Doctoral Thesis

Cognitive Behavioural Therapy for Anxiety in Informal Care-Givers of People with Dementia: A Meta-Analysis

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Doctorate in Clinical Psychology at the University of East Anglia

Submission Date: 22nd December 2017

Word Count: 35955

Abstract

Background and Aims

Caring for someone with dementia can be a source of significant stress, with many experiencing depression and anxiety (Pinquart & Sorensen, 2006). Despite showing promise for informal care-givers of people with dementia Cognitive Behavioural Therapy has received little systematic appraisal in isolation from other intervention models. The current review aimed to provide a systematic and quantitative appraisal of the evidence for CBT interventions with a primary focus upon anxiety outcomes, and secondary focus upon depression.

Methods

A systematic search of relevant databases was conducted. Study characteristics and effect size data were extracted. A series of random-effects meta-analyses were conducted. Subgroup analysis and meta-regression were performed to evaluate impact of intervention and care-giver characteristics. Publication bias and sensitivity analyses were examined.

Results

Fourteen studies comparing CBT to active or passive comparators for anxiety in informal dementia care-givers were identified. For both anxiety and depression significant “small” effect sizes, Hedge’s g=-0.15 and g=-0.21 respectively, were identified in favour of CBT over comparators combined. Effect sizes were generally reduced when studies deemed to be outliers were excluded. No significant treatment effects were found for anxiety or depression when CBT was compared to psychoeducation in isolation. Subgroup analysis for anxiety outcomes suggested that care-giver gender and relationship to care-receiver did not impact upon CBT intervention effectiveness. Interventions did not differ significantly according to delivery format; however, the magnitude of the effect was increased when studies without a relaxation component were excluded. Subgroup analyses were limited by lack of clear reporting within studies and therefore should be treated as preliminary.

Conclusions

There is a primary need to better understand whether dementia care-givers want help for anxiety and if they do then there is a need to establish what factors are driving their anxiety, specifically whether these factors lend themselves to the CBT model. If the answer is yes to both these questions then further methodologically rigorous clinical trials exploring the effectiveness of CBT for anxiety in informal dementia care-givers are warranted. In particular there is a need for trials employing CBT interventions specifically designed to target anxiety, with theoretically linked and well-defined primary outcomes, with attention given to baseline anxiety symptomatology.

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Acknowledgements

Firstly, I would like to take this opportunity to express my sincere thanks and appreciation to my Primary Supervisor, Professor David Peck. You have provided support and encouragement from the outset, always remaining positive. I am grateful for your expertise and the guidance you have provided in your revisions. I am extremely glad that you suggested completing a meta-analysis as I have learnt so much during this process and look forward to being able to draw on these skills again in the future. To my Second Supervisor, Dr Imogen Rushworth, thank you for helping me keep on top of all the other demands of training and for being a fantastic advisor throughout.

A big thank you must go to all the authors who responded to my requests for information, allowing me to complete such a comprehensive meta-analysis. Moreover thank you to all the care-givers who made this project possible by giving their time to participate in the studies synthesised in this research.

I would also like to thank Dr. Rhiannon Quann for assisting with the study inclusion process and for providing such great support. I also feel extremely fortunate for the constant encouragement, advice, and inspiration received from my fellow trainees, especially those of you who finished ahead of me and kept me motivated during tougher times.

Finally to my family, a heartfelt thanks goes to my husband, Dan, and to my mum, brother and sister for their unwavering support, unconditional love, and encouragement. You have been with me every step of the way. Between you all you have held everything else together allowing me to focus on my studies. Without your support I undoubtedly would not have made it this far. Thank you also to my funny, intelligent and loving son, Albert. You have been a source of immense joy throughout and have helped me to keep everything in perspective. Thank you.

Chapter One: Introduction

1.1 Introduction to Thesis

Over the last decade there has been a growing interest in interventions for informal care-givers of people with dementia. In particular research has looked to identify interventions that may have a positive impact upon care-givers psychological wellbeing. One such intervention which has shown some promise is Cognitive Behavioural Therapy (CBT). However, to date there has been only limited systematic appraisal of this approach with care-givers of people with dementia. In particular the present author could find no existing appraisal which focused exclusively on the impact of CBT interventions upon anxiety in dementia care-givers. Therefore the primary aim of the present research is to systematically appraise the studies investigating the impact of CBT upon informal care-giver anxiety. In addition it aims to consider whether the effectiveness of CBT in this population is moderated by care-giver and care-receiver characteristics or intervention format. A secondary aim is to appraise studies looking at depression in care-givers.

1.1.1 Overview of thesis structure.

There are four chapters presented in this thesis. The first provides an overview of dementia and the impact upon care-givers of people with dementia. It briefly summarises the CBT intervention research to date and the criticisms levelled at this research. The rationale for the present review will be outlined and finally the research aims are presented.

In the second chapter the methods used to address the research questions are presented, alongside the rationale for the techniques utilised. This chapter includes a summary of the search strategy, as well as a summary of the approach to study selection and data extraction. The details of quality appraisal are summarised and finally the methodology used for quantitative synthesis is described.

Chapter three is a detailed summary of the results including the outcomes of data collection and analysis. The pathway to study selection is presented and a summary of included study characteristics is provided. The findings of individual study quality appraisal are outlined. Finally, for each research question a summary is reported.

The final chapter in this thesis is the Discussion. Here the findings are discussed in relation to the research questions and existing literature. The clinical implications of the findings of the present review are highlighted. Limitations and strengths of this thesis will be presented, alongside recommendations for future research into CBT interventions for informal dementia care-givers.

