Inventory - activities of daily living (ADCS-ADL) scale (Galasko et al. 1997) for function; and the Neuropsychiatric Inventory (total score and score on the irritability subscale) to measure neuropsychiatric symptoms (Cummings et al. 1994).

Power Calculation

In order to detect a moderate (0.4 or above) correlation (with no correlation as the alternate hypothesis) between coping and anxiety scores at a significance level of 0.01 and power of 90%, a minimum of 87 carers would be required. Our sample size was thus adequate allowing for refusals and dropouts.

Statistical analysis

We used two-tailed tests throughout, and (in the light of the high number of statistical tests) $p < 0.01$ to indicate significance on univariate analysis. We used parametric tests for normally distributed data (defined as skewness statistic < twice standard error of the skewness mean) and otherwise non-parametric tests of significance. We tested our main hypothesis that coping strategies mediated the relationship between carer burden at T1

and anxiety score at T2, using Baron and Kenny criteria (Baron & Kenny 1986) to define mediation. Using SPSS version 12.0, we tested the association between carer HADS anxiety scores at T2 and mean scores on subscales of the brief COPE (using regression to enable relative scores to be considered) and other suggested risk factors (using appropriate univariate tests) which might be confounders. We also examined the Pearson's correlation coefficients for the relationship between the coping strategy scores and burden. We then conducted a stepwise linear regression. On step one, we entered burden score. On step two we entered T1 coping scores; on step three we entered baseline anxiety score; on step four we entered coping strategy subscale scores from T2, and on step five we entered all the other factors studied that approached significance ($p < 0.1$) on univariate analysis (Table 2). We repeated this analysis with HADS depression score as the dependent variable.

In order to ensure that collinearity did not affect our results, we then used structural equation modelling for confirmation of the model that emerged from these analyses. The factors were entered into a model using AMOS version 6 (Arbuckle, 2003). To obtain the most parsimonious model we used the accepted criterion that associations between variables were removed from the saturated model if the rise in χ^2 for the model (which tests the null hypothesis that the model could have occurred by chance) is smaller than the critical value for that association. We report the Normed Fit Index (NFI; a measure from 0 to 1 (perfect fit) of the extent to which the model fits the data); χ^2 test for the final model, and unstandardised regression estimates for each association. NFI ≥ 0.9 (Bentler & Bonett 1980) is generally accepted as evidence of a well fitting model.

Results

Ninety-five (75.4%) of family carers interviewed at time 1 were re-interviewed a year later. 31 carers were not re-interviewed - because the CR died ($n=13$), the carer refused ($n=8$), they had moved too far away ($n=1$) or they were no longer caring ($n=9$). Those not re-interviewed were more likely to be caring for someone with greater neuropsychiatric and ADL problems. There was also a non-significant trend towards them being more anxious

at T1, and this was accounted for by a high rate of baseline anxiety in those who refused to be re-interviewed (6/8) (Table 1). The only T1 factors studied that were significantly associated with anxiety score at T2 on univariate analysis were total burden score and self-rated health perception (see Table 2). Anxiety score at T2 was associated with: using relatively fewer emotion-focussed ($t=-2.1$, $p=0.039$), and more problem-focussed ($t=2.5$, $p=0.016$) and dysfunctional coping ($t=2.8$, $p=0.007$) at T1.

Dysfunctional ($r=0.58$; $p<0.001$), emotion-focussed ($r=0.34$; $p=0.001$) and problem-focussed coping strategy scores ($r=0.46$, $p<0.001$) were all significantly correlated with carer burden score at T1. On linear regression, caregiver burden was a significant predictor of T2 anxiety score ($t=3.1$, $p=0.002$) on step one; using more problem-focussed strategies at T1 ($t=2.2$; $p=0.028$) was the only predictor on step two; T1 anxiety score ($t=10.5$; $p<0.0005$), using fewer emotion-focussed ($t=-2.0$; $p=0.046$) and more problem-focussed strategies at T1 ($t=2.3$; $p=0.023$) were the only significant predictors on step three; T1 anxiety score ($t=9.2$; $p<0.0005$) and using fewer emotion-focussed strategies at T1 ($t=-0.13$; $p=0.036$) were the predictors on step four. In the final model, which explained 74.3% of T2 anxiety score variance and fully mediated the relationship between T1 burden and T2 anxiety scores, T1 anxiety score ($t=8.8$; $p<0.0005$), using relatively fewer emotion-focussed strategies ($t=-2.3$; $p=0.023$) and more problem-focussed strategies at T1 ($t=2.2$; $p=0.034$) and higher health perception at T1 ($t=-2.8$; $p=0.007$) were the only significant predictors (Table three).

Structural Equation Model

We entered coping strategy, burden and anxiety scores into a model. Figure 2 demonstrates the “best fit model” for these factors ($\chi^2=17.3$, $df=19$, $p=0.57$); this indicates that the null hypothesis, that our proposed model for the relationship of the coping, burden and anxiety scores was supported; a p value <0.05 would have indicated this model was disproved. The normed fit index was 0.96. The model confirms findings from the exploratory analyses that fewer emotion-focussed strategies and more problem-

focussed strategies mediated the relationship between carer burden and anxiety a year later, after controlling for potential confounders, but this relationship was not mediated by use of dysfunctional strategies.

