DO CHANGES IN COPING MEDIATE THE EFFECTS OF A PSYCHOLOGICAL INTERVENTION ON PSYCHOLOGICAL MORBIDITY IN CARERS OF PEOPLE WITH DEMENTIA?

Thesis submitted for PhD in Mental Health Sciences

Wing Yin Ryan Li

UCL

Supervisors Gill Livingston and Claudia Cooper

I, Wing Yin Ryan Li, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

Background: Family carers of people with dementia report high levels of anxiety and depression. More emotion-focused and less dysfunctional coping appear protective against symptoms in observational studies, but no randomised controlled trial (RCT) has investigated emotion-focused coping as a mechanism of effective therapy.

Method: We recruited 260 family carers of people with dementia (referred to services in past year) into a pragmatic RCT of 8-sessions manualised, individual-based coping skills intervention versus treatment-as-usual (TAU). Blinded raters measured carers' psychological morbidity (Hospital Anxiety and Depression Scale, HADS-T) and coping (Brief COPE: emotion-focused, problem-focused, dysfunctional subscales) at 4 and 8 months. My hypothesis that increased emotion-focused coping mediated treatment effects in reducing symptoms was tested using regression. As baseline symptoms moderated treatment effects on coping, *post-hoc* subgroup efficacy analyses were performed in carers with different baseline morbidity levels. Finally moderated mediation was tested using regression models.

Results: Emotion-focused coping did not mediate treatment effects in reducing psychological symptoms in the whole sample. It appeared to mediate such effects only in psychological morbidity cases (baseline HADS-T 16+). Increased emotion-focused coping over 4 months predicted reduced symptoms at 8 months regardless of treatment status (b = -0.24, p = 0.005). Intervention had no overall effects on coping, but more severe cases (HADS-T 20+) increased emotion-focused coping (b = 4.57 [95% CI: 1.83, 7.30]), and maintained dysfunctional coping while TAU decreased (b = 0.14 [95% CI: 0.02, 0.26]). Non-cases (HADS-T <8) in TAU increased dysfunctional coping versus intervention (b = -0.09 [95% CI: -0.17, -0.003], log).

Conclusions: Emotion-focused coping appeared to mediate treatment effects on psychological morbidity only in carers with high baseline symptoms. The most distressed increased helpful coping strategies and improved; the least distressed maintained low use of unhelpful strategies and remained well. Carers found different ways to benefit from standardised therapy.

Statement of contribution to the HTA-START (Strategies for Relatives) trial

My PhD investigation is nested in the HTA-START trial, a pragmatic randomised controlled trial (RCT) of a coping skills intervention versus treatment-as-usual (TAU) for family carers of people with dementia. The trial was designed by my supervisors Prof Gill Livingston and Dr Claudia Cooper, and funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme. During my employment as a research assistant (RAs) on the trial, I developed my PhD study proposal, formulated the hypotheses, designed and conducted the data analysis in the current PhD investigation. I was not involved in the selection of outcome measures. The team of 10 RAs, including I, collectively underwent training and supervision for the psychological intervention, recruited and obtained informed consent from the 260 trial participants (family carers), delivered the intervention, and collected and cleaned the trial outcome data (some of which I used for my PhD investigation). I was personally responsible for an intervention caseload of 12/173 carers and an assessment caseload of 118/260 carers.

Acknowledgments

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1 Background

1.1 Introduction

Dementia is a brain disorder associated with functional decline which affects the person, family and friends, and society. The prevalence of dementia is increasing due to ageing populations worldwide (Ferri et al. 2005). Carers of people with dementia are at a particularly high risk of experiencing anxiety or depression (Ory et al. 2000;Ory et al. 1999;Pinquart et al. 2003b). As more people are becoming family carers, the mental health needs of this population are rising.

There are many reasons why providing care for someone with dementia can be a particularly stressful responsibility. Dementia characteristically causes behavioural and personality changes, which are associated with fundamental losses in the relationship between carer and care recipient (CR) (Livingston et al. 1996a;Noyes et al. 2010;Ory et al. 2000). The person with dementia becomes increasingly unable to function in daily life, requiring progressively higher levels of care; the long hours of care often lead to social isolation for the carer (Noyes et al. 2010;Ory et al. 2000;Ory et al. 1999;Pearlin et al. 1990;Pinquart et al. 2003b). Carers are often grieving at the loss of their previous relationship as dementia is a progressive, terminal illness (Chan et al. 2012;Noyes et al. 2010). The variety of stressors in dementia caring, which are discussed in further detail in Section 1.2.5, imply that effective intervention to improve carer mental wellbeing might be complex in nature in order to address these multiple causal factors.

Although most carers for people with dementia experience stress or burden, many remain mentally well while others become anxious or depressed. Research into coping has sought to explain why this is so. Richard Lazarus, in his book *Psychological Stress*

and the Coping Process (Lazarus 1966), and later in a seminal text co-authored by Susan Folkman on the Transactional Theory of Stress and Coping (Lazarus et al. 1984), suggested that how a person copes with adversity can crucially determine the outcome. The implication is that by knowing what coping styles are associated with better psychological outcomes, we might be able to target and change coping in order to improve outcomes. In the current thesis I have sought to understand how dementia carers' coping styles affect their mental health, and to test whether an intervention to reduce carer psychological morbidity worked by modifying the coping styles they used.

1.1.1 *Family carers*

The words "carer" and "caregiver" are often used interchangeably in the academic literature. Caring and caregiving are two closely linked yet distinct concepts, as defined by Pearlin (1990): "Caring is the affective component of one's commitment to the welfare of another, whereas caregiving is the behavioural expression of this commitment." For simplicity, I shall use the terms "carer" and "caring" throughout this thesis.

I shall be focusing solely on unpaid family carers. Paid carers have different motivations for providing care, as well as differing emotional reactions, and research findings may not generalise across paid and unpaid carers. The term "carer" has been defined as someone who "provides unpaid care by looking after an ill, frail or disabled family member, friend or partner" (Carers UK 2012). I shall use the term "family carer" to mean any unpaid or informal carer, usually caring for a spouse or other immediate or extended family member, but sometimes friends and neighbours. People become carers for many different reasons, some practical reasons such as being the one who lives nearest the CR, some positive reasons such as having a close relationship with the CR,

and some less positive reasons such as guilt, or the refusal of others to take on the role (Camden et al. 2011). During the course of this study I have come across very different caring scenarios, including a lady who provided care for an older family friend because "he had been very good to my parents". These different scenarios may well have different implications regarding the carer's coping and mental wellbeing.

In this chapter I shall provide a background about dementia; why it is particularly associated with carer stress and psychological morbidity; the nature of depression and anxiety in carers, and how they relate to coping. Then in Chapter 2, I shall present a systematic review of observational studies of the relationship between carer coping and psychological morbidity; and in Chapter 3, a systematic review of intervention studies aiming to reduce morbidity through changing coping. In Chapter 4, I shall provide an overview of the START (Strategies for Relatives) Study, in which the current PhD investigation is nested. In Chapter 5, I shall outline my aims and hypotheses. In Chapter 6, I shall describe the methods of the study and data analysis. I shall describe my findings in Chapter 7, and finally in Chapter 8 discuss the clinical and research implications of the findings.

1.2   The caregiving context in dementia

1.2.1   What is dementia?

Dementia is a clinical syndrome characterised by chronic, global impairment in the patient's cognitive functioning relative to his or her previous level, attributed to organic brain changes of various aetiologies (American Psychiatric Association 2000). The most common forms of dementia are Alzheimer's disease, associated with amyloid plaques

and neurofibrillary tangles in the brain, followed by vascular dementia, which results from cerebrovascular disease (Stevens et al. 2002).

Among the various operational definitions of dementia, the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision) and ICD-10 (International Classification of Diseases, Tenth Revision) criteria are most commonly used. DSM-IV-TR defines dementia as the core deficit of memory impairment (the inability to learn new information or recall previously learned information), presenting with at least one of the following cognitive deficits: aphasia (language disturbance), apraxia (inability to carry out motor activities), agnosia (perceptual difficulties), and executive functioning (American Psychiatric Association 2000). The deficits must cause significant impairment in social or occupational functioning, and represent a significant decline from previous function (American Psychiatric Association 2000). Behavioural disturbance, such as agitation, may also be present.

The ICD-10 definition emphasises the pervasive nature of dementia: "…disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgment… commonly accompanied by deterioration in emotional control, social behaviour, or motivation." (World Health Organization 1992) It additionally requires the disorder to have been present for at least 6 months (World Health Organization 1992), in contrast with DSM-IV which allows for the diagnosis of dementia once symptoms have begun to impair daily living significantly (American Psychiatric Association 2000). The latter approach has prevailed in research and clinical practice, and is arguably more relevant to the everyday impact and meaning of the illness on the patient and carer. Finally it is worth

noting that there exist commonly used diagnostic criteria for dementia subtypes, for example the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable Alzheimer's disease (McKhann et al. 1984). In the current study we shall be recruiting carers of people who have received clinical diagnoses of dementia from psychiatrists or neurologists who use current criteria.

Recent advances in the understanding of dementia pathophysiology, particularly of biomarkers for Alzheimer's disease, have led to development of new research and diagnostic criteria for the different clinical and pre-clinical manifestations of dementia (Dubois et al. 2007). These may well shape our future conceptualisation of family carers' needs, and of psychosocial intervention approaches toward this population.

1.2.2 Subtypes of dementia

Different subtypes of dementia are diagnosed based on available aetiological evidence; for example vascular dementia (attributable to cerebrovascular disease), and dementia due to Parkinson's disease (American Psychiatric Association 2000). Under the DSM-IV, Alzheimer's disease is diagnosed where other aetiologies of dementia could be ruled out, with the caveat that these criteria sometimes fail to distinguish certain subtypes such as dementia with Lewy bodies (American Psychiatric Association 2000). There is broad consensus from autopsy, clinical, and epidemiological studies that Alzheimer's disease is the most common form of dementia followed by vascular dementia, yet different diagnostic criteria used across studies make it difficult to calculate the precise distribution of subtypes (Knapp et al. 2007). The following relative frequencies are taken from the most recent population-based study in the UK using standardised clinical criteria for each subtype (Stevens et al. 2002)

Alzheimer's disease accounts for approximately 41% of dementia cases in the community (Stevens et al. 2002). It is characterised by gradual and fairly consistent decline accelerating with time, although there may be brief troughs and plateaus during the course of illness (National Collaborating Centre for Mental Health 2007). Neuropsychiatric symptoms usually worsen as the dementia increases in severity. Vascular dementia (31% of cases; (Stevens et al. 2002) has a less predictable course with initial signs of stability, usually paving way to sudden and rapid deterioration following cerebrovascular events (National Collaborating Centre for Mental Health 2007). Dementia with Lewy bodies comprise around 8% of cases (Stevens et al. 2002), and is particularly associated with motor disorders and visual hallucinations. Frontal lobe dementia and Parkinson's disease with dementia each account for around 3% of cases (Stevens et al. 2002).

While memory impairment is the most recognisable symptom in most dementias, all dementias are pervasive and progressive such that most if not all aspects of daily functioning become compromised. The person with dementia may become unable to communicate, or to care for themselves (including eating and toileting appropriately), ultimately leading to death as the body becomes less able to cope with infections and other physical problems (National Collaborating Centre for Mental Health 2007).

Given that the dementias have more similarities than differences in the ways they affect family carers, and that the differences within a group of people with the same diagnosis may be more than that between diagnoses, I shall consider dementia as a broad clinical syndrome for the purposes of considering carers. This is the prevailing approach in the carer literature, and in the START study we have been similarly inclusive in recruiting carers of people with clinically diagnosed dementia of any

subtype (see Section 6.1.2). Certain subtypes, such as dementia with Lewy bodies and Parkinson's disease with dementia, do appear to be associated with increased carer needs and stress; this is mostly explained by increased presentations of particular neuropsychiatric symptoms such as mood problems, delusions, daytime somnolence and cognitive fluctuation (Lee et al. 2012). It is worth noting again that increased neuropsychiatric symptoms are a strong predictor of carer stress and morbidity regardless of dementia subtype (see Section 1.3.6: Correlates of depression and anxiety in family carers).

1.2.3 Prevalence of dementia

The occurrence of dementia increases dramatically with age, with various epidemiological studies showing prevalence rising from around 1% of individuals aged 60-65 to around 13% of those aged 80-85; alternatively, 5% of over 65s, and 20% of all over 80s (Hofman et al. 1991;Knapp et al. 2007;Medical Research Council Cognitive Function and Ageing Study (MRC CFAS) 1998). There are now an estimated 750,000 to 820,000 people in the UK living with a form of dementia (Alzheimer's Society 2012). With projected demographic changes this figure will rise steadily to 1 million by 2021, and over 1.7 million by 2051 (Alzheimer's Society 2012;Wancata et al. 2003).

1.2.4 Disease burden of dementia

Dementia is a chronic condition. Globally it is the leading cause of disability among people aged 60 or over, accounting for an estimated 11.2% of all disabled years lived; more than stroke (9.5%), musculoskeletal disorders (8.9%), cardiovascular disease (5.0%) and all cancers (2.4%) (World Health Organization 2004). In 2007, over 420,000

people, or almost two-thirds of those with late-onset dementia in the UK were living in their own homes, with most care provided by family members (Knapp et al. 2007).

Dementia is estimated to cost the UK economy some £23 billion per year, more than cancer (£12 billion) and heart disease (£8 billion) combined (Luengo-Fernandez et al. 2010). Perhaps even more striking is that the 1.5 billion hours of unpaid care provided by family carers represent over half (55%) of the total cost; the remainder (45%) by health and social care services (Luengo-Fernandez et al. 2010). A substantial portion of the cost will be incurred by family carers due to lost income from reducing or giving up work (Knapp et al. 2007). Long-term institutional care is yet more costly on a per patient basis, currently representing a sizeable 40% (£9 billion) of the total costs with over 300,000 people with dementia in care homes (Luengo-Fernandez et al. 2010). Given that carer burden and psychological distress are strong predictors of people with dementia requiring care home admission (Banerjee et al. 2003;Rozzini et al. 2006), there are strong health, economic and humanitarian rationales to improve the wellbeing of family carers.

1.2.5 Why caring for someone with dementia is particularly stressful

Caring for someone with dementia is stressful, and has consistently been linked with poor mental and physical wellbeing (Pinquart et al. 2003b). Providing care for someone with dementia appears to be particularly demanding even compared with caring in other chronic or terminal illnesses (Ory et al. 2000;Ory et al. 1999), for instance one study reported greater distress in dementia carers compared to cancer carers (Clipp et al. 1993). Demographic factors, such as the fact that dementia carers are more likely to be spouses, living with the care recipient, and older than carers of people without dementia (Ory et al. 2000;Parsons 2001), can only partly explain this difference. In representative

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studies that have controlled for sociodemographic factors and caregiving involvement, dementia carers reported as much as distress as cancer carers and greater distress than diabetes carers (Kim et al. 2008), and dementia status independently predicted physical, financial and emotional burden (Ory et al. 1999).

Why is caregiving for dementia so stressful? We can make sense of this by considering the different kinds of stressors facing the carer (Pearlin et al. 1990;Schulz et al. 2008). Some stressors are the objective needs or behaviours of the person with dementia, stemming directly from the illness: cognitive impairment, behavioural problems (neuropsychiatric symptoms), and functional impairment in activities of daily living (Pearlin et al. 1990;Pinquart et al. 2003b;Pinquart et al. 2007). These lead to other stressors, including the time pressures of caring for someone who needs a high level of supervision, alongside existing commitments such as work or childcare (Pinquart et al. 2003b). A population-based survey has found that dementia carers spend significantly more hours per week providing care than non-dementia carers, with some 28% of dementia carers providing at least 40 hours of care weekly versus 17% of non-dementia carers (Ory et al. 1999). This can lead to social isolation, less personal freedom, and less time for pleasurable activities (Noyes et al. 2010;Pinquart et al. 2003b). It is not surprising that longer hours spent caring over extended periods are associated with increased levels of depression and anxiety (Hirst 2003). Longer hours of care can also lead to occupational and financial difficulties, as family carers reduce their hours of paid employment (Ory et al. 1999).

Loss of a confiding or intimate relationship with the CR is another important stressor (Livingston et al. 1996a;Rankin et al. 2001). Decreased independence in activities of daily living, as well as dementia-specific behavioural symptoms, such as

disorientation, depression and personality changes, can contribute to this (Pinquart et al. 2003b). People with dementia may be less likely to express gratitude for the carer's help and indeed may actively resist help, reducing some of the positive aspects of caregiving (Pearlin et al. 1990;Pinquart et al. 2003b)

Grief is increasingly recognised as central to the caregiving experience of family carers of people with dementia, which is often compared to bereavement (Chan et al. 2012;Meuser et al. 2001;National Collaborating Centre for Mental Health 2007;Noyes et al. 2010). Survey studies have found prevalences of anticipatory grief among family carers as high as 47 to 71%, and this may occur at any stage from the CR's diagnosis, although severe grief reactions more commonly occur at the moderate and severe stages of dementia (Chan et al. 2012). Coping with loss may be even more challenging than coping with the practical demands of actually providing care. One study found that increased depressive symptoms in spousal carers were more likely to have resulted from diminished intimacy than with helping with activities of daily living (Rankin et al. 2001).

Furthermore, carers typically experience what is known as ambiguous loss, an unstable pattern of loss as the CR's ability to communicate, make decisions and maintain a relationship with the carer fluctuates with the course of dementia (Blieszner et al. 2007;Boss 1990;Noyes et al. 2010). Noyes and colleagues (2010) described this poignantly as a "revolving door of hope followed by disappointment and despair". The unpredictability of loss, coupled with the CR being physically present but no longer able to engage with the carer in a meaningful way, makes it difficult for carers to recognise the grief and to apply effective coping efforts (Blieszner et al. 2007;Boss 1990;Noyes et al. 2010;Sanders et al. 2007). Yet progressive deterioration of the dementia is inevitable,

and this further serves to diminish any visible positive long-term impacts of carer's engagement (Clipp et al. 1992;Ory et al. 2000).

1.2.6 Interim summary

Dementia is a chronic, terminal illness with a significant disease burden for patients, family carers and wider society. Caring for someone with dementia is stressful. We need to understand better how this stress causes psychological morbidity in some carers and not in others, in order to provide more effective interventions to reduce carer depression and anxiety.

1.3 Depression and anxiety in family carers

1.3.1 What is depression?

Depression is characterised by core symptoms of low mood and loss of positive affect, alongside a range of psychological and behavioural symptoms (American Psychiatric Association 2000;National Collaborating Centre for Mental Health 2009). As with anxiety disorders, low mood or lack of interest can be entirely normal reactions to everyday events, yet in depressive disorders such feelings are persistent and distressing to the extent of interfering with a person's daily functioning (American Psychiatric Association 2000). A clinical diagnosis of Major Depressive Episode can be made under DSM-IV-TR criteria, when at least one of the two core symptoms (low mood, and loss of positive affect) presents nearly everyday for at least two weeks, alongside at least four other symptoms, including: feelings of guilt and low self-esteem, low energy, irritability, suicidal thoughts, poor appetite and sleep, and other somatic symptoms (American Psychiatric Association 2000). The ICD-10 definition of a Depressive Episode is somewhat similar but requires 2 of 3 core symptoms (low mood,

loss of interest, and loss of energy) (World Health Organization 1992). In both

diagnostic systems, the severity of the depressive disorder is determined by number,

severity, duration and course of symptoms (American Psychiatric Association

2000;World Health Organization 1992).

Depressive symptoms may present differently in different populations, for example

in older people, somatic symptoms are more common than complaints of low mood

(Serby et al. 2003). The operationalisation of depression in psychometric questionnaires

will be discussed again in Section 6.4.2 (Carer assessments).

Depression presents a significant disease burden. It is a major cause of disability

across the world (Murray et al. 1994;World Bank 1993), due to its impact on social and

occupational functioning (Ormel et al. 1999), significant comorbidity with anxiety and

physical symptoms, and its exacerbating effect on existing chronic physical conditions

(Moussavi et al. 2007;Serby et al. 2003).

1.3.2 *Prevalence of depression*

General and older adult populations

Population-based surveys suggest that approximately 4 – 10% of the general adult

population worldwide will meet criteria for major depression in their lifetime (Waraich

et al. 2004), with an estimated point prevalence for a depressive episode at 2.6% in the

UK (Singleton et al. 2001). Depression is more common among women than men

(Singleton et al. 2001;Waraich et al. 2004). While reported estimates of prevalence in

older adults vary considerably (McDougall et al. 2007), depression certainly appears no

less common in this group, with the most recent population-based study across England

and Wales reporting a prevalence of 8.6% among older adults aged 65+ (McDougall et al. 2007).

Family carers of people with dementia

A systematic review found that 22.3% of approximately 800 family carers of people with dementia in 10 studies met clinical criteria for a depressive disorder (Cuijpers 2005), with prevalence ranging 15 – 32% across studies. The highest prevalence was being found in the only study with a representative sample (Livingston et al. 1996b). These are considerably higher figures than those reported in matched controls, as well as in the general population in other studies (Cuijpers 2005). As in the general population, carer depression is significantly associated with poorer physical health and daily functioning, frequently comorbid with anxiety (Mahoney et al. 2005a), and also a significant, independent predictor of abusive behaviours towards the CR (Cooper et al. 2009) (see Section 1.3.6).

1.3.3 What is anxiety?

The term "anxiety" comes from the Latin "anxietatem" meaning distress, worry and anguish. While everyone experiences anxiety as a normal reaction to stress, in anxiety disorders the worry and apprehension is abnormal and excessive; it is difficult to control and disproportionate to the circumstance, causing significant impedance to the person's daily functioning (American Psychiatric Association 2000;Bitran et al. 2009;Tyrer et al. 2006;World Health Organization 1992). The pathological features of worry are emphasised in the DSM-IV-TR definition of generalised anxiety disorder (GAD), the most common form of anxiety disorder (American Psychiatric Association 2000):

- Excessive, i.e. in duration and severity of distress relative to the actual likelihood or impact of the feared event(s)

- Pervasive, i.e. , permeating most events or activities, and occurring more days than not for at least 6 months

- Uncontrollable.

The anxiety and worry must also be associated with at least three of the following symptoms: restlessness, being easily fatigued, poor concentration, irritability, muscle tension, and sleep disturbance (American Psychiatric Association 2000).

In the ICD-10, generalised anxiety disorder is similarly defined with prominent tension, worry, and feelings of apprehension about everyday events and problems over 6 months, with a greater emphasis on physiological symptoms, including at least one core autonomic arousal symptom (palpitations or accelerated heart rate; sweating; trembling; dry mouth) plus three more, which may also include loose bowels, shortness of breath, dizziness, numbness, muscle tension and pains, etc. (World Health Organization 1992). In both DSM-IV-TR and ICD-10, a diagnosis of GAD excludes other anxiety disorders, such as panic disorder, post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, and specific phobias. People with GAD typically experience a range of the aforementioned psychological and physiological symptoms (Gelder et al. 2006), and GAD is typically a chronic condition with low rates of remission, significant burden of disability, and reduced quality of life (Sareen et al. 2006;Tyrer et al. 2006).

Since anxiety can present with diverse symptoms, the use of scientifically sound assessment measures becomes crucial in informing evidence-based treatment and evaluating outcomes. Anxiety symptom checklists, such as the widely used Spielberger

Trait Anxiety Inventory (STAI) (Spielberger et al. 1983), can generally detect anxiety disorders in different populations but are not designed to differentiate between specific disorders (Bjelland et al. 2002). Further discussion of instruments follows in the Methods (Section 6.4.2).

1.3.4 Prevalence of anxiety

General population

Anxiety typically exists alongside other psychiatric disorders, with GAD and comorbid depression being more common than 'pure' GAD (Tyrer & Baldwin 2006). The most recent Adult Psychiatric Morbidity Survey estimated the point prevalence of GAD in England as 4.4% (McManus et al. 2009). An international review of population surveys reported 12-month prevalence rates of 5.6% to 18.1% for all anxiety disorders, of which GAD and panic disorder accounted for over half (Baumeister et al. 2007). The worldwide lifetime prevalence of GAD is estimated at 0.8% to 6.4% (Grant et al. 2005;Kessler et al. 2008;Lieb et al. 2005).

Older adults

For adults aged 55+, a wide range of prevalence rates for any anxiety disorder have been reported in population-based or representatively sampled surveys, from 1.2% to 15% (Bryant et al. 2008;Wolitzky-Taylor et al. 2010). Many studies have found lower prevalence rates of anxiety disorders than those of general adult populations (Bryant et al. 2008;Wolitzky-Taylor et al. 2010), yet levels of anxiety symptoms appear to increase with age (Teachman 2006). A recent study concluded that findings of lower prevalence are likely due to measurement error, as both anxiety and depression tend to be experienced differently by older adults, and therefore under-recognised and under-

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diagnosed (McBride et al. 2013). Somatic complaints (such as fatigue and insomnia) and worries about physical health appear to be more common expressions of mood disorders in older populations, and symptoms from comorbid physical disorders further confound the diagnosis (Bryant et al. 2008;Jeste et al. 2005;McBride et al. 2013;Wolitzky-Taylor et al. 2010). Older adults are similar to the general adult population in that symptoms of anxiety are common across a range of psychological disorders, and anxiety with comorbid depression is particularly common (Bryant et al. 2008;Kvaal et al. 2005;Wolitzky-Taylor et al. 2010).

There is increasing research interest in sub-clinical anxiety, with studies suggesting a greater than twofold increase in the estimated prevalence of GAD if the DSM-IV threshold for diagnosis is reduced, but a similar profile of impairment and risks of subsequent psychological (co)morbidities (Kessler et al. 2005;Ruscio et al. 2007).

Family carers of people with dementia

Most research on the psychological morbidity of family carers has focused on depression rather than anxiety, and this is true of the general carer literature (Parks et al. 2000), as well as the dementia carer literature (Cooper et al. 2007a;Schulz et al. 1995;Schulz et al. 2008). A PubMed search in March 2012 for the terms "dementia AND carer AND depression" retrieved 1058 citations, while "dementia AND carer AND anxiety" retrieved only 325. This is in spite of anxiety being more prevalent than depressive disorders in family carers of people with or without cognitive impairment (Cochrane et al. 1997;Mahoney et al. 2005a). As in the general population, most carers with depression will also have comorbid anxiety but not vice versa (Mahoney et al. 2005a), therefore it is important also to consider carer anxiety (Cooper et al. 2007a).

Population studies found that around 25% of family carers of people with dementia meet criteria for clinical anxiety (Cooper et al., 2007a;Mahoney et al., 2005a), somewhat higher than the upper estimate of 18.1% of any anxiety disorder in the general population (Baumeister et al. 2007). Levels of anxiety symptoms are also high in carers of people with dementia compared to non-carers and carers of people without cognitive impairment (Cooper et al. 2007a;Crespo et al. 2005;Ulstein et al. 2012), and as high as those of geriatric inpatients (Ulstein et al. 2012). Consistent with these findings, a population-based study also found that family carers of people with dementia were almost twice as likely to be using psychotropic drugs as matched non-caregivers (Grafstrom et al. 1992); and a 4-year prospective study of 1222 family carers found use of anxiolytic drugs appears to increase significantly after institutionalisation of the person with dementia (Schulz et al. 2004).

1.3.5 Aetiology of depression and anxiety

The aetiologies of both depression and anxiety disorders are commonly thought to involve multiple biological and psychosocial factors. For example, the Theory of Triple Vulnerability posits GAD as a product of three vulnerabilities: generalised biological, generalised psychological, and specific psychological (Barlow 2000;Bitran et al. 2009). The general genetic factors predisposing individuals to a range of depressive and anxiety disorders have been recognised (National Collaborating Centre for Mental Health 2009;National Collaborating Centre for Mental Health 2011), and a range of early environmental factors such as certain parenting styles or attachment relationships, family disruption or childhood abuse may act as further triggers (Barlow 2000;Kendler 1996;Kendler et al. 2003). Recent life events seem to play an important role in the onset of depressive and anxiety disorders (Roemer et al. 1996). One study has found that

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stressful life events characterised by loss increased the risk of both depression and anxiety, whilst life events characterised by danger or threat (where the full impact of the event was yet to be realised) increased the likelihood of GAD (Kendler et al. 2003). Both types of life event are relevant to family carers of people with dementia, which is characterised by current loss and threat of further loss as dementia progresses.

1.3.6 Correlates of depression and anxiety in family carers

Caregiving and CR characteristics

Depression in family carers has been consistently associated with more severe CR neuropsychiatric behavioural symptoms, more caring tasks or hours, increased CR physical impairment (only for spousal carers), and the absence of uplifts in caregiving (Black et al. 2004;Mohamed et al. 2010;Pinquart et al. 2003a) As previously implied, there is a general paucity of research investigating the correlates of carer anxiety, both in terms of caseness and symptomatology (Cooper et al. 2007a). The LASER study, conducted with an English community sample that sought to be representative of people with dementia, using a clinically validated measure of anxiety, found the following significant independent risk factors for the carer meeting criteria for anxiety disorder: being female, living with the CR, and greater impairment in the CR's activities of daily living (Mahoney et al. 2005a). The study also found carer depression to be predicted by poor self-rated health, CR irritability, and a poorer quality of relationship with the CR (Mahoney et al. 2005a). With respect to symptoms, carers' coping strategies appeared to be the strongest modifiable predictor (Cooper et al. 2008b), although this study did not find a relationship for depressive symptoms. I shall be exploring these relationships at length in my systematic review in Chapter 2 (Li et al. 2012).

There is fairly consistent evidence to show that the care recipient's level of impairment in cognitive functioning or activities of daily living are *not* independently related to carer anxiety (Cooper et al. 2007a), but conflicting evidence regarding severity of the care recipient's behavioural symptoms (Cooper et al. 2007a;Garcia-Alberca et al. 2011). Behavioural disturbance is known to be strongly associated with carer burden (Beeri et al. 2002;Sink et al. 2005), which itself is associated with depression and anxiety (Cooper et al. 2007a;Cooper et al. 2008b). Certain behaviours such as aggression, agitation and night-time wandering are particularly associated with carer depressive symptoms (Gallicchio et al. 2002;Gaugler et al. 2005). The relationship between care recipient behavioural symptoms and carer anxiety remains to be established by sufficiently powered prospective studies (Cooper et al. 2007a).

Carer burden and physical morbidity have been consistently associated with depression and anxiety levels in cross-sectional and longitudinal studies (Cooper et al. 2007a;Cooper et al. 2008b;Schulz et al. 1995). The relationship between carer psychological and physical health is likely to be bidirectional (Pinquart et al. 2007), and anxiety is also independently associated with poor health perception (Valente et al. 2011).

Carer gender

The increased prevalence of depression and anxiety in female carers is consistent with a greater prevalence of such disorders among women in the general population (McManus et al. 2009). However there have been conflicting findings as to whether being a female carer is associated with higher levels of psychological morbidity symptoms (Cooper et al. 2007a;Yee et al. 2000). While female carers do generally appear to be at greater risk of psychological morbidity than male carers (Garcia-Alberca

et al. 2012;Mahoney et al. 2005a), higher quality studies report no significant unique association on multivariate analyses (Cooper et al. 2007a). At least some of the observed association is likely to be due to confounding factors, including women generally facing greater caregiving demands (Yee et al. 2000).

Grief

Grief appears to explain some of the psychological morbidity among dementia family carers (Chan et al. 2012). One small study of 27 female carers showed a significant correlation between the level of anticipatory grief with depressive and anxiety symptoms (Theut et al. 1991). In a larger study of 122 carers, grief predicted almost half of the variance in depressive symptoms, implying a large component of carer depression could be interpreted as a normal grief reaction (Sanders et al. 2005). This might also be expected to be the case with carer anxiety although no such study has yet been conducted (Chan et al. 2012). The current study will aim to recruit family carers of individuals who have been recently referred to services (within past year), thus anticipatory grief may be present but severe grief reactions will not be commonly expected in this population (Chan et al. 2012). However it is interesting to note that divorce, separation and death of a partner, all life events involving significant emotional loss, are risk factors for depressive and anxiety disorders in the general population (Gelder et al. 2006); a spousal carer of someone with dementia is losing their partner as the illness progresses.

CR outcomes

Carer depression and anxiety are associated with significant negative outcomes for the person with dementia. In a representative sample of carers of people with dementia

newly referred to secondary care services, increased carer depressive and anxiety symptoms were independently associated with increased self-reported abusive behaviour towards their CRs (Cooper et al. 2009). This relationship was also longitudinal, with increase in depressive and anxiety symptoms predicting increase in abuse scores a year later (Cooper et al. 2010). Regardless of the direction of causal relationship, carer depression and anxiety are clinically important targets of intervention for carers themselves, as well as for the people with dementia.

1.3.7 Natural history of depression and anxiety in family carers

In studies of family carers of people with or without dementia, psychological distress has generally shown little or no systematic change throughout the course of caregiving, suggesting recurrent or persistent distress (Ballard et al. 1996;Kiecolt-Glaser et al. 1991;Pevalin et al. 2003;RIS MRC CFAS 2000;Taylor et al. 1995). Given the known associations between CR neuropsychiatric symptoms and carer depression (and possibly anxiety), persistent psychological morbidity may partially reflect the course of CR neuropsychiatric symptoms; these are usually persistent over 6 months (Ryu et al. 2005), and increase over years as the dementia progresses. A 6-year follow-up study of spousal carers presenting at GP surgeries in the Netherlands found no significant increase in the incidence of anxiety disorders compared with matched controls, although it was possible that anxiety was underdiagnosed or confounded with depression (Joling et al. 2010). The natural course of psychological morbidity in family carers would be an expected worsening with dementia progression. Two recent representatively sampled cohort studies have confirmed this: family carers' depression and anxiety symptoms worsened over 12 months (Cooper et al. 2008b;Cooper et al. 2009). In summary, there

is good evidence that carer depression and anxiety do not decrease, and may increase over time in the absence of targeted intervention.

Carer distress is often higher at the time of diagnosis and at times of important transitions, for example when the person with dementia moves to 24-hour care (Hirst 2005;Pot et al. 1997;Schulz et al. 2004). The time of diagnosis may theoretically be a useful time for intervening; by helping carers to cope through provision of information and skills, this may reduce current distress and protect them from further distress.

1.3.8 Interim summary

Feelings of tension and low mood are normal in everyday life, but depressive and anxiety disorders are associated with a diverse range of psychological and physiological symptoms, which interfere with daily functioning. Depression and anxiety are frequently comorbid, and carers of people with dementia have an increased prevalence of both disorders compared to the general population. This is due to stressors inherent to caring, particularly behavioural and psychiatric symptoms of dementia (see Section 1.2.5). Nonetheless not all carers develop depression or anxiety even taking into account differences in stressors, implying that some carers may be better than others at coping with stress.

1.4 Coping

1.4.1 A historical perspective

Early psychological study of coping emerged from two distinct schools of thought: experimental psychology using animal studies, and psychoanalytic ego psychology (Lazarus et al. 1984). Animal models of stress and emotions focused on mechanistic

frameworks of general arousal, whereby encounters with pleasant or threatening

environments would lead to either positive or negative emotions, thought to be

physiologically measurable through pupil dilation, skin conductance and cortisol

secretion. Coping was often seen as behavioural acts to control aversive environments,

and largely focused on avoidance and escape behaviours; cognition was generally not

considered (Lazarus et al. 1984). The animal model did not allow for individual

differences in response to stress: a particular encounter may be stressful for one person

but not another, suggesting that stress is individual as well as environmental (Lazarus

1966).

In contrast with animal models, psychoanalytic models saw coping as flexible

thoughts and acts to solve problems and thereby reduce stress, with the emphasis on

cognition, i.e. how the individual thinks about his or her relationship with the

environment (Lazarus et al. 1984). Freud (1936) first described defence mechanisms

(such as aggressive outbursts and psychosis) as unconscious distortions of reality, as

means of dealing with stress. Ego psychology further proposed such mechanisms to be

at the bottom of a hierarchy of strategies for managing stressful encounters; coping was

at the top of this hierarchy and considered the most advanced and mature (e.g.

Menninger 1963, Vaillant 1977). In most psychoanalytic models, coping styles were

generally seen as dispositional traits. Thus this conceptualisation was also inadequate in

practice, as measures of coping traits were found not to be good predictors of how

people actually coped in different situations (Lazarus et al. 1984).

Certain environments, such as bombing combat flyers in battle, are objectively

threatening, and greater objective dangers are associated with greater harm; yet even

such extreme encounters reveal individual differences in psychological and

physiological outcomes (Lazarus 1994). Personality traits are important determinants of

coping responses, but do not seem to explain fully such individual differences in emotion (Lazarus 1994). These observations led Lazarus and Folkman to develop a relational approach to emotion, which sees emotion as an individual response to a given environment, determined in part by coping responses operating at both cognitive and behavioural levels (Lazarus et al. 1984;Lazarus 1994).

1.4.2 Conceptual models of coping

Coping is the planful, effortful process through which individuals attempt to manage stress (Lazarus et al. 1984;Lazarus 1994). In the influential theory of Transactional Model of Stress, coping is defined as "constantly changing cognitive, behavioural, [and emotional] efforts to manage particular external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus et al. 1984). The person's cognitive appraisal has two core functions during this process: to determine the level of threat caused by the stressor; and of one's capacity to deal with this perceived threat, giving rise to coping efforts. Coping could therefore been seen as a buffering process against stress.

The Transactional Model was elaborated in later works into the Appraisal Theory of Emotion, to provide a comprehensive framework not only for stress, but for emotions in general (Lazarus 1994;Lazarus 2001). The individual's beliefs and goals are core antecedents in the emotion process; the individual appraises not only degree of threat or capacity, but also how personally significant or meaningful the event is (i.e. how relevant to his or her core beliefs and goal priorities). Coping strategies in this context are planful efforts in adaptation: cognitions or behaviours to shape the personal meaning of an encounter in accordance with motivational goals. Emotions are the psychological consequences of these adaptational processes.

Generally speaking, emotions only arise when the person-environment encounter has some personal significance (i.e. relevant to the individual's goals), and negative emotions arise when the encounter is appraised as incongruent with the individual's underlying goals. Furthermore, a specific meaning is attached to each specific emotion (for example, sadness is conceptualised as being associated with irrevocable loss), thereby different person-environment encounters give rise to different emotions. This framework also explains why similar stressful encounters could result in anxiety for some and depression for others, because the underlying beliefs and goals are different for each individual and for each encounter.

1.4.3 Categorisation and measurement of coping strategies

Within a relational framework of emotion, coping strategies could be seen broadly as attempts either to change the environment (problem-focused coping: altering those demands appraised as challenging), or to change oneself (emotion-focused coping: regulating one's emotional response or reappraising the encounter) (Lazarus & Folkman, 1984; Lazarus 2001). Folkman and colleagues (1980) devised the Ways of Coping Scale, a self-report questionnaire aimed at capturing how frequently an individual used different coping strategies in a given stressful situation. Problem-focused coping strategies include: trying to come up with solutions to the problem, redoubling efforts to make things work, seeking practical advice. Emotion-focused strategies may include: efforts to reappraise the stressor (for example, trying to look for the bright side of things), seeking emotional support, as well as strategies to disengage from the difficult emotions (for example, hoping for a miracle, using drugs or alcohol).

Some commentators have argued that the dichotomisation between problem-focused and emotion-focused is too simplistic, as Folkman's (1980) emotion-focused category

includes behaviours that may be dysfunctional, i.e. impede adaptive coping in the long term (Carver et al. 1989;Carver 1997). In developing their Coping Orientation to Problems Experienced scale (COPE), Carver and colleagues (1989) proposed 13 dimensions of coping behaviours (on theoretical and empirical bases of whether behaviours would enhance or impede adaptation), and that these could be further grouped into three clusters: problem-focused, emotion-focused, and dysfunctional coping (Carver 1997). This conceptualisation of coping will be adopted throughout my thesis.

This represents only one of many possible conceptualisations for coping strategies. Despite decades of research there is still little consensus on the how coping strategies should be divided (Amirkhan & Auyeung 2007; Skinner et al., 2003). For example, within studies of dementia carers alone, coping is variously conceptualised as adaptive (positive) versus maladaptive (negative), approach (engagement) versus avoidance (disengagement), cognitive versus behavioural, etc. (see my review in Chapter 2). The aforementioned constructs are not necessarily mutually exclusive, and their differences may be nuanced. These broad constructs also do not fully capture more specific modalities of coping such as relationship-focused or religious beliefs (Berg et al. 1998;Bjorklof et al. 2013). Categorising coping into a dimensional construct might also be criticised (Coyne & Racioppo, 2000), although it could be argued that such constructs are useful insofaras they inform clinical interventions to improve coping skills for people facing stressful encounters, including in dementia caring.

1.4.4 Coping in normal human circumstances

The empirical evidence for the Transactional Model of Coping is relatively well-established in normal populations, having been built on Folkman and colleagues' (1980)

early work in administering coping questionnaires to various non-clinical samples, usually in relation to retrospectively recalled stressful scenarios (which could include major life events to relatively minor stressors). One of these studies involving a total of 246 adults in two community samples of adults (mean ages 40 and 69) provided preliminary evidence suggesting that coping processes mediated the relationships between recently experienced stressful encounters, and positive or negative emotion at different stages of these encounters (Folkman et al. 1988a). Another important finding was that across 1,300 reported stressful encounters, individuals endorsed multiple coping strategies for 98% of the encounters (Folkman et al. 1980). A review of surveys involving a total of 3,000 young people aged 12 – 20 similarly suggested that across a range of common stressors (such as problems with school or parents), healthy individuals used all coping strategies but mainly problem-focused and emotion-focused ones; in comparison, psychologically distressed individuals endorsed relatively more dysfunctional coping (Seiffge-Krenke 1993).

A consistent finding throughout the literature is that the characteristics of the stressor are important in determining coping responses, in terms of the perceived controllability and chronicity of the stressor (Lazarus et al. 1984), and also the social context. For example, spouses tend to endorse more empathic coping strategies when faced with martial conflict as compared with children's misbehaviour (Lee-Baggley et al. 2005). For a given stressor, the timing at which an individual is experiencing an ongoing event also has implications on the coping strategies selected; for example, the same student going through different stages of a college examination (preparing, sitting, and having completed it) (Folkman et al. 1985). These findings may have some relevance for the dementia carer population given they face broadly similar types of stressors, but which may vary at different stages of the illness. More recent

methodological developments in the daily process approach to coping, have seen researchers elucidate the relationships between actual stressors, appraisals, coping and emotion closer to real-time (Tennen et al. 2000).

Coping mechanisms across maturation, gender and other variables

Coping processes may be viewed as products of both personality and environment; they evolve alongside personality in adolescence and early adulthood shaped by childhood experiences, and cognitive and emotional maturation. They may continue to evolve in adulthood through changes in social roles and corresponding motivational goals, in addition to changes in coping options, resources, and the nature of stressors (Amirkhan et al. 2007;Compas et al. 1992;Folkman et al. 1988b;Lazarus 2001;Skinner et al. 1998). Specific personality traits and coping styles are related, for example optimism and conscientiousness with more engagement and less disengagement coping (Carver et al. 2010). Developmental theories in psychology are also relevant (Skinner et al. 1998). For example, attachment theory would suggest that a proximity-seeking coping style is likely to have arisen from experiencing mostly secure attachment parent-child interactions, while a more problem-focused coping style might reflect more experiences of avoidant attachment (Skinner et al. 1998). These associations were demonstrated in one study of family carers of people with dementia (Cooper et al. 2008a).

A comprehensive factor analytic study including various age groups (from 9–70 years old) showed that while people of all ages tended to use the same types of coping strategies, problem-focused coping generally increased with age whilst dysfunctional coping declined, when controlling for stressor type (Amirkhan et al. 2007). The authors speculated that perceived controllability of the stressor might be more important than its

objective controllability, and that older adults would typically have had many more experiences in solving a wide range of everyday problems than young people (Amirkhan et al. 2007).