1.2 Overview of Dementia

One of the most distinctive demographic events of the past two decades has been population ageing (World Health Organisation WHO, 2017). Globally there has been an unprecedented shift in the age of the population with older adults making up a proportionally larger percentage of the total population (United Nations, UN 2001). In the UK alone there has been a 1.7 million increase in the number of people over the age of 65 years since 1985 (UN 2010). Whilst this increase in ageing can largely be considered positive as it is a consequence of improved living environments, and health and social care systems, there is also another side which must be acknowledged. This change in population demographics will have profound impacts upon a range of political, economic, and social factors. In particular it will increase the demand for primary health care and for long-term care as it will drive significant growth in the number of people with health difficulties (Snell et al., 2011). This will be particularly true for dementia, as the greatest risk for the acquisition of dementia is ageing (Alzheimer's Society, 2007).

Dementia is amongst the most prominent cause of ill health for older adults, over the age of 65 years (UN, 2010). Defined as a clinical syndrome, dementia is caused when the brain is damaged either by one of the dementia diseases, such as Alzheimer's disease, or following a number of strokes. It can result in a cluster of symptoms including memory difficulties, language difficulties, changes in psychological and behavioural presentation, and impairments in activities of daily living (Burns & Lliffe, 2009). The symptoms will be dependent upon the disease that is causing the dementia and the corresponding parts of the brain that are damaged (Alzheimer's Society, 2007). It causes progressive, and irreversible decline, and presents a major challenge to health and social services (Donegan et al., 2017). Patients become increasingly dependent upon others to meet all their needs and over time many of their motor abilities are lost, and they may present in ways that are very challenging to those around them (Swearer, Drachman, O'Donnell & Mitchell, 1988).

In 2001 it was calculated that worldwide the number of people with Alzheimer's dementia, or related conditions, was 24 million. Researchers predict that this will increase in line with population ageing. By 2025 they estimate 43 million people will have the disease and this will rise to 100 million by 2050 (WHO, 2012). Globally there is some variation in prevalence, and it is predicted that much of the increase will occur in those countries which are of middle to low economic status. Currently approximately 58% of those with a diagnosis of dementia live within these countries, and this is predicted to rise to 68% by 2050 (Prince, 2000). This is in part due to the fact that ageing, once limited to developed countries, is expected to occur more readily in developing countries as standards of living improve, resulting in people living longer (Stephan & Brayne, 2009). Ferri et al. (2005) have suggested that by 2040 there will be as many people living with a dementia diagnosis in China alone as there will be living in developed countries combined.

In 2016 it was estimated that there were approximately 850,000 people living in England and Wales with a dementia diagnosis (Ahmadi-Abhari et al., 2017). This equates to one person in 84 living in the UK (Alzheimer's Society, 2007), and this figure is likely to be higher as not everyone with the disease will have sought help, or received a diagnosis (Elvish, Lever, Johnstone, Cawley & Keady, 2013). Subsequently there has been an international focus upon dementia (Department of Health (DoH), 2014). In 2012, and again in 2015, the Prime Minister's Challenge on Dementia identified areas of particular importance with the overarching aim to make England, by 2020, one of the best places for people with dementia and their care-givers to live (DoH, 2009; DoH, 2015).

1.3 Dementia Care-Givers

Within the UK the vast majority of people with dementia remain living in their own homes with care provided by family members (Boote, Lewin, Beverley & Bates, 2006). In 2009 it was estimated that in England alone there were over 500,000 family members caring for someone with dementia living in the community (DoH, 2009), and this number has likely risen in line with the increase in dementia diagnosis over the last 8 years. Over recent years there has also been a reduction in the number of psychiatric inpatient beds available and this has further increased the demands placed upon informal care-givers (Quirk et al., 2012). The cost of providing care for people with dementia in the UK is estimated to be higher than that for both cancer and heart disease at £17 billion per year (Alzheimer's Society, 2007), and is predicted to rise to £24 billion by 2026 (McCrone, Dhanasiri, Patel, Knapp, & Lawton-Smith, 2008). The Dementia UK update report by the Alzheimer's Society (2014) found that families and informal care-givers of those with dementia cover the cost of two thirds of this total (McCrone et al., 2008; Prince et al., 2014).

Not only are family care-givers bearing a large part of the financial responsibility, they also provide a crucial role as they facilitate the individual with dementia remaining at home, and this is often their preferred choice. In turn this means that expensive care in residential homes is avoided (Dickinson et al., 2017); without family care-givers people with dementia are likely to face earlier placement in institutions (Brodaty & Donkin, 2009:

Spijker et al., 2008). However, family care-givers of people with dementia, sometimes referred to as the ‘invisible patients’, are often overlooked (Brodaty & Donkin, 2009), with an assumption being made that relatives will automatically provide the care for elderly or unwell family members (Roth, Fredman, & Haley, 2015). In the UK the National Carers’ Strategy highlights the Government’s recognition of the contribution care-givers make, and it includes a commitment that by 2018 informal care-givers will “be supported to stay mentally and physically well and be treated with dignity” (DoH, 2008a).