Depression and coping

Depression score at T2 was significantly associated with: spending more time caring and caregiver burden on univariate analysis (Table two), and with dysfunctional ($t=2.2$, $p=0.027$) but not with emotion-focussed ($t=-1.01$, $p=0.31$) or problem-focussed ($t=1.0$, $p=0.30$) scores at T1. Repeating the above linear regression with depression score at T2 as the dependent variable, carer burden was a significant predictor of T2 depression score ($t=3.3$, $p=0.002$) on step one. On step two there were no predictors. On steps three and four only baseline depression score ($t=8.9$; $p<0.001$; $t=8.6$, $p<0.001$) predicted depression score at T2. In the final model, only depression score at T1 ($t=6.6$, $p<0.001$) and reporting ever consulting a professional about emotional problems ($t=2.5$, $p=0.016$) were significant factors, while using fewer emotional coping strategies ($t=-1.8$, $p=0.083$) was the only other factor to approach significance. Thus the hypothesis that coping mediated the relationship between burden and depression score a year later was not proved.

Overall psychological morbidity

In a post-hoc analysis, we repeated our linear regression analysis using total HADS score as the dependent variable, and including factors that approached a significant association with anxiety or depression score on univariate analysis in step five. Burden was a significant predictor on step one ($t=3.3$, $p=0.002$), and in the final model the only significant predictors were T1 emotion-focussed ($t=-2.5$, $p=0.016$) and problem-focussed coping ($t=1.9$, $p=0.050$), T1 total HADS score ($t=8.4$, $p<0.001$); ever having consulted a professional for emotional problems ($t=2.1$, $p=0.036$), and health perception HSQ score (-2.2 , $p=0.030$).

Discussion

This is the first longitudinal study to examine the role of coping in predicting anxiety in carers, and the first epidemiologically representative study to explore the relationship between coping and depression longitudinally. Using multivariate analysis, the only independent predictors of anxiety at one-year follow-up were using fewer emotion-focussed and more problem-focussed strategies, anxiety score and more positive health perception at baseline. Together with our findings that carer burden was significantly related to anxiety and coping scores on univariate analyses, this demonstrates that emotion-focussed and problem-focussed coping strategies mediate the relationship between burden and anxiety scores a year later (Baron & Kenny 1986). We confirmed these findings using structural equation modelling.

Our model demonstrates that carers responded to increasing burden with increased use of all three types of coping strategy. Those that particularly used problem-focussed strategies were more anxious a year later, indicating that these strategies did not, contrary to our hypothesis, protect against the impact of greater burden on psychological wellbeing. However, those that responded by using more emotion-focussed strategies (religion, emotional support, positive reframing, acceptance and humour) were less anxious a year later, upholding our second hypothesis, that use of these strategies is protective. Carers who used more dysfunctional strategies in response to burden were more anxious and most remained more anxious a year later, but those who used dysfunctional coping strategies but did not become anxious were no more likely to become highly anxious over the next year.

Problem-focussed strategies are widely accepted as being helpful to CG and associated with lower levels of morbidity cross-sectionally (Kneebone & Martin 2003) but in this, the first epidemiologically representative longitudinal study, we did not find them to be protective a year later. Perhaps anxious CG seek out information about coping, so know which strategies might be helpful and employ them maximally to try and bring caring situations under control. However, they also utilise the less helpful dysfunctional strategies and use fewer helpful emotion-focussed strategies and so become anxious nonetheless. Some of the problems associated with caregiving are intractable, so

perhaps successful coping for caregiver for people with a degenerative disease involves adapting emotionally rather than continuing with problem-focussed strategies that in the long term might prove to be frustrating and ineffective.

Clinical implications

Strengths of the study include the relatively large sample size, representative sampling and the comprehensive inclusion of potential mediators and confounders. The findings that emotion-focussed coping strategies protected those experiencing burden from higher anxiety levels a year later suggests that future interventions to reduce carer anxiety in dementia should focus on which psychological coping strategies carers use. This seems to be more important than all other factors including CR psychiatric symptoms and hours of care provided. This study provides a strong rationale for a well powered randomised controlled trial of a psychological therapy for anxiety, aimed at enhancing helpful emotion-focussed coping strategies, and reducing dysfunctional coping which led to greater anxiety immediately that persisted. As carer psychiatric morbidity is associated with CR institutionalisation there may be economic as well as health benefits to such an intervention. Emotion-focussed coping was also an important mediator of the impact of carer burden on overall psychological morbidity a year later, suggesting that such an intervention might also reduce overall psychological morbidity. Coping strategies were not predictive of depression by itself a year later, but as less use of emotion-focussed strategies approached significance on multivariate analysis, it seems likely that this was because our study was underpowered to detect this relationship due to the lower levels of depression in the sample. Emotion-focussed strategies have also been demonstrated to protect against mental health problems in other populations, for example carers of people with Multiple Sclerosis (Pakenham 2005) and the general USA population after the September 11th, 2001 terrorist attacks (Silver et al., 2002), so coping interventions based on emotion-focussed coping may be applicable across a range of populations.