As with different age groups, men and women tend to employ the same range of coping strategies given similar stressful situations, but there are consistent if small differences across studies between men and women in the amounts of different strategies they tended to use (Tamres et al. 2002). Women tended to be more likely than men to use emotion-focused coping, particularly involving verbal expression. The extent to which such differences could be accounted for by dispositional (including biological) versus social factors (gender role expectations) is debated (Washburn-Ormachea et al. 2004),.

1.4.5 *Coping in the caring context*

Models of coping

Various theoretical models have been used to conceptualise the processes of stress and coping among different groups of family carers. Despite some differences in the contributions of specific stressors or carer roles in the stress process, most models have been influenced by or derived from the Transactional Model of Stress framework (Lazarus et al. 1984), sharing the core premise that stressors exert an effect on psychological and health outcomes via appraisal and coping (Knight et al. 2000). The Transactional Model has been directly adopted and empirically supported in explaining the health outcomes of different carer groups, ranging carers of people with cancer (Fitzell et al. 2010), parents with a deaf child (Feher-Prout 1996), and mental health carers (Mackay et al. 2012). The cognitive model of caregiving in psychosis (Kuipers et

al. 2010), in which carer appraisals and expressed emotions are seen as having a relatively strong impact on the patient's illness, was explicitly informed by the Transactional Model of Stress (Lazarus et al. 1984). Another generic model of caring focuses on the carer's underlying beliefs and values, associated goals and objectives, which then determine the carer's behaviours (including coping strategies) (Hall 1990); at a conceptual level this is not dissimilar to concepts of motivation and goals as antecedents in the Appraisal Theory of Emotion (Lazarus 1994).

In summary, the various models of coping in caring share more fundamental similarities than there are differences in that most conceptualise coping as an intermediary mechanism between stressor appraisal and adaptational outcomes, first proposed by Lazarus and Folkman (1984). Although this implies a certain degree of transferrability of the principles of coping interventions for carers, the unique nature of stressors in dementia care should be carefully considered (see Section 1.2.5)

Relationship between coping and psychological morbidity

The links between coping and mental health have been studied extensively in various different populations. In an exhaustive systematic review and meta-analysis, 34 cross-sectional studies have investigated associations between coping (as measured by the Ways of Coping scale or its variants) and various physical and psychological health outcomes (Penley et al. 2002). Studies incorporated a range of clinical and non-clinical stressors, from being a carer or patient with chronic illness, to being made redundant from employment. Overall, problem-focused coping was correlated with better health outcomes whilst most other types of coping (including seeking social support) were correlated with poorer health outcomes (Penley et al. 2002). The study did not take into account confounding factors, such as the magnitude of the stressor. Greater stressors

would be expected to elicit more coping strategies as well as increasing anxiety and depression (Li et al. 2012); see my review in Chapter 2.

The duration of a stressor might also determine the types of coping strategies that would be successful (Suls et al. 1985;Taylor et al. 1986). For short-term stressors, "dysfunctional" coping strategies might well be adaptive for the context (Lazarus 1983), for example providing relief from dental treatment, a situation that is time-limited (Wong et al. 1986), whereas long-term stressors may require greater cognitive and emotional coping efforts (Suls et al. 1985;Taylor et al. 1986). There is good evidence from the general population as well as patient and carer populations that chronic use of dysfunctional coping is associated with increased psychological and physical morbidity, and even mortality (Holahan et al. 1986;Taylor et al. 2007). These findings may have important implications for caring in dementia, a long-term and progressively deteriorating condition.

1.4.6 Coping in the context of dementia care

Models of coping

Broader theoretical models have been developed to conceptualise the process of coping in dementia caring, perhaps because dementia caring is intrinsically complex, comprising multiple and chronic aspects of threats and losses that are likely to increase as the person with dementia deteriorates (see Section 1.2.5) (Pearlin et al. 1990;Schulz et al. 2008).

Pearlin's (1990) stress-process model of coping expanded upon the conceptualisation by Lazarus & Folkman (1984), in specifying two levels of stressors: primary stressors (objective and subjective burden which stems directly from care

recipient's symptoms) and secondary stressors (arising as a consequence of primary stressors, for example: family strains, occupational and financial difficulties, feelings of captivity in the caring role). Accordingly, coping strategies can reduce the impact of primary stressors, and also block the proliferation of secondary stressors. Nolan and colleagues' (1996) conceptualised a six-stage longitudinal descriptive model, based on interviews with carers of people with dementia, and this describes a stressor-appraisal-coping-outcome process occurring within each of the stages of the caring journey. Finally the Sociocultural-Stress Model of caregiving adds a cultural dimension (also based on evidence from dementia carers) (Knight et al. 2000); it assumes different culture groups share common processes of appraisal, and cultural values operate via coping strategies and coping resources.

Correlates of coping in dementia carers

There is little specific research on the correlates of dementia carers' coping styles. The finding that older people in the general population tend to use a more problem-focused coping style than younger people may have some implications given that most dementia carers are older adults (Amirkhan et al. 2007). Demographic factors may be of less importance, however, than the nature of the specific stressor in determining coping strategies of dementia carers versus the general population facing everyday challenges. The ambiguous, unpredictable, worsening and often uncontrollable nature of the stressors associated with dementia might explain why carers tend to use more dysfunctional styles of coping, such as denial, than the general population (Dempsey et al. 1998;Sanders et al. 2007).

Some preliminary evidence suggests that family carer coping also has an impact on CR outcomes, beyond the immediate impact on the family carers themselves. A recent

study found that increased use of coping strategies predicted slower cognitive and global decline of the person with dementia, as measured by MMSE (Mini-Mental State Examination) and CDR-SB (Clinical Dementia Rating, sum of boxes) (Tschanz et al. 2012). One prospective study even found that adjusted for CR impairments, carer's greater use of dysfunctional coping strategies (wishfulness-intrapsychic coping) independently predicted shorter survival time of the CR (McClendon et al. 2004).

Relationship between coping and psychological morbidity

There is no universally effective or ineffective coping strategy; the effectiveness of coping strategies depends partly on the situational demands of the stressors. Thus there is likely to be some commonality in the styles of coping that are helpful and unhelpful for carers of people with dementia.

In the dementia carer literature, psychological morbidity has been found to be even more strongly associated with the coping strategies used by the carer, than the demographic characteristics of the carer, and neuropsychiatric symptoms and illness severity in the person with dementia (Cooper et al. 2008b). Nonetheless earlier studies have reported conflicting results about the relationships between emotion-focused or dysfunctional coping styles and psychological morbidity (Crespo et al. 2005;Kneebone et al. 2003;Neundorfer 1991;Shaw et al. 1997;Vedhara et al. 2001). In the most recent systematic review, Kneebone and Martin (2003) considered 18 studies of carers of people with dementia, concluding that problem-solving and emotion-focused styles of coping appear to be beneficial for family carers. They acknowledged that their findings were limited because studies did not control for severity of stressors.

An additional source of differing conclusions may be use of the term "emotion-focused coping". In Folkman & Lazarus' Ways of Coping questionnaire the term

encompassed both acceptance-based strategies as well as avoidant and other dysfunctional strategies; whereas in other questionnaires such as COPE, emotion-focused referred only to the acceptance-based coping strategies and emotional support seeking.

To clarify the relationship between coping style and psychological distress in carers of people with dementia, I led a systematic review as part of my thesis (see Chapter 2; see Appendix A for published paper).

The longitudinal stability of dementia carers' coping

Longitudinal studies of dementia family carers suggest coping styles are amenable to change, but generally remain stable unless the environment or the nature of the burden changes, consistent with the Transactional Model (Lazarus et al. 1984). Goode and colleagues (1998) found that among 122 family carers of people with dementia, use of approach coping (encompassing positive aspects of both problem- and emotion-focused strategies) remained stable over 12 months. The LASER-AD study similarly found that over 24 months of follow-up, use of all coping strategies (problem-focused, emotion-focused and dysfunctional) were generally stable (Cooper et al. 2008a). Where problem-focused or dysfunctional coping did increase, this corresponded with an increase in carer burden. However, changes in emotion-focused coping appeared not to correlate directly with changes in carer burden. The researchers speculated that emotion-focused coping strategies might be more influenced by powerful external factors such as life events or therapeutic input (Cooper et al. 2008a).

1.4.7 Does coping respond to intervention?

There is mixed evidence of the efficacy of interventions to change coping, despite its theoretical and documented flexibility (Brown et al. 2008;Coyne et al. 2000;Skinner et al. 1998). This makes sense if coping is not only a 'strategy' but a deeply embedded mode of adaptation and related to personality (Skinner et al. 1998). From a developmental perspective, interventions should empower the individual through building skills to anticipate and manage stressful situations, and challenging faulty appraisal patterns (Lazarus 2001;Skinner et al. 1998). Cognitive reframing interventions could encourage attention to previously neglected facets of experience to give more complete and objective context and meaning (Lazarus 2001).

The evidence in various patient and carer populations suggests that interventions based around cognitive behavioural principles may be efficacious in changing coping. For example among 28 RCTs (randomised controlled trials) of interventions identified for HIV patients (Harding et al. 2011)., a small majority (16 studies) showed a positive intervention effect on improving coping; that is increased emotion-focused coping, or decreased dysfunctional coping versus control. The effective interventions consisted mostly of cognitive behavioural and stress management interventions, delivered in either individual or group format. In the asthma population, there is a smaller evidence base; Barton and colleagues (2003) found two RCTs respectively on children with asthma and parents of such children, suggesting that improvement in asthma and anxiety symptoms was mediated by improvement in parent coping strategies in the treatment groups.

Family carers of people with dementia

Several systematic reviews of family carer interventions have included coping as an outcome (Schulz et al. 2002;Selwood et al. 2007;Sorensen et al. 2002;Vernooij-Dassen

et al. 2011), but none have systematically explored intervention effects on different coping strategies, or considered coping as a potential mediator of treatment effects on psychological morbidity.

To establish the efficacy of interventions on specific coping styles and their consequent impact on psychological morbidity in carers of people with dementia, I conducted a second systematic review as part of this thesis (see Chapter 3; and Appendix A for published paper).

1.5 Summary

Dementia is a chronic illness with substantial disease and economic burden, on individuals and on the society. Most people with dementia in the UK are cared for at home by family carers (Knapp et al. 2007). Caring for someone with dementia presents particular challenges, both quantitative in terms of the excess hours of care required, and qualitative such as relationship changes and grief resulting from the symptoms and progression of dementia (Chan et al. 2012;Ory et al. 1999;Pearlin et al. 1990;Pinquart et al. 2003b). Therefore family carers are at high risk of psychological morbidity (Mahoney et al. 2005a;Pinquart et al. 2003b). With dementia becoming increasingly common due to demographic changes (Alzheimer's Society 2012;Wancata et al. 2003), the demand for family carers and the numbers with psychological morbidity will undoubtedly increase.

Coping strategies, the ways in which people manage stressful situations, appear to be important determinants of psychological morbidity among family carers of people with dementia (Cooper et al. 2007a;Cooper et al. 2008b). The use of coping strategies aimed at managing one's own emotions in response to caring burden (emotion-focused coping) appears to be protective against anxiety and depression, whereas anxiety and

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depression might worsen with other forms of coping, such as avoidance and denial (Cooper et al. 2008b). There is less clear evidence regarding how carers' coping styles may change over time, how they may respond to interventions, and how this may impact upon psychological morbidity. Further understanding of the role of coping in psychological morbidity could inform the development of effective carer interventions, which would improve outcomes not only for carers themselves but also for the people with dementia they care for.

In the following chapters, I shall present two systematic reviews: the first investigated the relationship between carer coping and psychological morbidity in observational studies (Chapter 2), and the second investigated whether changes in coping could explain the effectiveness of interventions for psychological morbidity (Chapter 3).

2 *Systematic review: Relationship between coping style and psychological morbidity among carers of people with dementia*

A paper describing this systematic review was published in the *Journal of Affective Disorders* (Li et al. 2012) (see Appendix A). This review was completed in collaboration with my supervisors Prof Gill Livingston (GL) and Dr Claudia Cooper (CC), and research assistants (RAs) in the START research team Jonathan Bradley (JB) and Amanda Shulman (AA).

2.1 Background

Many studies have explored the relationship between coping style and psychological morbidity in carers of people with dementia, with conflicting findings (Crespo et al. 2005;Kneebone et al. 2003;Neundorfer 1991;Shaw et al. 1997;Vedhara et al. 2001). The most comprehensive systematic review to date included 12 cross-sectional and 6 longitudinal studies, yet the conclusions of the review were limited because studies did not take into account the influence of the stressors (Kneebone et al. 2003). Greater stressors would be expected to elicit more coping strategies as well as increasing anxiety and depression.

One of the challenges of reviewing the coping literature is the vast number of different but similarly valid coping measures and nomenclatures in use, such that specific coping behaviours might be categorised under one heading in one measure, but a conceptually different heading in another measure. For example "sought help from persons or groups with similar experiences", categorised as an "active behavioural" coping strategy in the Health and Daily Living Form (HDLF) (Moos et al. 1983), could

be categorised as either a problem-focused or emotion-focused strategy in the Brief COPE (Carver 1997). Furthermore, the same heading (for example "emotion-focused coping") might be conceptually different in different measures. Consequently some authors of reviews have adopted an exclusive approach, for example only considering studies using variants of the Ways of Coping Checklist (WCCL) (Folkman et al. 1980), yet to our knowledge no review has provided an exhaustive synthesis of the entire literature.

2.1.1 *Aim*

The aim of this review was to identify and integrate existing studies and establish the relationships between coping and psychological morbidity in carers of people with dementia.

2.1.2 *Objectives*

The objectives of this review were twofold. First, to reclassify coping strategies (subscales of coping measures) using a common framework to ensure comparability between studies, and to remove any lack of clarity due to nomenclature. Second, taking coping strategies classified under this new taxonomy, to conduct meta-analysis of their statistical relationships with psychological morbidity, taking into account two specific stressors (CR's severity of dementia and neuropsychiatric symptoms), as the use of coping strategies is expected to increase as stressors increase.

2.1.3 *Hypothesis*

We hypothesised that carer depression and anxiety would be associated with greater use of emotion-focused coping strategies and less use of dysfunctional coping.

2.2 Method

2.2.1 Inclusion and exclusion criteria

We included primary, observational studies (cross-sectional or longitudinal), published in English up to March 2010 that reported a quantitative relationship between coping strategies and psychological morbidity in family/informal carers of people with any form of dementia. We adopted a broad definition of "family carer" as any unpaid carer. Studies that reported data on family carers of people without dementia were excluded, unless they reported the results for dementia carers separately. We included only studies that used standardised, quantitative measures of coping and psychological morbidity.

2.2.2 Search strategy

We searched EMBASE, MEDLINE, PsycINFO, Web of Science, CINAHL and AMED from inception to March 2010. The search terms were: (carer OR caregiver OR caring OR relative OR supporter OR family); (dementia OR Alzheimer OR cognitive impairment); coping; (anxiety OR depression OR mood OR psychiatric morbidity OR psychological morbidity).We hand searched relevant reviews, the references of included studies, and asked authors of included studies whether they were aware of any further studies.

2.2.3 Categorising coping strategies

Basis for the three-category framework for coping

Coping measures are typically divided into subscales (either driven by theory or factor analysis), and sometimes clusters of subscales formed higher-order coping

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categories. For example, the Coping Responses Inventory (CRI) comprised 8 subscales which collapsed into 2 higher-order categories, approach coping and avoidance coping (Moos 1988). To ensure comparability between studies in the current review, coping measures in all included studies had to be reclassified according to a common framework.

Our framework for coping strategies consisted of three higher-order categories: problem-focused, emotion-focused and dysfunctional strategies. These three headings were first used by Carver and colleagues (1989) to describe 14 conceptually distinct coping strategies (subscales) comprising the 60 items of the COPE Inventory, based on theory and as empirical evidence on the extent to which coping strategies might be adaptive or maladaptive . This categorisation was then validated against anxiety in older and younger adults by Coolidge and colleagues (2000). Finally, the same three headings were applied to the 14 subscales (28 items) in the Brief COPE in a sample of dementia carers, also demonstrating satisfactory psychometric properties (Cooper et al. 2008a). The three categories thus provided a useful, valid and reliable framework within which coping measures described in this review could be reclassified.

Table 2.1. Three-category structure of the Brief COPE

Problem-focused	Emotion-focused	Dysfunctional
Concentrating my efforts on doing something about the situation I'm in	Getting emotional support from others	Turning to work or other activities to take my mind off things
Taking action to try to make the situation better	Trying to see it in a different light, to make it seem more positive	Saying to myself "this isn't real"
Getting help and advice from other people	Getting comfort and understanding from someone	Using alcohol or other drugs to make myself feel better
Trying to come up with a strategy about what to do	Looking for something good in what is happening	Giving up trying to deal with it
Trying to get advice or help from other people about what to do	Making jokes about it	Refusing to believe that it has happened
Thinking hard about what steps to take	Accepting the reality of the fact that it has happened	Saying things to let my unpleasant feelings escape
	Trying to find comfort in my religion or spiritual beliefs	Using alcohol or other drugs to help me get through it
	Learning to live with it	Criticising myself
	Praying or meditating	Giving up the attempt to cope
	Making fun of the situation	Doing something to think about it less, such as going to the cinema, watching TV, reading, daydreaming, sleeping or shopping
		Expressing my negative feelings
		Blaming myself for things that happened

Reclassifying coping strategies

Source documents (original questionnaires, reports of item generation, psychometric validation) were retrieved for all coping measures included in the review. For each distinct coping measure, each of its coping subscales was reclassified into one of three higher-order coping categories within our new framework. This was done by my examining and interpreting the meaning of the individual questions comprising each subscale, then coded that subscale as "problem-focused", "emotion-focused" or

"dysfunctional" based on my judgment which of these three categories was the closest in function to the questions under consideration. This took into account any specific theoretical or empirical background information provided by the authors of the coping measure. My classification was then discussed with GL and CC, and finalised through consensus, including any revisions made as necessary. Coping subscales containing items that appeared to overlap substantially across two or more higher-order coping factors within our framework (for example, "seeking social support" in the Ways of Coping Questionnaire included both items for practical support and for emotional support) were categorised as such. We excluded any coping subscales used in the included papers that could not be categorised using this system (for example, a subscale consisting entirely of religious coping behaviours).

2.2.4 Quality assessment

The quality of each included study was rated independently by myself and one other author (AS or JB), blind to each other's ratings. Disagreements were resolved through discussion with GL. Our measure of study quality was adapted from Boyle (1998), a standardised checklist for evaluating bias in prevalence studies. The original checklist is a set of standardised criteria, originally developed for studies of psychiatric disorders (Boyle 1998), but has since been used more widely, for example in cancer (Gurunath et al. 2011), HIV (Chow et al. 2011), and also for prevalence studies in the dementia carer population (Cooper et al. 2007a). Given that many of the quality criteria for association studies are similar to those for prevalence studies, the checklist was adapted to operationalise the existing criteria, and to include additional items evaluating reliability and validity of both outcome measures of interest (psychological morbidity and coping), confounding factors, and relevant quality criteria for longitudinal studies. Therefore a

study that met more quality criteria would be seen as more valid in answering our hypothesis.

In our adapted checklist, we awarded points as follows for cross-sectional studies:

- Power analysis based on relationship between coping and depression/anxiety: 1 point
- Clearly defined population: 1 point
- Representative sample: 1 point for probability sampling, or whole population was recruited (for example, consecutive sampling).
- Participants and non-participants comparable: 1 point if demonstrated statistically, or if participation rate ≥80%
- Reliability and validity: for each, 0.5 point if measures of psychological morbidity and coping validated in target population, 0.25 points if validated only in another population.
- Confounding factors: 1 point if all of the following confounders were identified or addressed; carer gender and physical health, care recipient neuropsychiatric symptoms, carer burden.

For longitudinal studies, we applied two additional criteria: 1 point if participants were followed up for at least 6 months; 1 point if at least 80% of participants were followed up (or those lost to follow up were shown to be comparable). We categorised as "higher quality" those studies with quality score equal to or greater than the median score, respectively for cross-sectional and longitudinal studies.

2.2.5 Data extraction and analysis

From all included studies, we extracted correlation and regression coefficients for relationships between psychological morbidity (depression, anxiety, or mixed symptoms) and carer coping strategies. We categorised these coping strategies within our new framework, tabulating the direction and statistical significance of these relationships . For example, a reported correlation between depressive symptoms and avoidance coping measured using the Revised Ways of Coping Checklist (classified as dysfunctional coping within our framework) would be tabulated as an association between depression and dysfunctional coping.

As dementia severity was a known confounder in the relationship between carer coping and mental health, we only meta-analysed studies that controlled for severity of dementia (either by cognitive status or duration of illness) or neuropsychiatric symptoms. From these studies we extracted standardised beta regression coefficients for the relationships between psychological morbidity and coping strategies. We calculated regression coefficients from our own data (Cooper et al. 2008b;Cooper et al. 2010). Coefficients were pooled to produce a weighted mean correlation (WMC) coefficient, using a random effects model to account for heterogeneity (Hunter et al. 1990). We conducted statistical analysis using the SPSS 17 software package (SPSS Inc. 2008), and used StatsDirect 2.6.6 to produce forest plots (StatsDirect Ltd. 2008). We considered whether differences in study quality ratings could potentially explain some of the findings, and intended to prioritise the findings from the higher quality studies.

2.3   Results

2.3.1   Study description and methods

From 5396 publications identified by our systematic searches, we included 35 unique studies (28 cross-sectional and seven prospective) reported across 37 publications (see Figure 2.1: Flowchart of included/excluded studies). One paper reported different study procedures for its US and China samples (Shaw et al. 1997) and was therefore included as two separate studies.

Most of the studies (30/35) were from developed, English-speaking countries; of the remainder, two were from Taiwan (Fuh et al. 1999;Huang et al. 2006), and one each from Belgium (Schoenmakers et al. 2009), the Netherlands (Pot et al. 2000), and China (Shaw et al. 1997).

Figure 2.1: Flowchart of included/excluded studies.

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 │ Excluded: 305 did not report all required  │     │
 │              outcome measures              ├─────┤
 │ 77 not primary quantitative study          │     │
 │ 33 no specific data on carers of people    │     │
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 │ Excluded: 126 no measures of relationship  │     │
 │    between coping and anxiety/depression   ├─────┤
 │ 16 no specific data on carers of people    │     │
 │              with dementia                 │     │
 │ 13 intervention studies                    │     │
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2.3.2 Coping strategies

Table 2.2 shows how the 24 distinct coping measures utilised in the included studies, their original subscales/factors and how these were reclassified according to our framework. The same coping measure divided into different sets of subscales in different studies would be considered "distinct coping measures"; for example, the Revised Ways of Coping Checklist (RWCCL) was divided into two or eight factors owing to different factor analyses (Vitaliano et al., 1990, 1993).

Table 2.2. Coping strategies (subscales or factors) from validated coping measures, recategorised as problem-focused, emotion-focused or dysfunctional.

Representative item in [brackets]; * items overlapping across two or more factors.

| Coping measure | New categories | | |
	Problem-focused	Emotion-focused	Dysfunctional
Ways of Coping Checklist (WCCL) 2-factor (Folkman et al. 1980) – 68 items	**Problem-focused** [Made a plan of action and followed it.]	**Emotion-focused*** [Looked for the "silver lining", so to speak; tried to look on the bright side of things.]	**Emotion-focused*** [Tried to forget the whole thing.]
Ways of Coping Checklist (WCCL) 7-factor (Aldwin et al. 1987) – 42 items	**Problem-focused** – 9 items [Changed something so things would turn out all right.] **Mixed scale*** - 8 items [Asked someone I respected for advice and followed it.]	**Wishful thinking*** – 14 items [Accepted the next best thing to what I wanted.] **Growth** – 3 items [Came out of the experience better than when I went in.] **Seeks social support** – 2 items [Talked to someone about how I was feeling.]	**Minimized** – 2 items [Tried to forget the whole thing.] **Mixed scale*** – 8 items [Got mad at the people or things that caused the problem.] **Wishful thinking*** - 14 items [Hope a miracle would happen.] Blamed self [Realized you brought on the problem yourself.]

	New categories		
Coping measure	*Problem-focused*	*Emotion-focused*	*Dysfunctional*
Ways of Coping Questionnaire (WCQ) (Folkman et al. 1988b) – 50 items	**Planful problem-solving** – 6 items [I knew what had to be done, so I doubled my efforts to make things work] **Seeking social support*** – 6 items [Talked to someone to find out more about the situation]	**Positive reappraisal** – 7 items [Changed or grew as a person in a good way] **Distancing*** – 6 items [Made light of the situation; refused to get too serious about it] **Self-controlling*** [Tried not to burn my bridges, but leave things open somewhat] **Seeking social support*** – 6 items [Accepted sympathy and understanding from someone]	**Accepting responsibility** – 4 items [Criticized or lectured myself] **Escape-avoidance** – 8 items [Wished that the situation would go away or somehow be over with] **Self-controlling*** - 7 items [I tried to keep my feelings to myself] **Distancing*** – 6 items [Tried to forget the whole thing] **Confrontational coping** – 6 items [I expressed anger to the person(s) who caused the problem]
Shanghai Ways of Coping Questionnaire (WCQ) (Shaw et al. 1997) – 40 items	**Behavioural distancing/social support*** – 5 items [Talked to find out more about it]	**Cognitive distancing*** – 9 items [Made light of the situation] **Cognitive confronting*** – 7 items [Sometimes just bad luck] **Behavioural distancing/social support*** – 5 items [Talked to someone about feelings]	**Behavioural confronting** – 13 items [Brought the problem on myself] **Cognitive distancing*** – 9 items [Refused to think about it] **Cognitive confronting*** – 7 items [Wished that it would go away]
Revised Ways of Coping Checklist (RWCCL) (Vitaliano et al. 1987) – 42 items	**Problem-focused** – 15 items [Bargained or compromised to get something positive from the situation.] **Seeks social support*** – 6 items [Talked to someone to find out about the situation.]	**Seeks social support*** – 6 items [Accepted sympathy and understanding from someone.]	**Wishful thinking** – 8 items [Hoped a miracle would happen.] **Avoidance** – 10 items [Went on as if nothing had happened.] **Blamed self** – 3 items [Blamed yourself.]
Revised Ways of Coping Checklist (RWCCL) 3-factor (Vitaliano et al. 1990) – 42 items	**Problem-focused** – 15 items [Bargained or compromised to get something positive from the situation.] **Seeks social support*** - 6 items [Talked to someone to find out about the situation.]	**Seeks social support*** - 6 items [Accepted sympathy and understanding from someone.]	**Emotion-focused: wishful thinking, avoidance, blamed self** – 21 items [Hoped a miracle would happen.]

Coping measure	New categories		
	Problem-focused	Emotion-focused	Dysfunctional
Revised Ways of Coping Checklist (RWCCL) 8-factor (Vitaliano et al., 1993) – 57 items	**Problem-focused** – 15 items **Seeking social support*** - 6 items	**Counting one's blessings** – 6 items **Seeking social support*** **Religiosity** – 3 items	**Avoidance** – 10 items **Blame of others** – 6 items **Self blame** – 3 items **Wishful thinking** – 8 items
Revised Ways of Coping Checklist (RWCCL) with relationship-focused items (DeLongis et al. 1990) – 56 items	**Problem-focused** – 14 items [I came up with a couple of different solutions to the problem.]	**Positive relationship-focused** – 9 items [I imagined myself in my spouse's shoes.]	**Emotion-focused** – 21 items [I criticised or lectured myself.] **Negative relationship-focused** – 12 items[I expressed anger to my spouse.]
Modified Ways of Coping Checklist (MWOC) (Smyth et al. 1996) – 35 items	**Active coping*** - 15 items [Talked to someone who could do something concrete about the problem]	**Active coping*** - 15 items [Rediscovered what was important in my life] **Minimise the situation** – 10 items [Didn't let it get to me; refused to think too much about it]	**Avoidance coping** – 10 items [Had fantasies or wishes about how things might turn out]
Coping Orientation to Problems Experienced Scale (COPE) (Carver et al. 1989) – 54 items items	**Active coping** – 4 items [I take additional action to try to get rid of the problem] **Suppression of competing activities** – 4 items [I put aside other activities in order to concentrate on this] **Restraint coping** – 4 items [I force myself to wait for the right time to do something] **Seeking social support for instrumental reasons** – 4 items [I ask people who have had similar experiences what they did.] **Planning** – 4 items [I try to come up with a strategy about what to do]	**Seeking social support for emotional reasons** – 4 items [I talk to someone about how I feel.] **Positive reinterpretation and growth** – 4 items [I look for something good in what's happening.] **Acceptance** – 4 items [I learn to live with it.] **Turning to religion** – 4 items [I seek God's help.]	**Behavioural disengagement** – 4 items [I give up the attempt to get what I want.] **Mental disengagement** – 4 items [I turn to work or other substitute activities to take my mind off things.] **Focus on and venting of emotions** – 4 items [I get upset and let my emotions out.] **Denial** – 4 items [I refuse to believe that it has happened.] **Alcohol-drug disengagement** – 4 items [I drink alcohol or take drugs, in order to think about it less.] **Substance use** – 1 item [I've been using alcohol or other drugs to make myself feel better.]

	New categories		
Coping measure	*Problem-focused*	*Emotion-focused*	*Dysfunctional*
Coping Orientation to Problems Experienced Scale (COPE) 2-factor (Kim et al. 2007) – 60 items	**Active** (active coping, planning, positive reappraisal, restraint coping, suppression of competing activities)* – 16 items	**Active** (active coping, planning, positive reappraisal, restraint coping, suppression of competing activities)* – 16 items	**Avoidant** – 44 items
Brief Coping Orientation to Problems Experienced Scale (brief COPE) (Carver 1997) – 28 items	**Active coping** – 2 items [I've been concentrating my efforts on doing something about the situation I'm in] **Using instrumental support** – 2 items [I've been trying to get advice or help from other people about what to do.] **Planning** – 2 items [I've been thinking hard about what steps to take]	**Using emotional support** – 2 items [I'm been getting emotional support from others.] **Positive reframing** – 2 items [I've been trying to see it in a different light, to make it seem more positive] **Acceptance** – 2 items [I've been accepting the reality of the fact that it has happened.] **Religion** – 2 items [I've been trying to find comfort in my religion or spiritual beliefs.] **Humour** – 2 items [I've been making jokes about it]	**Behavioural disengagement** – 2 items [I've been giving up the attempt to cope.] **Self-distraction** – 2 items [I've been doing something to think about it less, such as going to the movies, watching TV, reading, daydreaming, sleeping or shopping.] **Venting** – 2 items [I've been saying things to let my unpleasant feelings escape.] **Denial** – 2 items [I've been saying to myself "This isn't real"] **Self-blame** – 2 items [I've been criticizing myself.]
Health & Daily Living Form (HDL) (Moos et al. 1983) – 40 items	**Active behavioural*** [Made a plan of action and followed it] – 13 items **Active cognitive*** [Considered several alternatives for handling the problem] – 11 items	**Active behavioural*** [Sought help from persons or groups with similar experiences] – 13 items **Active cognitive*** [Prayed for guidance and/or strength] – 11 items	**Avoidance** [Avoided being with people in general] – 8 items
Adapted Health & Daily Living Form (HDL) (Kirsch et al., 2000) – 40 items	**Active*** [Made a plan of action and followed it] – 24 items	**Active*** [Treated myself to something I liked] – 24 items	**Avoidance** [Avoided being with people in general] – 8 items

	New categories		
Coping measure	Problem-focused	Emotion-focused	Dysfunctional
Coping Responses Inventory (CRI) Billings & Moos, 1984 – 28 items	Problem-focused coping: seeking information – 5 items [Tried to find out more about the situation] Problem solving – 4 items [Made a plan and followed it] Appraisal-focused coping: logical analysis* – 4 items [Considered several alternatives for handling the problem]	Appraisal-focused coping: logical analysis* – 6 items [Tried to be more objective] Emotion-focused coping: affective regulation – 5 items [Tried to see the positive side of the situation]	Emotion-focused coping: emotional discharge – 4 items [Let my feelings out somehow]
Coping Responses Inventory (CRI) Moos, 1988 – 48 items	Approach coping: take problem-solving action – 6 items Approach coping: logical analysis* – 6 items Approach coping: seek guidance and support* – 6 items	Approach coping: logical analysis* – 6 items Approach coping: positive reappraisal – 6 items Approach coping: seek guidance and support* – 6 items	Avoidance coping: cognitive avoidance – 6 items Avoidance coping: acceptance-resignation – 6 items Avoidance coping: seek alternative rewards – 6 items Avoidance coping: emotional discharge – 6 items
Utrecht Coping List (UCL) (Turner et al., 2012) – 44 items	Active coping – 7 items	Seeking social support – 6 items Fostering reassuring thoughts – 5 items Expressing emotions – 3 items	Seeking distraction – 8 items Avoiding – 8 items Depressive reaction pattern – 7 items
Carers Stress Scale (Pearlin et al., 1990) – 21 items	Management of situation – 4 items [Do the things you really have to do and let other things slide]	Management of meaning: reduction of expectation – 3 items [Try to accept your relative as he/she is, not as you wish he/she could be.] Management of meaning: making positive comparisons – 3 items [Try to think of the good times you had in the past.] Management of meaning: constructing a larger sense of the illness – 3 items [Pray for strength to keep going]	Management of distress – 8 items [Smoke]

	New categories		
Coping measure	Problem-focused	Emotion-focused	Dysfunctional
Jalowiec Coping Scale (JCS) 3-factor (Jalowiec, 1988) – 40 items	Confrontive – 15 items [Try to look at the problems objectively and see all sides]	Palliative* - 15 items [Accept the situation as it is]	Palliative* - 15 items [Resign because things look hopeless] Emotive – 10 items [Get nervous]
Coping Strategy Indicator (CSI) (Amirkhan, 1990) – 33 items	Problem-solving – 11 items [Tried to solve the problem] Seeking support* – 11 items [Told people about the situation because talking about it helped you come up with solutions]	Seeking support* – 11 items [Confided your fears and worries to a friend or relative]	Avoidance – 11 items [Slept more than usual]
Gottlieb & Rooney (2004) – 15 items	Symptom management – 4 items [I say comforting, reassuring or calming things to my relative]	Acceptance – 4 items [I accept the problem; that's just the way it is] Positive framing – 4 items [I tell myself that things aren't so bad]	Emotional inhibition – 3 items [I tell myself not to let my feelings show]
Kiyak instrument (Kiyak et al., 1985) – 16 items	Instrumental – 5 items [Felt inspired to be creative in solving problem]	Acceptance – 4 items [Refused to let it get to you]	Wishfulness – 3 items [Wished you were a stronger person to deal with it better] Intrapsychic – 4 items [Had fantasies about how things might turn out]
Parks & Pilisuk (1991) – 36 items	Objectifying – 9 items [Rational, objective information gathering and planning]	n/a	Fantasy – 9 items [Wish for greater personal power and miraculous changes in prognosis or history] Withdrawal – 9 items [Unwilling to let people know how bad things really are] Internalising – 9 items [Passive turning inward, detachment from action]
Ways of Coping with Caring Questionnaire (Matson, 1994) – 34 items	Active-involved – 16 items [Having an organised routine]	Non-confronting coping* - 10 items [Confiding in others] Value coping – 8 items [Regarding caring as a privilege]	Non-confronting coping* - 10 items [Keeping busy doing anything to avoid thinking of caring]

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2.3.3 Cross-sectional studies

Table 2.3 summarises characteristics and findings of the included studies, with study quality rating ranging 2 – 5 (median 3). Four longitudinal studies additionally provided cross-sectional baseline data (Cooper et al. 2006;Kinney et al. 2003;Matson 1994;Vedhara et al. 2000) (see Table 2.4). Dysfunctional coping was most often associated with increased anxiety, while most papers evaluating problem-focused or emotion-focused coping reported non-significant associations with anxiety. For depression, a large majority of papers reported positive associations with dysfunctional coping; problem-focused coping and emotion-focused coping were most often reported as non-significant or negative associations. Overall, there were no observable differences between higher and lower quality studies in the direction and statistical significance of findings.

We extracted and meta-analysed regression coefficients from the 11 studies that controlled for severity of dementia or neuropsychiatric symptoms. All of these studies measured either depression or anxiety, except for the single study providing extractable data on mixed psychological morbidity (Hinrichsen et al. 1994).

Table 2.3. Cross-sectional studies reporting correlation or regression coefficients between psychological morbidity and coping strategies (as recategorised according to new framework).

Key: ↑ Positive association (p < 0.05), ↓ Negative association (p < 0.05) , ns No significant association. * Coping factors overlap into multiple categories thus strength of relationship to any single category will be overestimated. Study quality ratings rounded to nearest 1.

Cross-sectional studies: Higher quality (score ≥ 3)

Study	Carers	Recruitment source	N carers	Outcome measures Psych. morbidity	Coping	Results: Coping factors associated with morbidity Anxiety	Depression	Mixed measures	Study qual.
Batt-Leiba 1998	Spouses	Carer groups and day centres	32	CES-D	Revised WCCL		↓ Problem-focused ns Emotion-focused ↑ Dysfunctional		3
Cooper 2010	Family carers	Consecutive referrals to community psychiatric sevices	220	HADS	Brief COPE	ns Problem-focused ns Emotion-focused ↑ Dysfunctional	ns Problem-focused ns Emotion-focused ↑ Dysfunctional		5
Haley 1996	Family carers	Memory clinic	197	CES-D	CRI		↓ Problem-focused* ↓ Emotion-focused* ↑ Dysfunctional		3.75
Huang 2006	Family carers	Carer association and nursing home	148	CES-D	Modified WCCL		↓ Problem-focused* ↓ Emotion-focused ↑ Dysfunctional		3.75

Study	Carers	Recruitment source	N carers	Psych. morbidity	Coping	Outcome measures Anxiety	Depression	Results: Coping factors associated with morbidity Mixed measures	Study qual.
Kim 2007	Family carers	Random sample of households	160	CES-D, BSI	COPE		ns Problem-focused* ns Emotion-focused* ↑ Dysfunctional		3.75
Knight 2000	Family carers	Various sources	169	STAI, CES-D, BSI	WCQ			↓ Problem-focused* ↓ Emotion-focused* ↑ Dysfunctional	3.75
Knop 1998	Spouses	Support groups, health and day care services, nursing homes	63	CES-D	JCS		↓ Problem-focused ↑ Dysfunctional		3.5
Kramer 1993	Spouses	Media and community services	72	CES-D	Revised WCCL with relationship items		ns Problem-focused ns Emotion-focused ↑ Dysfunctional		3
Lutzky 1994	Spouses	Various community sources	92	CES-D, GSI	WCCL		ns Problem-focused ↑ Dysfunctional	ns Dysfunctional	3
Pot 2000	Family carers	Various community sources	165	GHQ-12	UCL			ns Problem-focused ns Emotion-focused ns Dysfunctional	3
Saad 1995	Family carers	Consecutive referrals to psychiatric and memory clinic services	109	RDC	CSS		↑/↓ Problem-focused* ↓ Emotion-focused* ns Dysfunctional*		4

Study	Carers	Recruitment source	N carers	Psych. morbidity	Coping	Anxiety	Depression	Mixed measures	Study qual.
				Outcome measures		*Results: Coping factors associated with morbidity*			
Schoen-makers 2009	Family carers	Health and social care professionals	50	BDI	WCCL		↓ Problem-focused ns Emot. support/acceptance ↑ Dysfunctional		3.75
Shaw 1997 (China)	Family carers	Probability sample	110	BSI, HamD	WCQ Revised	ns Problem-focused ns Emotion-focused* ns Dysfunctional	ns Problem-focused* ns Emotion-focused* ↑ Dysfunctional		5
(US)	Spouses	Community services inc. GPs (USA)	139	BSI, HamD	WCQ Revised	↑ Problem-focused ↑ Emotion-focused* ↑ Dysfunctional*	↑ Problem-focused* ↑ Emotion-focused* ↑ Dysfunctional*		3
Vitaliano 1987	Spouses	Part of stress vulnerability study	66	BDI, HamD	Revised WCCL	ns Problem-focused* ns Emotion-focused* ns Dysfunctional*	↓ Problem-focused ns Emotion-focused* ↑ Dysfunctional		3
Wilcox 2001	Wives and daughters	Part of exercise intervention trial	71	BDI	Revised WCCL		ns Problem-focused ↑ Dysfunctional		3
Williamson 1993	Family carers	Dementia diagnostic centres	174	CES-D	Williamson		ns Problem-focused ns Emotion-focused ↑ Dysfunctional*		3.5

Cross-sectional studies: Lower quality (score <3)

| Study | Carers | Recruitment source | N carers | Outcome measures | | Results: Coping factors associated with morbidity | | | | Study qual. |
				Psych. morbidity	Coping	Anxiety	Depression	Mixed measures		
Ashley 2002	Spouses	Carer resource centres	63	GDS	Coping Strategy Indicator		↓ Problem-focused* ↓ Emotion-focused* ↑ Dysfunctional			2.5
Brashares 1994	Female	Carer groups	73	RDC	HDLF		↑ Problem-focused* ↑ Emotion-focused* ns Dysfunctional			2.75
Fuh 1999	Family carers	Neurology clinic	74	GDS-S	CSS		ns Problem-focused ns Emotion-focused ↑ Dysfunctional			2.5
Haley 1987	Family carers	Various community sources	54	BDI	HDLF		↓ Problem-focused* ↓ Emotion-focused* ↑ Dysfunctional			2.75
Hinrichsen 1994	Family carers	Various health and social services settings	152	SCL-90	HDLF			ns Problem-focused ns Emot. support/acceptance ↑ Dysfunctional		2.75
Mausbach 2006	Spouses	Various community sources	95	BSI	WCQ		ns Problem-focused ns Emotion-focused ↑ Dysfunctional			2.75

| Study | Carers | Recruitment source | N carers | Outcome measures | | Results: Coping factors associated with morbidity | | | Study qual. |
				Psych. morbidity	Coping	Anxiety	Depression	Mixed measures	
Morano 2003	Family carers	Carer groups	204	CES-D	CSS		↓ Emotion-focused		1.75
Neundorfer 1991	Spouses	Research register and community services	60	BSI	WCQ	ns Problem-focused ns Emotion-focused ↑ Dysfunctional	ns Problem-focused ns Emot. Support /acceptance ↑ Dysfunctional		2.75
Parks 1991	Adult children	AD clinic, media and support groups	176	SCL-90	Parks	ns Problem-focused ↑ Dysfunctional	↑ Problem-focused* ns Dysfunctional		2
Proctor 2002	Family carers	Day hospitals and day centres	50	HADS	Miller Behavioral Style Scale	↑ Problem-focused ns Emotion-focused* ns Dysfunctional*	ns Problem-focused* ns Emotion-focused* ns Dysfunctional*		2.5
Pruchno 1989	Spouses	Various community sources	315	CES-D, HSC	Kiyak	ns Problem-focused ↓ Emotion-focused ↑ Dysfunctional	ns Problem-focused ↓ Emotion-focused Dysfunctional		2.75

Abbreviations:

Measures of psychological morbidity

BDI: Beck Depression Inventory; BSI: Brief Symptom Inventory; CES-D: Centre for Epidemiological Studies – Depression; GDS-S: Geriatric Depression Scale – Short Form; GHQ-12: General Health Questionnaire – 12; GSI: General Symptom Inventory; HADS: Hospital Anxiety and Depression Scale; HamD: Hamilton Rating Scale for Depression; HSC: Hopkins Symptom Checklist; RDC: Research Diagnostic Criteria; SCL-90: Hopkins Symptom Checklist – 90; STAI: Spielberg Trait Anxiety Index.