1.3.1 Definition of informal care-givers.

The term “informal care-givers” typically refers to those individuals who are providing assistance, without being paid, to help an individual with their day to day activities, or activities of daily living (ADLs). In contrast formal care-givers are individuals who are providing this care in their professional capacity, and in return for payment. Within the research there is some variation about who is considered an informal care-giver. Whilst some studies have considered any individuals who are living with the person receiving care as informal care-givers, other studies have set more formal criteria, for example, requiring them to provide a certain number of hours of care, or to be helping with more than one ADL. (Roth, Mittelman, Clay, Madan & Haley, 2005). For the purposes of this review, informal care-giver will be defined as anyone providing assistance with ADLs to an individual with a dementia diagnosis, regardless of whether they are co-habiting, as long as they are not receiving payment or employed in a professional care-giving capacity. Therefore this could include spouses, other relatives such as adult offspring, in-laws and siblings, or unrelated friends providing care for a person with dementia.

1.3.2 Experience of informal dementia care-givers.

Receiving a diagnosis of dementia has huge implications for that individual and also has enormous effects on those who care for them. Providing care for someone with a dementia diagnosis can involve providing support with a wide range of ADLs, including preparing meals, managing finances and legal affairs, attending to personal care, arranging medical appointments and assisting them to take medication correctly (Alzheimer's Association, 2010). In 2009 a survey of informal care-givers in the US revealed that on average individuals looking after someone with dementia were providing 21.9 hours of care per week. The amount of care provided has been shown to be significantly higher than that provided by people caring for older people without a dementia diagnosis, with up to 40% of care-givers for someone with dementia providing over 40 hours of care per week, compared to only 28% of those caring for older people without a dementia diagnosis (Metlife Mature Market Institute, 2006).

Those care-givers who are co-habiting with the individual they are caring for can be providing care up to 24 hours a day. This level of care is often required for individuals who cannot be left alone because of the chance of them hurting themselves or getting lost due to wandering. Cohabiting care-givers are often providing this level of support seven days a week, and this will include waking in the night to provide support and assisting with all ADLs (Mahoney, 2003; Schulz et al., 2003). This means that care-givers often do not get a lot of sleep (Ali & Bokharey, 2015). Approximately 32% of informal care-givers caring for someone with a diagnosis of dementia will provide this level of care for more than five years, and around 12% will provide care for over 10 years (Alzheimer's Association, 2010).

As those providing care for people with dementia have been shown to differ significantly from other care-givers with regards to the amount of time they dedicate to care-giving, some have suggested that the effects of care-giving are more negative for dementia care-givers, both in terms of the psychological and physical impact (Gilleard, 1984). As the amount of time required to care for someone with dementia increases, the amount of time available for a care-giver's own interests and hobbies reduces (Buckwalter, 1996). Care-givers' leisure time and opportunities to spend time with other family members, friends, or doing things for themselves is significantly reduced (Ory, Hoffman, Yee, Tennstedt & Schulz, 1999; Dupuis, Epp & Smale, 2004). Additionally, there may be conflict with other members of the family as individual family members disagree about decisions made by the primary care-giver (Ory et al., 1999).

As the disease progresses people with dementia may also behave in ways that can be challenging both psychologically, and behaviourally, for those who care for them (Burns & Lliffe, 2009; Nicolaou, Egan, Gasson & Kane, 2010). For example, there may be significant changes in their personalities, behaving in ways that they would not normally do, perhaps becoming aggressive towards those around them, or disinhibited. This is particularly true for individuals with a diagnosis of frontotemporal dementia (FTD) (Mendez, Perryman, Miller & Cummings, 1998). Friends and other family members may be less inclined to visit due to the behaviour of the patient (Buckwalter, 1996). This can bring a range of different challenges for informal care-givers, who may also still be adapting and learning to cope with the knowledge that their loved one has a terminal disease. They may have to start planning for future decisions, which can be extremely emotionally draining, such as deciding upon residential placements and making difficult medical decisions (Wilson, 1989). Care-givers also take over tasks that had previously been managed by the person with dementia, leaving them with a sense of relationship loss. Additionally, many individuals with a dementia diagnosis will also have physical health complaints, meaning care-givers are also responsible for managing these (Alzheimer's Association, 2010).

1.3.3 Negative effects of care-giving.

Of course care-giving is not entirely negative and there are positive outcomes associated with providing care for a family member with dementia (see Stansfield et al., 2014). However, not surprisingly, there is a large body of research demonstrating that providing care for someone with dementia can have a serious impact upon care-givers. Since the 80s multiple research studies have found long-term caring for a person with dementia to be associated with negative psychosocial impacts (Steffen, Gant & Gallagher-Thompson, 2008). A full review of all the literature is beyond the scope of this paper (for a full review see Liu & Gallagher-Thompson, 2009), as care-givers of people with dementia have been shown to be affected psychologically, socially and physically. A brief summary of some of the social and physical impacts will follow, before going on to review in more detail the psychological impact of providing care to someone with a diagnosis of dementia.

1.3.3.1 Impact on social functioning.

An early investigation found that up to 55% of care-givers reported having to give up pleasurable activities completely (Ory et al., 1999) and this of course has an impact upon their own well-being. Socially, care-givers find it more difficult to maintain relationships, and dementia spousal care-givers report higher marital conflict than non-caregiving couples (Narayan, Lewis, Tornatore, Hepburn & Corcoran-Perry, 2001). There is also an increase in general family conflict, particularly for dementia care-givers, and the consequence can be less social support and greater social isolation (Schulz, O'Brien, Bookwala & Fleissner, 1995). This can be further exacerbated by the need to give up employment in order to meet the demands of care-giving (Brodaty & Hadzi-Pavlovic, 1990). Care-givers may also have to balance the demands of providing care for a loved one with dementia, with caring for their own children; this can have consequences for these relationships, as well as for the child's wellbeing (Brodaty & Donkin, 2009).