Our results do not support the use of psychological interventions based on teaching problem-focussed strategies. We do not know how the anxious carers in this study were

evaluating situations and whether they were already selecting appropriate problem-focussed strategies. Our findings might explain why evidence is inconsistent for use of Cognitive Behavioural Therapy based interventions to treat anxiety morbidity in CG, as teaching and implementing problem-based strategies is a key component (Selwood et al. 2007). Further interventions for carers involving problem-based coping should perhaps focus on evaluating stressors and applying strategies effectively and not on didactic teaching of problem-focused strategies. Our results would support pilot studies investigating the impact of interventions, which focus on developing emotion-focussed strategies such as acceptance in CG.

Limitations

The extent to which participants' answers on coping strategy measures relate to how they actually manage caring situations is debatable (Kneebone & Martin 2003), and anxious carers may be more likely to report their coping strategies negatively. We asked all carers about how they cope with problems that arise in caring, but inevitably they will have been managing different situations. The generic measure we used to assess coping styles may not have fully captured the particular challenges associated with dementia caregiving. Those carers who were anxiety cases at T1 were more likely to refuse to be re-interviewed but as there were few refusals ($n=8$), we think our results are still applicable. Our sample size was insufficient to look separately at CR living with carers and those in institutional care.

Conclusions

Carers who used more emotion-focussed coping strategies in response to carer burden were protected from higher anxiety scores a year later, while those using problem-focussed strategies were not. There are no published randomised controlled trials of interventions to relieve psychological distress in CG which include anxiety as a primary outcome measure and demonstrate sufficient power to detect a clinically significant result (Cooper et al. 2006c). A randomised controlled trial of a psychological intervention

package to increase emotion focussed coping is therefore indicated to test this rational approach to reducing anxiety in CG.

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Figure 1: The Brief COPE (Carver et al., 1997)

<p>Emotion-focussed strategies</p> <p>acceptance (accepting the reality of the fact that it has happened/ learning to live with it)</p> <p>emotional support (getting emotional support/ comfort and understanding from others)</p> <p>humour (making jokes about it/ making fun of the situation)</p> <p>positive reframing (trying to see it in a different light, make it seem more positive/ look for something good in it)</p> <p>religion (trying to find comfort in my religious or spiritual beliefs/ praying or meditating)</p>
<p>Problem-focussed strategies</p> <p>active coping (concentrating my efforts on doing something about the situation I'm in/ taking action to try to make it better)</p> <p>instrumental support (getting help and advice from other people/ trying to get advice or help from others about what to do)</p> <p>planning (trying to come up with a strategy about what to do/ thinking hard about what steps to take)</p>
<p>Dysfunctional coping strategies</p> <p>behavioural disengagement (giving up trying to deal with it/ the attempt to cope)</p> <p>denial (saying to myself "this isn't real" /refusing to believe that it has happened)</p> <p>self-distraction (turning to work or other activities to take my mind off things/ doing something to think about it less)</p> <p>self-blame (criticising myself/ blaming myself for things that happened)</p> <p>substance use (using alcohol or other drugs to make myself feel better/ to help me get through it)</p> <p>venting (saying things to let my unpleasant feelings escape/ expressing my negative feelings)</p>

Figure 2: Model demonstrating the association of coping strategies, burden and anxiety score at T1 and T2 (numbers by arrows represent unstandardised regression coefficients; e= latent error)