Coping measures

COPE: Coping Orientation to Problems Experienced; CRI: Coping Resources Inventory; CSS: Carers' Stress Scale; HDLF: Health and Daily Living Form; JCS: Jalowiec Coping Scale; UCL: Utrecht Coping List; WCCL: Ways of Coping Checklist; WCQ: Ways of Coping Questionnaire.

Table 2.4. Longitudinal studies reporting correlation or regression coefficients between psychological morbidity and coping strategies (as recategorised according to new framework).

Key: ↑ Positive association (p < 0.05), ↓ Negative association (p < 0.05) , ns No significant association. * Coping factors overlap into multiple categories thus strength of relationship to any single category will be overestimated. Study quality ratings rounded to nearest 1.

				Outcome measures		*Results: Coping factors associated with morbidity*			
Study	Carers	Recruitment source	N carers	Psych. morbidity	Coping	Anxiety	Depression	Mixed measures	Study qual.
Cooper 2008	Family carers	Representative sample from community and care homes	126	HADS	Brief COPE	*Baseline (Cooper et al. 2006, Livingston et al. 2007)* ↑ Problem-focused ↓ Emotion-focused ↑ Dysfunctional *12-month follow-up* ↑ Problem-focused ↓ Emotion-focused ns Dysfunctional.	*Baseline (Cooper et al. 2006, Livingston et al. 2007)* ns Problem-focused ns Emotion-focused ↑ Dysfunctional *12-month follow-up* ns Problem-focused ns Emotion-focused ns Dysfunctional.		8
Goode 1998	Family carers	Memory clinic	197	CES-D	CRI		*12-month follow-up* ↓ Problem-focused* ↓ Emot. support/acceptance* ns Dysfunctional		5.75

| Study | Carers | Recruitment source | N carers | Outcome measures | | Results: Coping factors associated with morbidity | | | | Study qual. |
				Psych. morbidity	Coping	Anxiety	Depression	Mixed measures		
Kinney 2003	Spouses	Day programmes and carer support groups	64	CES-D	Revised WCCL		Baseline: ↑ Dysfunctional 1-month: ↑ Dysfunctional			3
Matson 1994	Family carers	Nursing home	37	BDI, Symptom Rating Test	Ways of Coping with Caring		*Baseline* ↑ Emotion-focused* ↑ Dysfunctional *6-month follow-up* ns Problem-focused ↑ Emotion-focused* ↑ Dysfunctional*	*Baseline* ns Problem-focused ↑ Emotion-focused* ↑ Dysfunctional* *6-month follow-up* ns Problem-focused ns Emotion-focused ns Dysfunctional		4.5
Powers 2002	Family carers	Adverts and clinician referral	89	BDI	CRI		*18-month follow-up* ns Problem-focused* ns Emotion-focused* ↑ Dysfunctional			3.75

| Study | Carers | Recruitment source | N carers | Outcome measures | | Results: Coping factors associated with morbidity | | | Study qual. |
				Psych. morbidity	Coping	Anxiety	Depression	Mixed measures	
Vedhara 2000	Spouses	Memory clinic	50	SPSS	WCQ	Baseline ns Problem-focused ns Emotion-focused ↑ Dysfunctional	Baseline ↓ Problem-focused ↓ Emotion-focused ↑ Dysfunctional *6-month follow-up* ↓ Problem-focused* ↓ Emotion-focused* ↑ Dysfunctional *12-month follow-up (Vedhara et al. 2001)* ns Problem-focused* ns Emotion-focused* ↑ Dysfunctional*		4.25
Wright 1994	Family carers	Purposive sample from agencies and churches	30	Short Zung	JCS		*24-month follow-up:* *subgroup analysis only* ↓ Problem-focused (nursing home placement spouses) ↑ Emotion-focused (widowed spouses)		4.5

Abbreviations:

Measures of psychological morbidity

CES-D: Centre for Epidemiological Studies – Depression; HADS: Hospital Anxiety and Depression Scale; BSI: Brief Symptom Inventory; BDI: Beck Depression Inventory; SPSS: Savage Personality Screening Scale; Short Zung: Short Zung Interviewer Assisted Rating Scale.

Coping measures

COPE: Coping Orientation to Problems Experienced; CRI: Coping Resources Inventory; WCCL: Ways of Coping Checklist; WCQ: Ways of Coping Questionnaire; JCS: Jalowiec Coping Scale.

Depression

Emotion-focused coping was associated with less depression (WMC = -0.196, 95% CI -0.283, -0.109; $p < 0.0005$; 5 studies; N = 848) (Figure 2.2)

. Dysfunctional coping was associated with more depression (WMC = 0.456, 95% CI 0.357 to 0.555; $p < 0.0005$; 10 studies; N = 1428), while problem-focused coping was not significantly associated with depression (WMC = -0.035, 95% CI -0.113 to 0.043; $p = 0.376$; 4 studies; N = 700). Higher and lower quality studies did not differ systematically in terms of the direction and size of effects.

Anxiety

Emotion-focused coping was associated with less anxiety (WMC = -0.220, 95% CI -0.259, -0.180; $p < 0.0005$; 3 studies; N = 628) (Figure 2.3). Dysfunctional coping was associated with more anxiety (WMC = 0.390, 95% CI 0.283 to 0.498; $p < 0.0005$; 4 studies; N=688), while problem-focused coping was not significantly associated with anxiety (WMC = 0.096, 95% CI -0.020-0.212; $p = 0.104$; 4 studies; N = 678). Higher and lower quality studies did not differ systematically in terms of the direction and size of effects.

Mixed psychological morbidity

Only one study provided extractable data on mixed psychological morbidity (Hinrichsen et al. 1994). This found dysfunctional coping to be associated with more distress (standardised beta = 0.350, $p < 0.001$, N = 152), but no significant association between problem-focused coping and distress (standardised beta = 0.090, ns, N = 152). It did not examine emotion-focused coping.

Figure 2.2. Standardised regression coefficients between coping styles and depression, and random effects WMCs, adjusted for CR neuropsychiatric symptoms and dementia severity.

Studies in bold are higher-quality, parentheses indicate 95% CI.

Problem-focused coping

Pruchno & Resch 1989	-0.05 (-0.16, 0.06)
Kramer 1993	-0.21 (-0.42, 0.02)
Cooper et al. 2006	0.11 (-0.09, 0.30)
Cooper et al. 2010	-0.02 (-0.16, 0.11)
Weighted mean correlation	-0.04 (-0.11, 0.04)

-1.0   -0.5   0.0   0.5   1.0

Emotion-focused coping

Pruchno & Resch 1989	-0.31 (-0.41, -0.21)
Kramer 1993	0.02 (-0.21, 0.25)
Cooper et al. 2006	-0.14 (-0.33, 0.05)
Huang et al. 2006	-0.15 (-0.30, 0.02)
Cooper et al. 2010	-0.16 (-0.29, -0.03)
Weighted mean correlation	-0.20 (-0.28, -0.11)

-1.0   -0.5   0.0   0.5   1.0

Dysfunctional coping

Pruchno & Resch 1989	0.48 (0.39, 0.56)
Neundorfer 1991	0.33 (0.08, 0.54)
Kramer 1993	0.63 (0.47, 0.75)
Brashares & Catanzaro 1994	0.12 (-0.11, 0.34)
Haley et al. 1996	0.74 (0.67, 0.80)
Cooper et al. 2006	0.41 (0.29, 0.52)
Huang et al. 2006	0.55 (0.43, 0.65)
Mausbach et al. 2006	0.29 (0.09, 0.47)
Kim et al. 2007	0.29 (0.14, 0.43)
Cooper et al. 2010	0.40 (0.22, 0.55)
Weighted mean correlation	0.46 (0.36, 0.56)

-1.0   -0.5   0.0   0.5   1.0

Figure 2.3. Standardised regression coefficients between coping styles and anxiety, and random effects WMCs, adjusted for CR neuropsychiatric symptoms and dementia severity.

Studies in bold are higher-quality, parentheses indicate 95% CI.

Problem-focused coping

Pruchno & Resch 1989	0.38 (0.11, 0.60)
Proctor et al. 2002	-0.01 (-0.12, 0.10)
Cooper et al. 2006	0.23 (0.04, 0.41)
Cooper et al. 2010	0.12 (-0.01, 0.25)
Weighted mean correlation	0.10 (-0.02, 0.21)

-1.0   -0.5   0.0   0.5   1.0

Emotion-focused coping

Pruchno & Resch 1989		-0.22 (-0.32, -0.11)
Cooper et al. 2006		-0.29 (-0.46, -0.10)
Cooper et al. 2010		-0.19 (-0.31, -0.05)
Weighted mean correlation		-0.22 (-0.26, -0.18)

-1.0   -0.5   0.0   0.5   1.0

Dysfunctional coping

Pruchno & Resch 1989		0.28 (0.17, 0.38)
Neundorfer 1991		0.53 (0.32, 0.69)
Cooper et al. 2006		0.44 (0.32, 0.54)
Cooper et al. 2001		0.56 (0.40, 0.68)
Weighted mean correlation		0.39 (0.28, 0.50)

-1.0   -0.5   0.0   0.5   1.0
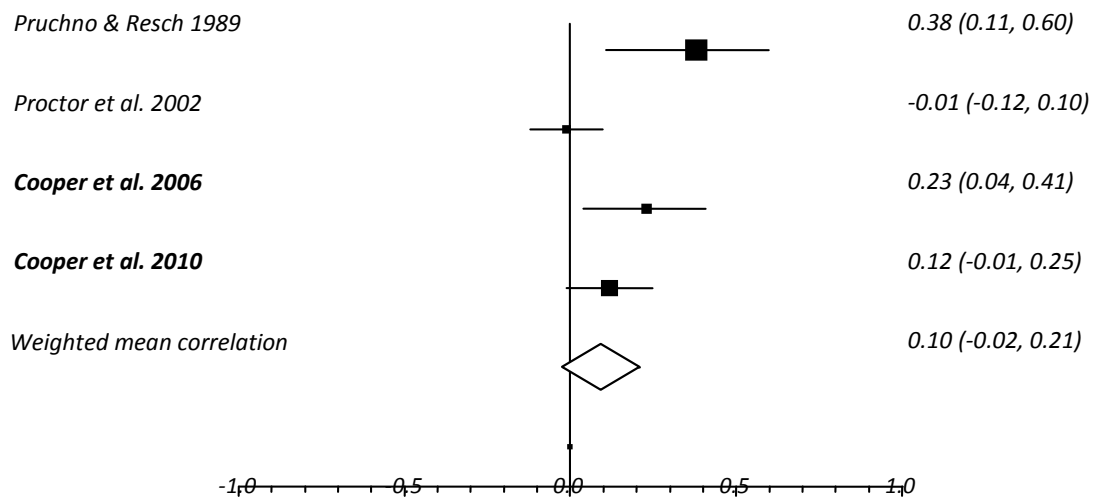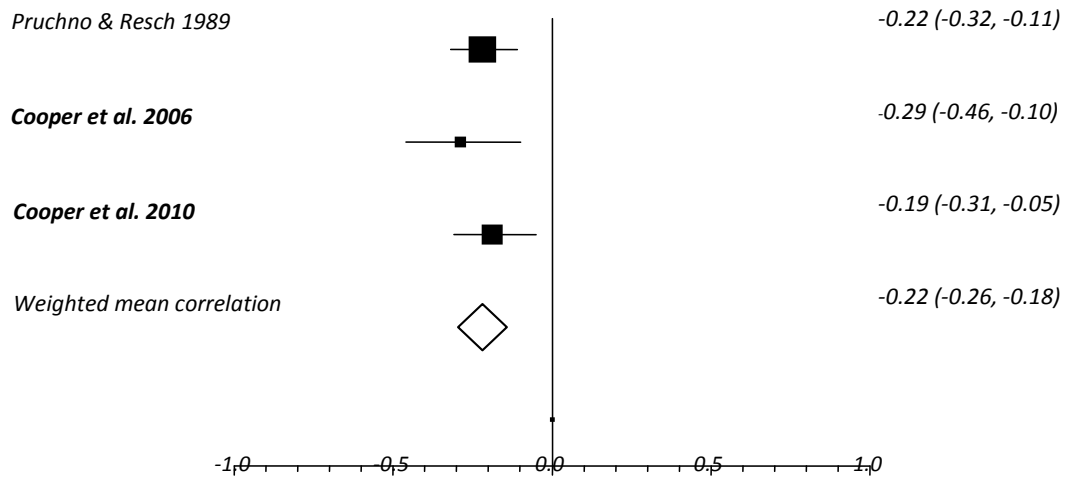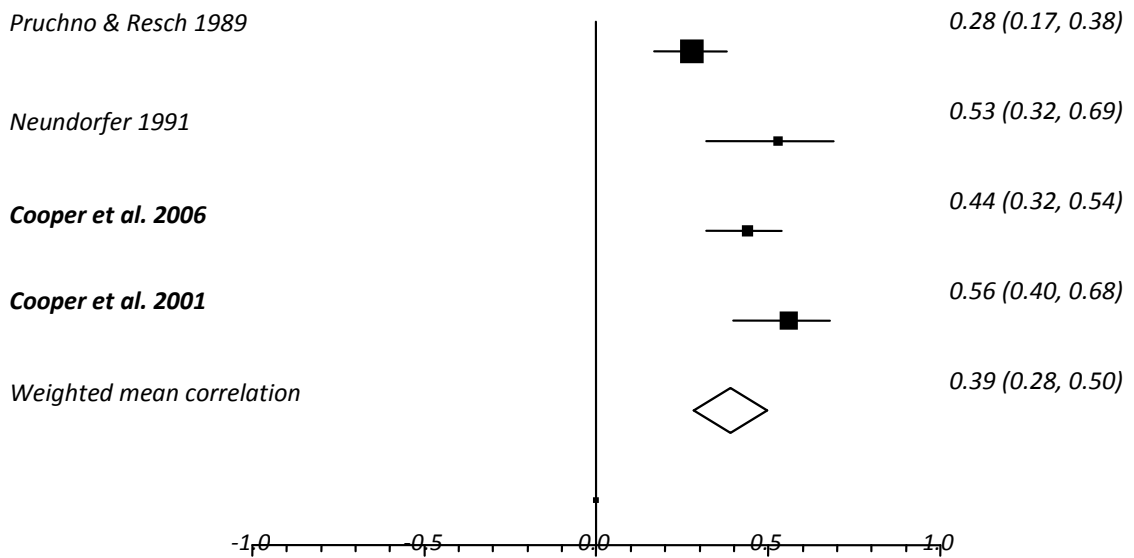
2.3.4 Longitudinal studies

Table 2.4 summarises characteristics and findings of the included longitudinal studies, with quality ratings ranging 3 – 8 (median 4.5). Two of these studies provided extractable data for meta-analysis (Cooper et al. 2008b;Vedhara et al. 2000).

Depression

Dysfunctional coping significantly predicted depression at follow-up (WMC = 0.321, 95% CI: 0.098, 0.544; p = 0.005; 2 studies; N = 143). Neither emotion-focused (standardised beta = -0.149, p = 0.28) nor problem-focused coping (standardised beta = 0.112, p = 0.46) significantly predicted depression a year later (N = 93) (Cooper et al. 2008b).

Anxiety

Emotion-focused coping was associated with less anxiety (standardised beta = -0.195, p = 0.020) and problem-focused coping with greater anxiety (standardised beta = 0.299, p = 0.002) a year later in the only included study to measure these types of coping (N = 93) (Cooper et al. 2008b). Dysfunctional coping at baseline did not significantly predict anxiety after 6 months (Vedhara et al. 2000) or 12 months (Cooper et al. 2008b) (WMC = 0.190, 95% CI: -0.158, 0.539; p = 0.284; 2 studies; N = 143).

2.4 Discussion

This is the first meta-analysis of the relationships between carer coping and psychological morbidity, and the first systematic review to reclassify different coping measures using a common framework to allow comparison as well as to take into account the effect of stressors. We found consistent evidence from higher quality cross-sectional studies that dysfunctional coping was moderately associated (WMC ≈ 0.4) with depression and anxiety. There was also evidence from two high quality longitudinal studies that dysfunctional coping predicted depression 6 and 12 months later. Emotion-focused coping strategies were correlated cross-sectionally to a lesser degree (WMC ≈ 0.2) with lower depression and anxiety in higher quality studies. In one study these coping strategies predicted lower depression and anxiety a year later

(Cooper et al. 2008b). Findings (size and direction of relationships between coping and psychological morbidity) were consistent between higher and lower quality studies.

Our meta-analysis suggests that problem-focused coping is not cross-sectionally associated with carer mental health, challenging a common generalisation in the literature that problem-focused coping is positive for carer mental health (for example, see (Kneebone et al. 2003)). The only study that explored such a relationship longitudinally found that carers reporting more problem-focused coping relative to other forms of coping at baseline tended to show more symptoms of depression and anxiety at 12 months follow-up (Cooper et al. 2008b). This might be explained by the inevitability of dementia as a progressive and incurable illness, and stressors associated with the illness become less amenable to problem-solving over time (Cooper et al. 2008b). This suggests for a family carer of someone with dementia, it becomes essential to have coping strategies in addition to those focused on solving the problem. Problem-focused behaviours might have other benefits, but our review focused on the outcome of carer psychological morbidity.

Studies that have investigated coping have tended to use a wide variety of coping measures (Kneebone & Martin 2003). This is the first review to synthesise studies of carer coping in dementia using a common classification system for different coping measures, enabling meaningful comparisons of results obtained with different measures.

2.4.1 Limitations

Coping strategies were classified by reading and re-reading items and through discussion with my supervisors; while I sought to do so objectively, the process was inevitably influenced by my subjective interpretation. Skinner and colleagues (2003)

used a similar method, and the process showed good agreement with coping categories derived by factor analysis. Nonetheless it is possible that the method used in the current study could have been more objective and reliable if others had independently classified coping strategies, and our interpretations compared.

In theory, a more robust method of recategorising coping measures would be to manually reassign each individual item into one of three categories, perform confirmatory factor analysis to validate the categorisation, then apply the categorisation to the studies of interest that also measured psychological morbidity, and calculate new correlation/regression coefficients using individual participant data. This was not feasible as the data were not available.

Our coping framework assumed the starting point of three higher-order coping strategies (problem-focused, emotion-focused and dysfunctional). Not all coping strategies from different instruments fit well into one category, and many overlapped across categories. This was perhaps unsurprising given that our framework presented only one possible way of conceptualising coping, and indeed our review of coping measures suggested other possible and valid conceptualisations, for example: positive versus negative, approach versus avoidance, cognitive versus behavioural. We selected our particular framework because a similar conceptualisation (the Brief COPE) had previously been validated in the dementia carer population (Cooper et al., 2008). Some coping subscales could not be extracted from otherwise relevant studies in our review, because the coping subscales did not fit into the framework, but we have no reason to think that this would have introduced a particular bias to our findings.

We could only include just over a quarter of the identified studies in our meta-analysis; the excluded studies did not report regression analyses with adjustments for

relevant confounding factors. There was a particular dearth of longitudinal studies, and only two included data that we could extract for analysis. The longitudinal relationships between carer coping style and psychological distress remains unclear; as Cooper and colleagues (2008b) measured coping only at baseline, it is not known whether changes in coping styles between baseline and follow-up might have contributed to depression or anxiety at follow-up.

2.4.2 Conclusion

Dysfunctional coping behaviours are performed by everyone to some degree (as are all coping behaviours). Coping scales are not all-or-nothing, but instead measure how much of a coping style is used, and have different implications for carer mental health.

Our meta-analysis provides good evidence that the greater use of dysfunctional coping and less use of emotion-focused coping are associated with anxiety and depression cross-sectionally; there is preliminary evidence (from one or two studies) that they also predict this morbidity from longitudinal studies. This suggests psychological interventions aimed at modifying coping style carers use would be rational interventions. In Chapter 3, I shall systematically review the RCT evidence base for such interventions.

3 Systematic review: Do changes in coping style explain the effectiveness of interventions for psychological morbidity in family carers of people with dementia?

A paper describing this review is now published in *International Psychogeriatrics* (Li et al. 2013) (see Appendix A). This review was conducted in collaboration with GL and CC, and Allana Austin (AA), an RA in the START Study team.

3.1 Background and aims

Carer coping appears an important and theoretically modifiable determinant of concurrent carer depression and anxiety, and as detailed in Chapter 2 there is preliminary evidence to suggest coping predicts such morbidity over time (Cooper et al. 2008b). Given that family carers of people with dementia experience high levels of depression and anxiety (Cooper et al. 2007a;Crespo et al. 2005;Pinquart et al. 2003b), and that coping styles generally do not appear to change in the absence of targeted intervention (Cooper et al. 2008a;Goode et al. 1998), it is theoretically important to identify interventions that are effective in changing coping style as means of reducing depression and anxiety.

Several systematic reviews of family carer interventions have included coping as an outcome measure of interest (Schulz et al. 2002;Selwood et al. 2007;Sorensen et al. 2002;Vernooij-Dassen et al. 2011). However none have systematically explored intervention effects on different types of coping, or considered coping as a potential mediator of treatment effects on psychological morbidity. For example, the recent Cochrane review of cognitive reframing interventions for family carers found no treatment effects on coping (Vernooij-Dassen et al. 2011), but the synthesis lacked

specificity as the authors treated "coping" as a unitary outcome measure rather than recognising the different types of coping strategies. Furthermore, no previous study has comprehensively reviewed all psychosocial interventions, including those involving the CR (in addition or instead of the carer), even though such interventions could nonetheless influence carer coping.

3.1.1 Aim

The aim of this review was to explore the role of coping as a potential treatment mechanism for reducing carer psychological morbidity, in existing efficacy studies of psychosocial interventions.

3.1.2 Objectives

The objectives of this study were to conduct a systematic review all RCTs of interventions measuring family carer coping and psychological morbidity as outcomes, to investigate whether interventions changed coping, and how this related to changes in psychological morbidity, in order to infer whether coping could have mediated treatment effects. For the first time in a review of intervention studies, we adopted a common classification of coping measures (developed in Chapter 2) to ensure comparability between studies.

3.1.3 Hypothesis

We hypothesised that interventions successful in decreasing carer depressive or anxiety symptoms would also decrease dysfunctional coping, or increase emotion-focused coping, directly based on cross-sectional and longitudinal observational study findings detailed in Chapter 2 that carer depressive or anxiety symptoms were

associated with both less dysfunctional and more emotion-focused coping. This also assumed that decreased dysfunctional coping or increased emotion-focused coping would mediate the effects of such interventions in reducing symptoms. We made no specific hypotheses regarding problem-focused coping as this was not shown to be associated with concurrent morbidity in observational studies.

3.2 Methods

3.2.1 Inclusion and exclusion criteria

We included peer-reviewed, RCTs of any psychosocial intervention, published in English up to July 2011 that reported baseline and follow-up quantitative outcomes for anxiety or depression, and coping in family carers of people with any form of dementia. We adopted a broad definition of "family carer" as any unpaid carer; but studies that reported outcome data on family carers of people without dementia were excluded, unless they reported the results for dementia carers separately.

There were no restrictions by any specific types of intervention, or on whether the CR, carer or both were involved in the intervention. From previous systematic searches we knew that the number of relevant studies was likely to be small, and we felt it important to conduct a comprehensive review of all intervention studies that measured carer coping, including those where carer coping was not explicitly mentioned as a target of intervention as long as coping was nonetheless measured (whether as a primary or secondary outcome). We included only studies that used standardised, quantitative measures of coping.

3.2.2 Search strategy

We searched EMBASE, MEDLINE, PsycINFO, Web of Science, Cochrane Library, CINAHL and AMED from inception up to July 2011 using search terms: (carer OR caregiver OR caring OR relative OR supporter OR family); (dementia OR Alzheimer OR cognitive impairment); (cope OR coping); (randomised OR controlled OR clinical) trial. We hand searched relevant reviews and the references of included studies. We also asked authors of included studies whether they were aware of any further studies.

3.2.3 Quality assessment

Two authors (AA and I) independently rated the quality of each study, blind to each other's ratings, using a checklist for RCTs adapted[1] from the Critical Appraisal Skills Programme (Public Health Resource Unit 2006). For any given study, one point was awarded where there was sufficient reporting to provide a "yes" answer to each of the following questions; where necessary we retrieved source studies for coping measures to determine their validity and reliability:

- Were participants appropriately allocated to intervention and control groups?

- Were study personnel 'blind' to participants' study group?

- Were all of the participants who entered the trial accounted for at its conclusion?

- Were the participants in all groups followed up and data collected in the same way?

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[1] The question "Were participants, staff and study personnel 'blind' to participants' study group?" from the original checklist was adapted to reflect the fact that it is usually not possible to blind participants and therapists in a psychosocial intervention. A new question was also added to assess the validity and reliability of the coping measure.

- Was there a power calculation with sufficient power and people included (>80%) to detect an effect on the primary outcome?

- Was a valid and reliable measure of coping used?

Disagreements were resolved through discussion with GL. As well as giving a total rating for each study, we labelled a study as "higher quality" if it met all three criteria that we judged the most important: using a valid and reliable measure of coping, blinding of study personnel, and sufficient accounting of all participants at trial conclusion (for example using intent-to-treat analysis). The first criterion was judged to be important, because if coping style was not being measured validly then we could not interpret the findings. The latter two criteria were also judged as important because they usually account for a substantial proportion of bias in RCTs (The Cochrane Collaboration 2011).

3.2.4 Data extraction

We categorised interventions based on the content of intervention, group- or individual- or dyad-based, and the number of sessions. For each study, we extracted endpoint and follow-up data for treatment and control as well as direction and statistical significance of any reported effects on carer anxiety, depression, and subscales of coping measures. For coping, subscales reported in each study were reclassified as 'problem-focused', 'emotion-focused', or 'dysfunctional' according to the taxonomy previously reported in Chapter 2 (Table 2.2: Classification of coping strategies). Where a reported coping subscale did not fit uniquely into one of the three categories (for example, the 'positive coping' subscale in the Revised WCCL comprises items

pertaining both to problem-focused and emotion-focused coping), we have specified this in our report of the findings.

We also reported relevant mediator, moderator or subgroup analyses relating to coping and psychological morbidity. If a study did not provide adequate data for our purposes, we wrote to the authors to request them (means and standard deviations).

3.2.5 Analysis

To test our hypothesis, we reported the coping changes for studies where intervention significantly decreased depression or anxiety; where intervention did not significantly improve morbidity; and for each type of intervention (including meta-analyses where sufficient data were available).

We conducted fixed-effect meta-analyses of intervention effects on each outcome measure, using Review Manager 5 software (The Cochrane Collaboration 2008). We employed a fixed-effect model because our meta-analyses were of similar interventions for similar populations (family carers of people with dementia), and a random-effects model is likely to be imprecise when there are few studies (Borenstein et al. 2010). For trials with multiple arms, we took treatment-as-usual or waitlist as the comparator. We calculated standardised mean differences (SMDs) for continuous outcomes, and relative risk (RR) for binary outcomes. We used intent-to-treat (ITT) data where available for continuous outcomes, and by using the number of participants initially randomised as the denominator for dichotomous outcomes.

3.3 Results

3.3.1 Description of studies

We identified 433 publications from our search (Figure 3.1 shows flow of papers from search to selection). We retrieved 154 abstracts of potentially relevant papers, of which 8 trials (published in 9 papers) met inclusion criteria. The most common reasons for excluding a study were not being an RCT, and not reporting coping outcomes.

Table 3.1 summarises the included studies. We obtained unpublished data for one study (Beauchamp et al. 2005). All studies were of psychological interventions involving family carers, conducted in North America with the exception of Au and colleagues (2010), which was of Chinese carers in Hong Kong. Most carers were female, with 4/8 trials including only women. Coon and colleagues (2003) reported results for two treatment arms in addition to their waitlist control group. These were labelled as Depression Management and Anger Management, and we categorised them respectively as group coping skills training with and without behavioural activation.

All studies used valid and reliable coping measures, and four were considered higher quality having also blinded study assessors and accounted for all participants (Au et al. 2010; Beauchamp et al. 2005; Coon et al. 2003; Gendron et al. 1996). There were no observable differences between studies that were of higher quality and those that were not, in terms of their significance and direction of findings (Table 3.1)

Figure 3.1. Flowchart of included/excluded studies.

433 hits (430 electronic search, 3 hand-search)

Excluded by title:
132 clearly irrelevant
23 not peer-reviewed journal
124 duplicates

154 potential references: abstracts retrieved

Excluded: 53 not RCT
16 not family carers of people with dementia
15 did not report extractable coping data

70 full texts retrieved

Excluded: 8 not RCT
2 not family carers of people with dementia
46 did not report extractable coping data
5 did not report extractable data for depression or anxiety

9 papers, covering 8 trials, included in review

Table 3.1. Effects of psychological interventions on carer depressive and anxiety symptoms, and subscales of carer coping measures, reported in RCTs.

↓ ↑ indicates significant decrease or increase versus control (p < 0.05), *ns* not significant, – not measured.

	Intervention				*Psych morbid-ity*	*Treatment effects*		*Coping*	*Treatment effects* – coping subscales reclassified according to taxonomy in Li et al. (2012)			*Quality appraisal*		
Study	**Category and content**	**Frequency/ duration**	**Control group**	**N**	**Symptom measure**	**Dep**	**Anx**	**Measure**	**Problem-focused**	**Emotion-focused**	**Dysfunc-tional**	**Total score**	**Blind raters**	**Account all N**
(Au et al. 2010)	**Group coping skills with behavioural activation** Cognitive-behavioural coping skills, problem solving, stress management, information on dementia and care planning, mutual support, behavioural activation	13 weekly	Waitlist	37	CES-D	ns	–	Chinese WOC	↑	ns	↑	3	Yes	Yes
(Beauchamp et al. 2005)	**Remotely-delivered video intervention** Information on common caregiving issues, cognitive-behavioural coping skills; no therapist input	Videos for 1 month	Waitlist	307	CES-D, STAI	↓	↓	Revised WCCL	ns	–	–	4	Yes	Yes
(Chang 1999)	**Remotely delivered-video intervention** Demonstrations of dressing and eating, communication, and behavioural activation ; nurses' telephone	Videos + weekly phone calls over 8 weeks	Minimal telephone support	71	BSI	↓	ns	CRI	ns	–	ns	3	No	Yes

Study	Intervention — Category and content	Frequency/ duration	Control group	N	Psych morbid-ity Symptom measure	Treatment effects Dep	Anx	Coping Measure	Treatment effects – coping subscales reclassified according to taxonomy in Li et al. (2012) Problem-focused	Emotion-focused	Dysfunc-tional	Quality appraisal Total score	Blind raters	Account all N
	support (cognitive reframing, problem solving, managing specific behavioural symptoms)													
(Coon et al. 2003)	**Group coping skills ('**Anger Management') Cognitive-behavioural coping skills, problem solving, stress management, information on dementia and care planning, mutual support	8 x 120min weekly, then 2 monthly, over 3-4 months	Waitlist	105	MAACL	ns	–	Revised WCCL	(↑ Positive coping)	ns		4	Yes	Yes
	Group coping skills with behavioural activation ('Depression Management') As above with behavioural activation			114		ns			(ns Positive coping)	ns				
(Gallagher-Thompson et al. 2003a)	**Group coping skills with behavioural activation** Cognitive-behavioural coping skills, problem solving, stress management, information on dementia and care planning, mutual support, behavioural activation	10 weekly, then monthly, over 8 months	Minimal telephone support	213	CES-D	Ns	–	Revised WCCL	(↑ Positive coping)	ns		3	No	Yes
(Gendron et al. 1996)	**Group coping skills** Cognitive-behavioural coping skills, problem solving, stress management, information on dementia	8 weekly	Information support group	39	HSC	ns Endpoint, 3 and 6 months	–	JCS	ns Endpoint, 3 and 6 months	ns Endpoint, 3 and 6 months	ns Endpoint, 3 and 6 months	4	Yes	Yes

Study	Intervention				Psych morbid-ity	Treatment effects		Coping	Treatment effects – coping subscales reclassified according to taxonomy in Li et al. (2012)			Quality appraisal		
	Category and content	Frequency/ duration	Control group	N	Symptom measure	Dep	Anx	Measure	Problem-focused	Emotion-focused	Dysfunc-tional	Total score	Blind raters	Account all N
	and care planning, mutual support													
(Quayhagen et al. 2000)	**Dyadic counselling** Couples therapy for CR and spousal carer (anger management, communication skills, conflict resolution); systemic and cognitive-behavioural approaches	8 x 90min over 3 months	Waitlist	44	BSI	ns	ns	CSI Revised	ns	ns	ns	2	Yes	No
	Cognitive training Training family carers to stimulate CR through memory-provoking, problem-solving and verbal fluency activities			36		ns	Ns		ns	ns	ns			
(Roberts et al. 1999)	**Individual behavioural management** Problem-solving therapy by nurses, based on cognitive-behavioural principles	10 over 6 months	Treatment-as-usual	77	PAIS Distress	ns Endpoint, 6 months	–	Indices of Coping	↑ 6 months	ns 6 months	ns 6 months	3	No	Yes

Abbreviations: Dep = depression, Anx = anxiety. BSI = Brief Symptom Inventory. CRI = Coping Resources Inventory. CSI = Coping Strategies Inventory. CST = cognitive stimulation therapy. CES-D = Centre for Epidemiologic Studies Depression Scale. HDLF = Health and Daily Living Index. HSC = Hopkins Symptoms Checklist. JCS = Jalowiec Coping Scale. MAACL = Multiple Affect Adjective Checklist. PAIS = Psychosocial Adjustment to Illness Scale. STAI = State-Trait Anxiety Index. WCCL = Ways of Coping Checklist. WOC = Ways of Coping.

3.3.2 Coping changes in interventions that significantly improved psychological morbidity

All eight studies reported depressive symptoms as an outcome measure. To test our hypothesis that interventions may decrease depression or anxiety through changing coping style, we identified the two studies in which depressive symptoms significantly decreased (Beauchamp et al. 2005;Chang 1999). Only one of the three studies reporting anxiety symptoms found they were decreased in the intervention group (Beauchamp et al. 2005).

Neither study measured emotion-focused coping. The smaller study (N = 71) found that both intervention and control used less dysfunctional coping over time but this reduction did not differ significantly between groups (Chang 1999). Chang (1999) also found no differences between groups in problem-focused coping at end of intervention and one-month post-intervention. The larger study did not measure dysfunctional coping, and found no significant treatment effects on problem-focused coping (N = 299, repeated measures ANOVA, F = 0.36, p = 0.547) (Beauchamp et al. 2005).

Summary

There was not much evidence, but that which existed found that neither dysfunctional nor problem-focused coping changed when depression or anxiety improved.

3.3.3 Coping changes in interventions that did not improve psychological morbidity

Four studies found that depression or anxiety were not significantly reduced, and reported a significant intervention effect on coping. All four interventions focused on

coping or behavioural management skills using cognitive behavioural principles. One study reported increased problem-focused and dysfunctional coping (Au et al. 2010), one reported increased problem-focused coping only (Roberts et al. 1999), and two reported increased positive coping (Coon et al. 2003;Gallagher-Thompson et al. 2003a). Positive coping is a mixture of problem-focused with emotion-focused strategies.

Positive coping

In both studies reporting a significant treatment effect on positive coping, Coon et al. (2003) (Anger Management arm, N = 89, F = 3.0, p < 0.05) and Gallagher-Thompson et al (Gallagher-Thompson et al. 2003a) (N = 213, F = 6.77, p < 0.05), the reduction in depressive symptoms versus control approached significance (F = 2.9, p = 0.06, Coon *et al*. (2003); F = 4.96, p = 0.06; Gallagher-Thompson et al (Gallagher-Thompson et al. 2003a).

Dysfunctional coping

Seven studies measured dysfunctional coping, and no intervention significantly decreased its use. Among the three studies in which the decrease in depression approached significance, one found a trend towards decreased dysfunctional coping versus control (N = 213, F = 2.86, p = 0.06) (Gallagher-Thompson et al. 2003a); one found no difference between groups (N = 130, F = 2.0, p = 0.14) (Coon et al. 2003); and one found significantly increased dysfunctional coping in the treatment group (N = 27, F = 5.65, p = 0.03) (Au et al. 2010).

Emotion-focused coping

The four studies measuring emotion-focused coping found no differences in its use between intervention and control at endpoint, but neither did they find a significant difference in psychological symptoms (Au et al. 2010;Gendron et al. 1996;Quayhagen et al. 2000;Roberts et al. 1999).

Summary

No intervention significantly decreased dysfunctional coping, including studies where there were trends towards decreased depression after intervention. No intervention increased emotion-focused coping, but it was not measured in the successful interventions. Interventions that increased problem-focused coping did not significantly decrease depressive symptoms.

3.3.4 Types of intervention

Two categories of interventions, group coping skills interventions with and without behavioural activation, provided sufficient outcome data for meta-analysis of depression and dysfunctional coping outcomes.

Group coping skills interventions (without behavioural activation)

Two studies delivered 8 to 10 sessions of group-based interventions for family carers, designed to teach coping skills, problem solving and stress management, alongside provision of information on dementia and care planning, and mutual support (Coon et al. 2003;Gendron et al. 1996). Both interventions used cognitive-behavioural techniques including behaviour modification, cognitive reframing, assertive communication and relaxation.

Coon and colleagues (2003) showed that those in the intervention group used more positive coping strategies after intervention, and a trend towards fewer depressive symptoms compared with the waitlist control post-intervention. Dysfunctional coping did not significantly differ between groups (Coon et al. 2003). Gendron and colleagues (1996) found no significant intervention effects on depression or coping style (emotion-focused, dysfunctional and problem-focused) up to 6 months after the intervention.

We found on meta-analysis of these two studies that depressive symptoms were significantly reduced immediately after the interventions (N = 120, SMD = 0.91, 95% CI 0.53 – 1.29, p < 0.0001), and dysfunctional coping was increased compared with the control groups (SMD = -0.39, 95% CI -0.75 – -0.03, p = 0.04; (Figure 3.2).

Figure 3.2. Fixed-effect meta-analyses for group coping skills interventions, showing significantly fewer depressive symptoms and more dysfunctional coping versus control, at endpoint of intervention (not adjusted for baseline).

Depression

Study	Control Mean	SD	n	Group Coping Skills Mean	SD	n	Weight	Standardized Mean Difference IV, Fixed, 95% CI
Gendron *et al.* 1996	22.1	5.5	18	19.3	7.3	17	32.0%	0.43 [-0.25, 1.10]
Coon *et al.* 2003 Anger Mgmt.	16.5	1.3	44	15	1.3	41	68.0%	1.14 [0.68, 1.60]
Total (95% CI)			62			58	100.0%	**0.91 [0.53, 1.29]**

Heterogeneity: $X^2(1)$ = 2.99, p = 0.08; I^2 = 67%
Test for overall effect: Z = 4.72 (p < 0.00001)

Dysfunctional coping

Study	Control Mean	SD	n	Group Coping Skills Mean	SD	n	Weight	Standardized Mean Difference IV, Fixed, 95% CI
Gendron *et al.* 1996	17.6	3.4	18	18.2	3.8	17	29.7%	-0.16 [-0.83, 0.50]
Coon *et al.* 2003 Anger Mgmt.	27.9	2	44	28.9	2.1	41	70.3%	-0.48 [-0.92, -0.05]
Total (95% CI)			62			58	100.0%	**-0.39 [-0.75, -0.03]**

Heterogeneity: $X^2(1)$ = 0.63, p = 0.43; I^2 = 0%
Test for overall effect: Z = 2.10 (p = 0.04)

Group coping skills interventions with behavioural activation

Three studies delivered 10 to 13 sessions of group-based, cognitive behavioural coping skills interventions with the additional component of behavioural activation, i.e. encouraging family carers to develop pleasant activities as a means to improving mood (Au et al. 2010;Coon et al. 2003;Gallagher-Thompson et al. 2003a). All were based on the Coping With Caregiving treatment manual (Gallagher-Thompson et al. 2002).

Au and colleagues (2010) found that in 37 family carers in Hong Kong, both dysfunctional coping and problem-focused significantly increased in the treatment group after accounting for baseline data, while there was a trend towards fewer depressive symptoms versus control. Gallagher-Thompson and colleagues (Gallagher-Thompson et al. 2003a) found that positive coping was significantly increased in the treatment group versus minimal telephone support, but decreases in dysfunctional coping and depression only approached significance. The Depression Management group in the Coon and colleagues (2003) study showed a trend towards decreased depressive symptoms versus waitlist, and no significant effects on positive coping or dysfunctional coping.

Meta-analysis showed significantly fewer depressive symptoms (3 studies, N = 329, SMD = 0.30, 95% CI 0.08 – 0.52, p = 0.007), more positive coping (2 studies, N = 302, SMD = 0.28, 95% CI 0.05 – 0.51, p = 0.02), and more dysfunctional coping (3 studies, N = 329, SMD = -0.26, 95% CI -0.48 – -0.04, p = 0.02) in the intervention group versus control at endpoint (Figure 3.3).

Figure 3.3. Fixed-effect meta-analyses for group coping skills interventions with behavioural activation, showing significantly fewer depressive symptoms, more positive coping and more dysfunctional coping versus control at endpoint (not adjusted for baseline).

Depression

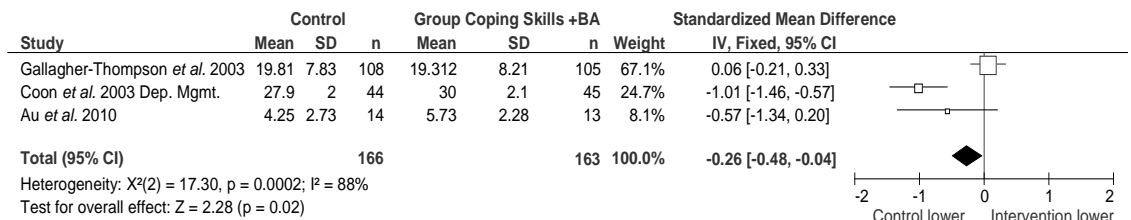| Study	Control Mean	SD	n	Group Coping Skills +BA Mean	SD	n	Weight	Standardized Mean Difference IV, Fixed, 95% CI
Gallagher-Thompson *et al.* 2003	15.77	12.24	108	14.996	10.72	105	66.5%	0.07 [-0.20, 0.34]
Coon *et al.* 2003 Dep. Mgmt.	16.5	1.3	44	15.4	1.3	45	25.5%	0.84 [0.40, 1.27]
Au *et al.* 2010	17.29	10.65	14	11.23	11.11	13	8.1%	0.54 [-0.23, 1.31]
Total (95% CI)			166			163	100.0%	0.30 [0.08, 0.52]

Heterogeneity: X²(2) = 9.18, p = 0.01; I² = 78%
Test for overall effect: Z = 2.70 (p = 0.007)

Dysfunctional coping

Study	Control Mean	SD	n	Group Coping Skills +BA Mean	SD	n	Weight	Standardized Mean Difference IV, Fixed, 95% CI
Gallagher-Thompson *et al.* 2003	19.81	7.83	108	19.312	8.21	105	67.1%	0.06 [-0.21, 0.33]
Coon *et al.* 2003 Dep. Mgmt.	27.9	2	44	30	2.1	45	24.7%	-1.01 [-1.46, -0.57]
Au *et al.* 2010	4.25	2.73	14	5.73	2.28	13	8.1%	-0.57 [-1.34, 0.20]
Total (95% CI)			166			163	100.0%	-0.26 [-0.48, -0.04]

Heterogeneity: X²(2) = 17.30, p = 0.0002; I² = 88%
Test for overall effect: Z = 2.28 (p = 0.02)

Positive coping

Study	Group Coping Skills +BA Mean	SD	n	Control Mean	SD	n	Weight	Standardized Mean Difference IV, Fixed, 95% CI
Coon *et al.* 2003 Dep. Mgmt.	54.4	1.8	45	53.6	1.7	44	29.0%	0.45 [0.03, 0.87]
Gallagher-Thompson *et al.* 2003	59.296	10.04	105	57.146	10.52	108	71.0%	0.21 [-0.06, 0.48]
Total (95% CI)			150			152	100.0%	0.28 [0.05, 0.51]

Heterogeneity: X²(1) = 0.92, p = 0.34; I² = 0%
Test for overall effect: Z = 2.41 (p = 0.02)

Remotely delivered interventions

Two studies tested the efficacy of delivering coping and behavioural management strategies through videos (Beauchamp et al. 2005;Chang 1999).