1.3.3.2. Impact on physical health.

Care-givers have also been shown to report poorer health and have more chronic illnesses than their age-matched peers (Stone, Cafferata, & Sangl, 1987; Haley, Levine, Brown, Berry & Hughes, 1987). For example, when compared to non-care-givers they report increased complaints of pain, higher diabetes prevalence, and higher intake of non-prescription pain medication (Pinquart & Sorensen, 2007; Vitaliano, Young & Zhang, 2004). The poor physical health has in part been explained by the impact of stress upon care-givers immunity (Kiecolt-Glaser, Glaser, Gravenstein, Malarkey & Sheridan, 1996), as there is consensus within the research that care-giving for someone with dementia is stressful for many family members (Schulz & Beach, 1999). Having a family member with dementia has been demonstrated to increase stress regardless of whether the relative is involved in providing their care (Amirkhanyan & Wolf, 2003). Additionally, care-givers are less likely to have time to rest and recover from injury and illness, to have time to get proper rest or to exercise to maintain their own physical health (Liu & Gallagher-Thompson, 2009). There is also evidence suggesting that care-givers have mortality rates which are up to 63% higher than those who are not providing care (Schulz & Beach, 1999).

1.3.3.3. Impact on psychological health.

The impact upon psychological wellbeing of care-givers of individuals with dementia has been shown to be significantly greater than that seen in other care-givers, and when compared to age matched non-care-givers the differences in levels of stress, and psychological distress, are even larger (Pinquart & Sorensen, 2003). Care-givers can experience various emotional problems as the dementia progresses. In 1984 Gilleard compared care-givers' levels of distress, as measured by Goldberg's General Health Questionnaire (GHQ) (Goldberg, 1978), and found significant differences between care-givers providing care for individuals with dementia and those caring for individual's with other health needs. Those providing care for people with dementia were more likely to report distress, and more likely to report levels of distress severe enough to indicate a psychological disorder. Additionally, care-givers of people with dementia have been found to experience more burden than family members who provide care for someone with a different chronic illness (Draper, Poulos & Cole, 1992; Ory et al., 1999).

1.3.3.3.1 Care-giver depression.

With regards to the specific psychological impact of care-giving for someone with dementia, and the associated high levels of burden, a lot of the research has been dedicated to exploring depression in dementia care-givers. A well-documented relationship has been observed between caring for someone with dementia and high rates of clinical depression or depressive symptomology seen (Brodaty & Donkin, 2009). Researchers have found prevalence rates of depressive disorders to be as high as 50% (Gallagher-Thompson, Rose, Rivera, Lovett & Thompson, 1989) and one study identified rates of depression between 23% and 85% in care-givers in developed countries (Clare et al., 2002). Depressed care-givers may then be less able to look after themselves, something which is already challenging due to increasing demands placed upon their time; consequently this further reduces their mood (Lu & Austrom, 2005).

Understanding care-giver depression is very important as it has a negative impact upon the care-giver, but can also affect the care-receiver or other family members as the care-giver is less able to provide care (Mok, Lai, Wong & Wan, 2007). This may increase the likelihood of the care-receiver being placed in residential care (Roth et al., 2005). There is also evidence to suggest that individuals with dementia are at higher risk of negative health consequences, including developing depression, if those caring for them are depressed (Schulz & Martire, 2001). If this occurs then it can further reduce the individual’s level of cognitive functioning beyond what they are already experiencing as a result of the dementia (Eisdorfer et al., 2003; Gitlin et al., 2003).

1.3.3.3.2 Care-giver anxiety.

Care-giver anxiety has not received quite as much attention as care-giver depression (Joling et al., 2015; Losada et al., 2014), but prevalence levels remain high, with dementia care-givers being estimated to be ten times more likely to meet the criteria for an anxiety disorder than care-givers of individuals without dementia (Dura, Stukenberg & Kiecolt-Glaser, 1991; Sallim, Sayampanathan, Cuttilan, & Chun-Man Ho, 2015). The London and South East Region Alzheimer's Disease (LASER-AD) study investigated the relationship between care-giving for someone with Alzheimer's disease (AD) and its impact upon care-givers' mental health (Mahoney, Regan, Katona & Livingston, 2005). The first section of the study sampled 153 people with AD and their care-givers; 23.5% of the care-givers scored within the range for a clinical diagnosis of anxiety (Mahoney et al., 2005). A more recent study, investigating a small number of care-givers of people with a diagnosis of Alzheimer's dementia, found that 46.7% met the criteria for a clinical diagnosis of anxiety (Ostojić, Vidović, Bačeković, Brečić, & Jukić, 2014) and the true rate is likely to be much higher given that many people struggling with anxiety often will not seek help (Kessler, Bennewith, Lewis & Sharp, 2002).

Cooper, Balamurali & Livingston, (2007) completed a systematic review of research investigating anxiety disorders in dementia care-givers, and suggested that anxiety may in fact be more prevalent than depression. This is due to co-morbidity with depression, with most care-givers who are depressed also being clinically anxious; however, the opposite was not true (see also Joling at al., 2015). Research exists investigating the impact of anxiety upon older adults in general; this is relevant given that many care-givers of people with dementia fall within this age group (Alzheimer's Association, 2007). This research has highlighted that those with high levels of anxiety perform poorly on tasks designed to assess their attention and concentration. They also show reduced capacity with regards to their working and episodic memory as well as a performing poorly on set-shifting tasks (Derousene, Rapin & Lacomblez, 2004). Considering the demands placed upon those providing care for people with dementia, any reduction in their cognitive functioning, as a consequence of being anxious, is likely to have a significant impact on their care-giving capacity.