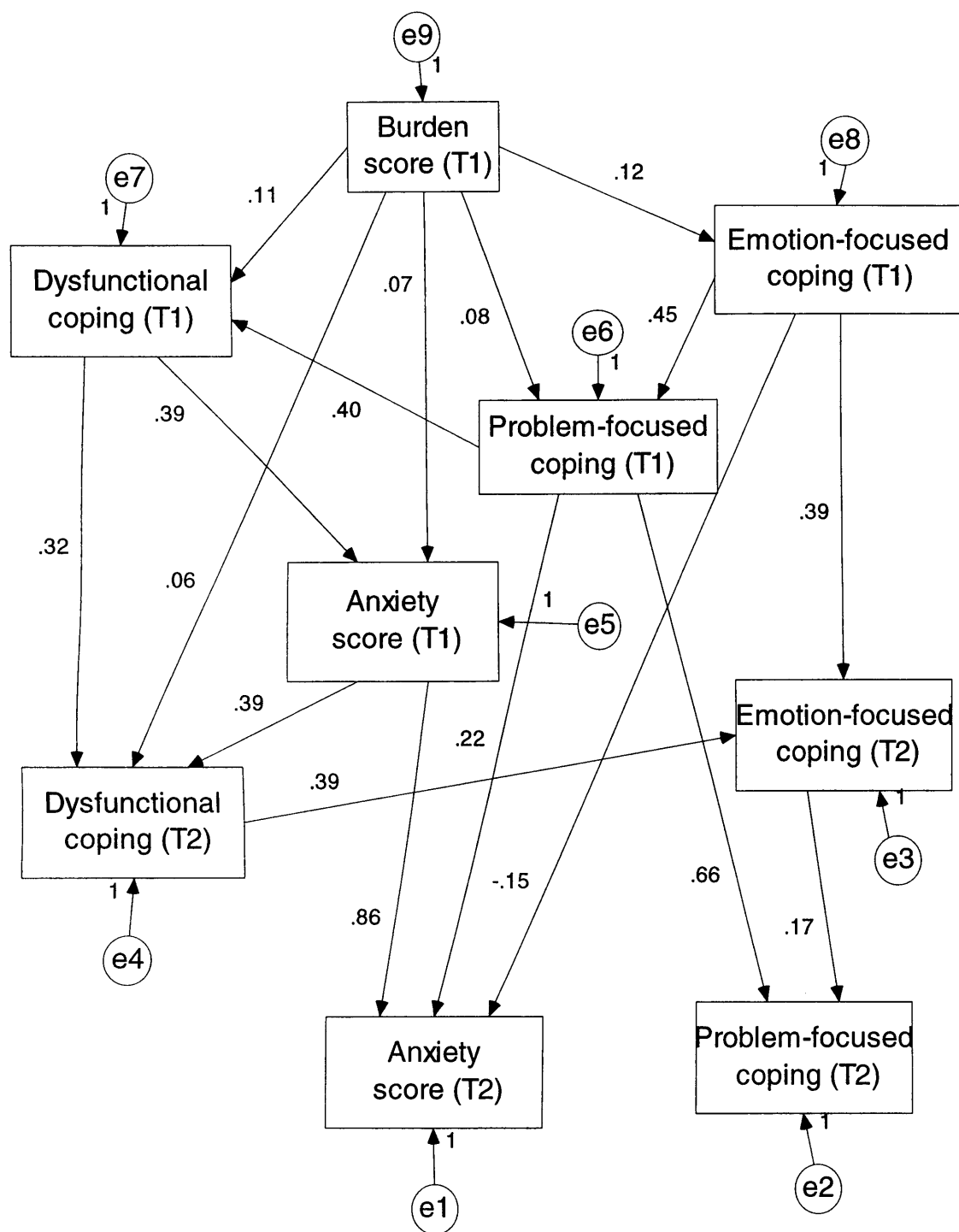


Table 1: A comparison of socio-demographic and morbidity characteristics of those recruited at baseline who were followed up at T2 and those who were not

Factor		Mean (%) in those reinterviewed (n=95)	mean (%) in those NOT reinterviewed (n=31)	χ^2/t	Significance
Carer	female	60(63.2%)	22(71.0%)	$\chi^2=0.63$	0.43
	age	63.7(14.7)	65.7(11.6)	t=0.81	0.47
	spouse of CR	42(44.2%)	12(38.7%)	$\chi^2=0.29$	0.59
	lives with CR	51(53.7%)	11(35.5%)	$\chi^2=3.1$	0.078
	burden score	26.6(14.1)	30.4(15.5)	t=1.3	0.20
	Anxiety score	5.7(4.0)	8(5.5)	t=2.5	0.012
Care recipient	MMSE	14.7(8.9)	11.4(9.3)	t=1.8	0.080
	NPI	17.7(14.7)	27.1(17.9)	t=2.9	0.004
	ADL-ADCS	33.7(21.3)	21.4(18.4)	t=2.9	0.004
	in 24 hour care	24(25.3%)	13(41.9)	$\chi^2=3.1$	0.077

Table 2: Factors at T1 and their univariate associations with anxiety and depression score at T2

Factor studied		n	Anxiety score			Depression score		
			Mean (sd)	t or r (correlation coefficient)	p	Mean (sd)	MWU or r (correlation coefficient)	p
CG gender	Male	34	5.6(4.0)	0.91	0.37	4.1(2.7)	932	0.57
	Female	59	6.5(4.7)			4.1(3.8)		
CG age		93		0.59	0.57		0.26	0.011
Carer married/ cohabiting	yes	76	5.9(4.5)	1.1	0.28	4.6(2.9)	531	0.025
	no	17	7.2(4.1)			4.0(3.5)		
Carer level of education	O Level or below	52	6.4(4.6)	1.0	0.31	4.60(3.7)	659.5	0.16
	Post 16 education	31	5.4(4.0)			3.32(2.8)		
CG hours spent caring		78		0.14	0.17		0.41	<0.001
CR in 24 hour care	yes	22	7.2(4.5)	1.3	0.21	3.9(3.2)	746	0.75
	no	71	5.8(4.4)			4.2(3.5)		
CR spouse/ partner of carer	yes	42	6.7(4.3)	1.0	0.31	4.9(3.3)	752	0.013
	no	51	5.7(4.6)			3.4(3.4)		
Relationship with CR "good/excellent"	yes	74	6.0(4.6)	0.62	0.54	3.9(3.4)	597	0.31
	no	19	6.7(4.2)			4.8(3.5)		