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Beauchamp and colleagues (2005) provided family carers with Web-based videos, containing information on common caregiving issues alongside cognitive-behavioural coping skills; there was no further therapist input. The intervention showed a small significant effect in decreasing both depressive and anxiety symptoms versus waitlist. There were no significant effects on problem-focused coping.

Chang (1999) provided family carers with video demonstrations of dressing and eating, communication and behavioural activation. Nurses made weekly telephone calls to provide support on cognitive reframing and problem solving, as well as specific advice on managing behavioural symptoms. The study found depression significantly decreased in the treatment group versus control over the 12 weeks of follow-up, but no significant treatment effect on anxiety. There were no significant treatment effects on dysfunctional or problem-focused coping.

Individual behavioural management

One study delivered 10 sessions of problem-solving therapy to individual family carers, based on cognitive behavioural principles (Roberts et al. 1999). There were no significant differences between treatment and control for depression and our hypothesised coping changes at endpoint and 6-month follow-up. The only significant effect was that problem-focused coping increased in the treatment group versus control at 6-month follow-up. A subgroup analysis found that problem-focused coping interacted significantly with treatment: carers who began with low use of problem-focused coping became less depressed after counselling, while carers who began with high use of problem-focused coping became less depressed in the control group.

Dyadic interventions

One study involved the spousal carer together with the care recipient in eight sessions of dyadic counselling aimed at promoting conflict resolution, anger and stress management, and improving communication (Quayhagen et al. 2000). There were no significant changes in the treatment group versus waitlist on depression or any of the three measures of coping.

Cognitive training

One study trained family carers to deliver an intensive cognitive training program to dementia patients (Quayhagen et al. 2000). This small study showed no significant effect on any outcome measure versus waitlist control, including carer coping, which was unsurprising as there was no direct intervention for the carer.

Summary

Most studies were of group coping skills interventions alone, or with a behavioural activation component. Meta-analysis found the former efficacious in reducing depressive symptoms, but it also increased dysfunctional coping. The latter showed a trend towards reducing depression; positive coping increased yet dysfunctional coping did not decrease.

The two different remotely delivered interventions were also shown to improve psychological morbidity, yet neither resulted in any change in measured coping.

3.4 Discussion

Many psychological interventions have been developed to reduce the high psychological morbidity in family carers of people with dementia. Despite this, we found only eight RCTs measuring the impact of the proposed treatments on carer coping

strategies, including studies where carer coping was included as a secondary outcome measure despite not being the primary focus of intervention (for example, cognitive training for the CR via the carer). These studies varied in methodological rigour (with half reporting blinding of raters and analyses adequately accounting for dropouts), nonetheless this did not appear to relate to direction and significance of findings and thus we do not think that findings are accounted for by study quality. Our most striking finding from meta-analysis was that group coping skills interventions were efficacious in decreasing depression, but also increased dysfunctional coping immediately post-intervention. The meta-analysis of group coping skills interventions with behavioural activation revealed findings in similar directions that did not reach statistical significance. They did however find a significant increase in positive coping. Our hypothesis that interventions successful in decreasing carer depression would also decrease dysfunctional coping was not supported.

There was some evidence to suggest that increasing positive coping strategies was helpful, and good evidence to suggest that improvement in depressive or anxiety symptoms was not related to change in the use of problem-focused strategies. As positive coping is a mixture of emotion-focused and problem-focused strategies, this gives preliminary support to our hypothesis that increasing emotion-focused coping is associated with improvement in depression and anxiety. Nonetheless there was no direct evidence for this. Neither of the two studies reporting a positive treatment effect on depression or anxiety specifically measured emotion-focused coping (Beauchamp et al. 2005;Chang 1999).

In these two studies, there were no significant effects on problem-focused coping (Beauchamp et al. 2005;Chang 1999). One of those studies was among the most

rigorous in the review and also the largest, with nearly 300 participants (Beauchamp et al. 2005). Correspondingly, the two studies showing significantly increased problem-focused coping found no treatment effect on depression (Au et al. 2010;Roberts et al. 1999) or anxiety (Roberts et al. 1999). These findings are in line with our meta-analysis of cross-sectional studies which found no significant association between problem-focused coping and psychiatric morbidity (Chapter 2).

A possible explanation of our findings is that interventions effective in promoting coping strategies may work by initially increasing carers' coping attempts in all domains, including those they are using already, so dysfunctional coping is initially reinforced. Strategies such as denial or disengagement may serve as protective mechanisms against stress in the short term (Au et al. 2010;Lazarus 1983). More proactive attempts at coping would also increase the likelihood of failures, resulting in self-blame (Curry et al. 1987). In consideration of our previous and current findings, we would expect an intervention effective in improving psychological morbidity to increase emotion-focused coping over a longer period of follow-up, even if dysfunctional coping may not decrease initially. No such study has yet been reported.

Four of eight trials in the current review showed a treatment effect on coping immediately after intervention (Au et al. 2010;Coon et al. 2003;Gallagher-Thompson et al. 2003a;Roberts et al. 1999). This is noteworthy because family carers' coping styles have generally been shown to remain stable over six months to two years in the absence of a targeted intervention (Cooper et al. 2008a;Goode et al. 1998;Powers et al. 2002). All four interventions delivered coping or behavioural management skills using cognitive behavioural principles, providing preliminary evidence that family carer coping is modifiable given the right kind of intervention. This is supported by a larger

evidence base in other populations, for example among HIV patients for whom RCTs of cognitive behavioural and stress management interventions have shown efficacy in increasing emotion-focused coping (Harding et al. 2011). An RCT that has shown a significant treatment effect on emotion-focused coping (cognitive reframing) also delivered coping skills training to carers of people with dementia using cognitive behavioural principles, but did not measure carer mental health (Ducharme et al. 2005). Similarly in a qualitative study of 30 carers in a psychoeducational group intervention, carers reported learning coping strategies, with reframing skills (an acceptance-based coping strategy) being more useful and better retained than problem solving or seeking social support (Lavoie et al. 2005).

3.4.1 Limitations

An important limitation of the review was that it included a wide range of different interventions, some of which had carer coping as a key therapeutic focus, and others which did not target carer coping primarily (or at all) yet this was included as a secondary outcome in the study. If an intervention effective in reducing carer depression or anxiety symptoms showed no effect in changing carer coping but could not reasonably have been expected do so, it would be a mistake to conclude that coping was not the treatment mechanism for *any* intervention. Nonetheless no such intervention was identified in the review (the cognitive training intervention described in Quayhagen et al. 2000, was not effective in reducing carer symptoms). Conversely, several studies reported coping skills-based interventions or described them as theoretically based on the Transaction Model of Stress and Coping (Lazarus et al. 1984), yet did not measure coping strategies as an outcome (Akkerman et al. 2004;Burgio et al. 2003;Hebert et al. 2003). We were therefore unable to include these studies in the review.

Many of the studies had small samples (which may have lacked statistical power). Possible ceiling and floor effects might have contributed to the difficulty in detecting significant changes (Zarit & Leitsch 2001). All three studies that showed efficacy in reducing psychological morbidity and changing coping were conducted on entirely female samples, thus it was not possible to separate out the effects of gender from that of the intervention (or an interaction effect between them). In general, the included studies showing efficacy all had waitlist or minimal control groups, thus it was not possible to rule out the possibility that effects could be explained by therapist attention.

Meta-analysis was useful in allowing us to pool studies, many of which were by the same research team following similar protocols, to increase effective statistical power, nonetheless we could not conduct meta-analyses for all outcome measures and interventions. As with any systematic review and meta-analysis, the current categorisation of interventions reflect only one of many possibilities based on the reviewers' judgment of commonalities and differences between studies; for example, it could also have been valid to pool all group-based interventions, and all individual-based interventions. We have been transparent in the way that we have chosen to enable replication and consideration of other methods.

Finally, no study reported relevant mediator or moderator analyses, which could have allowed us to draw more direct conclusions regarding coping as a treatment mechanism for psychological morbidity.

3.4.2 Conclusion

Group coping skills interventions increased dysfunctional coping in the short term relative to control, but this did not prevent psychological morbidity from improving. We

found consistent evidence that change in problem-focused coping was unrelated to change in carers' psychological morbidity. There was a lack of evidence about whether interventions can change carers' emotion-focused coping, whether this is helpful to them, and a general lack of studies with long term follow-up. Studies that specifically targeted coping style did appear to change the coping strategies carers used.

Given the high prevalence of depression and anxiety in family carers of people with dementia (Mahoney et al. 2005b), the anticipated growth of this population, and the relative lack of effective interventions (Selwood et al. 2007), we need to develop the evidence base on reducing their morbidity and identifying the components of effective interventions. My PhD investigation, and the START Study in which it is nested, aimed to address the gap in the evidence for a theory-driven intervention to promote family carers' emotion-focused coping, as a means of decreasing carer psychological morbidity.

4 The START Study

4.1 Background

There are no evidence-based psychological interventions recommended specifically for carers of people with dementia in England and Wales (National Institute for Health and Clinical Excellence et al. 2011), despite the prevalence of psychological morbidity in this population (see Section 1.3). The most promising treatments have been group interventions based on the Coping With Caregiving treatment manual (Gallagher-Thompson et al. 2002), in terms of their efficacy in reducing depressive symptoms, anger, and burden; and increasing positive coping strategies and self-efficacy (Coon et al. 2003;Gallagher-Thompson et al. 2003b;Selwood et al. 2007;Sorensen et al. 2002). There are no proven interventions that can effectively reduce anxiety in family carers of people with dementia (Cooper et al. 2007a). Thus there is a clinical need for effective interventions addressing both depression and anxiety that can be implemented in the NHS.

The current evidence suggests that an effective treatment package for carer psychological morbidity might include promoting emotion-focused coping strategies (Cooper et al. 2007a); see also Chapters 2 and 3). This is supported by a qualitative study of Italian family carers, many of whom expressed needs for emotional and psychological support, including coping with stress and grief, elaborating emotional reactions such as depression and anxiety, and acceptance, in addition to informational and medical needs relating to managing the dementia (Rosa et al. 2010).

Given the UK clinical context and that individual-based interventions appear to provide better treatment outcomes for carers compared to group-based interventions

(Sorensen et al. 2002), our study group decided to adapt the Coping With Caregiving programme for delivery to individual carers and for use in the UK, with permission from the original authors (Gallagher-Thompson et al. 2002). The START Study is an RCT of a coping skills intervention focused on reducing carer psychological morbidity. The study was designed by my supervisors Prof Gill Livingston and Dr Claudia Cooper, and funded by the National Institute for Health Research Health Technology Assessment programme.

4.2 Overview

The START Study is a pragmatic multi-centred single-blind parallel RCT of a coping skills intervention versus treatment-as-usual (TAU) for family carers of people with dementia. A total of 260 carers across four study sites were recruited and randomised. Methods and findings of the START Study are reported in detail elsewhere (Livingston et al., 2013), and in Chapter 6 within the context of my PhD study. Briefly, the intervention resulted in a clinically significant reduction in psychological morbidity symptoms versus TAU at 8-month follow-up (Livingston et al., 2013), and also good evidence that the intervention would be cost-effective for the NHS (Knapp et al. 2013) .

5 Aims of the current investigation

5.1 Design of current PhD investigation

My PhD investigation is nested in the START Study, and I developed my PhD
proposal during my employment as an RA on the START Study. Therefore I was not
involved in the initial design of the trial, including the selection of outcome measures. I
worked in a team of 10 RAs who delivered the intervention, recruited carers and
conducted the outcome assessments. I formulated the hypotheses, designed and
conducted the data analysis in the current PhD investigation.

5.2 Aim

The aim of the current study was to explore the role of coping style as a treatment
mechanism of the START intervention in the reduction of psychological morbidity.

5.3 Objectives

The primary objective of the present investigation was to establish whether change
in carers' emotion-focused coping mediated the effects of the START intervention in
reducing overall psychological morbidity. The secondary objective was to determine
whether similar mediating relationships were present for anxiety and depression
outcomes.

5.4 Hypotheses

5.4.1 Primary hypotheses

My primary hypothesis was that increase in emotion-focused coping between
baseline and 4-month follow-up (immediately post-intervention) mediated the

relationship between treatment assignment and symptoms of carer psychological

morbidity (combined anxiety and depression as measured by Hospital Anxiety and

Depression Scale – Total [HADS-T]) at 8-month follow-up.

Follow-up data were available at two different timepoints (4 and 8 months) and this

provided a good opportunity to strengthen my mediation hypothesis. A significant

mediator that preceded an outcome would provide a stronger claim of a causal

relationship (i.e. that the mediator caused the outcome) than if the mediator and

outcome were measured at the same time. Therefore HADS-T at 8-month follow-up

was chosen as the outcome in my hypothesis (also the primary endpoint of the START

trial); and coping at the preceding 4-month follow-up as the putative mediator.

Figure 5.1. Simplified path diagram for hypothesised causal relationship between carer intervention, coping and psychological morbidity.
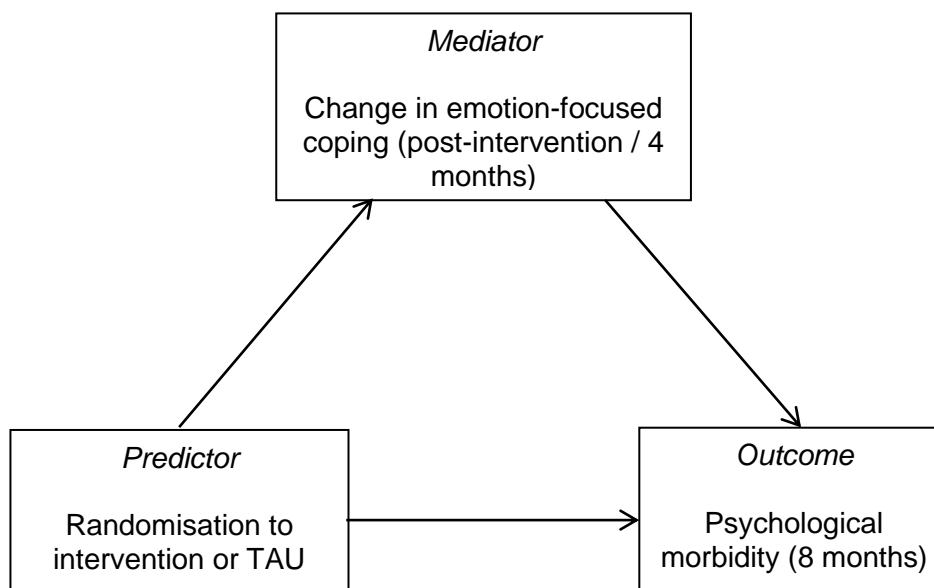
5.4.2 Secondary hypotheses

1. Increase in emotion-focused coping between baseline and 4 months mediated the relationship between treatment assignment and carer depression symptoms at 8 months.

2. Increase in emotion-focused coping between baseline and 4 months mediated the relationship between treatment assignment and carer anxiety symptoms at 8 months.

6 Method

This chapter describes the methods of the START Study relevant to my PhD investigation (which was nested in the START Study), and the methods specific to my PhD investigation but which were not part of the START Study protocol (for example, the analysis plans for establishing mediation).

6.1 Recruitment

6.1.1 Study sites

Trial recruitment began in November 2009 and finished in June 2011. All necessary ethical and local R&D approvals were obtained (see Appendix B and Appendix C), and we recruited carers from four sites. These included secondary dementia services from three NHS Mental Health Trusts in South East England:

- Camden and Islington NHS Foundation Trust (C&I)
- North Essex Partnership NHS Foundation Trust (NEPFT)
- North East London and Essex Foundation Trust (NELFT) Admiral Nurse service, who are specialist mental health nurses in dementia and family carers.

We also recruited from the Dementia Research Centre at the University College London Hospital (UCLH).

The sampling frame encompassed urban, suburban and rural areas, with the aim of recruiting people with different socioeconomic and demographic backgrounds, and those caring for people at different stages of dementia, to reflect the English population of carers for people with dementia.

C&I

Camden and Islington are urban inner London boroughs with diverse ethnic makeups, with black and minority ethnic (BME) groups accounting for 25-30% of their populations (GLA Intelligence Unit 2012). According to the Index of Multiple Deprivation (IMD), Islington ranked as the 6th most deprived area in England and 4th within London, while Camden ranked 55th in England and 14th within London (Greater London Authority 2011).

NELFT

North East London NHS Foundation Trust (NELFT) serves the London Boroughs of Waltham Forest, Redbridge, Barking & Dagenham and Havering, capturing a diversity of environments, from urban and suburban developments to affluent residential areas. The region has a diverse ethnic makeup, with white groups comprising only 50-58% of all four boroughs except Havering, which has a 95% white population (the highest among Outer London boroughs) (GLA Intelligence Unit 2012). The IMD ranks Waltham Forest and Barking & Dagenham as the 7th and 8th most deprived areas of England, while Redbridge and Havering rank 116th and 177th respectively (Greater London Authority 2011).

NEPFT

The North Essex trust covers two authorities, Epping Forest and Harlow, including suburban and rural areas. Both populations are predominantly white (88-95%). Overall deprivation levels are moderate in Epping Forest, although this is due to clusters of affluence existing alongside densely populated pockets of deprivation. Deprivation is higher in Harlow, ranked 8th most deprived authority in the East of England, and the 2nd most deprived in Essex (Greater London Authority 2011).

UCLH

The Dementia Research Centre accepts referrals for patients with dementia of all ages, with a higher proportion of young-onset dementias, familial dementias and other less common forms of dementia (such as frontotemporal dementias, posterior cortical atrophy). The Cognitive Disorders Service, which runs in parallel with the Dementia Research Centre, currently see between 250-275 new patients per year for diagnosis and assessment, and approximately 650 follow-ups for intervention, supportive management and ongoing assessment. Although UCLH accepts referrals from across England and Wales, it is located in Camden, and exclusion criteria of the START study (see Section 6.1.2: Exclusion Criteria) meant that participating family carers would come from London or South East England.

6.1.2 Eligibility criteria for carers

Carers who met all of the following eligibility criteria were recruited:

Inclusion criteria

- The CR had a clinical diagnosis of dementia, and lived at home at the time of recruitment (reflecting the intervention's intended point of delivery within the NHS)

- The family carer was providing emotional or practical support at least weekly, and self-identified as the CR's primary carer

- CR was referred to one of the study sites within the past year.

We included non-English speaking carers and used interpreters for assessments and interventions as necessary.

Exclusion criteria

- Carers unable to give informed consent, for example, because they had dementia themselves

- Participating in another RCT for themselves in their capacity as a family carer, and not solely as an informant for the CR

- Living more than 1.5 hours journey from the researchers' base.

In line with previous studies of carer coping interventions (Li et al 2013; Chapter 3), we did not include or exclude carers based on their current levels of clinical distress. Although the intervention could theoretically cause harm for carers who were otherwise coping well (for example, thinking about potential problem behaviours or care options associated with more severe dementia could be anxiety-provoking for the carer of someone with newly diagnosed mild dementia), no evidence of such harm has been reported in previous studies. Given our previous evidence that carers of adults with

dementia tend to become more depressed and anxious over time (Cooper et al. 2010), the study team felt that the potential benefits of offering the intervention early to all carers and equipping them for future stressful situations outweighed the potential risks. The potential benefits and risks, as well as the right to withdraw from the study, were clearly explained to all carers as part of informed consent.

6.1.3 Therapists and training

Two teams of RAs were recruited by the Chief Investigator to work on the START study both as outcome assessors and therapists. All recruited therapists held undergraduate degrees in psychology, had no professional qualifications in clinical psychology or psychotherapy, and underwent a formal, standardised training programme to deliver the START intervention.

Training of therapists

The Study Investigators, Clinical Psychologist and Trial Manager developed a formal training programme for the RAs, focusing on the clinical and practical skills needed to deliver the study intervention as well as to administer the assessments safely and effectively. Training was delivered through didactic lectures, group discussion and supervision, and role play. The three core training components included:

- Dementia-specific knowledge on salient issues such as: stages of dementia, end-of-life care, NHS and social care service organisation;
- Generic therapeutic competencies (Roth et al. 2007), such as: models for understanding carer distress, building therapeutic alliance, managing boundaries and risk;

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- Delivery of the START intervention. Therapists familiarised themselves with each session of the manual, practiced delivering it with each other and to one of the Investigators until deemed competent, at which point therapists were signed off and progressed to the next session. At all stages therapists received extensive feedback from their peers and supervisors, and were also encouraged to reflect on their own performance and development needs.

6.2 Procedures

6.2.1 Randomisation

Potentially eligible carers were asked by their clinicians, verbally or in writing, whether they agreed to be contacted by the research team, and either given a study information sheet or sent one by the research team. For carers who agreed to further contact, an RA arranged a face-to-face interview to obtain informed consent and baseline data. Interviews took place at a location convenient to the carers, usually their own homes. Consenting, eligible carers were then randomised to the intervention or treatment-as-usual (TAU), using an automated computerised system set up by an independent clinical trials unit ensuring concealed allocation. Randomisation was on a 2:1 ratio (intervention: TAU), stratified by treatment site with random permuted blocks.

6.2.2 Blinding

There were two teams of RAs, with each team responsible for conducting assessments for roughly half of the carers and managing the intervention caseload for the other half. To ensure that the assessing team remained blinded after baseline assessment of a carer, the Trial Manager disclosed the carer's randomisation status to the other team, who relayed this information to the carer and delivered any therapy as

allocated. The team that conducted baseline assessment was responsible for completing the remaining follow-up assessments, and reminded the carer at each assessment not to disclose treatment allocation. The only member of study personnel other than the Trial Manager routinely unblinded to all carers' randomisation status was the Clinical Psychologist, who provided fortnightly clinical supervision for therapists. The Trial Manager, Clinical Psychologist and the two teams of RAs were housed in separate offices, with case notes relating to intervention status in locked cabinets.

6.2.3 Follow-up assessments

We saw carers for follow-up assessments at 4, 8, 12 and 24 months post-baseline, regardless of the treatment arm. Carers randomised to the intervention were offered eight weekly sessions. As this was a pragmatic study, we offered carers some flexibility in scheduling sessions and expected that not all carers would finish the intervention within 8 weeks, and therefore set the follow-up point at 4 months. We aimed that carers completed all 8 sessions prior to the 4-month follow-up.

As I continued to be responsible for completing START Study assessments through 24 month follow-up, I had to remain blinded to individual carers' randomisation status. For my thesis, I used an anonymised dataset with 8 months of follow-up.

6.2.4 Allocation of therapists to carers

Each team of therapists allocated the given carer to one of the therapists within that team based on the current capacity and caseload of each therapist. Therefore carers receiving intervention were not randomly allocated to individual therapists.

6.3 Treatment conditions

6.3.1 Intervention: Coping with Caregiving

In addition to usual care detailed below, carers randomised to the intervention were offered eight sessions of the START intervention, each approximately 1 hour in duration. These were one-to-one sessions with the therapist taking place at a location convenient to the carer, usually his or her home, but sometimes in a clinical or academic setting as requested. Carers were given their own copy of the START treatment manual, which they read and worked through with the therapist during each session, and wrote in for homework. Carers also received an audio CD with recordings of the relaxation exercises. There were 10 therapists in total throughout the study due to staff turnover.

Content of sessions

The intervention was based on the stress appraisal and coping response model (Lazarus et al. 1984), and drew on cognitive behavioural therapy principles. A copy of the manual can be found here:

http://www.bmj.com/content/suppl/2013/10/25/bmj.f6276.DC1/livg009049.ww2_default.pdf . A key message underlying the intervention was that the CR could not change their own behaviour by themselves, and therefore the carer had to lead change. Carers were not expected or required to use all the taught techniques, and therefore therapists also emphasised that they should use the techniques that they found useful.

The intervention aimed for a balance of psychoeducation, information provision, and interactive exercises, with all sessions following a similar structure:

1. Session overview, and reviewing homework
2. Introducing new topic with mix of information, worked examples, and roleplay
3. Relaxation exercise

4. Summary, and setting homework task for next session.

The contents of each session, and the mechanisms through which session contents might promote emotion-focused coping, are listed in Table 6.1. Carers were asked to complete homework between each session, which generally involved observing and recording the CR's behaviours and the carer's own reactions (behaviours, thoughts, and emotions) during that week. Carers were encouraged to apply the strategies they learned in previous sessions, and to record these attempts and their outcomes. We also encouraged carers to use the relaxation exercise recordings. Throughout the intervention we encouraged carers to try different techniques to see what worked best for them.

Table 6.1. Contents of the START intervention, and potential impacts on emotion-focused coping.

Session	Contents	Components of emotion-focused coping upon which session might have positive impact (and possible mechanisms)
1. **Stress and wellbeing**	An overview of the symptoms of dementia, and introduced behaviour records, asking carers to write down any problem behaviours they noticed with the CR, and what effect these had on the their own emotions. Therapists explained the consequences of stress, and explored relaxation exercises with the carer as a method of managing stress.	Accepting the reality of the fact that it has happened; learning to live with it *(understanding of CR's diagnosis, problem behaviours and carer's own stress)*
2. **Reasons for behaviour**	Explored triggers for and reactions to CRs' problem behaviours, and developed strategies to change these triggers or reactions.	Accepting the reality of the fact that it has happened; learning to live with it *(understanding that CR problem behaviours stem from the illness and particular triggers; that there may be no solution, and the carer's response will have to change)*
3. **Making a behaviour plan**	Extending upon Session 2, we worked with carers to identify realistic goals and develop specific	Accepting the reality of the fact that it has happened; learning to live with it

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		behaviour plans, including the use of behavioural strategies such as rewarding positive behaviours.	*(understanding that problem behaviours do not always have solutions, and the need to be patient and creative)*
4.	**Behaviour strategies and unhelpful thoughts**	Introduced the idea of dysfunctional thoughts, and their negative effects on one's emotions. Explored cognitive strategies for changing such thoughts.	Trying to see it in a different light, to make it seem more positive; looking for something good in what is happening *(finding more positive interpretations and responses to the CR's problem behaviours)* Getting emotional support from others; getting comfort and understanding from someone *(seeking different perspectives from friends and family to challenge dysfunctional thoughts)*
5.	**Communication styles**	Explored different communication styles, and practiced asking for help from friends, family and professionals through a more assertive communication style. Also provided tips for communicating more effectively with people with dementia.	Getting emotional support from others; getting comfort and understanding from someone *(being able to express one's feelings more assertively such that others are more able to share and empathise)* Accepting the reality of the fact that it has happened; learning to live with it *(understanding that dementia limits CR's ability to communicate, and the need to be patient and persistent)*
6.	**Planning for the future**	Exploring the different health, social and residential care options available for the CR now and in the future, legal issues such as lasting powers of attorney, and end-of-life care. We encouraged carers to bring a family member or friend to this session whom might be useful to involve in planning for the future.	Accepting the reality of the fact that it has happened; learning to live with it *(understanding that CR's situation will deteriorate in the future but that proactive decisions can be taken to minimise crises and suffering)*
7.	**Introduction to pleasant events and your mood**	Introducing the principles behind behavioural activation, that taking part in pleasant activities has a direct effect on improving mood. We elicited a list of pleasant activities that the carer could do alone and with the CR, and worked with the carer to plan an activity schedule, identifying ways to overcome any possible barriers to carrying out such activities.	Trying to see it in a different light, to make it seem more positive; looking for something good in what is happening *(making the most out of a difficult situation through pleasant activities, especially involving the carer)* Making jokes about it; making fun of the situation *(joking and laughter as pleasant activities)*

			Getting emotional support from others; getting comfort and understanding from someone *(social contact with friends and family as pleasant activities)*
8.	**Putting it all together – refining your pleasant events and overcoming barriers**	Carers were asked to review and consolidate particular aspects of the intervention that they found most useful, and to identify the strategies that they were likely to continue using in the future.	All
Relaxation exercises (all sessions)		A variety of relaxation exercises including focused breathing, visual imagery, meditation, and mindful grounding (a distraction technique, based on focusing one's senses on the physical properties of the environment).	Trying to find comfort in religion or spiritual beliefs; praying or meditating *(experiencing relaxation and mediation as soothing and stress-relieving)*

Standardisation of the intervention

To ensure a standardised intervention as far as possible, all therapists were trained to deliver the START treatment manual in the same way (see Section 6.1.3: Therapists), assessed on their treatment fidelity, and clinically supervised as follows.

Assessment of treatment fidelity

Therapists took audio recordings of one randomly selected therapy session selected per carer, and this was rated for fidelity to the manual using a standard checklist by another therapist in the same team. Overall fidelity scores could range from 1 (low) to 5 (low). If fidelity scores were not high, this was discussed in clinical supervision.

Clinical supervision

Therapists received fortnightly group supervision with the Clinical Psychologist, and could seek additional individual supervision as required or pose urgent questions to

either the Clinical Psychologist or Chief Investigator. As well as addressing clinical dilemmas, supervision was also an opportunity for the Clinical Psychologist to ensure that therapists were adhering to the intervention.

Development of the manual

The START manual was developed with the authors' permission from the Coping With Caregiving manual (Gallagher-Thompson et al. 2002), for use within an NHS setting. First, it was changed from a group to an individual intervention so it was more flexible for individual carers (both for scheduling and tailoring of content). The study team identified key components of the 13 sessions and condensed these to eight sessions, adapting the content and wording for the British context (for example, information regarding England and Wales-specific legislations and service provision). Further information about the development of the manual can be found in Appendix H.

6.3.2 TAU

Carers in TAU received usual care with no additional contact from our research team other than for follow-up assessments. At all study sites, usual NHS care for CRs and their carers included diagnosis, education about the illness, management of risk, prescription of cholinesterase inhibitors if appropriate, referral for practical care services, and opportunities to take part in clinical research. Those on cholinesterase inhibitors at the time of the study typically received twice yearly reviews with a multidisciplinary memory service. CRs diagnosed with vascular dementia and their carers were usually referred back to primary care after appropriate signposting to social and voluntary services. A small minority of carers or CRs with severe or intractable behavioural or mental health problems, or who refused help, might receive care

coordination by a Community Mental Health team or treatment from a clinical psychologist. At the UCLH Dementia Research Centre, CRs and carers were offered an ongoing nurse-led information and advice service, and support groups catering to rarer forms of dementia (such as posterior cortical atrophy and primary progressive aphasia).

All carers in the NELFT site had been referred to admiral nurses, whose roles involved regular home visits, assessing patient and family carer needs, facilitating care coordination, and providing information, advice and emotional support (Dementia UK 2013)

6.4 Assessment

6.4.1 Baseline demographics

We asked carers for demographic information about themselves and the CR, including: age, gender, ethnicity, level of education, marital status, relationship to the CR (for example spouse, child), and whether they were living together.

6.4.2 Carer assessments

Carers completed the following assessments at baseline and each follow-up. (The instruments used in the case record forms can be found in Appendix D.)

Psychological morbidity: Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) is a self-report questionnaire (Zigmond et al. 1983). HADS-T, the total score, demonstrates good concurrent validity throughout the age range and in all settings with other established measures of depressive or anxiety symptoms (correlations range 0.68 – 0.77), and with clinical

diagnoses of depression and anxiety (Bjelland et al., 2002;Mykletun et al., 2001;Therrien and Hunsley, 2012). Its subscales have demonstrated high internal consistency (Cronbach's alpha for subscales: Anxiety [HADS-A] = 0.83, Depression [HADS-D] = 0.82) (Bjelland et al. 2002). It has also been used for carers of people with dementia (Cooper et al. 2010).

HADS contains 14 items (seven for anxiety and seven for depression) each scored out of 4 (0 – 3), assessing how the respondent has been feeling within the past week. Each subscale is summed to generate scores (0 – 21) for generalised anxiety and depression respectively. Zigmond and Snaith (1983) recommended a cut-off of 8+ to indicate clinically significant anxiety or depression on the respective scale. Optimal predictive values have, however, been obtained using a cut-off of 9+ for DSM and ICD diagnoses in numerous settings and populations (Bjelland et al. 2002). The Anxiety subscale (HADS-A) focuses on panic, excessive worry and restlessness, while the Depression subscale (HADS-D) focuses on low mood and positive affect. Some somatic items with possible physical causes (such as insomnia or dizziness) are omitted, making it theoretically more suitable for older adults compared with other commonly used questionnaires, such as the Spielberger State-Trait Anxiety Inventory (STAI) (Kvaal et al. 2001;Kvaal et al. 2005;Therrien et al. 2012). The relative brevity of HADS also increases acceptability (Dennis et al. 2007).

A potential weakness of HADS is that the high correlations between the anxiety and depression subscales could result in misclassification (Therrien et al. 2012), although this could arguably reflect shared aetiology of the two conditions (Burns et al. 1998;Herrmann 1997). Compared to the HADS-A or HADS-D alone, HADS-T has generally demonstrated equivalent or higher predictive values for depressive disorders

(with or without comorbid anxiety) in different populations when compared to ICD diagnosis (Bjelland et al. 2002;Mitchell et al. 2010). HADS-T is a valid, convenient and clinically meaningful measure of overall psychological distress (Crawford et al. 2001;Therrien et al. 2012), and the minimal clinically important difference has been determined at 1.60 (Puhan et al. 2008).

Coping: Brief COPE

As with the measure of psychological distress, the measure of coping had to be valid, reliable and acceptable in carers of people with dementia. The Study Investigators chose the Brief COPE (Carver 1997), a self-report questionnaire with 28 scales describing 14 conceptually different coping strategies. Carers indicated how often in the past month (from 1, not at all, to 4, a lot) they had performed each listed activity in order to help them to deal with problems. We used three subscales of the Brief COPE, taking the total scores for the items in each: problem-focused, emotion-focused, and dysfunctional coping (Carver et al. 1989;Coolidge et al. 2000;Cooper et al. 2008a). The Brief COPE has been used in this way in several studies of family carers of people with dementia (Li et al. 2012), with adequate psychometric properties established in this population (Cooper et al. 2008a). The three subscales demonstrate good internal consistencies ($\alpha = 0.72$ to 0.84), test-retest reliabilities ($r = 0.58$ to 0.72), convergent and concurrent validity with variables such as carer burden, attachment style and CR's functional impairment (Cooper et al. 2008a).

The Brief COPE was developed from the original 60-item COPE questionnaire (Carver et al. 1989) with the aim of improved acceptability, and has demonstrated satisfactory reliability and validity in a community sample (Carver 1997). The three divisions were first described but not formalised as subscales in the original COPE, and

only later used as subscales in a study of older and younger adults with anxiety disorders by Coolidge and colleagues (2000). They found that older and younger adults with anxiety respectively used more problem-focused and dysfunctional coping than their non-anxious counterparts (Coolidge et al. 2000). Factor analytic studies of the COPE have revealed similar (but non-identical) three-factor structures (Ingledew et al. 1996;Lyne et al. 2000).

Zarit Burden Interview

This is a self-report questionnaire measuring different aspects of caring burden (Zarit et al. 1980). Carers indicated on a Likert scale the extent to which they experienced the feelings in the 22 statements (from 0, never, to 4, nearly always). It is one of the most widely used scales for measuring burden among carers of people with dementia (Schulze et al. 2005). Psychometric properties have been established for this population (Hebert et al. 2003), and high scores on this scale have been consistently associated with poor carer physical and mental wellbeing (Pinquart et al. 2004).

6.4.3 CR assessments

As CRs were not interviewed, carers were informants for the CR in the following measures at each assessment. The instruments are found in Appendix E.

Neuropsychiatric Inventory (NPI)

This is a structured questionnaire for evaluating psychiatric and behavioural symptoms in 12 domains common in people with dementia (Cummings et al. 1994; 1997). We asked carers to indicate the presence or absence of each symptom in the past month, and for each group of symptoms rate its frequency (1, less than once a week, to

4, daily or continuously present) and severity (1, mild; 2, moderate; 3, severe) taking into account both CR and carer distress. The NPI has been used extensively in clinical practice and research, and has established psychometric properties (Cummings 1997).

Clinical Dementia Rating (CDR)

This is a clinical global staging scale of dementia severity based on semi-structured interviews (Hughes et al. 1982), in this case with the carer. The rater evaluated the CR's cognitive functioning in six domains: Memory, Orientation, Judgment and Problem Solving, Community Affairs, Home and Hobbies, and Personal Care. Based on information provided by the carer in the semi-structured interview, the rater gave for each domain a score 0 indicating no impairment, 0.5 questionable dementia, 1 mild dementia, 2 moderate dementia, or 3 severe dementia. From the domain scores we calculated the CDR Global rating as a measure of overall dementia severity, also out of 3, using the Washington University algorithm (Morris 1993). The CDR has been validated against other neuropsychological measures and survival, as well as neuropathological evidence for Alzheimer's disease (Morris 1997). The CDR Sum of Boxes (CDR-sb, or total scores of the six domains) has been used extensively as a measure of efficacy in dementia drug trials (Morris 1997), and a recent study found it sensitive to change in carer coping style (Tschanz et al. 2013).

6.4.4 Intervention characteristics

For carers randomised to the intervention group, we noted which therapist was assigned to the carer, and the number of therapy sessions completed. Carers were categorised as having "adhered to the intervention" if they completed at least 5/8

sessions, as the core components of coping and behavioural change were covered in the first five sessions of the treatment manual.

6.5 Statistical analysis

6.5.1 Data cleaning and preparation

SPSS 20.0 (IBM Corp. 2011) and STATA 10 Intercooled (StataCorp 2007) were used for data entry and analysis. Other RAs and I and cleaned the data by carrying out detailed checks of all relevant electronic data, where necessary against the paper case record forms and via discussion with the rater.

Missing data

Missing cells on the Brief COPE scale were imputed using the carer's own mean score for that particular subscale (Carver, personal communication). Single missing data cells on the HADS were imputed in a similar manner using the subscale mean, but cases with more than two missing cells in any given subscale were excluded as invalid (Snaith 2003).

Descriptive analyses

Tables of frequencies, means and standard deviations, scatterplots, and other charts were generated. For continuous variables, quartile-quartile (Q-Q) plots were inspected visually. Appropriate transformations were performed on variables that were not normally distributed, such that resulting data approximated the normal distribution.

6.5.2 Efficacy analyses

Coping

Mixed-models regression (also known as multilevel modelling) was used to estimate between-group differences in emotion-focused, problem-focused and dysfunctional coping scores across the 8 months of follow-up. The primary efficacy analyses designed by the START trial statisticians were adopted (see below).

Only carers who completed the Brief COPE at either or both 4- or 8-month follow-ups on the basis of ITT were included, i.e. in their randomly allocated groups regardless of the treatment actually received. The random effects component of the model accounted for clustering of carers by therapist in the intervention group (with assumed cluster size of 1 for each carer in TAU group), varying slopes between groups (Roberts et al. 2005), and repeated measures at 4 and 8 months. The fixed effects component included treatment allocation, time and study site as predictors, adjusting for total baseline coping and additional covariates (carer age and gender, carer burden, and CR neuropsychiatric symptoms) (Model 1). A sensitivity analysis was conducted, adjusted only for baseline coping and not for these additional covariates (Model 2). As I was interested in whether treatment showed an effect on coping strategies at 4 months for the purpose of testing my primary hypothesis, each model was repeated with an additional Randomisation × Time interaction term.

Psychological morbidity

The primary efficacy analyses for psychological morbidity were conducted by the START trial statisticians and have been reported elsewhere (Livingston et al., 2013). These showed carers in the intervention group reporting significantly lower scores at follow-up versus TAU for total morbidity (HADS-T: b = -1.78 [95% CI: -3.25, -0.29], p = 0.020), depression (HADS-D: b = -0.88 [95% CI: -1.68, -0.09], p = 0.029) and anxiety (HADS-A: b = -0.90 [95% CI: -1.74, -0.06], p = 0.036) (Table 6.2). The efficacy

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analyses for HADS Anxiety and Depression caseness showed a significantly lower proportion of depression cases in the intervention group than in TAU at follow-up (odds ratio = 0.25 [95% CI: 0.08, 0.75]), and a trend for reduction of anxiety caseness (odds ratio = 0.30, [95% CI: 0.08, 1.05]) (Table 6.3).

. Additional post-hoc repeated measures McNemar's tests were performed, detailed in Appendix F, suggesting the intervention to be efficacious versus TAU both in treating carers who were clinically depressed at baseline (HADS-T score 9+) and in preventing new cases of depression over 8 months among those were not.

Table 6.2. Psychological morbidity outcomes over 8 months. Mixed model regressions on ITT population, adjusted for baseline score, treatment site and additional baseline covariates. Coefficients (b) represent estimated mean difference between intervention and TAU.

		Intervention		TAU		Treatment effect	
HADS score	*Time*	n	Mean (SD)	n	Mean (SD)	b (SE)	P
Anxiety	Baseline	172	8.13 (4.39)	87	9.25 (4.32)	-0.90	0.036
	4 months	150	7.47 (4.16)	75	8.60 (4.16)	(0.43)	*
	8 months	133	7.63 (4.40)	71	8.79 (4.44)		
Depression	Baseline	172	5.40 (3.76)	87	5.51 (3.95)	-0.90	0.030
	4 months	150	4.92 (3.93)	75	5.68 (4.03)	(0.41)	*
	8 months	133	5.25 (4.01)	71	6.12 (4.16)		
Total	Baseline	172	13.53 (7.33)	87	14.76 (7.45)	-1.78	0.020
	4 months	150	12.39 (7.36)	75	14.28 (7.40)	(0.76)	*
	8 months	133	12.88 (7.87)	71	14.91 (7.96)		

Table 6.3. Numbers of anxiety and depression cases, respectively defined as HADS-A or HADS-D score of 9+, over 8 months. Mixed model logistic regressions on ITT population, adjusted for covariates.

HADS caseness	Time	Intervention	TAU	Odds ratio	95% CI
Anxiety	Baseline	85/172 (49.4%)	48/87 (55.2%)		
	4 months	54/150 (36.0%)	36/75 (48.0%)		
	8 months	53/133 (39.9%)	33/71 (46.5%)	0.30	0.08, 1.05
Depression	Baseline	36/172 (20.9%)	17/87 (19.5%)		
	4 months	25/150 (16.7%)	18/75 (24.0%)		
	8 months	28/133 (21.1%)	23/71 (32.4%)	0.24	0.07, 0.76*

6.5.3 Missing data mechanisms

Following the procedures described by Carpenter and colleagues (Carpenter et al. 2008), the patterns of missed follow-up assessments were examined using hierarchical logistic regression to identify variables significantly associated with dropout. Dropout was defined as carers who did not complete the Brief COPE at 4 months or HADS at 8 months, for the purpose of my analysis. In the first regression, all baseline sociodemographic and clinical variables were included, as well as adherence with the intervention, as predictors. After excluding predictors with non-significant p values, the regression was repeated until all remaining predictors were significantly associated with dropout ($p < 0.05$). It could then be inferred whether the data were missing completely at random, missing at random, or missing not at random.

Weighting for missing at random data

If the dataset were consistent with missing at random conditional on particular variables, I made inferences in the mediation analyses about the outcomes of carers who dropped out, using inverse probability weighting (Seaman et al. 2011). This technique involved using the predicted values frrom logistic regression to give extra weight to the

outcomes of carers whom remained in the trial, but whom shared characteristics with those who dropped out. For example, if non-White British carers had 50% probability of dropout, then all non-White British carers remaining in the trial would be given a weight of 2. I included these inverse probability weights in all mediation analyses described below (Sections 6.5.5, 6.5.6 and 6.5.9). I additionally performed sensitivity analyses using unweighted data with complete cases.