Exploring anxiety further, the factors that have been identified as predicting an anxiety disorder in care-givers are: living with the care-receiver, the degree of difficulty the care-receiver has with activities of daily living (ADLs), being female, reporting poor physical health, and having a poor relationship with the care-receiver (Mahoney et al., 2005; Ostojic et al., 2014). Cooper et al., (2007) also found some evidence to suggest that coping style might be an important determinant of anxiety, in particular confrontative and avoidant coping. Caring for someone with dementia can be particularly challenging due to the changing nature of the care-needs of that individual, and the changing impact of the disease upon the behaviour of the care-recipient (Quirk et al., 2012), meaning that behaviour is not always easily predictable and this can cause care-givers to feel anxious.

1.3.4 Factors that may moderate the impact of dementia caregiving.

Care-givers are often talked about as if belonging to a homogenous group (Roth et al., 2005). However, as already mentioned there are considerable differences between care-givers on a number of characteristics. Many of these characteristics have been investigated to gain a better understanding of the impact they may have upon how care-givers cope with their role, and the levels of distress, or psychological difficulties they experience. These factors are important to consider as they may also have an impact upon how care-givers respond to interventions designed to support them.

1.3.4.1 Relationship to care-receiver.

Informal care-givers may have a range of different relationships with the person with dementia. The most investigated relationships are those of spousal care-givers and adult children providing care to a parent with dementia (Liu & Gallagher-Thompson, 2009). Spousal care-givers may face different challenges as, unlike adult children, they are most likely to be living with the care-recipient (Capistrant, Moon, Berkman & Glymour, 2011). This may mean that they have less choice about whether to take on the care-giving role (Adelman, Timanova, Delgado, Dion & Lachs, 2014). They may also be spending more time in that role as they are sharing the same accommodation, making it more difficult for them to have a break. Care-giving that is "around the clock" has been associated with increased risk of care-giver burden (Monin & Schulz, 2009). In addition spousal care-givers may be in poorer physical health due to their older age (Bauer & Sousa-Poza, 2015; Burton, Newsom, Schulz, Hirsch & German, 1997).

There is research which suggests that spouses of individuals with dementia may be less likely than adult offspring to seek support from outside agencies (Schofield et al., 1998). This has been hypothesised to be due to a sense of greater emotional commitment stemming from commitments made at the time of marriage, and also the investment already placed into that relationship over the years. This in turn may mean that spouses experience higher levels of burden as they struggle to manage all the care independently, which in turn can manifest as anxiety and depression (Liu & Gallagher-Thompson, 2009).

Due to the cognitive changes in their partner, spousal care-givers experience a loss of companionship. The reciprocal exchange of affection may also diminish, as well as experiencing the loss of a confidant with whom the carer may have previously shared the day-to-day running of their household. This in turn can also lead to an increased risk of depression and anxiety (Beeson, 2003). Loneliness has also been suggested as a significant contributing factor to the development of poorer mental health in dementia care-givers (Liu & Gallagher-Thompson, 2009). Loneliness may be greater for spousal care-givers as they are often living with the person with dementia. In comparison adult child care-givers may live independently, or be surrounded by their own family, thus reducing the experience of loneliness (Beeson, 2003; Bergman-Evans, 1994). Adult children who are in a care-giving role have been shown to receive higher emotional rewards than spousal care-givers (Raschick & Ingersoll-Dayton, 2004). However, reports of positive outcomes are rare in the literature (Bauer & Souza-Poza, 2015).

1.3.4.2 Care-giver gender.

It is estimated that 60% of informal care-givers providing care to someone with a dementia diagnosis are female (Alzheimer's Association, 2010). Whilst some studies have found no difference between male and female care-givers' distress (Beeson, 2003), there is a growing body of evidence highlighting differences in how different genders respond to their care-giving role (Liu & Gallagher-Thompson, 2009). Male care-givers might be more likely to assume a role not dissimilar to the care-manager, whereas female care-givers have been shown to be more likely to be attending to the emotional and personal needs of the person with dementia (Billings & Moos, 1984; Draper, 2004). Generally research has found female care-givers to be more vulnerable to anxiety and depression. A study by Schulz & Williamson (1991) found that whilst 16% of male care-givers met the criteria for clinical depression, 39% of females were categorised as being depressed (see also Pinquart & Sorensen, 2006a).

One explanation for this difference is linked to the different roles that male and female care-givers might take on, as outlined above. In line with this, wives have been found to report more subjective burden, anger, and lower satisfaction with their involvement in leisure activities than husbands of females with Alzheimer's dementia (Lieberman & Fisher, 1995; Yin, Zhou & Bashford, 2002). Additionally, for female care-givers there is also an increased risk of financial difficulties (Wakabayashi & Donato, 2006), which further adds to the strain they are experiencing. Some researchers have also argued that female care-givers are less likely to seek support in their care-giving role (Stoller, 1990). However, this suggestion was not supported in a meta-analysis investigating care-giver gender differences. Pinquart & Sorensen (2006a) concluded that men and women did not differ with regards to their use of both informal and formal support.