Carer ever had consult for mental health problems	yes	25	7.9(4.4)	2.3	0.022	5.4(3.8)	595	0.032
	no	67	5.5(4.4)			3.6(3.2)		
No. confidants for personal/ private matters		91		-0.043	0.69		-0.099	0.35
Life event score (in last 6 months)		92		0.20	0.057		0.10	0.32
Serious, threatening life event	yes	43	6.9(4.8)	1.4	0.15	5.0(3.8)	778	0.030
	no	49	5.5(4.3)			3.2(2.8)		
Serious, independent life event	Yes	17	7.71(5.2)	1.6	0.11	5.8(3.9)	433	0.038
	No	75	5.79(4.3)			3.7(3.2)		
Zarit burden score		95		0.37	<0.001		0.33	0.001
Carer physical health	Health perception	93		-0.34	0.001		-0.41	<0.001
	Physical functioning	93		-0.26	0.013		-0.36	<0.001
	Role physical	93		-0.25	0.018		-0.31	0.002
MMSE		93		-0.19	0.075		-0.043	0.69
ACDS-ADL		93		-0.18	0.094		-0.068	0.52
NPI Total score		93		0.14	0.17		0.19	0.063
NPI irritability score 4+	Yes	13	7.85(5.2)	-1.46	0.15	6.4(4.5)	337	0.041
	No	80	5.19(1.4)			3.7(3.1)		
ADAS-Cog		93		0.20	0.055		0.047	0.66

Table 3: Linear regression of factors associated with anxiety score at T2

	R squared	Factor	Standardised Beta	t	P
Step 1	0.100	Carer burden	0.316	3.122	0.002
Step 2	0.223	Carer burden	0.122	1.057	0.293
		Dysfunctional coping T1	0.254	1.962	0.053
		Emotion-focused coping T1	-0.256	-1.984	0.051
		Problem-focused coping T1	0.324	2.238	0.028
Step 3	0.665	Carer burden	-0.037	-0.476	0.635
		Dysfunctional coping T1	-0.010	-0.115	0.909
		Emotion-focused coping T1	-0.174	-2.026	0.046
		Problem-focused coping T1	0.223	2.315	0.023
		Anxiety score T1	0.776	10.526	<0.0005
Step 4	0.668	Carer burden	-0.045	-0.556	0.580
		Dysfunctional coping T1	-0.027	-0.279	0.781
		Emotion-focused coping T1	-0.199	-0.127	0.036
		Problem-focused coping T1	0.237	1.877	0.064
		Anxiety score T1	0.755	9.159	<0.0005
		Dysfunctional coping T2	0.042	0.432	0.667
		Emotion-focused coping T2	0.050	0.586	0.559
		Problem-focused coping T2	-0.018	-0.174	0.862
Step 5	0.743	Carer burden	-0.100	-1.260	0.212
		Dysfunctional coping T1	-0.014	-0.143	0.887
		Emotion-focused coping T1	-0.210	-2.325	0.023
		Problem-focused coping T1	0.279	2.159	0.034
		Anxiety score T1	0.746	8.794	<0.0005
		Dysfunctional coping T2	-0.047	-0.450	0.654

	Emotion-focused coping T2	0.048	0.582	0.562
	Problem-focused coping T2	0.030	0.293	0.770
	Health perception score	-0.262	-2.769	0.007
	Consultation for emotional problems	0.087	1.343	0.183
	Total life event score	-0.073	-1.059	0.293
	Physical functioning score	0.031	0.345	0.731
	Role physical score	0.040	0.382	0.704
	ADAS-Cog total score	0.155	0.680	0.499
	ADCS-ADL total score	-0.056	-0.491	0.625
	MMSE score	0.046	0.205	0.838

References

- Almberg, B., Grafstrom, M., & Winblad, B. 1997c, "Major strain and coping strategies as reported by family members who care for aged demented relatives", *Journal of Advanced Nursing*, vol. 26, no. 4, pp. 683-691.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th edition). 1994. Washington DC, American Psychiatric Association.
- Arbuckle JL. Amos 5.0 Update to the Amos User's Guide. [Smallwaters Corporation, Chicago IL.]. 2003. Chicago IL., Smallwaters Corporation.
- Baron, R. M. & Kenny, D. A. 1986, "The Moderator Mediator Variable Distinction in Social Psychological-Research - Conceptual, Strategic, and Statistical Considerations", *Journal of Personality and Social Psychology*, vol. 51, no. 6, pp. 1173-1182.
- Bentler, P. M. & Bonett, D. G. 1980, "Significance Tests and Goodness of Fit in the Analysis of Covariance-Structures", *Psychological Bulletin*, vol. 88, no. 3, pp. 588-606.
- Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. 2002, "The validity of the Hospital Anxiety and Depression Scale: An updated literature review", *Journal of Psychosomatic Research*, vol. 52, no. 2, pp. 69-77.
- Brugha, T., Bebbington, P., Tennant, C., & Hurry, J. 1985, "The List of Threatening Experiences - A Subset of 12 Life Event Categories with Considerable Long-Term Contextual Threat", *Psychological Medicine*, vol. 15, no. 1, pp. 189-194.
- Carver, C. S. 1997, "You want to measure coping but your protocol's too long: Consider the brief COPE", *International Journal of Behavioral Medicine*, vol. 4, no. 1, pp. 92-100.
- Carver, C. S., Scheier, M. F., & Weintraub, J. K. 1989, "Assessing Coping Strategies - A Theoretically Based Approach", *Journal of Personality and Social Psychology*, vol. 56, no. 2, pp. 267-283.

Coolidge, F. L., Segal, D. L., Hook, J. N., & Stewart, S. 2000, "Personality disorders and coping among anxious older adults", *Journal of Anxiety Disorders*, vol. 14, no. 2, pp. 157-172.