6.5.4 Establishing statistical mediation

The main objective of this study was to investigate whether increased carers' emotion-focused coping post-intervention mediated the effect of psychological therapy on reducing morbidity.

A mediator is a mechanism through which a predictor variable exerts influence on an outcome variable (Baron et al. 1986;Kraemer et al. 2002;Rose et al. 2004). For example, coping style has been shown to mediate the relationship between burden and anxiety in family carers of people with dementia (Cooper et al. 2008b). In contrast, a moderator is a contextual variable that influences the strength or direction of a relationship between two variables (Baron et al. 1986;Kraemer et al. 2002;Rose et al. 2004). For example, the carer's relationship to CR has been shown to moderate the effects of adult day services on carer stress, with daughters reporting greater reduction in stress compared to wives (Kim et al. 2012). Models of mediation and moderation are therefore important tools for illustrating causal relationships (Rose et al. 2004). There is a growing literature on more complex models such as mediated moderation, in which the strength of mediation varies depending on the moderator (Muller et al. 2005). For example, the effect of Alcoholics Anonymous groups on reducing problem drinking was shown to be mediated by improved social functioning, but this relationship was much

stronger in men (implying that women reduced their drinking more through other mechanisms) (Kelly et al. 2012) This particular model will be discussed further in relation to the current study in Section 6.5.9.

Mediation models have particular strengths in the context of randomised intervention trials (Rose et al. 2004). They can be informative about the mechanisms of successful or unsuccessful intervention (Kraemer et al. 2002;Rutter et al. 2001;Weersing et al. 2002), particularly in elucidating causal pathways or "active ingredients" of complex psychosocial interventions (Dunn et al. 2005). This can in turn inform the development of more effective interventions in research and clinical practice. On a theoretical level, if a manipulated variable (the randomly assigned intervention) is associated with change in the mediator which in turn is associated with change in the outcome, this significantly strengthens the hypothesis of the mediator as a causal mechanism (Collins et al. 2000).

Conventional mediation methods

Various methods have been used to establish statistical mediation, including regression techniques and structural equation modelling. A widely accepted approach is the Baron and Kenny (1986) method, which uses hierarchical ordinary least squares regressions to test whether the effect of a predictor variable on an outcome variable is attenuated after controlling for the mediator variable. I shall be using a variation of this method to test my hypotheses that change in coping mediated the effects of the intervention in reducing psychological morbidity (Mackinnon et al. 2002) (Figure 6.1).

Figure 6.1. Path diagram showing my hypothesis, and criteria for significant mediation based on MacKinnon joint significance test.
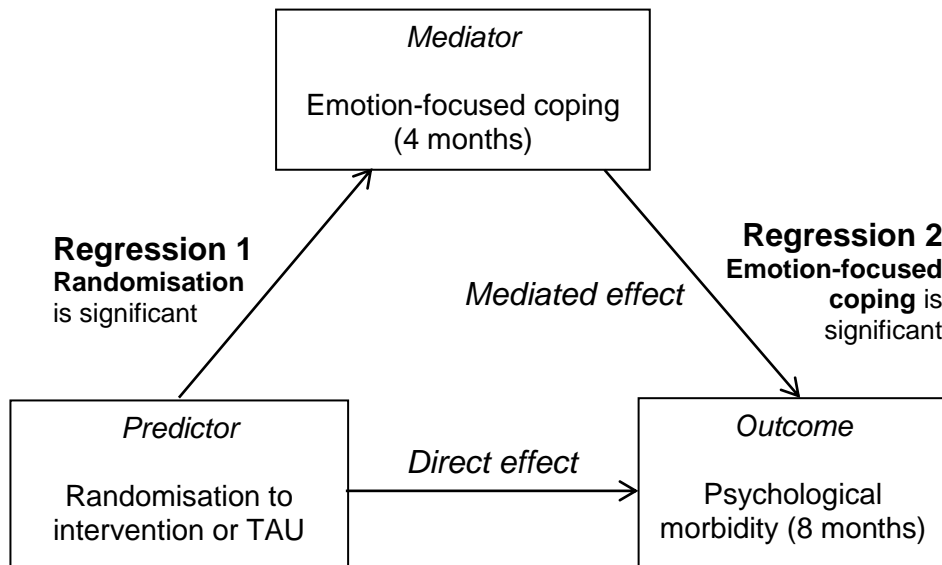
Ordinary regression techniques may produce biased estimates when used to test mediation of treatment effects in an RCT, because of hidden confounding influencing both the post-randomisation mediator and the outcome (Dunn et al. 2005;Emsley et al. 2010;Gelman et al. 2007;Herting 2002). Randomisation does not remove this confounding; while participants are randomly allocated to different levels of treatment, they are *not* randomly allocated to different levels of the post-randomisation mediator (Gelman et al. 2007). A typical example is adherence as a potential mediator of the effects of psychological therapy on mood outcomes. Hidden confounding is likely, because participants are not randomised to different levels of adherence; and those who are likely to achieve poor outcomes are also those least likely to engage with treatment, thus the observed relationship between the two would be exaggerated under conventional regression techniques (Dunn et al. 2005;Emsley et al. 2010;Gelman et al. 2007;Herting 2002). In the current context, if carers whose emotion-focused coping
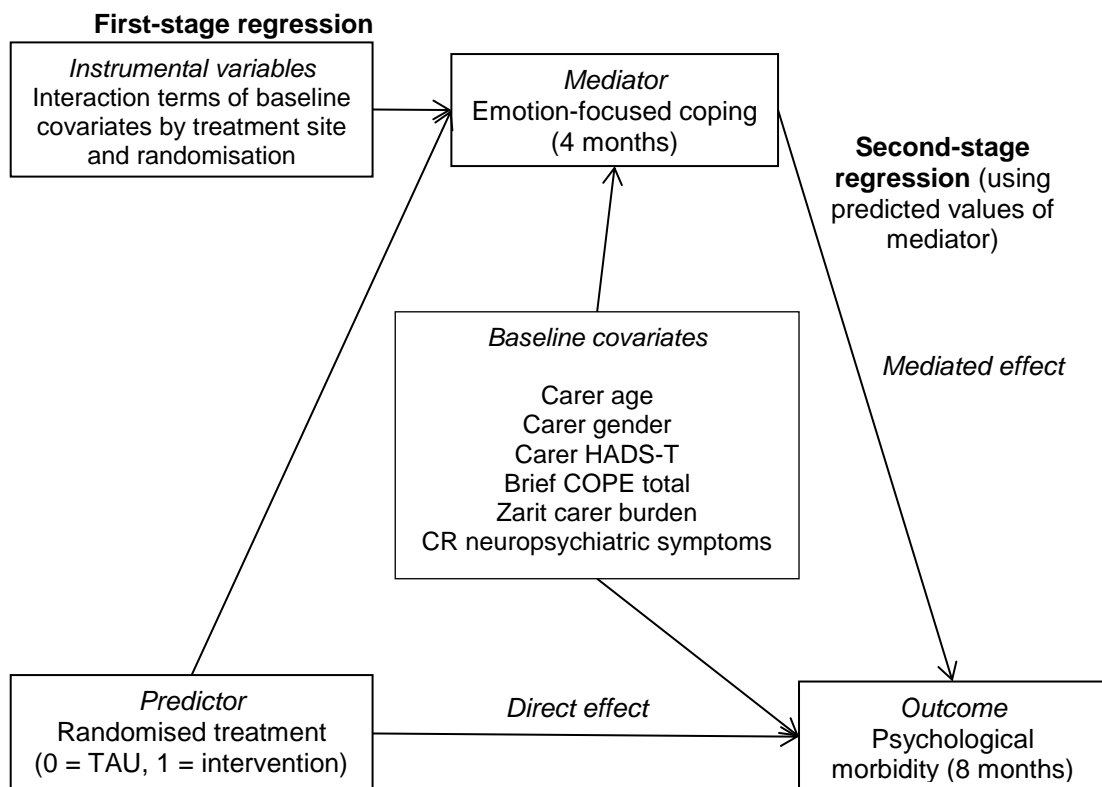
increases with treatment differs from those whose emotion-focused coping decreases, in ways that also affect their psychological morbidity, then any association between change in coping and psychological morbidity could be spurious. Traditional structural equation modelling methods are also not immune from this problem (Emsley et al. 2010).

Causal inference using instrumental variables

Causal inference approaches acknowledge hidden confounding and are designed to obtain less biased estimates of mediation effects in RCTs (Angrist et al. 1996;Emsley et al. 2010;Gennetian et al. 2008). These approaches aim to model the predicted outcomes for each participant had they been randomised to each possible treatment group, at each possible level of the mediator, given the participant characteristics and outcomes actually observed. One method uses instrumental variables, defined as variables that correlate with the mediator and that influence the outcome solely via the mediator, to improve the estimates of the regression (Angrist et al. 1996;Dunn et al. 2005;Emsley et al. 2010). Conceptually speaking, instrumental variable methods discard all natural variation in the mediator (due to individual and environmental factors), and estimate the causal effects of treatment by utilising only the experimentally-driven variation in the mediator (Lynch et al. 2008). An additional assumption is that the outcome for any participant is not influenced by treatment status of any other participants (Angrist et al. 1996). Instrumental variable methods have been successfully used to elucidate treatment mechanisms for various psychological therapy trials, for example how reduced reliance on non-study therapy mediated the effect of cognitive therapy on depression (Ten Have et al. 2007).

In an RCT, randomisation status would be an ideal instrumental variable because the treatment could by definition only affect the outcome via the treatment mechanism (Dunn et al. 2005;Emsley et al. 2010;Gennetian et al. 2008). However as I was interested in randomisation status as a predictor in the regression model, it would be necessary to generate additional instrumental variables, by taking the interaction terms of randomisation status with baseline covariates that are strongly associated with both mediator and outcome (Emsley et al. 2010). I could then perform a two-stage least squares regression procedure incorporating all the instrumental variables (Figure 6.2): the first stage to estimate potential values of the mediator, then using these values in the

Figure 6.2. Path diagram of instrumental variable model, illustrating hypothesised causal relationships between treatment, emotion-focused coping and psychological morbidity.

First-stage regression

Instrumental variables
Interaction terms of baseline covariates by treatment site and randomisation

Mediator
Emotion-focused coping
(4 months)

Second-stage regression (using predicted values of mediator)

Mediated effect

Baseline covariates

Carer age
Carer gender
Carer HADS-T
Brief COPE total
Zarit carer burden
CR neuropsychiatric symptoms

Predictor
Randomised treatment
(0 = TAU, 1 = intervention)

Direct effect

Outcome
Psychological
morbidity (8 months)

second stage to estimate effects of treatment on the outcome (Angrist et al. 1996;Dunn et al. 2005;Emsley et al. 2010;Gennetian et al. 2008).

Selection of mediators

My primary hypothesis was that for family carers in the START study, increase in emotion-focused coping post-intervention mediated the relationship between treatment assignment and reduced carer psychological symptoms at later follow-up. I had to consider whether to include all three subscales of the Brief COPE (emotion-focused, problem-focused, and dysfunctional) as putative mediators. (These subscales correspond to the categories of coping defined in my systematic review; see Chapter 2.) While "coping style" conceptually relates to the levels of use of different coping strategies (Cooper et al. 2008a;Li et al. 2012), including three mediators simultaneously would reduce the power of an instrumental variable mediation model, and require additional assumptions that are unlikely to be justified (Reardon et al. 2010).

Nonetheless the relationships between morbidity and the three coping strategies are of interest, given that my systematic review of intervention studies produced no definitive findings regarding any single coping strategy (see Chapter 3). Thus three sets of analyses were conducted, each exploring one of the coping subscales (emotion-focused, problem-focused, and dysfunctional) measured post-intervention as the sole putative mediator of intervention effects on psychological morbidity, and including the baseline score for that particular subscale as covariate. Each mediation analysis was performed twice: using an ordinary regression method (Section 6.5.5), then using two-stage least squares regression designed for RCTs (Section 6.5.6), and compared the findings.

Multiple statistical tests were performed during the course of this investigation, and thus there was a theoretically increased risk of Type I errors (significant chance findings). The proposed models of mediation on HADS symptoms, mediation on HADS caseness, and moderated mediation could be seen as comprising three different 'families' of tests for which the alpha level could potentially be adjusted.

Statistical advice from the START Study statistician was that Bonferroni corrections would not be appropriate; such corrections, as applied to classical multiple testing scenarios, assume tests to be statistical independent to each other, which would not be the case with the various tests of mediation (Barber, J., personal communication). Bonferroni correction would likely be overly conservative at the expense of unjustifiably increased risk of Type II errors (a true effect failing to reach significance) (Gelman et al. 2012;Perneger 1998).

6.5.5 Analytic procedure: Ordinary regression

To test the primary hypothesis that increase in emotion-focused coping mediated effects of treatment in reducing psychological morbidity, I first conducted mediation analyses using hierarchical ordinary least squares regressions, following MacKinnon and colleagues' (2002) revision of the Baron and Kenny (1986) method (see Figure 6.1):

- Regression 1: Emotion-focused coping at 4 months was the outcome variable, and randomisation was the predictor variable

- Regression 2: HADS-T at 8 months was the outcome variable, with emotion-focused coping at 4 months as predictor while controlling for randomisation.

In both regression equations, I included the *a priori* baseline covariates listed in Table 6.4. I incorporated inverse probability weights into the regressions to adjust for missing data, and conducted sensitivity analyses using unweighted complete cases. I reported coefficients, the model's R^2, and used the MacKinnon's joint significance test to assess goodness-of-fit.

Table 6.4. Baseline covariates for mediation analysis.

Experimental variables	Demographic variables	Baseline clinical variables
Study site	Carer age Carer gender	Psychological morbidity (HADS-T) Coping (Brief COPE: Emotion-focused, problem-focused, or dysfunctional) Carer burden (Zarit Burden Inventory) CR neuropsychiatric symptoms (VNPI)

Statistical mediation is established if: randomisation is significantly associated with emotion-focused coping (Regression 1), emotion-focused coping is significantly associated with psychological morbidity after controlling for randomisation (Regression 2), and the two coefficients are jointly significant (Mackinnon et al. 2002). The MacKinnon test removes the Baron and Kenny (1986) requirement for a significant association between treatment and outcome (i.e. a significant direct effect on HADS-T), both for increased statistical power and because the mediating effect of coping would be of interest even in the absence of a significant treatment effect (Mackinnon et al. 2002).

6.5.6 Analytic procedure: Two-stage regression

I also used an alternative procedure for establishing mediation in RCTs, documented in various sources (Angrist et al. 1996;Dunn et al. 2005;Emsley et al. 2010;Gennetian et

al. 2008). The mediator of interest was emotion-focused coping at 4 months (i.e. immediately post-intervention), and the primary outcome variable was HADS-T at 8 months (Figure 6.2).

Generating instrumental variables

I included baseline covariates that were correlated with emotion-focused coping and HADS-T at follow-up, same as those used in the ordinary least squares regression analyses (Table 6.4). I generated instrumental variable interaction terms by taking the product of each baseline covariate with randomisation (Randomisation $\times$ Baseline HADS-T, Randomisation $\times$ Carer gender, etc.) (Emsley et al. 2010). I made the assumption that baseline covariates influenced the effect of randomisation on the level of mediation (i.e. change in emotion-focused coping), but neither the direct effect of treatment on the outcome (psychological morbidity) nor the effect of mediator on the outcome (Emsley et al. 2010).

Two-stage regression

I constructed a two-stage least squares regression model to estimate: 1) the direct effect of treatment on HADS-T at 8 months; 2) the mediated effect of treatment via coping, i.e. the causal effect of emotion-focused coping at 4 months on HADS-T at 8 months as a result of receiving treatment, as follows:

First-stage: Emotion-focused coping at 4 months was the outcome variable, and randomisation was the predictor variable, controlling for baseline covariates and instrumental variables (Randomisation $\times$ Covariate interaction terms). For the initial model, I used all *a priori* specified interaction terms for the covariates specified in Table 6.4. I then saved the estimated values of emotion-focused coping.

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Second stage: HADS-T at 8 months was the outcome variable, with estimated values of emotion-focused coping at 4 months as predictor variable, controlling for randomisation and baseline covariates.

As before I incorporated inverse probability weights (Section 6.5.3) into the instrumental variable regressions to adjust for missing data (Dunn et al. 2007), and conducted sensitivity analyses using unweighted complete cases.

Testing and optimising model validity

I reported coefficients for the direct and mediated effects of treatment. To assess the validity of the instrumental variables, I reported the following diagnostic tests:

- First-stage regression F-test: $F < 10$ suggests that the instrumental variables do not sufficiently explain the relationship between randomisation and coping, and the model may be imprecise (Stock et al. 2002).
- Durbin-Wu-Hausman χ^2 test for endogeneity: This tests whether the estimated coefficients are significantly different from that of a conventional regression (Cameron et al. 2009).
- Sargan χ^2 test of overidentification: A significant result suggests that there are too many instruments that lack explanatory power in the model (Sargan 1958).

Following procedures outlined by Berry (2011), if these tests suggested the instrumental variable model lacked validity, I repeated the analysis using a more parsimonious model including only the single instrumental variable with the greatest explanatory power, in order to increase precision and reduce bias (Hahn et al. 2002).

Given that the assumptions of instrumental variable models were met, statistical

mediation was established by the presence of a significant indirect (mediated) effect, i.e.

if increased emotion-focused coping were significantly associated with reduced

psychological morbidity, for those carers whose emotion-focused coping would increase

had they been randomised to treatment. I compared the results to those obtained using

conventional regression models (see Section 6.5.5).

6.5.7 Secondary analyses

To test my secondary hypotheses that increase in emotion-focused coping mediated

the effects of treatment on reduced anxiety and depression, and to explore whether other

coping strategies (problem-focused or dysfunctional) might have mediated treatment

effects, I repeated all regression procedures detailed previously (Sections 6.5.5 and 6.5.6)

for the variables listed in Table 6.5.

**Table 6.5. Putative treatment mediators for different outcome measures in the
START intervention.**

Mediator: Coping (at 4 months)	Outcome (at 8 months)
Problem-focused	HADS-T
Dysfunctional	HADS-T
Emotion-focused	HADS-A
Emotion-focused	HADS-D
Emotion-focused	Anxiety caseness
Emotion-focused	Depression caseness

6.5.8 Post-hoc subgroup efficacy analyses

In generating instrumental variables for the mediation analyses, I found that the

Randomisation $\times$ Baseline HADS-T interaction term independently and significantly

predicted change in coping strategies over 4 months (Section 6.5.3).

To elucidate how clinically different levels of morbidity affected response to treatment, I conducted post-hoc efficacy analyses for subgroups of carers defined by baseline HADS-T. I categorised carers as non-cases (HADS-T $0 - 7$), possible cases ($8 - 15$) and cases (16+), based on the range of cut-offs for clinical caseness for anxiety or depression used in previous studies (Bjelland et al. 2002). As the cut-offs used could influence subgroup effects, I performed sensitivity analyses using alternative cut-offs of $0 - 11$, $12 - 19$, and 20+, based on two studies in the same review that found optimal cut-offs of 20+ for major depressive disorder (Bjelland et al. 2002).

I conducted mixed model regression analyses for each subgroup, with each Brief COPE subscale over 4 months as the outcome, and randomisation as the predictor. I included all previously specified baseline covariates (baseline coping, treatment site, carer age and gender, Zarit Burden Inventory, and $\sqrt{NPI}$; see Table 6.4). Although not of key interest to my primary hypothesis, I conducted sensitivity analyses with Brief COPE outcomes over 8 months, adjusting for repeated measures, as it would be nonetheless interesting to see whether treatment effects on coping continued. Following the recommendations by Lagakos (2006) for maximising the validity of subgroup analyses, I inspected the confidence intervals of treatment effect for the various subgroups to infer a plausible range of treatment differences consistent with the trial results.

6.5.9 Analytic procedure: Moderated mediation

Given that baseline psychological morbidity moderated treatment effects on coping (Sections 6.5.3 and 7.7), and that change in emotion-focused coping over 4 months predicted psychological morbidity at 8 months irrespective of randomisation (Section 7.6), this raised the possibility of the data being consistent with moderated mediation

(Muller et al. 2005). That is, the mediating effects of coping strategies on psychological morbidity might vary according to baseline morbidity. On the basis of the subgroup efficacy findings (Section 6.7), I hypothesised that increase in emotion-focused coping over 4 months would more strongly mediate the effect of treatment in reducing psychological morbidity at 8 months among those with higher levels of baseline distress, compared to those with lower baseline distress.

Figure 6.3. Path diagram and criteria for hypothesised moderated mediation, based on Muller et al. (2005).

Overall treatment effect

| *Predictor*

Randomisation to intervention (+1) or TAU (-1) | **Regression 1**

Randomisation is significant;
Randomisation × HADS-T is *not* | *Outcome*

Psychological morbidity (8 months) |

| *Moderator*

Psychological morbidity (baseline) | *Mediator*

Emotion-focused coping (4 months) | |

Regression 2
Randomisation × HADS-T is significant

Mediated effect

Regression 3
Emotion-focused coping is significant

| *Predictor*

Randomisation to intervention (+1) or TAU (-1) | *Direct effect* | *Outcome*

Psychological morbidity (8 months) |

To test this hypothesis, I followed the procedure described by Muller and colleagues (2005). This sought to establish moderated mediation in an RCT using a series of

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regression equations adapted from the Baron & Kenny (1986) procedure, but including the putative moderator in all of the equations. In this instance, baseline HADS-T score was the moderator, and the mediation analysis included interaction terms for Randomisation $\times$ Baseline HADS-T, and Coping (4 months) $\times$ Baseline HADS-T. Emotion-focused coping at 4 months was the mediator of interest. Randomisation was contrast coded (+1 representing intervention, -1 TAU), and predictor variables were centred around their means to facilitate interpretation of interaction terms (Muller et al. 2005). All regression equations were adjusted for previously specified baseline covariates (Table 6.4), and for missing data using previously calculated inverse probability weights (see Section 6.5.3: Weighting for MAR data).

- Regression 1: HADS-T at 8 months was the outcome variable. Randomisation, and Randomisation $\times$ Baseline HADS-T were predictor variables, controlling for baseline covariates;

- Regression 2: Emotion-focused coping at 4 months was the outcome variable. Randomisation, Randomisation $\times$ Baseline HADS-T were predictor variables, controlling for emotion-focused coping and other covariates at baseline;

- Regression 3: HADS-T at 8 months was the outcome variable. Emotion-focused coping at 4 months was the predictor, controlling for emotion-focused coping and other covariates at baseline, randomisation, and all possible moderating effects of baseline morbidity, i.e. Emotion-focused coping (4 months) $\times$ Baseline HADS-T, and Randomisation $\times$ Baseline HADS-T.

To establish moderated mediation, all of the following criteria must be met (Figure 6.3):

- Regression 1: there is a statistically significant overall effect of treatment on psychological morbidity at 8 months, which was not moderated by baseline morbidity (i.e. non-significant Randomisation × Baseline HADS-T);

- Regression 2: the Randomisation × Baseline HADS-T interaction is significant (The overall effect of treatment on coping may or may not be significant;)

- Regression 3: the effect of coping on psychological morbidity is significant.

For each regression, I estimated the total mediated effects of treatment via coping, by multiplying estimated effects of treatment on coping with estimated effects of coping on psychological morbidity, taking the mean baseline HADS-T within each of the three psychological morbidity caseness subgroups (non-cases, possible cases, and cases), to better illustrate varying levels of mediation at different level of the moderator (Muller et al. 2005). Finally, I repeated all steps above using HADS-D and HADS-A as the final outcome variable, and all again using problem-focused coping and dysfunctional coping as putative mediator. For ease of interpretation of the estimated effects, I used non-transformed dysfunctional coping.

6.5.10 Power calculations

Primary efficacy analysis

The START Study was powered for a primary outcome of the HADS-T score. It was calculated that a sample size of 260 carers (173 intervention, 87 TAU) would be sufficient to detect a difference in HADS-T of at least 2.4 points (with 80% power, at 5% significance), a difference exceeding 1.6 points that would be considered clinically important (Puhan et al. 2008). This calculation assumed a standard deviation for HADS-T of 7.4 from pilot data (Livingston et al. 2013), allowing for analysis of covariance

(assumed correlation 0.5), repeated follow up measurements at 4 and 8 months

(assumed correlation 0.7), a 10% dropout rate at 8 months, and a design effect of 1.4

applied for the intervention arm (based on an average cluster size of 15 carers per

therapist and an intraclass correlation of 0.03) (Fossey et al. 2006),

Mediation analysis

I conducted an *a priori* power calculation for my primary hypothesis based on a

mediation model using the MacKinnon joint significance method (Mackinnon et al.

2002). There is no single standardised approach for calculating sample size

requirements in instrumental variable models, but very small samples are known to

result in biased estimates (Gennetian et al. 2008).

I based effect size estimates on:

1. My meta-analysis of group coping skills interventions with behavioural
   activation (see Chapter 3), which found a treatment effect size of SMD = 0.28 on
   positive coping;
2. The LASER study which reported a standardised beta of -0.195 for the
   association between emotion-focused coping and later anxiety (Cooper et al.
   2008b).

Both effect sizes would be considered small-to-medium (Cohen 1988). Therefore

for the current study, I assumed effect sizes of 0.26 (halfway between small and

medium effects) (Cohen 1988)) for both: a) treatment on emotion-focused coping at 4

months, and b) emotion-focused coping on HADS-T at 8 months. To achieve 80%

power to detect significant mediation ($p < 0.05$) using the MacKinnon joint significance

test would require a minimum sample size of 159 (Fritz et al. 2007). With an estimated

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dropout rate of 10% at 8-month follow up, this would require recruitment of 177 carers, within the 260 needed for the primary HADS-T analysis.

7 Results

7.1 Sample

We recruited the participants between November 2009 and June 2011 (see CONSORT diagram, Figure 7.2). We screened 472 potentially eligible carers, of whom 260 provided informed consent, completed baseline assessment and were randomised. The most common reason for exclusion was declining consent (181/212). Carers who did and did not consent were generally comparable on known demographic variables (carer and CR gender, relationship with CR; Table 7.1), demonstrating external validity of the included sample. However carers who gave consent were slightly more likely to be married to the CR (109/260, 42%) than those eligible but not randomised (65/190, 34%).

Table 7.1. External validity of eligible carers who consented to the trial compared with those who were not randomised.

	Randomised (N=260)	Eligible but not randomised (N=190)
Female carer	179 (31%)	134 (29%)
Female CR	142 (42%)	115 (39%)
Carer relationship to CR		
Spouse or partner	109 (42%)	65 (34%)
Child	113 (44%)	90 (47%)
Friend	6 (2%)	8 (4%)
Daughter- or son-in-law	12 (5%)	4 (2%)
Nephew or niece	8 (3%)	8 (4%)
Grandchild	6 (2%)	4 (2%)
Sibling	4 (2%)	5 (3%)
Other	**2 (1%)**	6 (3%)

For the current investigation, 145/173 (83.8%) of the Intervention group and 72/87 (82.8%) of TAU completed the Brief COPE at 4 months. Overall, 208/260 carers

(80.0%) remained in the study and provided HADS psychological morbidity measures at 8 months.

Figure 7.1. CONSORT diagram illustrating flow of participants for the START study.
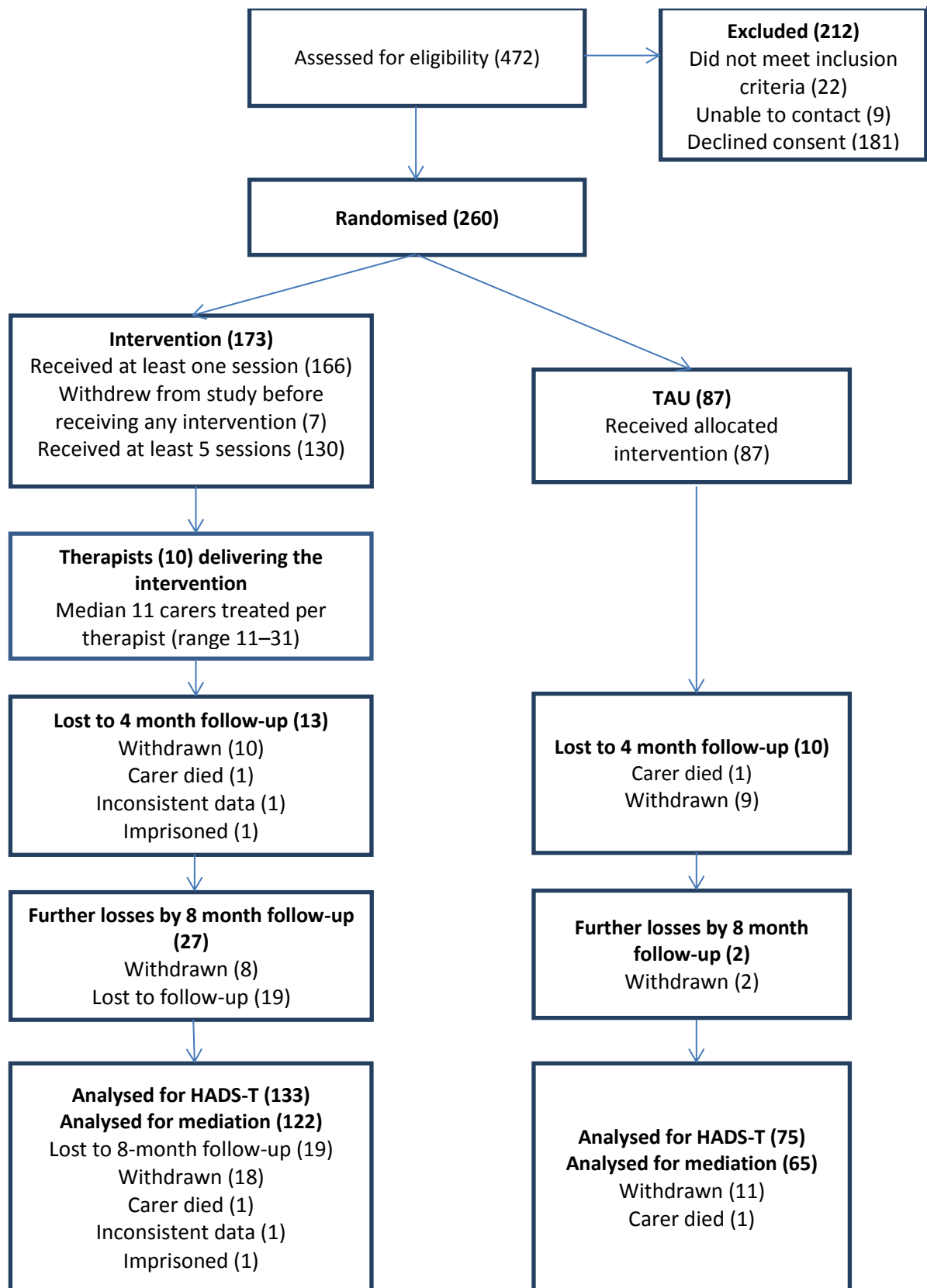
7.2   Descriptive statistics

7.2.1   Carer and carer recipient characteristics

Carers had a mean age of 60; most were female (179/260, 68.5%), either a spouse/partner (109/260, 41.9%) or child (113/260, 43.5%) of the CR, living with the CR (163/260, 62.7%), educated to school level or beyond (197/260, 75.8%), and White British or Irish (187/260, 72.2%) (Table 7.2). CRs had a mean age of 79, most were female (152/260, 58.5%) and White British (168/260, 71.9%), and just over half were educated to school level or beyond (133/260, 51.1%).

Intervention and TAU groups were generally comparable, except those in the intervention group were slightly older on average, and more likely to be male, unmarried, living with CR, and have no qualifications (Table 7.2). On the advice of the START Study statistician, formal tests for significant differences between intervention and TAU groups were not performed, in order to minimise the number of statistical tests (Barber, J., personal communication).

Table 7.2. Carer demographics overall and by randomisation status.

		Intervention n = 173 (66.5%)		TAU n = 87 (33.5%)		Overall N = 260	
Carer demographics		Mean or number	SD or %	Mean or number	SD or %	Mean or number	SD or %
Age		62.0	14.6	56.1	12.3	59.8	14.6
Gender	Female	116	67.0%	63	71.3%	179	68.5%
Marital status	Single or unmarried	37	21.4%	14	16.1%	51	19.6%
	Married or couple	112	64.7%	62	71.3%	174	66.9%
	Divorced or separated	17	9.8%	8	9.2%	25	9.6%
	Widowed	5	2.9%	3	3.4%	8	3.1%
	Other	2	1.2%	0	0%	2	0.8%
Relationship to CR	Spouse or partner	78	45.1%	31	35.6%	109	41.9%
	Child	71	41.0%	42	48.3%	113	43.5%
	Friend	2	1.2%	4	4.6%	6	2.3%
	Child-in-law	7	4.1%	5	5.8%	12	4.6%
	Nephew or niece	6	3.5%	2	2.3%	8	3.1%
	Grandchild	4	2.3%	2	2.3%	6	2.3%
	Sibling	3	1.7%	1	1.2%	4	1.5%
	Other	2	1.2%	0	0%%	2	0.8%
Living with CR		113	65.3%	50	57.5%	163	62.7%
Education	No qualifications	45	26.0%	18	20.7%	63	24.2%
	School level	51	29.5%	33	37.9%	84	32.3%
	Further education	77	44.5%	36	41.4%	113	43.5%
Work	Full-time	36	20.8%	28	32.2%	64	24.6%
	Part-time	27	23.0%	20	15.6%	47	18.1%
	Retired	80	46.2%	23	26.4%	103	39.6%
	Not working	30	17.3%	16	18.4%	46	17.7%
Ethnicity	White British	125	72.7%	62	71.3%	187	72.2%
	White Other	16	9.3%	8	9.1%	24	9.1%
	Black or Asian	31	18.0%	17	19.5%	48	18.5%
	Did not disclose	1	0.6%	0	0%	1	0.4%

Table 7.3. CR demographics overall and by carer randomisation status.

		Intervention n = 173 (66.5%)		TAU n = 87 (33.5%)		Overall N = 260	
CR demographics		Mean or number	SD or %	Mean or number	SD or %	Mean or number	SD or %
Age		79.9	8.3	78.0	9.9	79.3	8.9
Gender	Female	102	59.0%	50	57.5%	152	58.5%
Marital status	Single or unmarried	11	6.4%	2	2.3%	13	5.0%
	Married or couple	81	46.8%	40	46.0%	121	46.5%
	Divorced or separated	22	12.7%	13	14.9%	35	13.5%
	Widowed	58	33.5%	32	36.8%	90	34.6%
	Other	1	0.6%	0	0	1	0.4%
Education	No qualifications	73	44.5%	44	51.2%	117	45.0%
	School level	28	17.1%	16	18.6%	44	16.9%
	Further education	63	38.4%	26	30.2%	89	34.2%
Ethnicity	White British or Irish	114	65.9%	54	62.1%	168	71.9%
	White Other	26	15.0%	13	14.9%	39	15.0%
	Black or Asian	33	19.1%	20	23.0%	53	20.4%

Baseline clinical characteristics

Clinically significant psychological morbidity was common in this sample of carers, with around half of carers meeting criteria for anxiety caseness (133/259), and around a fifth for depression (53/256), defined respectively by scores of 9+ on HADS-A and HADS-D (see Section 6.4.2). Roughly 40% (105/259) met criteria for overall psychological morbidity caseness, defined by HADS-T scores of 16+ (see Section 6.5.8). Most CRs had mild-moderate dementia (212/259, 81.8%), as expected given the inclusion criteria of the study. The intervention and TAU groups were broadly comparable on baseline carer and CR clinical characteristics (see Table 7.4), although in the TAU group carers presented slightly greater psychological distress, and CRs

exhibited greater neuropsychiatric symptoms, compared to the intervention group. Formal tests for significant differences between intervention and TAU groups were again not performed, on the advice of the START trial statistician.

Table 7.4. Baseline carer and CR clinical characteristics overall and by randomisation status.

	Intervention	TAU	Overall
N	173	87	260
Carer characteristics	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
HADS-A	8.13 (4.39)	9.25 (4.32)	8.51 (4.39)
HADS-D	5.40 (3.76)	5.51 (3.95)	5.44 (3.82)
HADS-T	13.53 (7.33)	14.76 (7.45)	13.94 (7.38)
	n (%)	*n (%)*	*n (%)*
Anxiety case	85/172 (49.4%)	48/87 (55.2%)	133/259 (51.4%)
Depression case	36/172 (20.9%)	17/87 (19.5%)	53/259 (20.5%)
Psychological morbidity case	71/172 (41.3%)	34/87 (39.1%)	105/259 (40.5%)
Brief COPE			
Emotion-focused	22.51 (5.19)	22.81 (5.20)	23.42 (5.19)
Problem-focused	15.84 (4.57)	17.26 (4.09)	16.32 (4.46)
Dysfunctional	19.24 (5.35)	20.48 (6.19)	19.66 (5.66)
Zarit Burden Inventory	35.26 (18.39)	38.14 (17.01)	36.23 (17.95)
CR characteristics			
NPI Total	23.97 (18.96)	26.63 (20.12)	24.86 (19.36)
CDR	*n (%)*	*n (%)*	*n (%)*
0.5	30/172 (17.4%)	12/87 (13.8%)	42/259 (16.2%)
1	91/172 (52.9%)	43/87 (49.4%)	134/259 (51.7%)
2	48/172 (27.9%)	30/87 (34.5%)	78/259 (30.1%)
3	2/172 (1.2%)	2/87 (2.3%)	4/259 (1.5%)

All baseline continuous variables approached the normal distribution (as demonstrated by approximately linear Q-Q plots), except for dysfunctional coping and NPI Total (Figure 7.3). These were transformed into log dysfunctional coping and square root NPI Total, and the resulting distributions approximated the normal distribution.

Figure 7.3. Q-Q plots for baseline dysfunctional coping and NPI Total were non-linear, suggesting non-normally distributed data.

Normal Q-Q Plot of COPE Dysfunctional

Normal Q-Q Plot of NPI Total
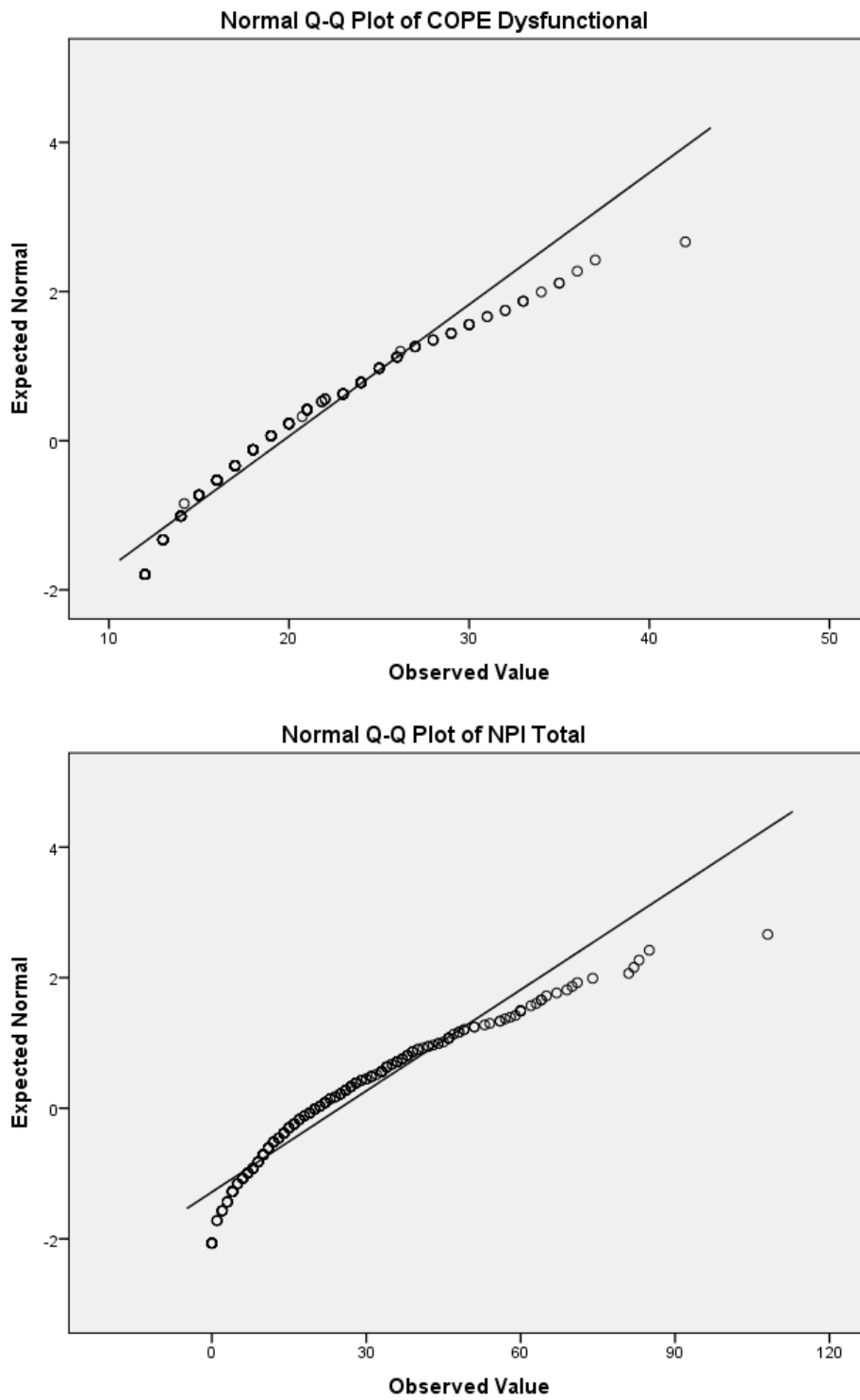
7.2.2 Baseline characteristics by centre

Most (183/260, 70%) carers and CRs were recruited from C&I. Carers and CRs in the four study sites were broadly similar in key characteristics (Table 7.5), although carers in the C&I site were slightly younger (58.3 years) than the average across the study (59.8 years). CRs in UCLH were younger (67.6 years) than the study average (79.3 years), as expected at a service specialising in younger onset dementias. NELFT, the admiral nurse service was the smallest site with only 16 carers, most of whom were female (14/16, 85%), with above average scores on psychological distress (18.0) and all coping strategies; this site also had the greatest portion of male CRs (12/16, 25%) and above average neuropsychiatric symptoms (31.5).

Table 7.5. Mean (SD) or n (%) for baseline characteristics by study site.

	C&I	UCLH	NELFT	NEPFT	Overall
n	183	35	16	26	260
Carer characteristics					
Carer age	58.3 (15.1)	61.1 (13.5)	63.4 (15.1)	66.2 (10.1)	59.8 (14.6)
Female carer	123 (67.2%)	20 (57.1%)	14 (87.5%)	21 (80.8%)	178 (68.5%)
Living with CR	100 (54.6%)	32 (91.4%)	13 (81.3%)	18 (69.2%)	163 (62.7%)
HADS-T	13.7 (7.8)	13.7 (6.5)	18.0 (5.5)	13.9 (6.1)	13.9 (7.4)
Brief COPE					
Emotion-focused	23.0 (5.2)	22.0 (5.3)	24.3 (5.6)	21.8 (5.1)	22.8 (5.2)
Problem-focused	16.4 (4.6)	16.7 (4.3)	17.1 (3.0)	14.9 (4.3)	16.3 (4.5)
Dysfunctional	19.5 (5.9)	19.5 (4.7)	23.1 (4.4)	19.0 (5.3)	19.7 (5.7)
Zarit Burden Inventory	35.0 (18.7)	34.7 (14.9)	49.0 (12.8)	39.2 (16.1)	36.2 (18.0)
CR characteristics					
CR age	81.8 (7.0)	67.6 (8.3)	76.3 (7.9)	78.9 (9.3)	79.3 (8.9)
Female CR	114 (62.3%)	18 (51.4%)	4 (25.0%)	16 (61.5%)	152 (58.5%)
NPI Total	24.7 (19.4)	24.5 (22.0)	31.5 (15.5)	22.9 (17.1)	24.9 (19.4)
CDR					
0.5	24 (13.3%)	10 (28.6%)	1 (6.2%)	7 (26.9%)	42 (16.3%)
1	96 (53.0%)	20 (57.1%)	6 (37.5%)	12 (46.2%)	134 (51.9%)
2	58 (32.0%)	5 (14.3%)	8 (50.0%)	7 (26.9%)	78 (30.2%)
3	3 (1.7%)	0	1 (6.2%)	0	4 (1.6%)

7.3   Implementation of interventions

7.3.1   Therapists

The therapists were 7 women and 3 men, all UK graduate level psychologists aged in their 20–30s. Each therapist treated a median of 17 carers (interquartile range 7.5, range 11–31). The therapist intracluster correlations for the primary HADS-T outcomes were 0.01 (95% CI: 0.00, 0.09) at 4 months and 0.00 (95% CI: 0.00, 0.07) at 8 months, suggesting a negligible therapist effect.