1.3.4.3 Type of dementia diagnosis.

The most common form of dementia in both older and younger people with the diagnosis is Alzheimer's disease, although there are many different causes of dementia (Alzheimer's Society, 2007). The impact upon the person with dementia and their presentation can be very different depending on the specific diagnosis, and as such research has started to investigate the different impact this might have upon care-givers. In particular much of the research has investigated the difference between care-givers of individuals with a diagnosis of Frontotemporal dementia (FTD) and those caring for someone with a diagnosis of Alzheimer's dementia (AD). In individuals with FTD, changes in personality and behaviour can often precede cognitive decline in other domains (Nicolaou et al., 2010). Consequently care-givers of people with FTD may have a very different experience, exacerbated by the fact that individuals with a FTD diagnosis may be more likely to experience early-onset changes (Diehl, Mayer, Forstl & Kurz, 2003).

Nicolaou et al. (2010) compared 30 care-givers of people with FTD to 30 care-givers of people with AD with a view to investigating their potentially different needs, levels of burden and presence of depressive or anxious symptomatology. They concluded that the needs of FTD care-givers were significantly greater than those of AD care-givers, particularly with regards to financial difficulties and access to services. However, there were no significant differences in terms of levels of burden, anxiety or depression. This contrasts with the earlier research by De Vugt et al. (2006) who also compared FTD care-givers with AD care-givers and concluded that those providing care for people with FTD were significantly more distressed. Despite these differences considering the type of dementia diagnosis could be important when designing interventions; in the same way that care-givers do not belong to a homogenous group neither do care-receivers. Care-receivers will differ with regards to the nature and number of problems they pose for the care-giver, for example, the level of attention or supervision required and the demandingness of the care-receiver can all have a negative impact on care-giver wellbeing (Gilleard, 1984). Therefore, care-givers may need different support, even if it is only with regards to the specific information they require (Nicolaou et al., 2010).

1.4 Models of Care-Giver Distress

Over the years a number of different models have been developed to explain the relationship between care-giving and the negative outcomes associated with it (Liu & Gallagher, 2009). The most frequently cited model of care-giver distress is Transactional Theory by Lazurus and Folkman (1984) (Levesque et al., 2002). This is a model which is based upon the ideas of stress and coping.

Lazarus and Folkman (1984) define stress as “a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her wellbeing” (p. 19). According to this definition and model, care-giver stress results when a transaction occurs between the care-giver and his environment. This transaction is then appraised by the care-giver with regards to their abilities to cope and the resources they feel are available to them. If the care-giver appraises the situation as being beyond their capabilities, or if they appraise themselves as not possessing adequate resources to overcome the environmental stressor, then this is when a negative impact upon well-being occurs (Levesque et al., 2002).

Folkman expanded upon this model to outline a primary and secondary appraisal in response to a stressor (Folkman, 1997). The primary appraisal is the assessment of how threatening the situation is. The secondary appraisal is the care-giver’s assessment of their ability to cope. This will include their perception of both their personal and their physical resources. The care-giver will then apply their coping skills to the situation and these can include problem-focussed coping, using social support networks, or emotion-focussed approaches. The choice of coping skill will be dependent on the appraisal. For example, if the care-giver appraises the situation as threatening and appraises themselves as lacking the skills to cope, then they may employ emotion-focussed approaches such as avoidance. Folkman & Moskowitz (2004) argue that the type of coping skill employed can lead to negative emotional, behavioural and psychological responses; these in turn are hypothesised contribute to the development of physical and mental health difficulties (Beauchamp, Irvine, Seeley & Johnson, 2005).

This model lends itself easily to the development of care-giver interventions (Knight, Silverstein, MaCallum & Fox, 2000; Levesque et al., 2002). Using this framework interventions aim to target care-giver skill deficits through psychoeducation in order to assist them to become more effective in dealing with environmental stressors, such as challenging behaviour in the care-receiver (Crespo, Lopez & Zarit, 2005). If the care-givers are more skilled then they feel more able to cope and therefore are less stressed and more likely to employ helpful, rather than unhelpful, coping skills (Gitlin & Hodgson, 2015).

1.5 CBT Interventions in Care-Givers

The increased focus upon dementia, and care-givers, has highlighted the need for greater support for care-givers to enable them to remain able to care for their loved ones whilst also ensuring they are able to attend to their own health needs (DoH, 2015; Laver et al., 2016). The need to support those who are providing care for people with dementia has been recognised across communities internationally (Prince, Bryce & Ferri, 2011; Stoltz, Uden & Willman, 2004).

As summarised by research investigating the impact of care-giving upon dementia care-givers, the problems experienced can be wide ranging, including mental health, physical health, and social difficulties (Czaja, Schulz, Lee & Belle, 2003). Therefore any intervention needs to be able to address each of these areas. CBT as a model has the potential to target a number of different difficulties. Within the science of psychology, the cognitive model is perhaps the theoretical approach with the most empirical support (Clark, Beck & Alford, 1999; Salkovskis, 1996) and CBT is the psychological intervention which has been most tested within psychological research (Butler, Chapman, Forman & Beck, 2006; DeRubeis & Lorenzo-Luaces, 2017; Marquez-Gonzalez, Losada, Izal. Perez-Rojo, & Montorio, 2007).