Coope B, Ballard C, Saad K, Patel A, Bentham P, Bannister C, Graham C, & Wilcock G 1995, "The prevalence of depression in the carers of dementia sufferers", *International Journal of Geriatric Psychiatry*, vol. 10, no. 3, pp. 237-242.

Cooper, C., Katona, C., Orrell, M., & Livingston, G. 2006a, "Coping strategies and anxiety in caregivers of people with Alzheimer's disease: The LASER-AD study", *Journal of Affective Disorders*, vol. 90, no. 1, pp. 15-20.

Cooper, C., Balamurali T, & Livingston G. A systematic review of the prevalence and associates of anxiety in caregivers of people with dementia (in press: *International Psychogeriatrics*) 2006b.

Cooper, C., Balamurali T, Selwood A, & Livingston, G. A systematic review of the treatment of anxiety in caregivers of people with dementia (in press: *International Journal of Geriatric Psychiatry*) . 2006c.

Crespo M, Lopez J, & Zarit SH 2005, "Depression and anxiety in primary caregivers: a comparative study of caregivers of demented and nondemented older persons", *International Journal of Geriatric Psychiatry*, vol. 20, pp. 591-592.

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. 1994, "The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia", *Neurology*, vol. 44, no. 12, pp. 2308-2314.

Dura JR, Stukenberg KW, & Kiecolt-Glaser JK 1991, "Anxiety and depressive disorders in adult children caring for demented parents", *Psychology and Aging*, vol. 6, no. 3, pp. 467-473.

Ferri, C. P., Prince, M., Brayne, C., Brodaty, H., Fratiglioni, L., Ganguli, M., Hall, K., Hasegawa, K., Hendrie, H., & Huang, Y. 2005, "Global prevalence of dementia: a Delphi consensus study", *The Lancet*, vol. 366, no. 9503, pp. 2112-2117.

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*, vol. 12, no. 3, pp. 189-198.

Fratiglioni L 1998, "Epidemiology," in *Health Economics of Dementia*, Wimo A et al., eds., John Wiley & Sons Ltd, USA, pp. 13-31.

Galasko, D., Bennett, D., Sano, M., Ernesto, C., Thomas, R., Grundman, M., & Ferris, S. 1997, "An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. The Alzheimer's Disease Cooperative Study", *Alzheimer Dis.Assoc.Disord.*, vol. 11 Suppl 2, p. S33-S39.

Gallagher, T. J., Wagenfeld, M. O., Baro, F., & Haepers, K. 1994, "Sense of Coherence, Coping and Caregiver Role Overload", *Social Science & Medicine*, vol. 39, no. 12, pp. 1615-1622.

Goode, K. T., Haley, W. E., Roth, D. L., & Ford, G. R. 1998, "Predicting longitudinal changes in caregiver physical and mental health: A stress process model", *Health Psychology*, vol. 17, no. 2, pp. 190-198.

Haley, W. E., Roth, D. L., Coleton, M. I., Ford, G. R., West, C. A. C., Collins, R. P., & Isobe, T. L. 1996, "Appraisal, coping, and social support as mediators of well-being in black and white family caregivers of patients with Alzheimer's disease", *Journal of Consulting and Clinical Psychology*, vol. 64, no. 1, pp. 121-129.

Hayes, S.C., Luoma, J.B., Bond, F.W., Masuda, A., Lillis, J. Acceptance and commitment therapy: model, processes and outcomes. *Behaviour research and therapy*. 2006;44(1):1-25.

Hebert R, Levesque L, Vezina J, Lavoie JP, D. F., Gendron C, Preville M, Voyer L, & Dubois MF 2003, "Efficacy of a psychoeducative group program for caregivers of demented persons living at home: a randomised controlled trial", *Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*, vol. 58, no. 1, p. S58-S67.

Hinrichsen, G. A. & Niederehe, G. 1994a, "Dementia Management Strategies and Adjustment of Family Members of Older Patients", *Gerontologist*, vol. 34, no. 1, pp. 95-102.

- Holmes, T. H. & Rahe, R. H. 1967, "Social Readjustment Rating Scale", *Journal of Psychosomatic Research*, vol. 11, no. 2, pp. 213-218.
- Kessler, R. C., Davis, C. G., & Kendler, K. S. 1997, "Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey", *Psychological Medicine*, vol. 27, no. 5, pp. 1101-1119.
- Kneebone, I. I. & Martin, P. R. 2003, "Coping and caregivers of people with dementia", *British Journal of Health Psychology*, vol. 8, pp. 1-17.
- Livingston, G., Katona, C., Roch, B., Guilhaume, C., & Rive, B. 2004, "A dependency model for patients with Alzheimer's disease: its validation and relationship to the costs of care--the LASER-AD Study", *Curr.Med.Res.Opin.*, vol. 20, no. 7, pp. 1007-1016.
- Logsdon R, Gibbons LE, McCurry SM. Quality of Life in Alzheimer's Disease: Patient and Caregiver Reports. *Journal of Mental Health and Aging* 5, 21-32. 1996.
- Mahoney R, Regan C, Katona C, & Livingston G 2005, "Anxiety and depression in family caregivers of people with Alzheimer's disease - the LASER-AD study", *American Journal of Geriatric Psychiatry*, vol. 13, no. 9, pp. 795-801.
- Mausbach, B. T., Aschbacher, K., Patterson, T. L., Ancoli-Israel, S., von Kanel, R., Mills, P. J., Dimsdale, J. E., & Grant, I. 2006, "Avoidant Coping Partially Mediates the Relationship Between Patient Problem Behaviors and Depressive Symptoms in Spousal Alzheimer Caregivers", *American Journal of Geriatric Psychiatry*, vol. 14, no. 4, pp. 299-306.
- Mckee, K. J., Whittick, J. E., Ballinger, B. B., Gilhooly, M. M. L., Gordon, D. S., Mutch, W. J., & Philp, I. 1997, "Coping in family supporters of elderly people with dementia", *British Journal of Clinical Psychology*, vol. 36, pp. 323-340.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. 1984, "Clinical-Diagnosis of Alzheimers-Disease - Report of the Nincds-Adrda Work Group Under the Auspices of Department-Of-Health-And-Human-Services Task-Force on Alzheimers-Disease", *Neurology*, vol. 34, no. 7, pp. 939-944.