7.3.2   Adherence with intervention

Carers in the intervention arm completed a mean of 6.4 sessions (SD = 2.71), with most carers (130/173, 75.1%) completing at least 5 sessions and thus considered to have adhered to the intervention programme; and 125/173 (72.3%) completing all 8 sessions.

7.3.3   Blinding

Blinding was fairly successful as only 12% (31/260) of carers had unblinded themselves to the rater by 8-month follow-up.

7.4   Efficacy analyses

There were no significant differences between intervention and TAU groups for any coping strategy over 8 months of follow-up, whether or not adjusting for baseline covariates (Table 6.6). Adding an interaction term for Randomisation $\times$ Time and post-hoc pairwise comparisons confirmed that there were no significant effects of treatment on any coping strategy at 4 months (Table 7.7).

Table 7.6. Coping outcomes over 8 months by randomisation group. Mixed model regressions on ITT population accounting for therapist effect and repeated measures. Model 1 was adjusted for all *a priori* baseline covariates; Model 2 was adjusted for baseline coping and treatment site only.

		Intervention		TAU		Model 1 (N = 213)		Model 2 (N = 221)	
Coping	*Time*	n	Mean (SD)	n	Mean (SD)	b (SE)	p	b (SE)	p
Emotion-focused	Baseline	171	22.51 (5.19)	87	23.42 (5.19)	0.30 (0.64)	0.643	0.44 (0.65)	0.493
	4 months	143	23.39 (5.85)	72	23.16 (5.46)				
	8 months	125	22.06 (5.75)	67	23.18 (5.48)				
Problem-focused	Baseline	171	15.84 (4.57)	87	17.26 (4.09)	-0.23 (0.56)	0.684	-0.33 (0.53)	0.540
	4 months	145	15.89 (4.64)	72	16.10 (4.79)				
	8 months	126	14.75 (4.53)	67	16.45 (4.24)				
Dysfunctional (log scale)	Baseline	172	19.24 (5.35)	87	20.48 (6.19)	0.02 (0.03)	0.454	0.03 (0.03)	0.288
	4 months	145	18.97 (5.23)	72	19.10 (5.43)				
	8 months	126	19.10 (5.16)	67	19.29 (5.05)				

Table 7.7. Effects of treatment on coping strategies at 4-month follow-up after adding in Randomisation × Time interaction, adjusted for baseline covariates.

Outcome	**Treatment effect**	
Coping	Contrast (SE)	p
Emotion-focused	0.67 (0.73)	0.364
Problem-focused	0.47 (0.68)	0.485
Dysfunctional (log)	0.02 (0.03)	0.552

7.5 Mediation analyses: Did change in coping over 4 months mediate treatment effects on psychological morbidity at 8 months?

Although the efficacy analyses did not show any significant main effects of treatment on coping, I proceeded with the regression analyses as planned to explore the relationship between treatment assignment, coping and morbidity, as it would be useful to know whether particular styles of coping predicted morbidity irrespective of treatment. In three sets of regression analyses, I tested each coping strategy individually as a putative mediator of the relationship between treatment assignment and psychological morbidity.

7.5.1 Predictors of missingness

I found using hierarchical logistic regression that completion of both Brief COPE at 4 months and HADS-T at 8 months was significantly associated with the characteristics shown in Table 6.8.

Table 7.8. Sociodemographic and clinical characteristics associated with completion of Brief COPE (4 months) and HADS-T (8 months).

Variable	OR	95% CI	p
Adhered with at least 5 sessions of therapy, if assigned to intervention	4.14	2.07, 8.30	<0.0005*
From North Essex NHS Trust	0.29	0.11, 0.81	0.018*
Carer's number of children	3.06	1.30, 7.21	0.010*
Lived with CR	0.42	0.18, 0.98	0.044*
Relationship to CR	(versus spouse)		
Nephew or niece	0.12	0.02, 0.76	0.025*
Grandchild	0.11	0.02, 0.86	0.035*
White British CR	2.21	1.06, 4.61	0.033*
Dysfunctional coping (log)	0.30	0.09, 1.00	0.050*

I therefore inferred that the dataset were consistent with MAR, and used the logistic regression to generate inverse probability weights to account for missing data in the mediation analyses (Section 6.5.3).

7.5.2 Analysis: Ordinary regression

The following mediation analyses utilised the MacKinnon joint significance method (Mackinnon et al. 2002), and were adjusted for baseline covariates and weighted for MAR data. The unweighted complete case analyses can be found in Appendix G.

Emotion-focused coping

Randomisation status did not predict change in emotion-focused coping between baseline and 4 months ($b = 0.676$, SE = 0.700, $p = 0.336$) (Figure 6.6). Therefore my hypothesis that emotion-focused coping mediated the relationship between treatment assignment and change in psychological morbidity was not supported. Increased emotion-focused coping at 4 months did significantly predict reduced psychological morbidity at 8 months ($b = -0.345$, SE = 0.082, $p < 0.0005$), controlling for randomisation and baseline covariates. The final model explained around 58% of the variance in psychological morbidity at 8 months ($R^2 = 0.583$). The sensitivity analysis with complete cases unweighted for missing data gave very similar results (see Appendix G).

Figure 7.4. Emotion-focused coping did not mediate the relationship between treatment and psychological morbidity, although it predicted the latter (N = 184).
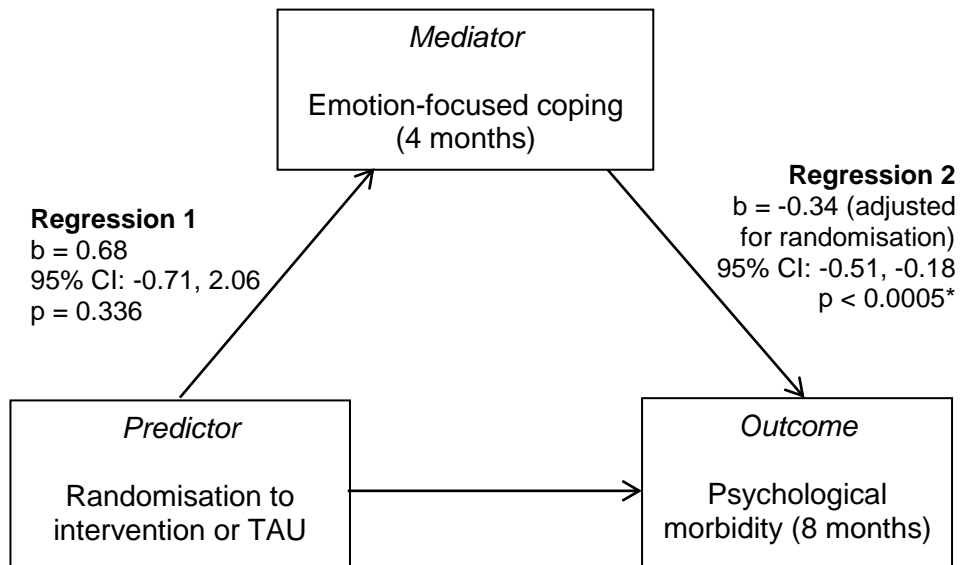
Problem-focused coping

After controlling for baseline covariates, there was neither a significant effect of randomisation status on problem-focused coping at 4 months (b = 0.575, SE = 0.686, p = 0.403), nor of problem-focused coping on psychological morbidity at 8 months adjusted for randomisation (b = -0.150, SE = 0.095, p = 0.117) (Figure 7.5). Therefore mediation was not established. The final model explained over half of the variance in psychological morbidity at 8 months ($R^2 = 0.551$). The sensitivity analysis based on unweighted complete cases gave similar results (see Appendix G).
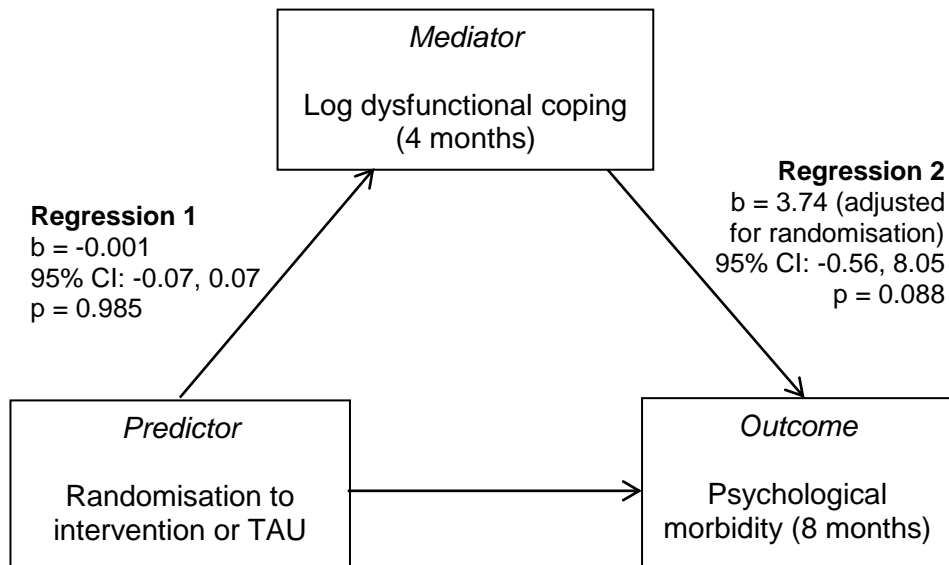
Figure 7.5. Problem-focused coping did not mediate the effect of treatment on psychological morbidity (N = 187).
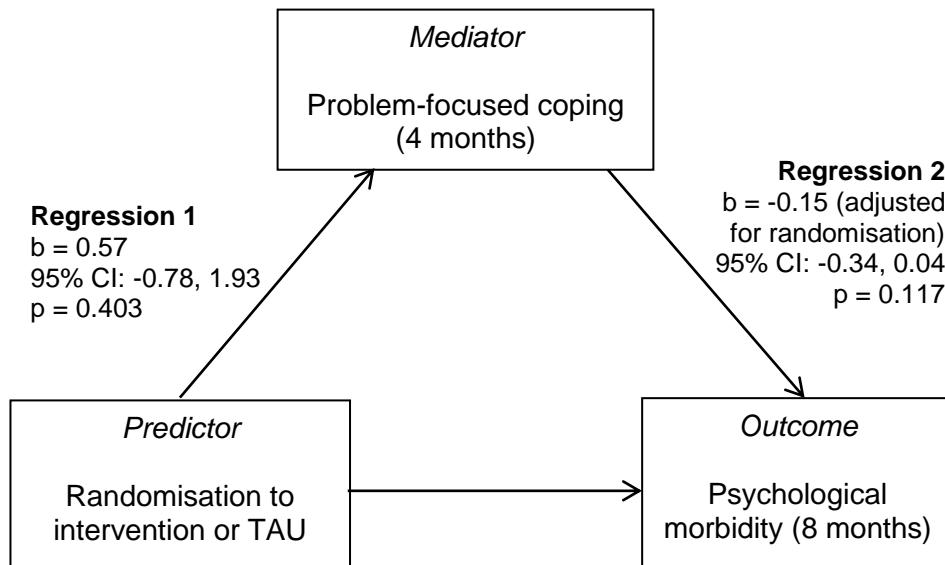
Dysfunctional coping

After controlling for baseline covariates, there was neither a significant effect of randomisation status on dysfunctional coping at 4 months (b = -0.001, SE = 0.033, p = 0.985, log scale), nor of dysfunctional coping on psychological morbidity at 8 months adjusted for randomisation (b = 3.74, SE = 1.90, p = 0.088) (Figure 6.8). Therefore mediation was not established. The final model explained over half of the variance in psychological morbidity (R^2 = 0.557). The sensitivity analysis based on unweighted complete cases gave similar results (see Appendix G).

Figure 6.8. Dysfunctional coping did not mediate the effect of treatment on psychological morbidity (N = 187).

Mediator

Log dysfunctional coping (4 months)

Regression 1
b = -0.001
95% CI: -0.07, 0.07
p = 0.985

Regression 2
b = 3.74 (adjusted
for randomisation)
95% CI: -0.56, 8.05
p = 0.088

Predictor

Randomisation to intervention or TAU

Outcome

Psychological morbidity (8 months)

Summary

Treatment assignment was not associated with overall change in emotion-focused coping over 4 months on univariate or multivariate analyses, therefore my primary hypothesis that emotion-focused coping mediated treatment effects on psychological morbidity was not supported. On multivariate analysis, carers who increased their use of emotion-focused coping between baseline and 4 months reported reduced psychological morbidity at 8 months.

Neither change in problem-focused coping nor change in dysfunctional coping between baseline and 4 months mediated treatment effects on psychological morbidity at 8 months.

7.5.3 Analysis: Two-stage regression

Initial model

The initial two-stage least squares regression analysis weighted for missing data included all interactions of randomisation status with *a priori* covariates as instrumental variables (Appendix G). This model demonstrated very poor fit (first-stage $F[11, 160] = 1.725$, $p = 0.072$), failing to reach the threshold of 10, conventionally accepted as minimum to indicate model validity; and a significant Sargan χ^2 ($p = 0.033$) indicated that it contained too many instrumental variables with little influence on coping. To improve validity and precision of the model, I needed to eliminate unnecessary instrumental variables.

Reducing the model

I inspected the first-stage regression to identify the instrumental variable with the greatest explanatory power, and this was the Randomisation $\times$ Baseline HADS-T interaction term ($b = 0.35$, $p = 0.005$). In other words, baseline psychological morbidity was the strongest predictor of change in emotion-focused coping as a result of treatment. The positive coefficient indicated that higher baseline psychological morbidity was associated with greater increase in emotion-focused coping in the intervention group over 4 months, relative to TAU. I optimised the two-stage regression by dropping all instrumental variables except the Randomisation $\times$ Baseline HADS-T interaction term, which remained strongly significant ($b = 0.300$, $p = 0.002$; Table 7.9).

I repeated the above procedures treating problem-focused coping and dysfunctional coping as putative mediators. For each coping strategy, the Randomisation $\times$ Baseline HADS-T interaction was the strongest instrumental variable (Table 7.9), with higher

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baseline morbidity significantly predicting greater increase in coping (approaching significance for problem-focused coping) in the intervention group over 4 months relative to TAU. I proceeded with the reduced models in the following mediation analyses.

Table 7.9. Significant Randomisation × Baseline HADS-T interactions from first-stage regressions predicting coping strategies at 4 months. All regressions adjusted for baseline covariates and weighted for missing data.

Outcome	N	Randomisation × Baseline HADS-T interaction		
Coping		b (SE)	95% CI	p
Emotion-focused	184	0.30 (0.09)	0.11, 0.49	0.002*
Problem-focused	187	0.18 (0.10)	-0.04, 0.37	0.056
Log dysfunctional	187	0.016 (0.006)	0.004, 0.029	0.012*

Emotion-focused coping

The reduced model demonstrated good fit (first-stage $F_{(1,172)} = 10.19 > 10$, p = 0.0017). The model coefficients did not differ significantly from those obtained of an ordinary regression (Durbin $\chi^2 = 0.49$, p = 0.485), indicating the absence of significant hidden confounding. Change in emotion-focused coping over 4 months did not significantly mediate the effects of treatment on psychological morbidity at 8 months (b = -0.565, SE = 0.356, p = 0.113). The sensitivity analysis with unweighted complete cases gave similar results (Appendix G). In summary, the model findings are compatible with those of the ordinary regression (Section 7.5.2), and statistical mediation was not established.

Figure 7.6. Instrumental variable regression model for emotion-focused coping did not support its mediation of treatment effects (N = 184).
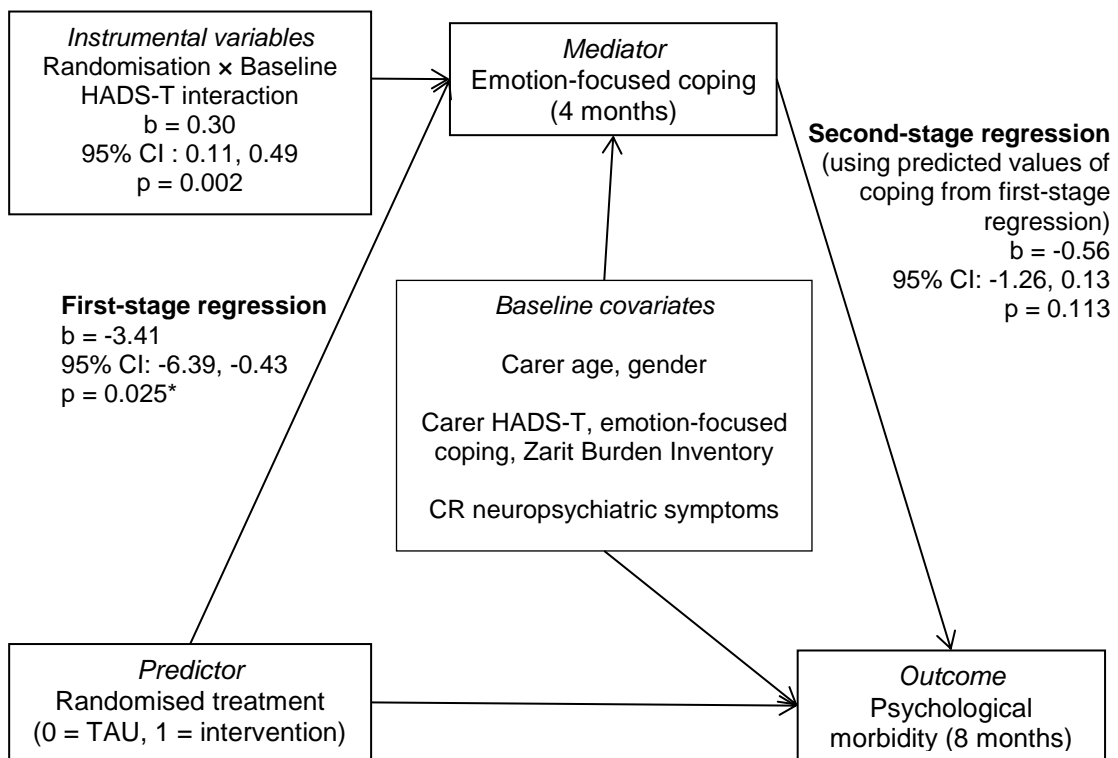

Problem-focused coping

The two-stage regression analysis demonstrated poor fit (first-stage F[1, 175] = 3.78 < 10, p = 0.05), and there was no evidence of significant hidden confounding (Durbin χ^2 = 1.11, p = 0.292). Therefore the model was compatible with ordinary regression (Section 7.5.2), and statistical mediation was not established.

Dysfunctional coping

The two-stage regression analysis demonstrated less than ideal fit (first-stage F[1,175] = 6.62 < 10, p = 0.0210), suggesting the results should be interpreted with caution. Change in dysfunctional coping over 4 months did not significantly mediate the effect of treatment on psychological morbidity at 8 months (b = -8.10, SE = 8.38, p =

0.334) (Figure 7.7). The sensitivity analysis with unweighted complete cases showed

improved fit (first-stage F > 10), otherwise gave very similar results. In summary,

statistical mediation was not established.

Figure 7.7. Instrumental variable model for dysfunctional coping (unweighted for missing data) did not support its mediation of treatment effects (N = 187).
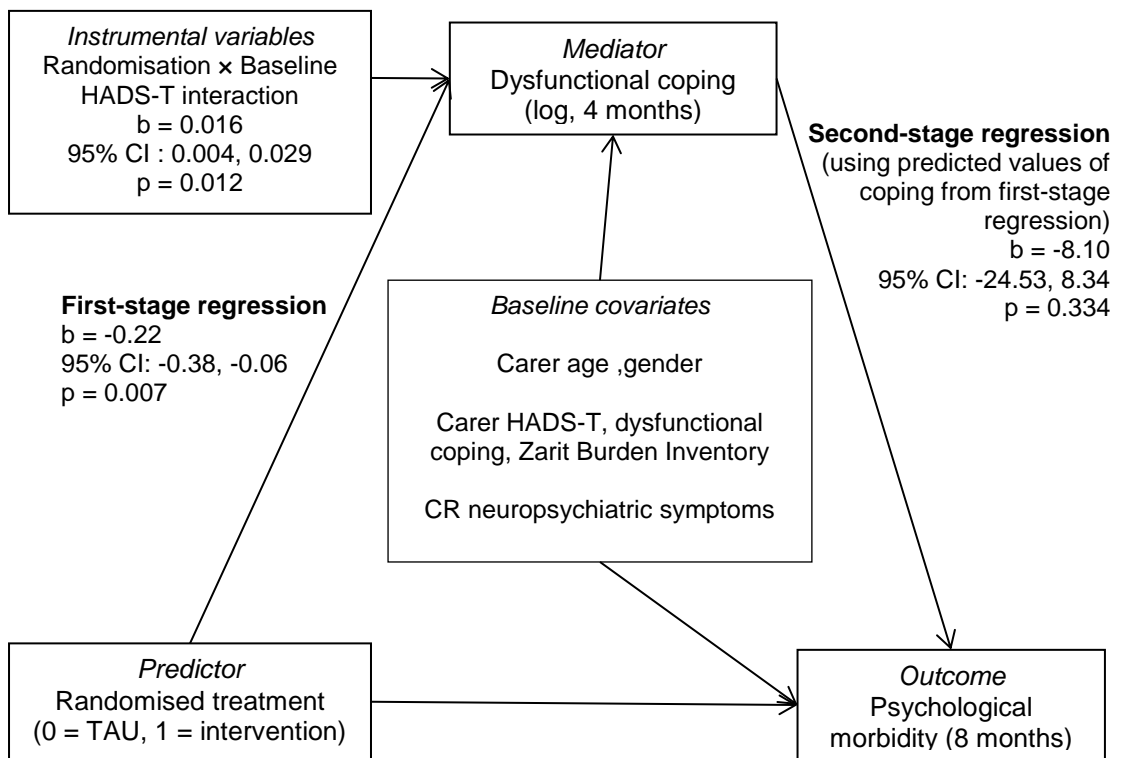
Summary

The two-stage regression analyses generally produced findings consistent to those of

ordinary regression models (Section 7.5.2), and none of the coping strategies mediated

the effects of treatment on reduced psychological morbidity. Baseline HADS-T

significantly moderated the effects of treatment on emotion-focused and dysfunctional

coping in the first-stage regressions, such that those who were initially more distressed

also showed greater increase in coping relative to TAU.

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7.5.4 Overall summary

My primary hypothesis that an increase in emotion-focused coping mediated the treatment effect of the START intervention on reducing later psychological morbidity was not supported. By definition, treatment mediation requires treatment to have a significant effect on the mediator (Baron et al. 1986). This study found no significant main effects of treatment on emotion-focused, problem-focused or dysfunctional coping, therefore the criteria for mediation were not met for any coping strategy. I did not repeat the analyses with HADS-A and HADS-D scores as outcome variables, because the first part of the mediation analysis (effects of treatment on coping) would remain non-significant, and criteria for mediation would not be met.

In the process of generating instrumental variables for the two-stage regressions, I found that increased baseline psychological morbidity significantly interacted with randomisation to predict increased coping for the treatment group. This was a novel finding, which I explore further in a post-hoc analysis in Section 7.7.

The ordinary regression analysis showed that increases in emotion-focused coping between baseline and 4 months predicted reduced morbidity at 8 months, regardless of randomisation status. This will be explored further in Section 7.6: Secondary analysis.

7.6 Secondary analysis: Did change in coping over 4 months predict caseness of psychological morbidity at 8 months?

My secondary hypotheses were that for carers receiving the START intervention, increase in emotion-focused coping between baseline and 4 months mediated intervention effects on reducing depression and anxiety. Although the mediation hypothesis was not supported, it would be clinically useful to know whether change in

coping, regardless of intervention, predicted caseness of depression or anxiety at follow-up.

I conducted logistic regressions with caseness at 8 months as the outcome, based on the previously specified cut-off of 9+ on HADS-D or HADS-A for depression and anxiety respectively (see Section 6.4.2), as well as a caseness indicator for overall morbidity (scores of 16+ on HADS-T), based on optimal cut-offs for HADS-T validated in previous studies (Bjelland et al. 2002). Predictor variables were randomisation, all three coping subscales at 4 months, and previously specified baseline covariates (Table 6.4).

7.6.1 Results

Total morbidity

In the logistic regression, psychological morbidity caseness was significantly predicted by lower emotion-focused coping at 4 months (odds ratio = 0.85, p = 0.005), and neither problem-focused (p = 0.684) nor dysfunctional coping (p = 0.111) (Table 6.9).

Depression

Depression caseness at 8 months was significantly predicted by lower emotion-focused coping at 4 months (odds ratio = 0.86, p = 0.022), and neither problem-focused (p = 0.873) nor dysfunctional coping (p = 0.158) (Table 6.9).

Anxiety

Anxiety caseness at 8 months was not significantly predicted by any coping strategy at 4 months (p values range 0.316–0.608) (Table 6.9).

Table 7.10. Coping as predictors of psychological morbidity at 8 months, controlling for randomisation and baseline covariates (N = 184).

Outcome	HADS-T		HADS-D		HADS-A	
Predictor (coping)	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Emotion-focused	0.85 (0.76, 0.95)	0.005	0.87 (0.77, 0.98)	0.022	0.98 (0.86, 1.05)	0.334
Problem-focused	1.03 (0.91, 1.16)	0.684	1.01 (0.88, 1.16)	0.873	0.97 (0.86, 1.09)	0.608
Dysfunctional (log)	5.92 (0.66, 52.74)	0.111	5.75 (0.51, 65.17)	0.158	2.93 (0.36, 24.11)	0.316

7.6.2 Summary

Reduced emotion-focused coping between baseline and 4 months independently and significantly predicted 8-month caseness for overall psychological morbidity and for depression at 8 months. None of the coping strategies significantly predicted anxiety caseness.

7.7 Post-hoc subgroup analyses: Did baseline psychological morbidity moderate the effects of treatment on coping?

Although treatment had no overall effect on coping strategies (Section 7.4), baseline psychological morbidity was the strongest predictor of whether an individual carer used more of each coping strategy in response to treatment, with more baseline symptoms predicting more coping of all kinds versus TAU (Section 7.5.3 and Table 7.9). Reduced emotion-focused coping was also shown to predict depression and overall morbidity caseness independently of randomisation status (Section 7.6).

To elucidate how treatment affected coping strategies for carers with different levels of baseline morbidity, post-hoc subgroup analyses of treatment effects on coping following were conducted as detailed in Section 6.5.8, with carers defined by baseline HADS-T.

7.7.1 Results

Descriptive statistics for subgroups

Table 7.11 and Table 7.12 show the categorisation of the subgroups, and their key characteristics. Baseline carer burden and CR neuropsychiatric symptoms generally increased with psychological morbidity, as would be expected (Table 7.12). Coping strategies at baseline and follow-up for the subgroups are shown in Table 7.13.

Table 7.11. Subgroups by baseline HADS-T score (N = 259).

Category	*Main analysis*		*Sensitivity analysis*	
	HADS-T range	**n (%) at baseline**	**HADS-T range**	**n (%) at baseline**
Non-cases	**0 – 7**	55 (21.2%)	**0 – 11**	105 (40.5%)
Possible cases	**8 – 15**	99 (38.2%)	**12 – 19**	93 (35.9%)
Cases	**16 – 42**	105 (40.5%)	**20 – 42**	61 (23.6%)

Table 7.12. Carer characteristics for subgroups by baseline HADS-T (non-cases, possible cases, and cases) in main analysis.

	Non-cases (0 – 7)				*Possible cases (8 – 15)*				*Cases (16 – 42)*			
	Intervention		*TAU*		*Intervention*		*TAU*		*Intervention*		*TAU*	
Measure	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*
HADS-T Baseline	43	4.44 (2.14)	12	4.25 (2.09)	58	11.38 (2.23)	41	11.51 (2.46)	71	20.79 (4.04)	34	22.38 (4.75)
4 months	37	5.70 (3.89)	12	6.58 (4.48)	52	10.88 (4.99)	36	12.81 (4.59)	61	17.74 (6.76)	27	19.67 (7.66)
8 months	32	6.13 (4.34)	11	6.64 (4.74)	47	11.02 (6.02)	36	12.94 (6.30)	54	18.50 (7.00)	24	21.67 (6.01)
Zarit Burden	43	21.05 (14.18)	12	22.75 (13.99)	58	30.36 (13.50)	41	34.72 (15.64)	71	48.40 (15.37)	34	47.79 (13.91)

Inventory												
CR NPI	43	14.58 (12.59)	12	15.00 (11.90)	58	19.19 (15.31)	41	21.95 (17.02)	71	33.70 (20.64)	34	36.67 (21.96)

Table 7.13. Brief COPE scores for subgroups at baseline and follow-up.

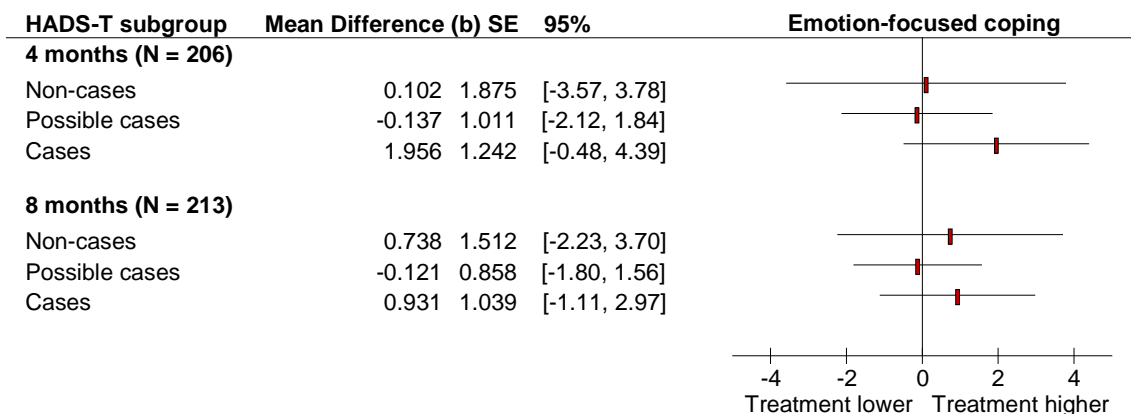|	Non-cases (0 – 7)				Possible cases (8 – 15)				Cases (16 – 42)			
Coping measure	*Intervention*		*TAU*		*Intervention*		*TAU*		*Intervention*		*TAU*	
Emotion-focused	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*
Baseline	43	21.07 (5.50)	12	23.25 (4.99)	58	22.53 (4.79)	41	24.20 (5.54)	71	23.36 (5.18)	34	22.54 (4.80)
4 months	37	21.03 (5.37)	12	22.17 (6.87)	50	23.22 (5.67)	34	24.23 (5.57)	56	25.10 (5.84)	26	22.23 (4.49)
8 months	32	21.52 (5.76)	11	22.45 (5.52)	44	21.97 (5.14)	33	23.91 (6.39)	50	22.48 (6.32)	23	22.60 (3.94)
Problem-focused												
Baseline	43	13.84 (4.43)	12	19.08 (3.63)	58	15.71 (4.67)	41	16.78 (3.95)	71	17.19 (4.14)	34	17.21 (4.34)
4 months	37	13.43 (4.72)	12	15.17 (5.32)	51	16.03 (4.71)	34	16.21 (4.45)	57	17.35 (3.86)	26	16.38 (5.12)
8 months	31	13.61 (5.00)	11	18.27 (4.36)	45	14.28 (4.23)	33	16.30 (4.60)	50	15.88 (4.28)	23	15.79 (3.52)
Dysfunctional												
Baseline	43	15.37 (3.54)	12	15.33 (3.77)	58	18.53 (4.60)	41	20.00 (5.31)	71	22.16 (5.18)	34	22.89 (6.71)
4 months	37	14.78 (2.64)	12	17.00 (5.72)	51	18.74 (4.87)	34	19.18 (5.37)	57	21.88 (4.94)	26	19.96 (5.31)
8 months	31	15.56 (3.80)	11	18.82 (5.89)	45	18.51 (4.71)	33	18.00 (3.72)	50	21.83 (4.83)	23	21.37 (5.79)

Subgroup analyses

Figure 7.8 illustrates subgroup treatment effects on coping strategies, using mixed models regression adjusted for baseline covariates (including demographic variables, carer burden and CR NPI). As these analyses were based on the ITT population (i.e. carers who completed at least one follow-up assessment for coping) and the 8-month analyses accounted for repeated measures, numbers of carers in each subgroup differ from those reported in Table 7.13.
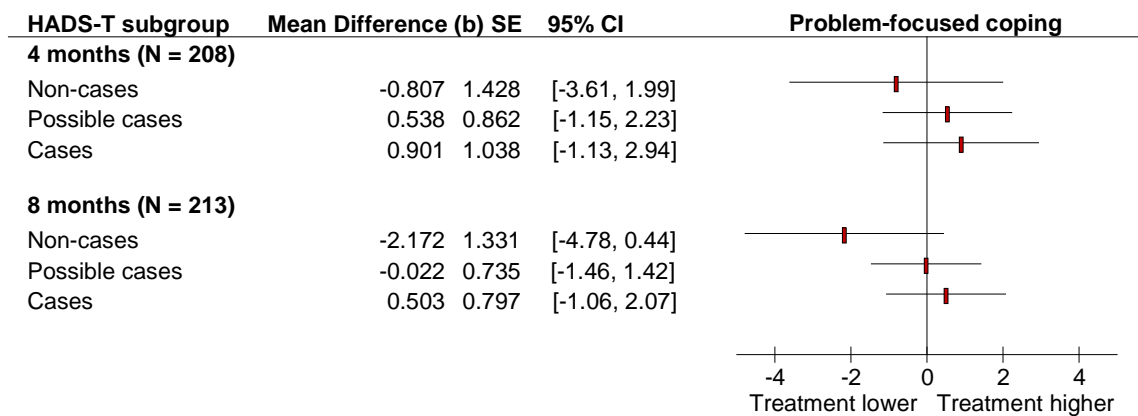
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For dysfunctional coping, there were clear differences in subgroup treatment effects, with non-cases and cases showing no overlap in their 95% CIs over 4 or 8 months (Figure 7.8). Visual inspection of the mean scores revealed that within TAU, non-cases reported increasing dysfunctional coping over time, while cases reported decreasing dysfunctional coping over time. Within the intervention group, both non-cases and cases reported no change in dysfunctional coping over time (Table 7.13). There were no clear subgroup differences for emotion-focused or problem-focused coping (Figure 7.8), although for cases in intervention there was a trend towards an increase in emotion-focused coping at 4 months.

Figure 7.8. Treatment effects on coping by HADS-T caseness subgroups (cut-offs: 8+ for possible cases, 16+ for cases). 8-month analyses included both 4- and 8-month outcomes to account for repeated measures. Dysfunctional coping in log scale except 'Converted MD', in unitary scale for ease of interpretation.
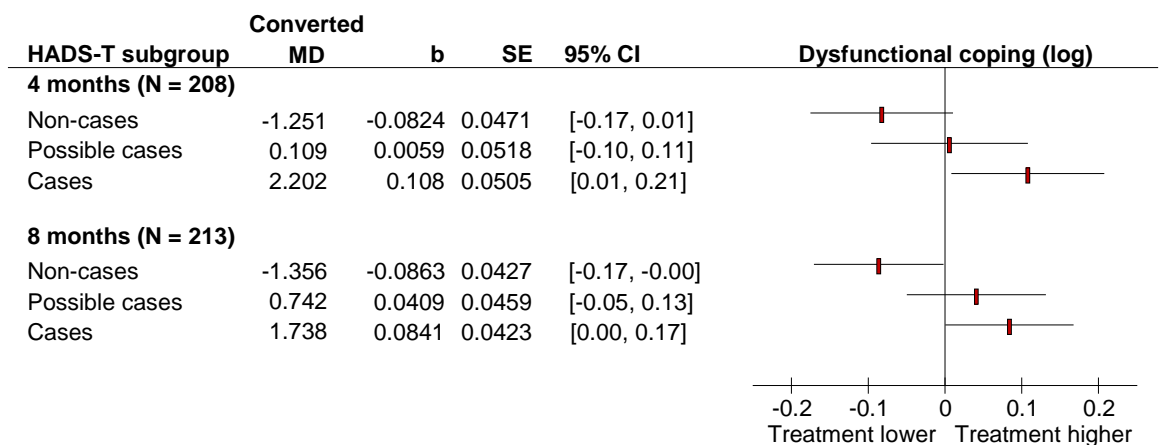
Emotion-focused coping

HADS-T subgroup	Mean Difference (b)	SE	95%
4 months (N = 206)			
Non-cases	0.102	1.875	[-3.57, 3.78]
Possible cases	-0.137	1.011	[-2.12, 1.84]
Cases	1.956	1.242	[-0.48, 4.39]
8 months (N = 213)			
Non-cases	0.738	1.512	[-2.23, 3.70]
Possible cases	-0.121	0.858	[-1.80, 1.56]
Cases	0.931	1.039	[-1.11, 2.97]

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Problem-focused coping

HADS-T subgroup	Mean Difference (b)	SE	95% CI	Problem-focused coping
4 months (N = 208)				
Non-cases	-0.807	1.428	[-3.61, 1.99]	
Possible cases	0.538	0.862	[-1.15, 2.23]	
Cases	0.901	1.038	[-1.13, 2.94]	
8 months (N = 213)				
Non-cases	-2.172	1.331	[-4.78, 0.44]	
Possible cases	-0.022	0.735	[-1.46, 1.42]	
Cases	0.503	0.797	[-1.06, 2.07]	

-4   -2   0   2   4
Treatment lower   Treatment higher

Dysfunctional coping

HADS-T subgroup	Converted MD	b	SE	95% CI	Dysfunctional coping (log)
4 months (N = 208)					
Non-cases	-1.251	-0.0824	0.0471	[-0.17, 0.01]	
Possible cases	0.109	0.0059	0.0518	[-0.10, 0.11]	
Cases	2.202	0.108	0.0505	[0.01, 0.21]	
8 months (N = 213)					
Non-cases	-1.356	-0.0863	0.0427	[-0.17, -0.00]	
Possible cases	0.742	0.0409	0.0459	[-0.05, 0.13]	
Cases	1.738	0.0841	0.0423	[0.00, 0.17]	

-0.2   -0.1   0   0.1   0.2
Treatment lower   Treatment higher

Sensitivity analyses using higher cut-offs

Figure 7.9 shows that subgroup effects for dysfunctional coping remained apparent
when using higher HADS-T cut-offs to categorise possible cases (HADS-T 12–19) and
cases (HADS-T 20+). Within TAU, non-cases reported significantly increased
dysfunctional coping, and cases reported significantly decreased dysfunctional coping
versus intervention, with no overlap in the 95% CIs of non-cases and cases. Cases in the
intervention group reported increased emotion-focused coping versus TAU, with CIs
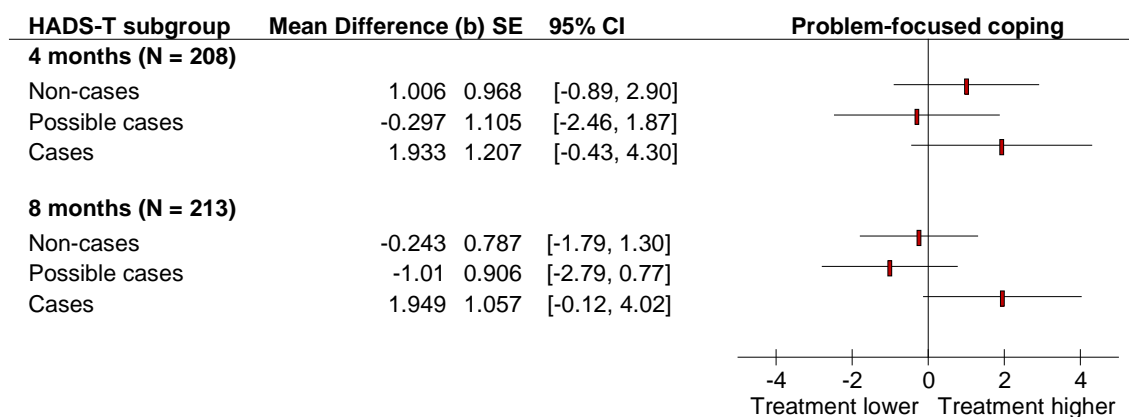
not overlapping with those of non-cases at 4 months (for whom there was no treatment effect on emotion-focused coping).

Figure 7.9. Treatment effects on coping using higher cut-offs for HADS-T subgroups (12+ for possible cases, 20+ for cases). The 8-month analyses included both 4- and 8-month outcomes to account for repeated measures.
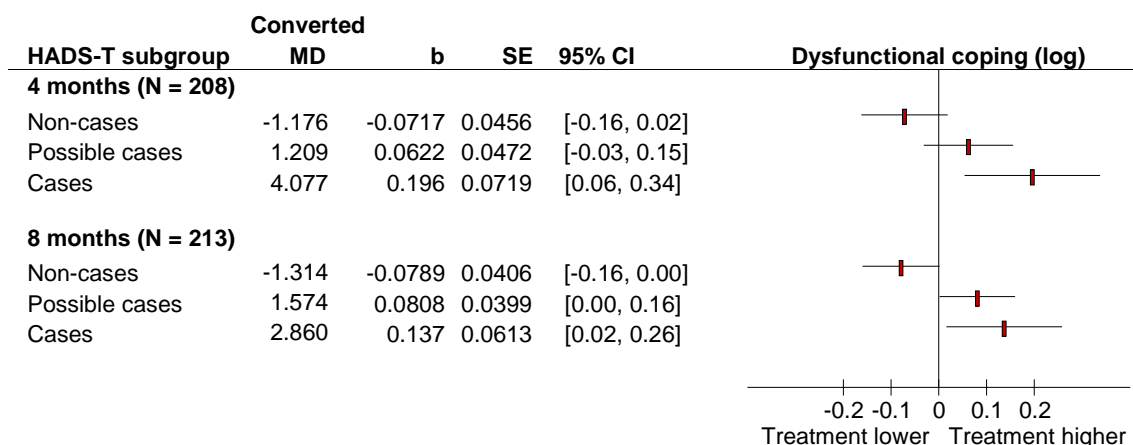
Emotion-focused coping

HADS-T subgroup	Mean Difference (b)	SE	95% CI	Emotion-focused coping
4 months (N = 206)				
Non-cases	-0.564	1.197	[-2.91, 1.78]	
Possible cases	0.158	1.322	[-2.43, 2.75]	
Cases	4.567	1.395	[1.83, 7.30]	
8 months (N = 213)				
Non-cases	-0.394	0.963	[-2.28, 1.49]	
Possible cases	-0.165	1.096	[-2.31, 1.98]	
Cases	2.963	1.268	[0.48, 5.45]	

-4 -2 0 2 4
Treatment lower   Treatment higher

Problem-focused coping

HADS-T subgroup	Mean Difference (b)	SE	95% CI	Problem-focused coping
4 months (N = 208)				
Non-cases	1.006	0.968	[-0.89, 2.90]	
Possible cases	-0.297	1.105	[-2.46, 1.87]	
Cases	1.933	1.207	[-0.43, 4.30]	
8 months (N = 213)				
Non-cases	-0.243	0.787	[-1.79, 1.30]	
Possible cases	-1.01	0.906	[-2.79, 0.77]	
Cases	1.949	1.057	[-0.12, 4.02]	

-4 -2 0 2 4
Treatment lower   Treatment higher

Dysfunctional coping

HADS-T subgroup	Converted MD	b	SE	95% CI	Dysfunctional coping (log)
4 months (N = 208)					
Non-cases	-1.176	-0.0717	0.0456	[-0.16, 0.02]	
Possible cases	1.209	0.0622	0.0472	[-0.03, 0.15]	
Cases	4.077	0.196	0.0719	[0.06, 0.34]	
8 months (N = 213)					
Non-cases	-1.314	-0.0789	0.0406	[-0.16, 0.00]	
Possible cases	1.574	0.0808	0.0399	[0.00, 0.16]	
Cases	2.860	0.137	0.0613	[0.02, 0.26]	

-0.2 -0.1 0   0.1 0.2
Treatment lower   Treatment higher

7.7.2 Summary

Baseline psychological morbidity moderated the effects of treatment on coping strategies. The most consistent subgroup differences were found for dysfunctional coping. This increased in the TAU group for carers with the fewest baseline symptoms (non-cases), and decreased in the TAU group carers with the most symptoms (cases), but showed no change for both non-cases and cases who received intervention. There were no overlaps in the 95% CIs for non-cases and cases, and these findings were replicated in sensitivity analysis using higher HADS-T cut-off values (12 / 20) to define subgroups, suggesting a robust effect.