1.5.1 Definition of CBT.

CBT is a therapy based upon both cognitive and behavioural theory and their associated therapies. Cognitive therapy is defined as “attempts to reduce dysfunctional emotions and behaviour by altering individual appraisals and thinking patterns” (Brewin, 1996, p. 34). Behavioural therapy is defined as “direct attempts to reduce dysfunctional emotions and behaviour by altering behaviour” (Brewin, 1996, p. 34). CBT is a talking therapy which is time-limited and structured. It uses techniques derived from cognitive and behavioural models of human behaviour to alleviate psychological distress (Laidlaw, Thompson, Gallagher-Thompson & Dick-Siskin, 2003). CBT interventions can involve a range of elements. These include cognitive restructuring through thought identification, monitoring and challenging, alongside a behavioural element which can include behaviour activation, activity scheduling, graded exposure tasks, emotional management strategies including relaxation, and/or problem solving skills training (Gallagher-Thompson & Steffen, 1994).

1.5.2 How might CBT interventions with care-givers work?

Many of the CBT interventions have drawn on the stress and coping framework (Beauchamp et al., 2005; Lazarus & Folkman, 1984; Levesque et al., 2002). Investigating the link between the demands a care-receiver's presentation places upon the care-giver and the subsequent care-giver stress suggests a way of intervening from a CBT perspective. The relationship will be partially determined by the way the care-giver perceives the behaviour. This links to the idea of stress appraisal (Folkman, 1997) but can also be conceptualised from a CBT theoretical framework by considering dysfunctional thoughts. Losada, Montorio, Knight, Marquez & Izal (2006) noted that whilst interventions existed which were looking to change the cognitive appraisals of care-givers there was no CBT model explaining how this might work.

There is research to show that not all care-givers experience stress and there is in fact evidence to suggest that some elements of care-giving can be rewarding (Stansfield et al., 2017; Tarlow et al., 2004). This suggests that if the care-giver's appraisals (thoughts) are altered and reframed as more positive then the outcomes for the care-giver will also become more positive (Losada et al., 2006). In general, interventions based upon CBT are aimed at training care-givers to be more flexible and adaptive in their thinking. This helps them to face the daily demands of care-giving in a more realistic way, challenging cognitive distortions (Rodriquez-Sanchez et al., 2013). Losada et al. (2006) also highlighted the importance of considering the impact of the care-giver's life experience upon the beliefs they might hold about care-giving. Their early experiences also shape the beliefs they hold about themselves and this may further impact on the way they respond to their situation (Crespo et al., 2005).

Cognitive distortions, or unrealistic beliefs, shape the content of an individual's automatic thoughts through errors in logic (Beck & Emery, 1985; Leahy, 2003). When faced with challenging situations an individual will produce a number of automatic thoughts. Cognitive distortions associated with care-giving, or with the person with dementia, lead to a narrowed focus of attention and this can intensify behavioural responses to that situation (Friedman & Thase, 2006). Within the literature it is possible to find examples of these unrealistic beliefs about care-giving, for example, believing that the care-receiver's behaviour is deliberately intended to cause the care-giver distress. Such erroneous beliefs may be particularly likely during the early stages of the disease and in care-givers who have not had access to educational information about dementia (Mittelman, Epstein & Pierzchala, 2003, p. 184). They may also be linked to beliefs about the care-giving role, for example, that family members "must" provide care that no one else will be able to provide care, or that other family members will frown upon requests for help (Arai, Sugiura, Miura, Washio & Kudo, 2000).

Losada et al. (2006) linked the care-giver's life experiences to the development of their beliefs about care-giving and the subsequent automatic thoughts, feelings and behaviours that arise from these in their model proposing a theoretical cognitive model for CBT interventions (see Figure 1). Based upon this model, Losada et al. (2006) argued that CBT should look to change maladaptive cognitions because they are identified as the antecedents of emotional distress in care-givers (Dick & Gallagher-Thompson, 1995; Leahy, 2003; Losada et al., 2006). If care-givers are able to challenge these cognitions then they are better placed to cope with the stressors associated with care-giving. CBT interventions also aim to increase the number of pleasant activities within a care-giver's life as a way of increasing self-care, and this in turn helps them to be more able to manage the daily demands they face (Rodriquez-Sanchez et al., 2013).

1.5.3 Evidence base for CBT for informal dementia care-givers.

Interventions targeting dementia care-givers have been developed from a range of different theories and concepts and focus upon many different targets (Moniz-Cook et al., 2008). Consequently there is a wide range of interventions available and these are based upon a variety of different delivery methods. Research exploring their effectiveness has in turn used a wide range of outcomes to assess these interventions. The result is a complex evidence base and several authors have conducted systematic reviews over the last decade to try and synthesise the available literature (see Dickinson et al., 2017).

Trying to unpick the evidence base explicitly for CBT is challenging as to the best of the present author's knowledge there are no systematic reviews which have focussed solely upon CBT interventions (Dickinson et al., 2017; Gilhooly et al., 2016; Parker, Arksey & Harden, 2010). Rather, CBT interventions have been included as part of reviews investigating a range of care-giver interventions and the definition of CBT has not always been clearly or consistently defined, with some reviews referring to interventions that utilise either behavioural or cognitive therapy, as opposed to those interventions that include both techniques (see Beck, 2005, p.955). To complicate matters further, CBT interventions have often been grouped with interventions drawing on different therapeutic approaches, and even these categories have been defined differently by different review authors, or not explicitly defined at all (Gaughler, Jutkowitz, Shippee & Brasure, 2017; Gilhooly et al., 2016; Parker et al., 2010).