- Morano, C. L. 2003, "Appraisal and coping: Moderators or mediators of stress in Alzheimer's disease caregivers?", *Social Work Research*, vol. 27, no. 2, pp. 116-128.
- Morris, L. W., Morris, R. G., & Britton, P. G. 1988, "The Relationship Between Marital Intimacy, Perceived Strain and Depression in Spouse Caregivers of Dementia Sufferers", *British Journal of Medical Psychology*, vol. 61, pp. 231-236.
- Neundorfer MM 1991, "Coping and health outcomes in spouse caregivers of persons with dementia", *Nursing Research*, vol. 40, no. 5, pp. 260-265.
- Pakenham, K. I. 2005, "Relations between coping and positive and negative outcomes in carers of persons with multiple sclerosis (MS)", *Journal of Clinical Psychology in Medical Settings*, vol. 12, no. 1, pp. 25-38.
- Pettit, T., Livingston, G., Manela, M., Kitchen, G., Katona, C., & Bowling, A. 2001, "Validation and normative data of health status measures in older people: the Islington study", *International Journal of Geriatric Psychiatry*, vol. 16, no. 11, pp. 1061-1070.
- Pinquart M & Sorensen S 2003, "Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis", *Psychology and Aging*, vol. 18, no. 2, pp. 250-267.
- Pratt, C., Schmall, V., & Wright, S. 1985, "Burden, Coping and Health - Family Caregivers to Community-Dwelling and Institutionalized Dementia Patients", *Gerontologist*, vol. 25, p. 149.
- Pruchno, R. A. & Resch, N. L. 1989a, "Mental-Health of Caregiving Spouses - Coping As Mediator, Moderator, Or Main Effect", *Psychology and Aging*, vol. 4, no. 4, pp. 454-463.
- Radosevich D & Pruitt M. Twelve-Item Health Status Questionnaire: HSQ-12 Version 2.0. 1995. Health Outcomes Institute, Bloomington.
- Regan, C., Katona, C., Walker, Z., & Livingston, G. 2005, "Relationship of exercise and other risk factors to depression of Alzheimer's disease: the LASER-AD study", *International Journal of Geriatric Psychiatry*, vol. 20, no. 3, pp. 261-268.

- Rosen, W. G., Mohs, R. C., & Davis, K. L. 1984, "A new rating scale for Alzheimer's disease", *Am.J.Psychiatry*, vol. 141, no. 11, pp. 1356-1364.
- Russo J, Vitaliano PP, Brewer DD, Katon W, & Becker J 1995, "Psychiatric disorders in spouse caregivers of care recipients with Alzheimer's disease and matched controls: a diathesis-stress model of psychopathology", *Journal of Abnormal Psychology*, vol. 104, no. 1, pp. 197-204.
- Saad, K., Hartman, J., Ballard, C., Kurian, M., Graham, C., & Wilcock, G. 1995, "Coping by the Carers of Dementia Sufferers", *Age and Ageing*, vol. 24, no. 6, pp. 495-498.
- Schulz R, O'Brien T, & Bookwala J 1995, "Psychiatric and physical morbidity effects of dementia caregiving: prevalence, correlates, and causes", *Gerontologist*, vol. 35, no. 6, pp. 771-791.
- Selwood A, Johnston K, Katona C, & Livingston G. Systematic review of the effect of psychological interventions on family caregivers of people with dementia; *Journal of Affective Disorders* (in press)
- Silver, R. C., Holman, E. A., McIntosh, D. N., Poulin, M., & Gil-Rivas, V. 2002, "Nationwide longitudinal study of psychological responses to September 11", *Jama-Journal of the American Medical Association*, vol. 288, no. 10, pp. 1235-1244.
- Stansfeld, S. & Marmot, M. 1992, "Deriving A Survey Measure of Social Support - the Reliability and Validity of the Close Persons Questionnaire", *Social Science & Medicine*, vol. 35, no. 8, pp. 1027-1035.
- Vedhara K, Shanks N, Wilcock G, & Lightman SL 2001, "Correlates and predictors of self-reported psychological and physical morbidity in chronic caregiver stress", *Journal of Health Psychology*, vol. 6, no. 1, pp. 101-119.
- Vitaliano, P. P., Russo, J., Young, H. M., Teri, L., & et al 1991, "Predictors of burden in spouse caregivers of individuals with Alzheimer's disease.", *Psychology and Aging*, vol. 6, no. 3, pp. 392-402.
- Winslow, B. W. 1997, "Effects of formal supports on stress outcomes in family caregivers of Alzheimer's patients", *Research in Nursing and Health*, vol. 20, no. 1, pp. 27-37.
- Zarit, S. H., Reever, K. E., & Bachpeterson, J. 1980, "Relatives of the Impaired Elderly - Correlates of Feelings of Burden", *Gerontologist*, vol. 20, no. 6, pp. 649-655.