For emotion-focused coping, clear subgroup differences were seen only in the sensitivity analysis: non-cases showed no treatment effect, and cases in the intervention group reported significantly increased emotion-focused coping versus TAU. The 95% CIs for non-cases and cases did not overlap. These subgroup differences were not seen in the main analysis using lower cut-offs (8 / 16), nor for problem-focused coping. This could partly reflect lack of statistical power, particularly among non-cases who comprised just over one-fifth of the entire sample (55/259, 21.2%).

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In summary, carers with the greatest psychological morbidity at baseline responded to treatment by maintaining use of dysfunctional strategies, and possibly by increasing use of emotion-focused strategies (for those scoring 20+ on HADS-T). Carers who were least distressed responded to treatment by not increasing dysfunctional strategies (which increased for carers not receiving treatment). The findings could not be attributed to the fact that carers reporting more distress at baseline were facing greater burden and generally attempting more coping, as the regression analyses were adjusted for these covariates. The results were generally consistent for the 4- and 8-month analyses, suggesting that moderated treatment effects on coping might persist, and might predict similar findings at 12 months follow-up.

7.8 Moderated mediation: Did baseline psychological morbidity moderate the extent to which coping mediated the effects of treatment?

Given that change in emotion-focused coping over 4 months independently predicted psychological morbidity at 8 months (Section 6.6), and that carers with the highest baseline morbidity appeared to respond to treatment using more emotion-focused coping (Section 7.7), I hypothesised that increase in emotion-focused coping over 4 months would mediate the effect of treatment in reducing psychological morbidity at 8 months more strongly among those with high morbidity than among those with low morbidity.

7.8.1 Results

Treatment effects on psychological morbidity

As expected there was a significant overall effect of treatment in reducing HADS-T at 8 months (b = -1.255, p = 0.005), which was not significantly moderated by baseline HADS-T (b = -0.087, p = 0.099), after adjusting for covariates (Figure 7.10). Thus I proceeded to test whether baseline morbidity moderated the mediating effects of coping strategies at 4 months on subsequent morbidity (Muller et al. 2005).

Figure 7.10. Overall effect of treatment on reducing psychological morbidity was not moderated by baseline morbidity.

Overall treatment effect
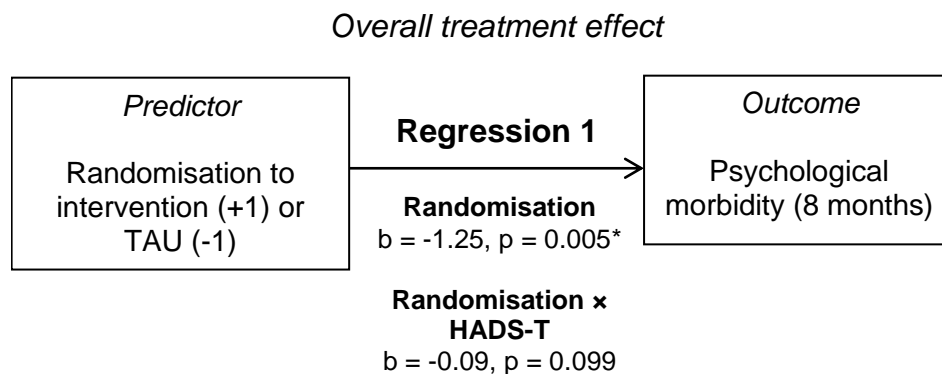
Emotion-focused coping

In Figure 7.11, the overall effect of treatment on increasing emotion-focused coping at 4 months was non-significant (b = 0.381, SE = 0.336, p = 0.259), however this relationship was strongly significantly moderated by baseline HADS-T (b = 0.150, SE = 0.047, p = 0.002). Increased coping at 4 months (mediator) significantly predicted reduced HADS-T at 8 months (outcome) (b = -0.351, SE = 0.084, p < 0.0005), and this relationship was not significantly moderated by baseline HADS-T (b = -0.010, SE =

0.009, p = 0.303). As Randomisation × Baseline HADS-T and coping were both significant predictors in the above relationships, moderated mediation was established.

The estimated effects of treatment and emotion-focused coping for subgroups of psychological morbidity caseness are given in Table 7.14. Numbers under "Randomisation → Emotion-focused coping (4 months)" represent the absolute effect of treatment on emotion-focused coping, at the mean baseline HADS-T score within each subgroup (see Table 7.14). For cases, randomisation to treatment led to 1.560 points higher emotion-focused coping at 4 months versus TAU, whereas for non-cases treatment resulted in 1.050 points lower emotion-focused coping versus TAU.

Numbers under "Emotion-focused coping (4 months)→ HADS-T (8 months)" represent the absolute effect of each point increase in emotion-focused coping on HADS-T, showing that for all subgroups increased emotion-focused coping predicted decreased subsequent HADS-T (Table 7.14). Total mediated effect is obtained by multiplying the effects in the two columns. Thus for cases there was a mediated effect of treatment (via increased emotion-focused coping) which reduced HADS-T at 8 months (by 0.631 points); for possible cases there was no mediation; for non-cases, the treatment effect appeared to increase psychological morbidity by a small amount (0.269 points) via lowered emotion-focused coping versus TAU (Table 7.14).

Note that these estimates do not take other covariates into consideration, nonetheless they illustrate the differences in magnitude and directionality of the mediated effect at different levels of the moderator (baseline psychological morbidity).

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Figure 7.11. Baseline psychological morbidity significantly moderated the effects of treatment, mediated via emotion-focused coping at 4 months, on psychological morbidity (HADS-T) at 8 months (N = 184).
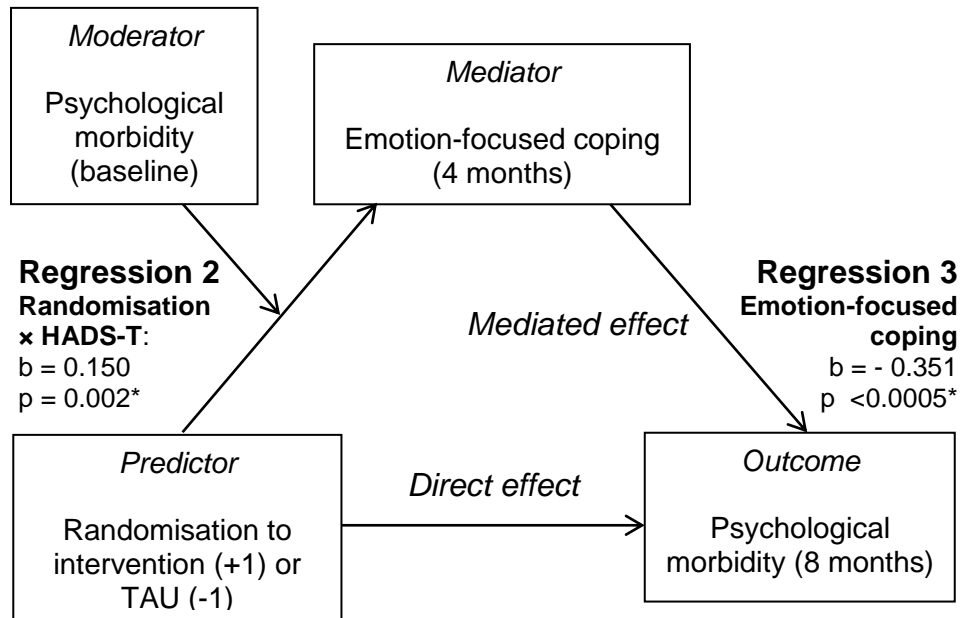
Table 7.14. Estimation of absolute treatment effects mediated via emotion-focused coping, for subgroups of baseline psychological morbidity caseness.

HADS-T subgroup	Randomisation → Emotion-focused coping (4 months)	Emotion-focused coping (4 months)→ HADS-T (8 months)	Total mediated effect
Non-cases	-1.050	-0.256	0.269
Possible cases	0.005	-0.356	-0.002
Cases	1.485	-0.425	-0.631

Replacing the outcome with HADS-D and HADS-A, increased emotion-focused coping at 4 months significantly predicted both reduced depressive symptoms (b = -0.151, SE = 0.050, p = 0.003) and reduced anxiety symptoms (b = -0.201, SE = 0.050, p < 0.0005). Therefore, emotion-focused coping mediated the effects of treatment on

reducing overall psychological morbidity through reducing both depression and anxiety, and the levels of mediation were stronger at higher baseline levels of morbidity.

Problem-focused coping

The Randomisation × Baseline HADS-T interaction approached significance in predicting problem-focused coping at 4 months (b = 0.092, SE = 0.047, p = 0.054), but problem-focused coping at 4 months did not significantly predict HADS-T at 8 months (b = -0.133, SE = 0.100, p = 0.188) (Figure 7.12). Therefore moderated mediation was not established, and I did not repeat the analysis with HADS-D and HADS-A as 8-month outcomes.

Figure 7.12. Problem-focused coping did not show moderated mediation of treatment effects on psychological morbidity (HADS-T) (N = 187).
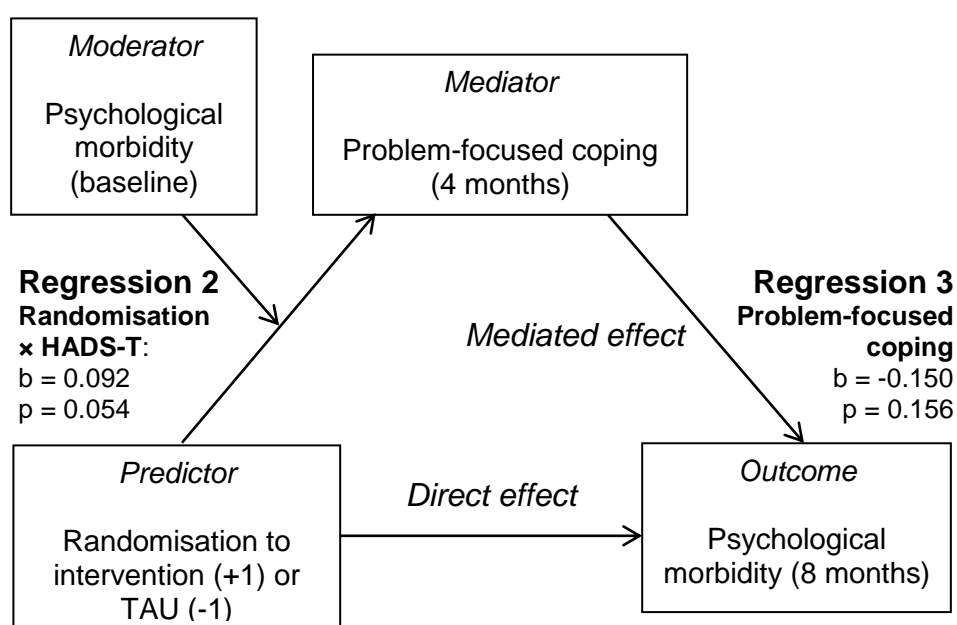
Dysfunctional coping

The overall effect of treatment on dysfunctional coping at 4 months was non-significant (b = 0.025, SE = 0.333, p = 0.940), however this relationship was significantly moderated by baseline HADS-T (b = 0.172, SE = 0.069, p = 0.013). Increased dysfunctional coping at 4 months (mediator) significantly predicted increased HADS-T at 8 months (outcome) (b = 0.256, SE = 0.114, p = 0.026). As both Randomisation × Baseline HADS-T and coping were significant predictors, moderated mediation was established.

Figure 7.13. Baseline psychological morbidity significantly moderated the effects of treatment, mediated via dysfunctional coping at 4 months, on psychological morbidity (HADS-T) at 8 months (N = 187).
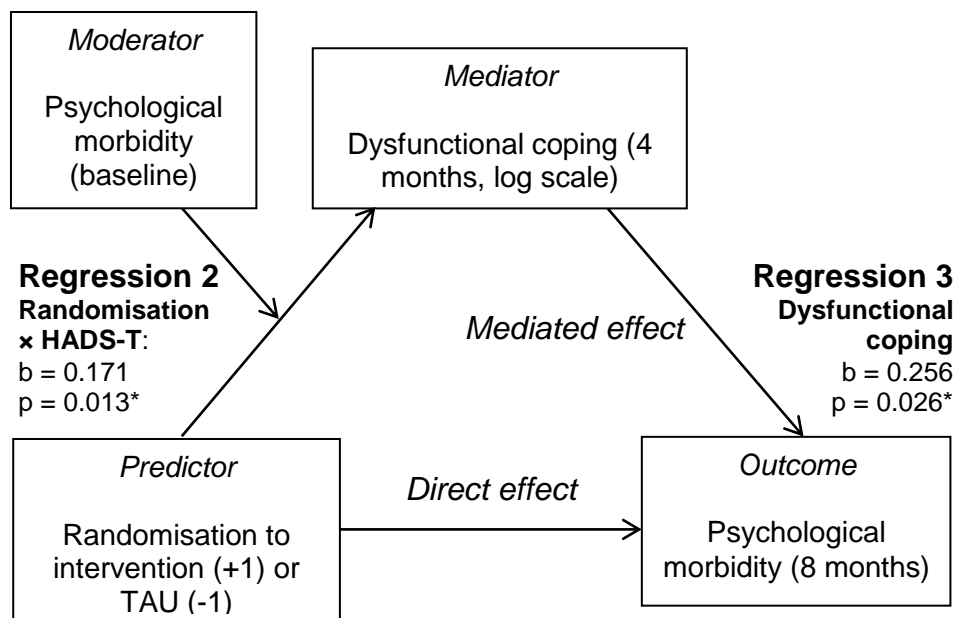
The estimated effects of treatment and dysfunctional coping for subgroups of psychological morbidity caseness are given in Table 7.15. For non-cases and possible cases, treatment resulted in lower psychological morbidity versus TAU (by 0.269 and 0.097 points respectively) via reduced dysfunctional coping. For cases, treatment resulted in higher psychological morbidity versus TAU (by 0.407 points) via increased

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dysfunctional coping. Each point increase in 4-month dysfunctional coping predicted 0.256 points increase on 8-month HADS-T across all subgroups, as there was no moderation of this relationship by baseline HADS-T (b = 0.008, SE = 0.012, p = 0.483).

Table 7.15. Estimation of absolute treatment effects on HADS-T mediated via dysfunctional coping.

HADS-T subgroup	Randomisation → Dysfunctional coping (4 months)	Dysfunctional coping (4 months) → HADS-T (8 months)	Total mediated effect
Non-cases	-1.616	0.180	-0.291
Possible cases	-0.406	0.240	-0.097
Cases	1.291	0.315	0.407

Replacing the outcome with HADS-A, increased dysfunctional coping at 4 months significantly predicted increased anxiety at 8 months (b = 0.172, SE = 0.062, p = 0.006). There was no significant association between dysfunctional coping at 4 months and HADS-D at 8 months (b = 0.084, SE = 0.066, p = 0.204). In summary, dysfunctional coping mediated treatment effects on anxiety but not depression, and the level of mediation was moderated by baseline psychological morbidity.

7.8.2 Summary

Increased emotion-focused coping at 4 months mediated the effects of treatment on decreasing psychological morbidity (whether depression, anxiety, or overall) at 8 months, only among carers with high initial levels of psychological morbidity. The level of mediation varied systematically with baseline morbidity. For cases (HADS-T 16+), the effect of treatment was more strongly mediated through increased emotion-focused coping (relative to TAU), but for non-cases (HADS-T 0–7) and possible cases (HADS-T 8–15) the mediating process was not through emotion-focused coping but via other

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mechanisms, possibly including reduced dysfunctional coping versus TAU. These findings also explain why my primary hypothesis, that emotion-focused coping mediated the effects of treatment on psychological morbidity overall, was not supported by the data.

8 Discussion

8.1 Key findings

The findings did not support my primary hypothesis that change in emotion-focused coping strategies mediated the overall effects of treatment on carer psychological morbidity. Randomisation status was not associated with significant change across the sample in any of the coping strategies between baseline and follow-up (at 4 or 8 months), thus criteria for mediation were not met. There was some evidence to suggest the treatment worked as hypothesised, via increasing emotion-focused coping, only for carers with high initial levels of morbidity.

In multivariate analyses controlling for baseline covariates and treatment status, increased emotion-focused coping over 4 months significantly predicted reduced psychological morbidity symptoms, as well as reduced likelihood of caseness for overall psychological morbidity, depression, and anxiety at 8 months. Furthermore, treatment effects via emotion-focused coping systematically differed for carers with varying levels of baseline morbidity. Clinically distressed carers (cases) scoring 16+ on baseline HADS-T and particularly those with baseline HADS-T 20+, appeared to respond to treatment by using more emotion-focused coping relative to TAU, and therefore improved. Counterintuitively they also maintained high levels of dysfunctional coping versus TAU (which showed a decrease). For non-cases (HADS-T < 8) and possible cases (HADS-T 8–15) however, treatment did not lead to increased emotion-focused coping versus TAU, and therefore the mediated effect was minimal, implying that they remained well through other mechanisms including maintaining low use of dysfunctional coping versus TAU (which showed an increase). Although treatment for non-cases appeared to result in small increase in distress mediated via a small decrease

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in emotion-focused coping versus TAU, this was unlikely to be clinically significant especially considering that overall positive effects for this subgroup were mediated via other mechanisms.

These subgroup effects might explain why there were no overall treatment effects on any coping strategy. The most robust subgroup effects were for dysfunctional coping, with non-overlapping 95% CIs for non-cases and cases in all analyses.

Dysfunctional coping in carers of people with dementia has generally been regarded as detrimental, and there is good observational evidence that it is associated with, and also appears to predict carer anxiety and depression (Cooper et al. 2008b;Li et al. 2012) (see Chapter 2). The current study suggests that for carers who are highly distressed, initial maintenance of high dysfunctional coping may be consequential to engaging with therapy, but its harmful effects appear to be counteracted by the simultaneous increase in emotion-focused coping strategies. It would also imply that high-distress carers who undergo intervention first improve in mood (via increased emotion-focused coping) before they successfully reduce dysfunctional coping, which should in turn help them further maintain mental wellbeing. This hypothesis is testable in long term follow-up of the START study. Coping is nonetheless a constantly changing process (Lazarus et al. 1984), and the same strategies, including "dysfunctional" ones, may be adaptive in some contexts and maladaptive in others.

The current findings show that a manualised psychological intervention aimed at promoting emotion-focused coping strategies was effective, potentially both as prevention and treatment for psychological morbidity in carers of people with dementia. Different carers found different ways to benefit from the intervention.

8.2 Comparison with other studies

The finding that increase in emotion-focused coping predicted decreased subsequent morbidity regardless of treatment are consistent with those of observational studies (Cooper et al. 2008b;Li et al. 2012) (see Chapter 2), and also potentially explains the counterintuitive RCT findings that standardised group coping skills interventions appear effective in reducing depression while increasing both positive coping and dysfunctional coping versus control (Li et al 2013; Chapter 3). It seems likely that different carers may respond differently to the same intervention. Carers with relatively little distress at the outset appeared to remain well following therapy because it prevented increases in dysfunctional coping. For carers with the greatest distress (particularly cases with HADS 20+, in the sensitivity analysis for subgroup effects), the intervention appeared to have encouraged them to attempt more emotion-focused coping, but also to maintain their high use of dysfunctional strategies, consistent with previous RCTs reported in Chapter 3 (Li et al., 2013). The failures that result from proactive coping attempts might initially perpetuate self-blame, also a dysfunctional coping behaviour (Curry et al. 1987). This should have increased psychological morbidity, yet such carers improved (see Section 6.5.2: HADS caseness), possibly because the beneficial effects of their increased emotion-focused coping outweighed harmful effects of their maintained dysfunctional coping.

A further effect of therapy could be that it made distressed carers more aware of their dysfunctional coping behaviour, such that they reported this more accurately; denial could arguably be expressed as under-reporting of dysfunctional coping behaviours. Increased awareness is an important prerequisite for behaviour change (Miller et al. 1992).

Denial or disengagement coping strategies could have been adaptive in relieving or protecting against stress in the short term (Lazarus, 1983; Au et al., 2010), even if not over 8 months. For cancer patients, certain kinds of denial or distraction do appear to be associated with lower initial distress, perhaps by allowing time to process the distressing situation at a manageable rate (Rabinowitz et al. 2006;Vos et al. 2007). The START intervention actively encouraged carers to seek pleasant activities (see Section 6.3.1), which would have been consistent with a reported increase in some of the those listed in the Brief COPE Behavioural Disengagement items ("turning to work or other activities to take my mind off things", and "doing something to think about it less, such as going to the cinema, watching TV, reading, daydreaming, sleeping or shopping").

The strong subgroup effects might also explain why intervention studies on carers of people with dementia on the whole have failed to report consistent significant treatment effects on coping (Li et al 2013; Chapter 3), despite robust relationships between coping and psychological morbidity in observational studies (Li et al. 2012; Chapter 2). All coping intervention RCTs have to date been conducted with diverse, non-clinical carer samples (Li et al 2013; Chapter 3). Therefore I would expect a study of a similar intervention, targeted only at carers who are clinically distressed (e.g. HADS-T exceeding 20), to show statistically significant effects on coping, and also clinically significant effects on reducing psychological morbidity.

The Cochrane review on cognitive reframing interventions for carers concluded that such interventions seem to be effective in reducing anxiety or depression without changing coping, but appeared to do so via changing attributions and appraisals (Vernooij-Dassen et al. 2011). The START intervention included components that would be defined as cognitive reframing according to the Cochrane review. According

to the Transactional Model of Stress and Coping, appraisal is both an important precursor and an outcome of coping (Lazarus et al. 1984). Thus emotion-focused coping (trying to see the matter in a more positive light, looking for a something good in what is happening, learning to accept and live with it) might be seen as conscious, planful manifestations of positive appraisal. Neither the current study nor any of the studies included in the Cochrane review measured psychological attributions or appraisals; these would be useful to measure in future trials of cognitive-behavioural and coping interventions.

The current study provides stronger evidence that the intervention was effective in reducing overall psychological morbidity and depression than anxiety, as anxiety caseness showed a trend for reduction in intervention versus TAU (despite the reduction in anxiety symptoms being statistically significant). The reason for this is unclear, except it should be noted that the evidence base for interventions for carer anxiety has always been smaller and weaker than that for carer depression, and that the only previous RCT reporting a significant effect in reducing anxiety symptoms had specifically targeted anxiety (Cooper et al., 2007). The current intervention was not specifically targeted at anxiety, and was considered clinically useful if it successfully reduced overall psychological morbidity either through reduced depression or anxiety.

8.3 Strengths and Limitations

8.3.1 Strengths

A priori hypotheses and analytic plan

My hypotheses for the study were *a priori* based on my findings from two systematic reviews. In the analytic plan, I recognised the possibility of hidden

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confounding in applying conventional mediation models in an RCT context, and devised different analyses taking this into consideration. I also considered the mechanisms of missing data *a priori*, and used various techniques to account for missing data.

Study design and sample size

The current study was nested in the START study, a pragmatic RCT with broad inclusion criteria. It included carers from varied geographic and sociodemographic backgrounds, drawn from NHS clinical practice, and there were no substantial demographic differences between carers who did and did not consent to the study, ensuring that the results are directly applicable to the general UK population.

The START study had an *a priori* sample size calculation powered on the primary outcome, HADS-T psychological morbidity, and which I also calculated to be adequate for my proposed analyses. The overall follow-up rate of 88% at the primary endpoint of 8 months was good, similar to that reported in a recent RCT of befriending for carers of people with dementia (Charlesworth et al. 2008). For the efficacy and subgroup analyses I used mixed model regression, which not only took into account possible therapist effects, but also made full use of the available data from all participants who completed at least one follow-up assessment. For the mediation analyses, I also specified *a priori* strategies for identifying the predictors and mechanism of missing data. Although I could have used multiple imputation methods to replace participants excluded from the efficacy analyses, this would have required further assumptions about the missing data, and such imputed data would not have been appropriate for the proposed mediation analyses using instrumental variable regression (White et al. 2011).

Weighted complete-case analysis was a valid strategy given that I found the data to be missing at random (White et al. 2011).

Assessment and blinding

We used only standardised instruments, previously shown to be valid and reliable in carers of people with dementia. In the case of HADS, it has been validated against gold-standard DSM and ICD diagnoses of depression and anxiety (Bjelland et al. 2002). Most of the measures were self-complete (including HADS and Brief COPE), and independent researchers conducted assessments and delivered therapy for any given carer, minimising the likelihood of rater bias. Furthermore, all raters received standardised training on the study assessments, and we made best efforts to ensure that allocation was concealed and that raters were blinded to carers' randomisation status. Blinding was fairly successful, as the unblinding rate was only 12% by 8-month follow-up (see Section 7.3.3).

Standardised intervention

The START intervention was standardised and manualised, and therapists received standardised training and clinical supervision to ensure consistency in their delivery of the intervention. The high fidelity ratings and the negligible intra-cluster correlations within therapists suggested that the intervention was delivered consistently.

8.3.2 Limitations

Nesting of PhD study within a predesigned clinical trial

The current PhD study was embedded within the HTA-START trial, which had already been designed and commenced at the time I formulated my hypothesis, to

address a related but different hypothesis (that the psychological intervention would be effective in reducing carer depression and anxiety symptoms, irrespective of the mechanism). Therefore some of the strengths and limitations of my study reflect aspects of the START study design over which I had no control, and the design of my PhD study was focused on using relevant statistical analyses to establish mediation within an RCT.

My specific hypothesis addressed whether coping mediated the effects of a specific psychological intervention (the START programme). Testing this hypothesis implies drawing inferences to answer more fundamental hypothesis that in general, "changing coping is an effective mechanism for reducing psychological morbidity" (a hypothesis which follows from the Transactional Model of Stress; Lazarus & Folkman 1984). In a 'perfect' experiment, this would be tested by manipulating participants' coping strategies. Given that this is unlikely to be possible in practice, the next best alternative would be to provide a well-controlled intervention that could, as far as possible, influence only coping and not other potential parallel pathways to psychological morbidity. However I would also measure and take into account variables along the same stressor-appraisal-coping-outcome pathway, for example dysfunctional thoughts (appraisal), self-efficacy and coping resources such as availability of social support (which might influence whether changes in coping strategies actually had an impact). Some of these possible variables are further discussed in Section 8.4.

While the START intervention was theoretically informed by a psychological model of coping, it also included other components aimed at reducing depression and anxiety without necessarily involving coping, thus any mediation effects might have been diluted. It is possible that my findings might differ had I designed a study from scratch

centred around coping outcomes; nonetheless the current findings add an arguably important and clinically relevant dimension to the outcome of the START clinical trial.

Blinding and non-specific effects of therapy

We inevitably could not blind family carers to randomisation status, and we did not include a waitlist control group, or an attentional control group (i.e. who would receive therapist contact but without the proposed "active ingredients" of the psychological intervention). Thus it was not strictly possible to separate out placebo effects and non-specific effects of therapist contact from the specific effects of intervention. There could also have been demand effects, for example carers assigned to active intervention reporting more positive outcomes to appease the researchers, although independent raters and therapists should have minimised this. Nonetheless, given that other recent RCTs of psychosocial interventions have been ineffective in reducing psychological morbidity or changing coping (Charlesworth et al. 2008;Waldorff et al. 2012), the current findings are unlikely to be explained by therapist attention alone.

Statistical power

The START study was powered to detect significant treatment effects on psychological morbidity, and not on coping outcomes. It is possible that true treatment effects on coping not detected in the current study (a Type II error) might be detectable in a larger sample, however this is unlikely because the p values for changes in emotion-focused and dysfunctional coping did not approach statistical significance, and subgroup treatment effects were found. Furthermore, given the sample was powered to show a significant treatment effect on HADS-T, and succeeded in doing so, it would

have been unethical to continue randomising carers for the sake of increasing statistical power to answer questions about the treatment mechanism.

Sensitivity of the Brief COPE

A lack of statistical power could have been compounded if the Brief COPE was not sensitive to all relevant ways of coping (especially those encouraged by the intervention), or for instance if some of the intended effects of therapy such as increased pleasant activities were reported as dysfunctional coping strategies (see Section 8.2: Comparison with other studies). Reflecting on my experiences in administering the questionnaire, some common coping strategies, such as exercising or smoking were not readily captured by the questionnaire. From a systemic perspective, the Brief COPE had relatively little to say on more collaborative modes of coping which might be particularly salient in the context of dementia caring (as family members often shared caring responsibilities) (Berg et al. 1998), and which the intervention would have encouraged. Introducing additional coping questions or measures could be a way of building a more complete picture of coping, however the potential gains of this would need to be balanced against the additional burden on study participants; the Brief COPE was a fairly pragmatic choice of coping measure given it was readily validated in the carer population.

The derivation of Brief COPE subscales by factor analysis and their validation in the dementia carer population assumes that all items in a subscale are equally weighted, and have a unidirectional effect (i.e. a higher score on a dysfunctional coping correlating with higher distress). In practice, certain coping behaviours may have greater impact on psychological distress than others even within the same subscale; and some behaviours may be harmful if done in excess but beneficial in moderation (e.g. disengagement

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strategies). These and other limitations (such as aspects of timing and sequencing) are likely to be inherent to coping measures based on summary scores such as the Brief COPE (Coyne et al. 2000). Qualitative methods could complement coping measures and help to overcome some of their limitations. For example, qualitative interviews could potentially elicit richer descriptions of coping strategies used and the contexts in which they were used.

Long-term or non-coping outcome measures

The conclusions of the current study are limited by the length of follow-up, which was 8 months from baseline, and may not generalise to longer term outcomes or relationships between them. If 'good' coping interventions foster personal growth and greater adaptiveness in managing stressful encounters in the long term (Skinner et al. 1998), then analytic methods that better capture the dynamics of change in caring encounters, as opposed to snapshots, over longer follow-up periods should be more informative as to the intervention's ultimate success.

Although we included a variety of outcome measures to assess carer coping strategies and burden, we did not include measures of other possible mechanisms of the START intervention (including ones that may be related to coping), such as: self-efficacy, attachment and relationship, grief, illness attribution and perceptions, and social support (see Section 8.4: Other psychosocial mechanisms of treatment). We did not measure other factors that could have influenced psychological morbidity or coping regardless of treatment status, such as prior psychiatric history or recent life events (Cooper et al. 2010). As dementia is a progressive disease with changing demands on the family carer through heterogeneous illness trajectories, it is important that coping and intervention research takes these factors into consideration.

Non-English speaking carers

In practice, we found it difficult to engage non-English speaking carers in the intervention even using interpreters. However as there were only four such carers in the study, three of whom randomised to intervention, they would have had little impact on overall study findings; if anything, their lack of engagement would have strengthened the current findings of intervention efficacy. There is some evidence from North America that Coping With Caregiving-based interventions tailored for specific ethnic groups can be efficacious (Napoles et al. 2010).

Subgroup analyses and multiple testing

The subgroup analyses were post-hoc, and multiple testing would have increased the likelihood of chance significant findings. Subgroup effects where subgroup membership is defined exclusively by cut-offs in symptom severity (as per HADS-T caseness) are inevitably subject to variation depending on the cut-offs chosen. However, they were informed by *a priori* demonstration of significant interactions of treatment allocation with baseline psychological morbidity. I tried to minimise chance findings by pre-defining subgroups using two alternative and similarly valid sets of cut-offs based on existing validation studies (Bjelland et al. 2002), which not only aided interpretation of the findings but also added robustness to the findings, as results were largely consistent across multiple tests.

Mediation analyses

The three coping strategies (emotion-focused, problem-focused and dysfunctional) were not considered simultaneously in the mediation analyses, mainly on practical

considerations as this would have reduced statistical power and required additional assumptions that might not have been justified (see Section 6.5.4: Establishing statistical mediation). Although "coping style" conceptually relates to relative amounts of each coping strategy, there was no strong reason to believe this would more clinically relevant to psychological morbidity outcomes than individual coping strategies (Li et al., 2012). Nonetheless some studies have successfully explored multiple mediator models of burden, coping and psychological morbidity using alternative techniques such as structural equation modelling (Cooper et al. 2008b).

On a more fundamental level, a single direction of causality from the predictor variable (receiving randomised treatment) through the mediator (coping strategies) to the outcome variable (psychological morbidity) was assumed. However it is also likely that changes in psychological morbidity also influence coping; for example, individuals who become less depressed may consequently engage in less self-blame and denial, and seek more social contact. Indeed Lazarus and Folkman (1984) explicitly proposed a bidirectional relationship between stress and coping in the Transactional Model. I accounted for this to some extent by hypothesising that changes in coping over 4 months mediated effects of treatment on psychological morbidity over 8 months.

Appropriateness of the instrumental variable regression methods

Regression methods that aim to account for hidden bias have previously been used to explore potential mediating mechanisms of psychological therapies for depression and psychosis, for example adherence to study and non-study therapy, and therapeutic alliance (Emsley et al. 2010). Such models assume that there exists an instrumental variable that is randomly allocated, and strongly associated with the putative mediator. This assumption was violated in the current study as randomisation was not strongly

associated with coping strategies, and this was reflected in the poor fit for the various instrumental variable regression models. Nonetheless their findings were consistent with those of the ordinary regression models.

8.4 Other psychosocial mechanisms of treatment

Increased emotion-focused coping did not explain how the least distressed carers benefited from the current intervention, suggesting that the intervention also worked through other mechanisms. A range of mechanisms could have operated in isolation from coping, but they could also have been subcomponents within the stress-appraisal coping framework, operating as further moderating or mediating factors for coping (and these factors could have differed between subgroups). It is unlikely that a single factor could fully explain complex psychological behaviours (Judd et al. 1983), and for dementia carers there are likely to be multiple pathways between stressor and psychological morbidity (Mausbach et al. 2012), some of which are outlined below and which can be empirically tested in future trials of carer interventions.

Quality of the relationship between carer and CR

Dementia is typically associated with a decline in communication, shared activities, and often intimacy (for reviews, see (Ablitt et al. 2009;Quinn et al. 2009). A consistent body of evidence suggests that worse premorbid or current relationship quality are associated with higher levels of carer strain and depression (Ablitt et al. 2009;Ballard et al. 1995;Mahoney et al. 2005a;Quinn et al. 2009;Rankin et al. 2001). Carer attachment style can predetermine the relationship quality with the CR; and carers with less secure or more avoidant attachment styles tend to report higher anxiety, which is partially mediated by their greater use of dysfunctional coping strategies (Cooper et al. 2008c).

There is also some evidence that a poor relationship exacerbates loss of function in the CR (Burgener et al. 2002), which might further reduce relationship quality (Morris et al. 1988;Spruytte et al. 2002). In relation to my hypothesis, relationship quality and attachment would at the very least influence the choice of coping strategies used. Although attachment styles cannot be changed (Bretherton 1992), a successful intervention might improve current relationship quality through increasing acceptance (emotion-focused coping) and decreasing dysfunctional coping, which would in turn further improve the relationship and further impact on coping strategies.

In the START Study we did not directly measure the quality of the relationship, but the intervention could have improved this in various ways such as: encouraging positive reappraisal of the relationship through accepting that problem behaviours are caused by the illness rather than intentional (see also Attribution below); improving communication and reducing conflict; and encouraging shared pleasant activities. The latter could have been particularly powerful in introducing "uplifts" in the caring experience which might otherwise dominated by stressors (Kinney et al. 1989)

Increased social support

Carers of people with dementia often experience feelings of social isolation, partly because care demands reduce opportunities for leisure, social activities, and employment (Brodaty et al. 2009). The positive relationship between social support and health is well established in the general population (Cohen 2004), and this is true for dementia carers in terms of physical health, and to some extent mental health (Brodaty et al. 2009;Schulz et al. 1995). One RCT found an intervention successful at increasing social support for carers of people with dementia, and more importantly this mediated a reduction in depressive symptoms (Roth et al. 2005). Within the Transactional Model

(Lazarus et al. 1984), social support could have multiple points of impact in my hypothesised coping pathway, both as a coping resource and also in modifying appraisal. That is, an intervention successful in encouraging social support seeking would lead to an increase in emotion-focused coping (i.e. seeking emotional support and empathy from others), leading to increased actual social support. Those with more social support might in turn appraise the stressor as less demanding and feel more able to cope. All of these consequences could contribute to improved psychological outcomes.

In the current study, although the Brief COPE measured support-seeking behaviour, we did not fully measure the extent to which carers received or perceived informal social support. Seeking social support was a core theme throughout the START intervention, from direct encouragement to engage with carer support groups or other pleasant social activities; seeking support from family and friends; involving them in planning for the future; or improving carers' ability to ask for support by teaching assertive communication skills.

Processing of grief

Grief, discussed in detail in Section 1.2.5, is increasingly recognised as a central part of family carers' experience (Chan et al. 2012;Noyes et al. 2010), and is closely related to aforementioned losses in communication and relationship (Ablitt et al. 2009;Quinn et al. 2009). There is significant overlap between anticipatory grief (feelings of loss before the death of a loved one actually occurs) and symptoms of depression in carers of people with dementia (Ott et al. 2007). Ambiguous loss, an unstable pattern of loss fluctuating with the course of dementia, makes it difficult for carers to recognise and process grief (Blieszner et al. 2007;Boss 1990;Noyes et al. 2010). Qualitative interviews with 44 carers with high levels of grief suggested that this group tended to use emotion-

focused coping strategies of spiritual faith and social support, although carers with low

and moderate grief appeared to use similar strategies (Sanders et al. 2008). Within the

framework of the Appraisal Theory of Coping (Lazarus 1994), grief would probably

operate at the level of fundamental beliefs and goals, and thus strongly influence the

stress appraisal process. An intervention successful in addressing the consequences of

grief might influence appraisal by enabling the carer to recognise their loss, which

might 'legitimise' further use of emotion-focused coping, particularly holding on to the

social and spiritual support that the carer might already likely be using.

The START intervention did not specifically address grief, though it have might

helped carers cope better in recognising and coming to terms with (rather than deny) the

diagnosis and the resulting loss, through sessions providing education about dementia

and its symptoms, and planning for the future; and encouraging carers to seek emotional

support from friends and family.

Self-efficacy

Self-efficacy is an individual's perception of his or her ability to achieve a goal

(Bandura 1997). In the context of the Transactional Model of Stress and Coping

(Lazarus et al. 1984), it could be conceptualised as the carer's appraisal of whether his

or her coping attempts will be effective (Gottlieb et al. 2004). Thus increased emotion-

focused coping efforts might not necessarily achieve positive outcomes if the individual

did not believe they would do so. A growing literature suggests that higher self-efficacy

is associated with reduced carer depression, either directly or by acting as a buffer to

moderate the otherwise harmful effects of carer burden (Gilliam et al. 2006;Rabinowitz

et al. 2009;Romero-Moreno et al. 2012). One RCT of female carers, based on the

Coping With Caregiving manual, found that increased self-efficacy for controlling

dysfunctional thoughts explained reduced depressive symptoms (Coon et al. 2003). In the current study, the Brief COPE did not capture carers' perceived effectiveness of specific coping strategies. Carers' positive appraisals of their coping strategies could be self-fulfilling, and render coping more effective in reducing psychological distress, even if actual coping strategies did not change.

Self-efficacy could also directly influence how carers appraise the stressful situation, including their own distress. If treatment succeeded in increasing self-efficacy, this could lead to the situation being appraised as less threatening and more manageable. It could also enable carers to interpret their physiological symptoms (such as sweating and shallow breathing) as normal under stress, rather than as signs of failure (Bandura 1997). Both eventualities would decrease distress, and possibly decrease coping attempts (balancing out any increases in coping as a direct result of treatment).

Fostering self-efficacy is explicit throughout the START intervention, through emphasising that the carer can and must lead change; specifically, through changing unhelpful thoughts, assertiveness skills training, and the use of behaviour and thought records (Tee et al. 2011). The relaxation exercises might have helped carers recognise and feel more in control of symptoms of stress.

Attribution

Individuals make attributions as to whether events are good or bad, and why they happened (Heider 1958;Weiner 1985). Carers of people with Alzheimer's disease typically may not attribute symptoms to the illness, despite being aware of the diagnosis, and often believe that behaviours are within the CR's control (Hinton et al. 2009;Paton et al. 2004). Carers may resent behaviours they perceive as wilful or manipulative

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(Martin-Cook et al. 2003). One study suggested that carers who lay less blame on the CR and express less criticism tend to show less burden, more efficient coping, and lower distress (Bledin et al. 1990), consistent with the evidence base on carers for people with psychosis or diabetes (Barrowclough et al. 2003;Wearden et al. 2006). In the context of my hypothesis, attribution would influence appraisal and thus determine the selection of coping strategies. An intervention that successfully improved the accuracy of attributions might thus lead to more emotion-focused coping strategies (and probably also fewer dysfunctional ones) being used, leading to improved psychological outcomes.

The START intervention aimed to foster more objective attributions, from reinforcing important messages such as that CR 'problem behaviours' result from dementia and are not intentional, to specific exercises on causes of behaviour, and challenging unhelpful thoughts. Improved behavioural management and communication skills could also have resulted in carers becoming more aware of CR needs, and this could potentially reduce problem behaviours.

Illness perception

The Common Sense Model of illness perception (Leventhal 1984) suggests that patients and carers use their prior knowledge and experience to form "common-sense hypotheses" about an illness: its identity, cause, timeline (illness duration and trajectory), consequences, and curability/controllability. This could influence their coping strategies. The relatively sparse research on dementia carers' illness perception finds that carers tend to rate CR functioning as poorer than CRs would rate it themselves (Onor et al. 2006), whereas people with early dementia tend not to see themselves as ill (Clare et al. 2006). Some carers or other close relatives have

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expectations that the condition will improve by itself, or that a cure will be available in the near future (Paton et al. 2004;Roberts et al. 2000). It is not known how carer illness perception relates to carer outcomes in dementia. It is possible there may be some parallels with the evidence bases for psychosis (Kuipers et al. 2010) and physical illnesses (Hagger et al. 2003), which suggest carer illness perceptions to be stronger predictors of carer outcomes than CR illness severity. In psychosis, carers who perceive the illness as outside of their control and persistent tend to experience more depression (Onwumere et al. 2009), especially if their perception disagrees with that of the CR (Kuipers et al. 2007). For spousal carers of myocardial infarction patients, an intervention aimed at promoting more positive illness representations has reduced carer anxiety (Broadbent et al. 2009). Within the context of my hypothesis, more positive illness representations resulting from successful intervention would probably influence coping and psychological outcomes in a similar way to improved attribution.