Zigmond, A. S. & Snaith, R. P. 1983, "The Hospital Anxiety and Depression Scale", *Acta Psychiatrica Scandinavica*, vol. 67, no. 6, pp. 361-370.

List of presentations

University College London

January 2006 Departmental meeting (upgrade presentation)

September 2006 Centre for Aging and Mental Health, UCL

UK conferences

June 2006 Royal College of Psychiatrists' AGM, Glasgow (poster)

International conferences

June 2006 World Federation of Societies of Biological Psychiatry

Conference: Vienna

May 2007 International Psychogeriatric Association conference:
Istanbul

Poster presented at Royal College of Psychiatrists' AGM Glasgow June 2006

The role of coping strategies in predicting anxiety in caregivers of people with Alzheimer's disease: the LASER-AD study

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Introduction

Caregivers of people with dementia (CGPD) frequently develop psychological disorders, with anxiety symptoms most common (Mahoney et al., 2005). It seems likely that these may relate to coping strategies employed in caring but there is little information about their association with coping strategies. Our primary hypothesis, informed by previous research, was that CGPD with clinically significant anxiety were more likely to use dysfunctional and emotion-focused coping strategies than non-anxious caregivers.



Methods

126 people with Alzheimer's disease and their family caregivers living in the community were recruited from local psychiatric services, the voluntary sector and through managers of care homes. Sampling was designed to ensure that the sample was epidemiologically representative in terms of dementia severity, gender and care setting. The anxiety subscale of the Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and the Brief COPE was used to measure coping strategies. Measures of demographic factors, life events, carer physical health, caregiver burden, quality of the caregiver-care recipient (CR) relationship, CR cognitive, neuropsychiatric morbidity and dependency were also included.

Results

Of all the factors measured, only those listed in table one were significantly associated with carer anxiety on univariate analysis. When all the factors in table 1 were entered in a logistic regression, only dysfunctional coping strategies (OR 1.3, CI 1.2-1.5; $p=0.007$) predicted HADS anxiety caseness.

Limitations

Anxious caregivers may be more likely to report their coping strategies negatively. We measured coping strategies and caregiver morbidity at the same time, so we cannot comment on the direction of causality from these results.

Conclusion

Dysfunctional coping strategies predicted caregiver anxiety, and appear to be more important than any other factor in doing so. Our findings suggest that addressing coping strategies may be a helpful intervention for alleviating caregiver anxiety.

Coping strategies used by anxious and non-anxious caregivers

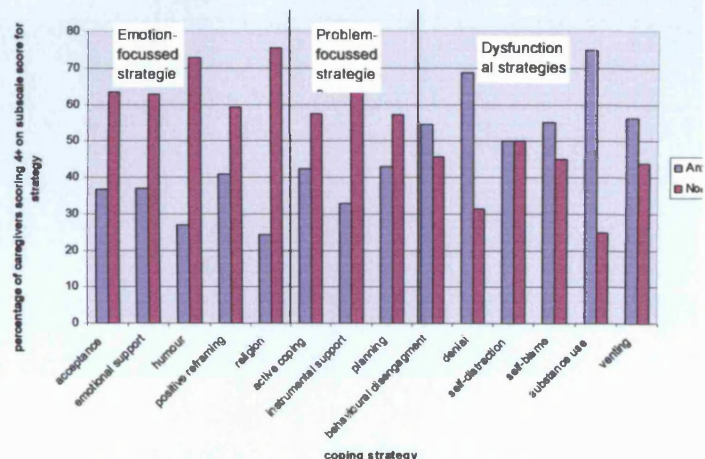


Table 1: Mean(sd) for association of coping strategies and factors investigated that were significantly associated with HADS anxiety caseness on univariate analysis

		HADS anxiety Case (8+) (n=40)	Not anxiety case (n=86)	Z/t	Significance
COPE subscale total scores	emotion-focussed	20.0(4.9)	19.1(5.5)	t=0.88	0.38
	problem-focussed	12.7(4.2)	11.1(4.5)	Z=2.1	0.032
	Dysfunctional	18.9(4.9)	14.8(3.4)	Z=5.0	<0.001**
Life events (in last 6 months)	Total score	85.5(75.8)	50.6(55.4)	Z=2.8	0.006*
Zarit burden score total		35.2(15.0)	24.0(12.8)	t=4.3	<0.001**

Reference: Mahoney R, Regan C, Katona C, Livingston G (2005) Anxiety and depressive disorders in family caregivers of people with Alzheimer's Disease - the LASER-AD study *Am J Geriatr Psychiatry* 13(9):795-801.

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