The START intervention contained various psychoeducational components, including introduction to dementia and behaviours, behavioural management techniques, changing unhelpful thoughts, decision-making (CHOICE leaflets) and planning for the future. These might have reduced distress by positively shaping different facets of the carer illness perception.

Self-monitoring and collaborative empiricism

Collaborative empiricism in psychological therapy refers to the therapist and client working together to gather objective data that are relevant to the therapeutic goals (Tee et al. 2011), and is thought to be a key ingredient of effective cognitive behavioural interventions (Cohen et al. 2012). Self-monitoring, the client's systematic observing and recording of thoughts, emotions and problem behaviours, is one way of achieving this

(Cohen et al. 2012), as it fosters curiosity in challenging assumptions, provides objective evidence to refute distorted cognitions, and puts the client in control of monitoring change. Within the context of my hypothesis, an intervention successful in encouraging self-monitoring would provide better information from which the carer could appraise the objective threat level of the stressor as well as the effectiveness of his or her coping strategies, and make refinements to coping accordingly, with consequent impacts on psychological outcomes. Self-monitoring was a core component throughout all sessions of the START intervention, through the use of behaviour, thought and communication records.

Behavioural activation

Behavioural activation is a treatment that involves planning, scheduling and reinforcement of pleasant activities, and its positive effects on mood and wellbeing for clinical depression and in non-clinical populations are well established (Mazzucchelli et al. 2010). Carers of people with dementia tend to partake in few hobbies or pleasant activities due to caring demands (Brodaty et al. 2009), and this explains a significant proportion of their depressive symptoms (Mausbach et al. 2008;Thompson et al. 2003), therefore carers may particularly benefit from behavioural activation. Various intervention studies with positive effects on reducing depression have included behavioural activation components (Selwood et al. 2007). In the START Study, performing pleasant activities was not well captured in the Brief COPE questionnaire (see Section 8.3.2), although if some of the pleasant activities involved meeting with friends and family this could be captured as emotion-focused coping. Nonetheless this mechanism of change may have been missed in the measurement of coping. The START intervention devoted one session to planning pleasant activities; this was

followed up in the final session and was often emphasised as one of the plans for the future.

Specific effects of relaxation

Relaxation techniques are an accepted treatment for anxiety symptoms (Manzoni et al. 2008), and to a lesser extent for depressive symptoms (Jorm et al. 2008). Some of the effective trials of interventions for anxiety in carers of people with dementia also include relaxation components (Cooper et al. 2007b). The START intervention provided carers with a range of relaxation exercises. The Brief COPE asked how often carers "[prayed or meditated]", but this would not have detected whether those in the treatment group were using relaxation exercises.

8.5 Clinical implications

The START intervention demonstrated clinically important effects in reducing psychological morbidity, in particular depressive symptoms and caseness, in carers of people with dementia who were not specifically selected as a clinical sample. The intervention appeared useful both in reducing symptoms to sub-clinical levels, and in preventing new cases (see Section 6.5.1: Efficacy analyses), highlighting its potential both as a preventative and treatment strategy. Furthermore, carers appeared to benefit in different ways from the standardised therapy. The least distressed learned to maintain low use of unhelpful coping, while the most distressed appeared to respond by using more of helpful strategies while maintaining high use of unhelpful ones. The intervention was acceptable to most carers, as demonstrated by their high rate of adherence to sessions, despite the demands of being a carer. In summary, the findings

lend strong support to START as an early intervention for all family carers of people with dementia in the community.

Psychological morbidity is common in carers of people with dementia (Livingston et al. 2007), tends to worsen over time without intervention even among those not initially considered clinical cases, and is associated with poorer carer and CR outcomes including abusive behaviour (Cooper et al. 2008b;Cooper et al. 2010). In the absence of any current proven psychological interventions specifically recommended for this population in the NHS (National Institute for Health and Clinical Excellence et al. 2011), the demonstrated short-term effectiveness and cost-effectiveness of the START intervention provide strong rationale for its routine implementation in clinical practice (Livingston et al., submitted). This is now beginning to happen in the Camden & Islington Foundation Trust, where I have been assisting the trial Clinical Psychologist in training five graduate mental health workers to roll out the intervention as part of the low-intensity IAPT (Increasing Access to Psychological Therapies) service.

8.6   Implications for further research

8.6.1   Long-term follow-up of the START study

The current study showed no overall treatment effect on coping style, but it is not known whether this will hold true in the longer term. Also, as there were consistent subgroup effects of treatment on coping at 4 and 8 months (Section 7.7.1), it is possible that these trends could continue into future follow-up. The START study is ongoing with carers being followed up for 24 months post-baseline. The longest follow-up for coping outcomes in any published RCT to date is 6-months post-intervention (Gendron et al. 1996;Roberts et al. 1999) (Chapter 3), thus the START Study will become the

only study to have investigated the long-term effects of a time-limited intervention on coping strategies.

It is possible that treatment has less of an effect over time as carers forget what they have learnt, and no longer maintain the coping skills. Alternatively, it is possible that previously undetectable treatment effects on coping become detectable at 24 months, if treatment has a lagged effect, for example particular coping strategies requiring months of practice to become familiar and habitual. It is also possible that carers consolidate and adopt different coping strategies from the intervention as the CR's dementia progresses. Preliminary qualitative feedback from carers in the treatment group at the 24-month follow-up suggests that some carers, even if they did not find the sessions useful at the time, found it helpful to refer to the treatment manual at a later stage as the CR's condition worsened. It would be clinically useful to measuring subsequent use of the manual and show whether this were related to coping and psychological morbidity over the course of 24 months.

Longer follow up should also allow further disentangling of the casual relationships between psychological morbidity and coping. It is likely that psychological symptoms also influences coping, and long-term follow-up could allow the reverse of my hypothesis to be tested, i.e. that carers' depressive or anxiety symptoms have to improve first as a result of therapy before they are able to use more emotion-focused coping strategies.

8.6.2 Delivery and other characteristics of the therapy

The START study is the first trial of an individual-based coping skills intervention adapted for carers of people with dementia in the UK, and there are many empirical

questions about how the delivery of the intervention could be optimised for cost- and clinical effectiveness. As the protocol of eight sessions was effective in reducing psychological morbidity, it would be clinically useful to show whether more than eight sessions could deliver superior effectiveness, although the potential burden on the carer (and CR) on attending more sessions should be considered. On the other hand, fewer than eight sessions are unlikely to be as effective if carers needed broad exposure to the intervention in order to adopt and benefit from the components that would work for them. The optimal timing of any additional sessions can also be considered; whether optimal effects are achieved with sessions added immediately after the existing course, or as booster sessions spread further apart in time (allowing a greater likelihood that the CR will deteriorate, perhaps providing fresh opportunity for intervention to reinforce the carer's adaptive coping strategies). It would be interesting to explore all of this in the context of coping as a mediating or moderating mechanism.

8.6.3 Moderators of psychological intervention

Baseline psychological morbidity significantly moderated the effects of intervention on coping strategies, and this was additionally supported by post-hoc subgroup analyses. This naturally provides two avenues for further research. First, by repeating the intervention RCT but restricting the inclusion criteria to carers showing clinically significant psychological morbidity, we should expect to see all coping strategies increasing significantly following treatment; and if so, my original hypothesis that changes in coping mediated the effect of the intervention on psychological morbidity could be retested in this specific population. Second is the possibility of tailoring the intervention to further optimise its clinical effects for different subgroups (although carers already appeared to be quite good at taking what they found useful from the

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standardised intervention); for instance with the most distressed carers, it might be worthwhile reinforcing any and all attempts at coping.

It might also be clinically useful to identify the different sociodemographic and clinical factors associated with better or worse clinical outcomes, to enable more effective targeting and tailoring of the intervention. A previous meta-analysis suggested that carer age, gender and relationship with CR might influence treatment outcomes (indirect associations of sample-level characteristics with overall effect size) (Sorensen et al. 2002), but there has been relatively little direct evidence from RCTs to identify moderators of treatment effect at the individual level. Similarly a review of psychosocial intervention RCTs in North America has found 11 interventions (many of which based on Coping With Caregiving) tailored to specific ethnic groups, in terms of language, including culturally relevant themes, or matching of therapist ethnicity); but again very few of these RCTs directly compared outcomes across ethnic groups (Napoles et al. 2010),. It is also unclear how well this evidence translates to the UK setting.

Cultural sensitivity is a valuable and needed dimension in psychological therapies (Sue et al. 2009). Given that there were higher rates of dropout and non-adherence among non-White British carers in the current study, it would be useful to know how else ethnicity might affect outcomes, which might inform future trials of more culturally-sensitive adaptations of START.

8.6.4 Treatment mechanisms of complex psychological intervention

Multi-component interventions tend to be more effective than single-component interventions in reducing carer burden and psychological morbidity (Acton et al.

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2001;Selwood et al. 2007). While carers who received the START intervention appeared to benefit from it by adapting their coping strategies in different ways, it would be also informative to measure psychosocial mechanisms other than coping in future trials, for example grief, self-efficacy, and quality of the relationship between carer and CR (see Section 8.4).

8.7 Conclusion

The START study was designed to reduce carer psychological morbidity through an intervention aimed at changing their coping strategies. I hypothesised that the effect of the intervention on reducing morbidity would work through increasing carers' emotion-focused coping. This hypothesis was not supported, as the intervention did not significantly change coping strategies across the sample. However, treatment effects on coping varied systematically with baseline psychological morbidity. The most distressed carers responded to intervention both by using more helpful coping strategies and maintaining high use of unhelpful strategies, while intervention for the least distressed prevented their unhelpful strategies from increasing. Once this was taken into account, I showed the intervention to work via increasing emotion-focused coping only in the most distressed subgroup.

Complex interventions work in different ways for different people, and the current findings suggest that a diverse, non-clinical sample of carers may gain benefits in different ways from a standardised psychological intervention. The START intervention appeared to be effective both as a preventative and treatment strategy, and appeared to achieve this via different psychological mechanisms. Most importantly it benefited carers as a whole, providing strong support for the intervention to be made available to all carers of people with dementia recently referred to NHS services. On the other hand,

given the range of viable therapeutic pathways other than coping through which the intervention could also have exerted its effects, these mechanisms and their potential interactions with coping should be further researched in order to inform more effective interventions.

Appendix A.   Peer-reviewed publications

Coping strategies and psychological morbidity in family carers of people with dementia: A systematic review and meta-analysis

This paper describing my systematic review in Chapter 2 is published in the *Journal of Affective Disorders* (Li et al. 2012). Note that problem-focused is referred to here as "solution-focused coping", and emotion-focused coping as "emotional support and acceptance-based coping", at the suggestion of a peer reviewer.

[Manuscript removed to exclude copyrighted material]

Do changes in coping style explain the effectiveness of interventions for psychological morbidity in family carers of people with dementia? A systematic review and meta-analysis

This paper describing my systematic review in Chapter 3 is published in *International Psychogeriatrics* (Li et al. 2013).

[Manuscript removed to exclude copyrighted material]

Appendix B.   Ethics approval for START study

On 11 August 2009, the East London and the City Research Ethics Committee granted a favourable ethical opinion of the START study, in which the current PhD study is nested.

East London and the City Research Ethics Committee 1
Room 24, 2nd Floor
Burdett House
Mile End Hospital
Bancroft Road
London
E1 4DG

Telephone: 020 8223 8602

Prof Gill Livingston
Prof of psychiatry for of older people/consultant old age psychiatry
University College London
Dept of Mental Health Sciences
UCL Holborn union building, Archway
Highgate Hill London
N19 5NL

11 August 2009

Dear Prof Livingston

Study Title:	**START (STrAtegies for RelaTives) study: a pragmatic randomised controlled trial to determine the effectiveness of a manual based coping strategy programme in promoting the mental health of carers of people with dementia**
REC reference number:	**09/H0703/84**

Thank you for your letter of 23 July 2009, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered by a sub-committee of the REC at a meeting held on 11 August 2009. A list of the sub-committee members is attached.

Confirmation of ethical opinion

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

Ethical review of research sites

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

Conditions of the favourable opinion

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

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

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

available in the Integrated Research Application System or at http://www.rdforum.nhs.uk. *Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.*

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

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

Approved documents

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

Document	Version	Date
Research Protocol	0.1	18 May 2009
Applicant's checklist		
Investigator CV		21 May 2009
Application		
Caregiver HSQ-12		
Caregiver Questionnaire		
Clinical Dementia Rating (CDR)		
Caregiver Assessment		
Confirmation of funding		07 April 2009
UCL Clinical research insurance registration form (non-CTIMP)		
Statement of indemnity arrangements		01 August 2008
Copy of manual/intervention		
Participant Consent Form	0.2	24 July 2009
Participant Information Sheet	0.2	23 July 2009
Response to Request for Further Information		23 July 2009

Statement of compliance

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

After ethical review

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

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

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

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports

- Notifying the end of the study

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

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

09/H0703/84	**Please quote this number on all correspondence**

Yours sincerely

P.P. Senior Research Ethics Administrator
A. T. Tucker BSc(Hons) PhD SRCS
Chairman
East London and The City Research Ethics Committee 1

Enclosures: List of names and professions of members who were present at the meeting "After ethical review – guidance for researchers"
Copy to: Dr O Avwenagha

East London and the City Research Ethics Committee 1

Attendance at Sub-Committee of the REC meeting on 11 August 2009

Committee Members:

Name	Profession	Present	Notes
Professor Atholl Johnston	Professor of Clinical Pharmacology	Yes	
Dr Arthur T. Tucker	Principal Clinical Scientist & Senior Lecturer (REC Chairman)	Yes	

Appendix C.   Local NHS trust R&D approvals for START study

Between 2009 and 2010, the Research and Development (R&D) offices of the four NHS study sites granted R&D approvals for the START study, in which the current PhD study was nested.

Provider Services

Camden NHS
Primary Care Trust

North Central London Research Consortium
3rd Floor, West Wing
Camden PCT, St Pancras Hospital
4 St Pancras Way, London, NW1 0PE

Telephone: 020 7530 5375

Facsimile: 020 7530 3235
www.camdenproviderservices.nhs.uk

21st October 2009

Professor Gill Livingston
Professor of psychiatry for older people/consultant old age psychiatry
University College London
Department of Mental Health Sciences
UCL Holborn union building, Archway
Highgate Hill
London
N19 5NL

Dear Professor Livingston,

Title: START (STrAtegies for Relatives) study: a pragmatic randomised controlled trial to determine the effectiveness of a manual based coping strategy programme in promoting the mental health of carers of people with dementia

LREC Ref: 09/H0703/84

CSP Reference Number: 21355

I am pleased to confirm that the above study has received **provisional** R&D approval, and you may now start your research in **Camden& Islington NHS Mental Health Foundation Trust**. Full R&D approval will be granted pending the following Research Assistants getting their Research Passports: **Amanda Schulman**, **Shilpa Bavishi, Lisa Shanley and Eleanor Lewis-Holmes** . May I take this opportunity to remind you that during the course of your research you will be expected to ensure the following:

- **Patient contact:** only trained or supervised researchers who hold the appropriate Trust/NHS contract (honorary or full) with each Trust are allowed contact with that Trust's patients. If any researcher on the study does not hold a contract please contact the R&D office as soon as possible.
- **Informed consent:** original signed consent forms must be kept on file. A copy of the consent form must also be placed in the patient's notes. Research projects are subject to random audit by a member of the R&D office who will ask to see all original signed consent forms.
- **Data protection:** measures must be taken to ensure that patient data is kept confidential in accordance with the Data Protection Act 1998.
- **Health & safety:** all local health & safety regulations where the research is being conducted must be adhered to.
- **Adverse events:** adverse events or suspected misconduct should be reported to the R&D office and the Ethics Committee.
- **Project update:** you will be sent a project update form at regular intervals. Please complete the form and return it to the R&D office.
- **Publications:** it is essential that you inform the R&D office about any publications which result from your research.
- **Ethics:** R&D approval is based on the conditions set out in the favourable opinion letter from the Ethics Committee. If during the lifetime of your research project, you wish to make a revision or amendment to your original submission, please contact both the Ethics Committee and R&D Office as soon as possible.

Please ensure that all members of the research team are aware of their responsibilities as researchers. For more details on these responsibilities, please check the R&D handbook or NoCLoR website: http://www.noclor.nhs.uk

We would like to wish you every success with your project

Yours sincerely,

Angela Williams
Research & Development Manager

University College London Hospitals **NHS**

NHS Foundation Trust

Joint UCLH/UCL Biomedical Research (R&D) Unit
Professor Monty Mythen

Office Location:
1st Floor Maple House
149 Tottenham Court Road
London W1T 7DN

Postal Address:
Rosenheim Wing, Ground Floor
25 Grafton Way
London, WC1E 5DB

Email: philip.diamond@uclh.nhs.uk Tel: 020 7380 9833 Fax: 020 7380 9937 Web-site: www.uclh.nhs.uk

04 November 2009

Dr C Mummery,
Consultant Neurologist
NHNN

Dear Dr Mummery,

Project ID: **08/0288** *(Please quote in all correspondence)*
Title: **START (STrAtegies for RelaTives) study**

Thank you for registering the above study with the UCLH/UCL Biomedical Research Unit. I am pleased to give the approval of UCL Hospitals NHS Foundation Trust for the study to proceed.

You will be aware that as principal investigator you have various responsibilities under the Department of Health's *Research Governance Framework for Health and Social Care*. Please note that you are required:

- to comply with the UCLH Information Security Policy (the data protection toolkit "Consent and Security" will help you meet the requirements of the Data Protection Act and is available at http://www.uclh.nhs.uk/services/research/.
- to ensure that any co-investigator who is not an employee of UCLH has in place an up-to-date honorary contract.
- to keep copies of all consent forms with your project documentation. UCLH carries out audits of informed consent and if your project is selected for audit, you will need to provide access to the consent forms.
- To use an investigator file to store all the documentation relating to this research project (the attached list of headings is designed to help you assemble your investigator file).

This approval is conditional upon you having addressed any outstanding issues raised by the research ethics committee (REC) and having full ethical approval in place for the project. You should also be aware that your REC approval requires that you comply with all the requirements of the ethics committee regarding progress reports, notification of protocol amendments and adverse event reporting.

Also please can the following researcher have honorary contracts in place (copies must be sent to R&D) before they start within UCLH: Mr R Li, Ms S Bavishi, Ms A Shulman, Ms E Lewis-Holmes, Mr J Bradley, Ms R Shanley and Dr M Manela.

This approval is awarded on the basis of all the project documents you included in your submission to the UCLH/UCL Biomedical Research Unit, including any research agreements or contracts. In the event that the terms of any research contracts or agreements change or a new contract is issued this approval may be invalidated while the terms of the contract are negotiated.

Yours sincerely

Professor Monty Mythen
Director of R&D, UCL Hospitals NHS Foundation Trust

HOSPITALS

UCL Hospitals is an NHS Foundation Trust comprising: The Eastman Dental Hospital, The Heart Hospital, Hospital for Tropical Diseases, National Hospital for Neurology and Neurosurgery, The Royal London Homoeopathic Hospital and University College Hospital (incorporating the former Middlesex and Elizabeth Garrett Anderson Hospitals).

North East London NHS
NHS Foundation Trust

Research and Development Office
North East London NHS Foundation Trust,
1st Floor Maggie Lilley Suite,
Goodmayes Hospital,
Barley Lane,
Goodmayes,
Essex, IG3 8XJ

Date: 28.01.2010

Dear Prof. G. Livingston,

Re: START Study, Ref; 21355

I am pleased to inform you that the above named study has been granted approval and indemnity by Professor Martin Orrell, Director of Research and Development North East London NHS Foundation Trust. You must act in accordance with the North East London NHS Foundation Trust's policies and procedures, which are available to you upon request, and the Research Governance Framework. Should any untoward events occur, it is **essential** that you contact your Trust supervisor and the Research and Development Office immediately. If patients or staff are involved in an incident, you should also contact the Governance and Assurance department, in Goodmayes Hospital, and complete the Incident and Reporting Form, namely the IR1 form.

You must inform the Research and Development Office if your project is amended and you need to re-submit it to the ethics committee or if your project terminates. This is necessary to ensure that your indemnity cover is valid and also helps the office to maintain up to date records.

You are also required to inform the Research and Development Office of any changes to the research team membership, or any changes in the circumstances of investigators that may have an impact on their suitability to conduct research.

Yours sincerely,

Sandeep Toot

Research and Development Manager, North East London NHS Foundation Trust

UKCRN Portfolio No: 6721

Essex & Hertfordshire CLRN Office
Colchester Hospital University NHS Foundation Trust
R&D Office, Villa 3
Colchester General Hospital
Turner Road
Colchester
CO4 5JL

TEL: 01206 744242
http://www.crncc.nihr.ac.uk/index/networks/comprehensive/clrns/essex.html

14 November 2011

Prof Gill Livingston
University College London
Dept of Mental Health Sciences
UCL Holborn union building, Archway
Highgate Hill
London N19 5NL

Cc: (by email)
Stephen Davies, NHS Trust R&D Lead
Kieran Wing, R&D Manager
Dr Zuzana Walker, Principal Investigator
Dr O Avwenagha, Sponsor contact

Dear Prof Livingston,

RE: START (STrAtegies for RelaTives) study: a pragmatic randomised controlled trial to determine the effectiveness of a manual based coping strategy programme in promoting the mental health of carers of people with dementia

Amendment Number and date: AM01, 01 September 2011

NRES Reference: 09/HO703/84

Protocol Reference: Version 0.2, 01 September 2011

NHS Organisation: North Essex Partnership NHS Foundation Trust

This letter is issued by the Essex & Hertfordshire CLRN on behalf of North Essex Partnership NHS Foundation Trust, confirming that the amendments for the above study (defined by those documents listed below) have been reviewed and accepted by the NHS Organisation therefore I am pleased to confirm approval for the study to continue with these changes.

Description	Version	Date
REC Approval (NRES Committee London – City & East)	-	19 September 2011
Questionnaire: HADS	-	01 September 2011
Participant Information Sheet	1.0	01 September 2011
Protocol	0.2	01 September 2011
Consent Form	1.0	01 September 2011

Please note that this permission only relates to the above named NHS organisation. If your research involves other organisations then you are recommended to contact them to find out if you require their permission.

The responsibilities for Chief Investigator, Principal Investigator and other researchers are described in the Research Governance Framework for Health and Social Care. A reminder of the original approval conditions for Essex & Herts are given overleaf.

Very best wishes for your study, and please do not hesitate to contact me for any assistance during the project.

Yours sincerely,

E Slater

Miss Elizabeth Slater
Assistant Research Management & Governance Facilitator
Essex & Hertfordshire Comprehensive Local Research Network (E&HCLRN)

Version 3 – 14/06/10

APPROVAL CONDITIONS

1.0 Communications with E&H CLRN Office

1.1 Communications during the study with the Essex and Hertfordshire Comprehensive Local Research Network (E&H CLRN) Office are the personal responsibility of the Chief Investigator, unless a Principal Investigator has been appointed for the site.

1.2 The preferred method of contact must be communicated to the E&H CLRN Office at the beginning of the study. Changes in the point of contact must be notified in writing as soon as possible after the change, but certainly within 30 days.

1.3 The E&H CLRN Office may disclose information acquired as part of its research governance function to relevant authorities where such information is deemed necessary to assist such bodies in carrying out their functions in relation to regulation and monitoring of R&D.

1.4 The E&H CLRN Office is always willing to sign confidentiality agreements if required.

2.0 Trust Approval

2.1 The approval is only valid for the research described in the submission to Trust and has been approved by the relevant Research Ethics Committee.

2.2 The Approval for the research generally applies for the duration of the research. If it is proposed to extend the duration of the study as specified in the application form, the E&H CLRN Office should be contacted, and permission for an extension should be sought.

2.3 The research study may not be extended to any additional Essex or Hertfordshire site until the local Principal Investigator (PI) or Local Collaborator has obtained research governance approval from the E&H CLRN Office.

2.4 Should the research study not commence within 6 months, the Chief Investigator should give written notification of the delay. It will be the decision of the E&H CLRN Office to allow the research to commence in the approved local site/s.

2.5 In the case of studies having been given 'No Local Investigator' status, a listing of ALL involved sites will be required by the E&H CLRN Office. Studies given 'No Local Investigator' status will NOT be required to submit individual applications for each Research Site though a 'Local Collaborator' must be identified for each site. Research at a site must not commence until the Chief Investigator has a letter of Trust Approval indicating that the site is approved.

3.0 Communications with Research Ethics Committees

3.1 The E&H CLRN Office should be sent copies of all information submitted to Research Ethics Committees that relate to research approved by Essex or Hertfordshire organisations. This includes research taking place at General Practices. This is to include, but not be limited to,
  • progress reports
  • safety information,
  • substantial amendments
  • non-substantial amendments
  • termination reports

3.2 If the research is terminated early, the Chief Investigator should notify the E&H CLRN Office within 15 days of the date of termination. An explanation of the reasons for early termination should be given.

4.0 Amendments

4.1 It is conditional that any proposed amendments to the original protocol gain approval from the relevant NHS Research Ethics Committee.

4.2 Substantial amendments, defined in accordance with guidance issued by the National Research Ethics Service, can only be implemented with prior Ethical and Trust approval. The Chief Investigator is required to seek Trust approval by submitting the appropriate notification for substantial amendment, and the relevant Research Ethics Approval letter to the E&H CLRN Office.

4.3 Non-substantial amendments, defined in accordance with guidance issued by the National Research Ethics Service, can be implemented without prior Ethical or Trust approval on the condition that the non-substantial amendment is notified to both the Research Ethics Committee and the E&H CLRN Office.

4.4 Changes in Chief Investigator must be notified to this E&H CLRN Office immediately. It is the responsibility of the Sponsor to ensure that a new Chief Investigator is qualified and fully able to take over the title and the responsibilities thereof. This will also be viewed as a 'substantial amendment' by the Main Research Ethics Committee (REC).

4.5 Changes in Principal investigator should be treated in the same way as adding a new Site to a study. All relevant documentation must be sent to the E&H CLRN Office.

4.6 Changes in Administrative staff / research team should be notified to the E&H CLRN as changes in contact information. This should be done as soon as possible, in order for a smooth flow of information to be maintained.

5.0 Urgent safety measures

5.1 The sponsor or the Chief Investigator, or the local Principal Investigator at a study site, must take appropriate urgent safety measures in order to protect research participants against any immediate hazard

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to their health or safety. These actions are to be reported using the relevant NHS Organisation Policy and copies of such reports are to be submitted to the E&H CLRN Office. This is in line with current regulations, and contains local arrangements to fulfil the current regulation and legislation in addition to reporting requirements required by other regulatory bodies.

6.0 Reports to the E&H CLRN

6.1 The Chief Investigator is required to submit to the E&H CLRN Office a brief progress report every 12 months for the duration of the study to monitor the number of participants recruited and any adverse events, or complaints about the study. It is a condition of Approval that this is completed and submitted at each 12 month anniversary. It is acceptable to provide a copy of the report submitted to the Research Ethics Committee.

6.2 Upon completion of the study please note that the Chief Investigator or local Principal Investigator will be required to provide the E&H CLRN office with a copy of the final report, or publications related to findings, along with any recommendations that the local health care services may wish to adopt.

7.0 Review of Trust Approval

7.1 Each NHS Organisation may review its opinion at any time in the light of any relevant information it receives.

8.0 Breach of approval conditions

8.1 Failure to comply with these conditions may lead to suspension or termination of Approval.

9.0 Audit of the Research

9.1 As part of the monitoring of R&D activities and compliance with research governance, the E&H CLRN Office will contact randomly selected services participating in research, to check that the research is being conducted as per the approved Protocol, and any Participant consent forms are collected and stored correctly in accordance with current guidance and regulation.

9.2 Although this may not affect your study directly, any study files relevant to the study conducted at this site should be made available for the audit purposes.

10.0 Data Protection

10.1 This is a reminder that no identifiable data should be released to any party including commercial organisations without participant's written consent.

10.2 It is also NHS Organisation Policy that the researcher must remove person identifiers before any research data is transferred to a third party. If you are planning to share research data with colleagues abroad, a special undertaking may have to be signed prior to the transfer of data.

10.3 Where appropriate, an Access to Patient Records Form should be completed and returned to the E&HCLRN office on completion of the research study. A copy of this form will be sent to you if appropriate with the final letter of Approval.

10.4 It is expected that all clinical and non-clinical information obtained during the trial is recorded, handled and stored in such way that it is traceable, accurate and protected. Clear arrangements for archiving data collected from/at local research sites should be in place from the outset of the trial.

11.0 Support for studies on NIHR Portfolio

11.1 For research that has been adopted by the UK Clinical Research Network it maybe possible to obtain funds to offset any additional service support costs. These are those costs that are over and above the costs of a 'standard treatment' but exclude any excess treatment or 'project' costs.

12.0 Health and Safety Issues

12.1 ALL researchers should make themselves aware of standard health and safety good practice. Regulations applied during the course of a usual 'working day' should be carried across to encompass the time spent on a research study.

12.2 Holders of Honorary Contracts, Research Passports or Letters of Access are accountable to the E&H CLRN Office. All such holders should ensure that an appropriate risk assessment is made.

13.0 Freedom of Information

13.1 You shall note that all NHS organisations operate under the Code of Practice on Access to Government Information 1997, the Code of Practice on Openness in the NHS and the Freedom of Information Act 2000 (the 2000 Act), therefore, you are required to notify this office promptly on becoming aware of any person involved this study, exercising any rights or making a complaint under one or both of such Codes or the 2000 Act. You should notify the E&HCLRN office within five Business Days of receipt of any such complaints and / or Request for Information.

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Appendix D.   Carer assessment instruments

The following instruments are reproduced as presented in the case record forms for carers to self-complete.

Hospital Anxiety and Depression Scale

HADS

[Copyrighted material removed]

Brief COPE Inventory

COPE Inventory

There are many ways to try to deal with problems. Obviously people deal with things in different ways, but we are interested in how you have tried to deal with it. Each item says something about a particular way of coping. 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:	1 I haven't been doing this at all	2 I have been doing this a little bit	3 I have been doing this a medium amount	4 I have been doing this a lot
1. I've been turning to work or other activities to take my mind off things				

How often have you:	1 I haven't been doing this at all	2 I have been doing this a little bit	3 I have been doing this a medium amount	4 I have been doing this a lot
2. I've been concentrating my efforts on doing something about the situation I'm in				
3. I've been saying to myself "this isn't real"				
4. I've been using alcohol or other drugs to make myself feel better				
5. I've been getting emotional support from others				
6. I've been giving up trying to deal with it				
7. I've been taking action to try to make the situation better				
8. I've been refusing to believe that it has happened				
9. I've been saying things to let my unpleasant feelings escape				
10. I've been getting help and advice from other people				
11. I've been using alcohol or other drugs to help me get through it				
12. I've been trying to see it in a different light, to make it seem more positive				
13. I've been criticising myself				
14. I've been trying to come up with a strategy about what to do				
15. I've been getting comfort and understanding from someone				
16. I've been giving up the attempt to cope				
17. I've been looking for something good in what is happening				

How often have you:	1 I haven't been doing this at all	2 I have been doing this a little bit	3 I have been doing this a medium amount	4 I have been doing this a lot
18. I've been making jokes about it				
19. I've been doing something to think about it less, such as going to the cinema, watching TV, reading, daydreaming, sleeping or shopping				
20. I've been accepting the reality of the fact that it has happened				
21. I've been expressing my negative feelings				
22. I've been trying to find comfort in my religion or spiritual beliefs				
23. I've been trying to get advice or help from other people about what to do				
24. I've been learning to live with it				
25. I've been thinking hard about what steps to take				
26. I've been blaming myself for things that happened				
27. I've been praying or meditating				
28. I've been making fun of the situation				

Zarit Burden Interview

Zarit Interview

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.

	0 Never	1 Rarely	2 Sometimes	3 Quite frequently	4 Nearly always
1. Do you feel that your relative asks for more help than he/she needs?					
2. Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?					
3. Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?					
4. Do you feel embarrassed over your relative's behaviour?					
5. Do you feel angry when you are around your relative					
6. Do you feel that your relative currently affects your relationships with other family members or friends in a negative way?					
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?					
9. Do you feel strained when you are around your relative?					
10. Do you feel your health has suffered because of your involvement with your relative?					
11. Do you feel that you don't have as much privacy, because of your relative?					
12. Do you feel that your social life has suffered because you are caring for your relative?					
13. Do you feel uncomfortable about having friends over, because of your relative?					
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?					
15. Do you feel that you don't have enough money to care for your relative, in addition to the rest of your expenses?					
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?					
18. Do you wish you could just leave the care of your relative to someone else?					
19. Do you feel uncertain about what to do about your relative?					
20. Do you feel you should be doing more for your relative?					
21. Do you feel you could do a better job in caring for your relative?					
	Not at all	A little	Fairly	Quite a bit	Very
22. Overall, how burdened do you feel in caring for your relative?					

Appendix E.   CR assessment instruments

Raters completed the following CR assessments through semi-structured interviews with the carer.

Neuropsychiatric Inventory (NPI)

[Copyrighted material removed]

Clinical Dementia Rating (CDR)

	None 0	**Questionable 0.5**	**Mild 1**	**Moderate 2**	**Severe 3**
Memory	No memory loss or slight inconstant forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographical disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only
Judgment and problem-solving	Solves everyday problems and handles business and financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, and differences	Moderate difficulty in handling problems, similarities, and differences, social judgment usually maintained	Severely impaired in handling problems similarities, and differences; social judgment usually impaired	Unable to make judgments or solve problems
Community affairs	Independent function at usual level in job, shopping, and volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities although may still be engaged in some; appears normal to casual inspection	No pretence of independent function outside home; Appears well enough to be taken to functions outside a family home	No pretence of independent function outside home; Appears too ill to be taken to functions outside a family home

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Home and hobbies	Life at home, hobbies and intellectual interests well maintained	Life at home, hobbies and intellectual interests slightly impaired	Mild but definite impairment of function at home; more difficult chores abandoned more complicated hobbies and interests abandoned	Only simple chores preserved; very restricted interests, poorly maintained	No significant function in home
Personal care	Fully capable self-care	Fully capable self-care	Needs prompting	Requires assistance in dressing, hygiene, keeping of personal effects	Requires much help with personal care; frequent incontinence

Global rating: None 0 / Questionable 0.5 / Mild 1 / Moderate 2 / Severe 3

Appendix F. Efficacy analysis: Improvement and worsening in depression and anxiety caseness

Comparing the caseness of individual carers before and after intervention, 13/22 (59.1%) of the depression cases at baseline were no longer cases ("improved") following intervention, versus only 1/6 (16.7%) showing improvement in the TAU group at 8-month follow-up. Similarly, only 10/111 (9.0%) of non-cases at baseline became cases ("worsened") following intervention, versus 14/65 (21.5%) in the TAU group. I performed post-hoc repeated measures tests for each group, and found that the TAU group as a whole demonstrated significantly worse outcomes after 8 months (McNemar's χ^2, p = 0.001), whereas this was not the case for the treatment group (McNemar's χ^2, p = 0.678). Overall, the results suggest that the intervention was effective versus TAU both in treating carers who were depressed at baseline, as well as preventing new cases of depression over 8 months.

Appendix G. Sensitivity analyses for mediation

Ordinary regression: Unweighted complete cases

Table 8.1: Mediation analyses based on MacKinnon (Mackinnon et al. 2002) method. All regressions included baseline covariates: study site, carer age and gender, HADS-T, coping (emotion-focused, problem-focused, log dysfunctional), carer burden, CR neuropsychiatric symptoms ($\sqrt{\text{NPI}}$).

Putative mediator	Regression step	Outcome	Predictors	b (SE)	95% CI	p
Emotion-focused coping	*Step 1*	Emotion-focused coping (4m)	Randomisation	0.739	-0.715, 2.193	0.317
	Step 2	HADS-T (8m)	Emotion-focused coping (4m), controlling for randomisation	-0.338	-0.511, -0.164	<0.0005 *
Problem-focused coping	*Step 1*	Problem-focused coping (4m)	Randomisation	0.567	-0.718, 1.853	0.385
	Step 2	HADS-T (8m)	Problem-focused coping (4m), controlling for randomisation	-0.159	-0.364, 0.046	0.128
Log dysfunctional coping	*Step 1*	Log dysfunctional coping (4m)	Randomisation	0.002	-0.060, 0.064	0.954
	Step 2	HADS-T (8m)	Log dysfunctional coping (4m), controlling for randomisation	3.550	-0.713, 7.813	0.102

Two-stage regression: Unweighted complete cases

Emotion-focused coping

First stage regression				
Outcome	**Emotion-focused coping (4m)**	**b (SE)**	**95% CI**	**p**
Predictors	Randomisation	-3.180	-6.162, -0.199	0.037*
	Emotion-focused coping (baseline)	0.673	0.514, 0.831	<0.0005*
	HADS-T (baseline)	-0.095	-0.272, 0.083	0.300
Instrumental variable	Randomisation × HADS-T	0.294	0.097, 0.490	0.004*
			First-stage F = 8.719 < 10	0.004*
Second-stage regression				
Outcome	**HADS-T (8m)**	**b (SE)**	**95% CI**	**p**
Predictors	Emotion-focused coping (4m)	*Mediated effect = -0.742*	-1.539, 0.054	0.068
	Randomisation	*Direct effect = -1.993*	-3.784, -0.202	0.029*
			Durbin-Wu-Hausman χ^2 = 1.171	0.279
			Sargan χ^2	n/a

Problem-focused coping

First stage regression				
Outcome	**Problem-focused coping (4m)**	**b (SE)**	**95% CI**	**p**
Predictors	Randomisation	-1.879	-4.551, 0.793	0.167
	Problem-focused coping (baseline)	0.363	0.206, 0.521	<0.0005*
	HADS-T (baseline)	-0.073	-0.233, 0.086	0.367
Instrumental variable	Randomisation × HADS-T	0.183	0.007, 0.358	0.041*
			First-stage F = 4.225 < 10	0.041*
Second-stage regression				
Outcome	**HADS-T (8m)**	**b (SE)**	**95% CI**	**p**
Predictors	Problem-focused coping (4m)	*Mediated effect = -0.992*	-2.474, 0.490	0.190
	Randomisation	*Direct effect = -1.808*	-3.946, 0.331	0.098
			Durbin-Wu-Hausman χ^2 = 1.586	0.210
			Sargan χ^2	n/a

First stage regression				
Outcome	**Log dysfunctional coping (4m)**	**b (SE)**	**95% CI**	**p**
Predictors	Randomisation	-0.202	-0.327, -0.077	0.002*
	Log dysfunctional coping (baseline)	0.470	0.321, 0.618	<0.0005*
	HADS-T (baseline)	-0.008	-0.015, -0.000	0.037*
Instrumental variable	Randomisation × HADS-T	0.015	0.007, 0.023	<0.0005*
		First-stage F = 13.395 > 10		0.0003*
Second-stage regression				
Outcome	**HADS-T (8m)**	**b (SE)**	**95% CI**	**p**
Predictors	Log dysfunctional coping (4m)	*Mediated effect* = -11.894	-29.142, 5.356	0.176
	Randomisation	*Direct effect* = -2.349	-4.258, -0.440	0.015*
		Durbin-Wu-Hausman χ^2 = 4.054		0.046
		Sargan χ^2		n/a

Appendix H. Development of the START intervention manual

This was written by the START trial investigators, and outlines how and why the START intervention was adapted from the Coping With Caregiving programme (Gallagher-Thompson et al. 2002).

Development of the intervention manual

Having obtained permission from the Authors of the 'Coping with Caregiving' programme in the USA to adapt the manual for use with individuals in an NHS setting, we, the applicants (CC, PR, GL) and trial manager, DL began by familiarising ourselves with the structure and content of the manual which utilises the stress appraisal and coping response model, and principles from cognitive behavioural therapy.

Why change from group to individual intervention?

As noted in the original research protocol, through our clinical and personal involvement in caring for people with dementia, we are aware of the difficulties carers face in attending a group intervention, as it can be very difficult to make alternative care arrangements and to be available at a pre-specified time. Individual therapy also has the advantage that it can be tailored to the specific problems faced by the carer and our previous systematic review found that therapies worked better with individuals than groups. Therefore the first stage of development was adapting the manual for use with individuals in the UK. Individual therapies are quicker to deliver, since in groups time is

needed for all group members' problems to be discussed, therefore it was agreed that the number of sessions would be decreased.

Reducing the number of sessions

We identified the key components of the intervention and began reducing the 13 sessions to 8 sessions. This was a collaborative process.

In the original manual the sessions were: 1. Stress and wellbeing, 2. Target behaviours, 3. Strategies for changing behaviour, 4. Refining our behaviour plans, 5. Behaviours and thoughts, 6. Changing unhelpful thoughts, 7. Communication styles, 8. Communication and memory problems, 9. Planning for the future, 10. More planning for the future, 11. Pleasant events, 12. Refining your pleasant events and 13. Review and conclusion

The START manual which we produced for use with individual family carers in the UK NHS has eight sessions entitled: 1. Stress and wellbeing, 2. Reasons for behaviour, 3. Making a behaviour plan, 4 Behaviour strategies and unhelpful thoughts, 5. Communication styles, 6. Planning for the future, 7. Introduction to pleasant events and your mood, 8. Refining your pleasant events and overcoming barriers. Session six was completely rewritten so it was in accordance with UK law, e.g. Mental Capacity Act and services and also so that it focussed on earlier rather than end of life planning. An appendix was developed which included information on UK helplines and the CHOICE leaflets which we had developed in earlier research project about carers making decisions for people with dementia without capacity.

Finalising the content of sessions

Having produced the 8 session manual, each session was revised to ensure that the content was written in appropriate UK English, without jargon, was comprehensive and included both theoretical components and exercises for the participants to work through their own examples and experiences. Attention was given to ensuring a balance between psychoeducation and information provision, and interactive exercises inviting the carer to reflect upon their own experiences and strategies for coping as well as relaxation exercises. We piloted the manual by the researchers trying to deliver it and altered it whenever it did not flow or was unclear or repetitive.

At this early stage we took care to adapt the language and tone of the American manual to ensure that the language of the revised manual was suitable for its target audience, and to ensure that it was written in a clear and accessible style. Although the content of each session varied, each session followed a broadly similar structure which included an introduction and a review of homework task from the previous session (from session 2 onwards), one or more specific topics including worked examples and space for carers to identify their own examples, a stress reduction / relaxation technique, a session summary and a homework task, for example keeping a diary of challenging behaviours for the following week. During this process we consulted the trial management committee for feedback on drafts of the sessions. Particular focus was given to specific dilemmas such as how much to focus the manual on end of life care.

Having developed the eight sessions each one was practiced by the researchers whose job it would be to deliver the manual. We would meet in groups, practice delivering the sessions and obtain oral and written feedback on how to improve the sessions and increase the accessibility and clarity of the session content. This process was repeated until we all agreed that the sessions were ready for use. Sessions were

practiced with each other to ensure that all researchers had the same understanding of how to deliver the therapy. Two separate versions of the manual, one for the carer to keep and one for the therapist to use, which included additional prompts and guidance to the therapist, were produced. In addition to the text, pictures and images were included to make the manual more user friendly.

At this point the sessions were piloted by an experienced clinical psychologist (PR) with a carer of a person with dementia who would have met the criteria for inclusion in the study. After each session, the clinical psychologist provided feedback to the team on how both the process and content was received by the carer, including the ease of delivery and timing of the sessions and adjustments were made accordingly. Final versions of both the therapist and carer versions of the manual were then produced for use within the study.

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