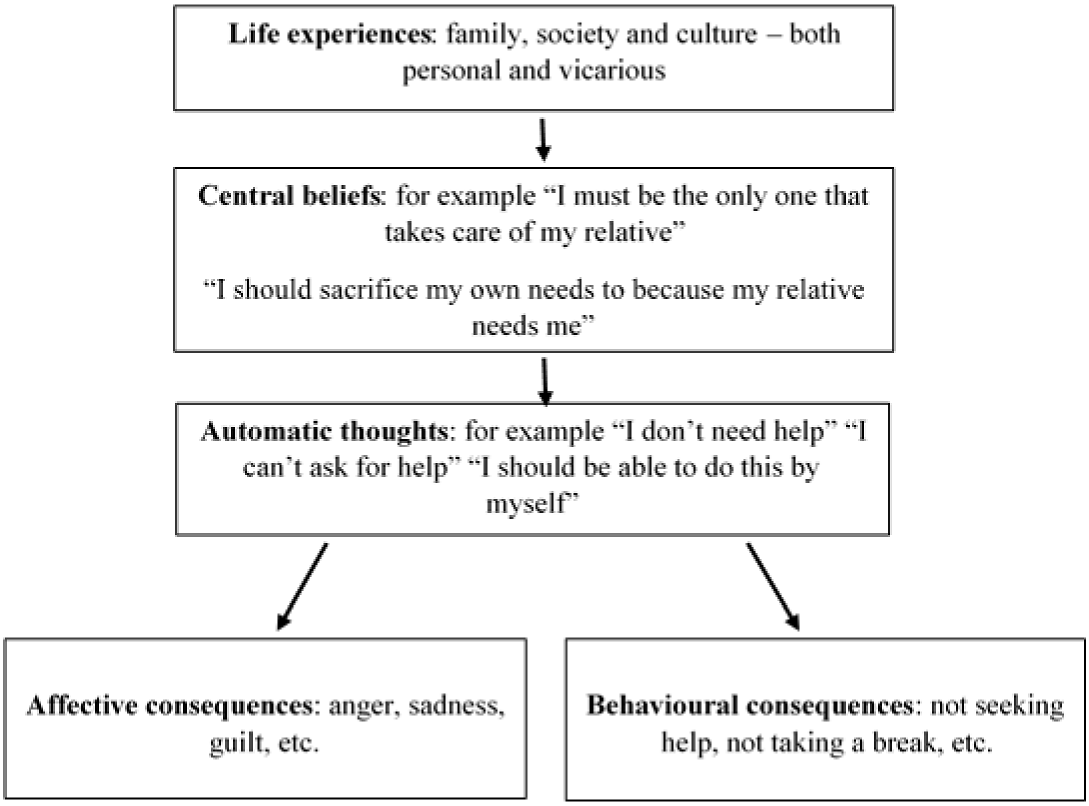
For example, a systematic review completed by Cooke, McNally, Mulligan, Harrison & Newman (2001) looked specifically at a category of psychosocial interventions for dementia care-givers. They defined psychosocial interventions as those which employed techniques drawing on cognitive, behavioural or social mechanisms of action. Forty studies met their inclusion criteria, and of these only two of these studies explicitly identified themselves as being based upon CBT. In contrast, in the review completed by Gallagher-Thompson & Coon (2007), CBT interventions were included in the category of psychotherapy. Again only three studies based on CBT were included, despite this small number of studies they concluded that CBT enjoys strong empirical support. To confuse matters further an earlier study by the same first author described their CBT intervention as psychoeducational (Gallagher-Thompson et al., 2000).

A later systematic review by Elvish et al. (2013) grouped reviews into psycho-education, psychotherapy-counselling, multicomponent, and technology based. They also placed CBT interventions in the psycho-education category, alongside interventions that were purely educational. Once again only a very small number of CBT interventions were included (k = 3). However, again despite this limited empirical evidence the authors concluded that interventions underpinned by CBT were able to produce the most meaningful change.

1.5.3.1 CBT for depression in informal dementia care-givers.

Three reviews were identified which included categories specifically for CBT interventions. These were the reviews completed by Pinquart & Sorensen (2006b) and by Vandepitte et al. (2016). The third review investigated the use of pure technology based CBT interventions (Scott et al., 2015). The review by Pinquart & Sorensen (2006b) is frequently cited in the dementia care-giver intervention literature, and has been rated as methodologically strong (Dickinson et al., 2017). This review included 127 intervention studies which were published between 1982 and 2005, 11 of which were included in the CBT category. To be included in this category interventions had to apply techniques from CBT, with a focus upon modifying thoughts and beliefs, as well as developing and changing care-giver behavioural patterns. Significant and large effect sizes for the impact of CBT on depression were demonstrated (Cohen's $d = -0.70$), leading the authors to conclude that CBT interventions had the highest effect size amongst interventions aimed at reducing care-giver depression (Pinquart & Sorensen, 2006b).

Figure 1. Cognitive model for CBT interventions with care-givers: pathological pathway (Losada et al., 2006 p. 122)



Vandepitte et al., (2016) completed a systematic review which identified 52 papers for inclusion. These papers were categorised by the dominant components the intervention contained, and this included a category of CBT, for which they identified three studies that met their eligibility criteria. They concluded that CBT had a positive impact upon dysfunctional thoughts. However, with regards to mental health outcomes findings were mixed with two studies demonstrating a positive impact on depression (Losada, Marques-Gonzalez, & Romero-Moreno, 2011; Rodriguez-Sanchez et al., 2013), but one study demonstrating no difference from the control group (Passoni et al. 2014).

Scott et al. (2015) conducted a systematic review of pure technology-based CBT interventions for dementia care-givers. They required studies to be CBT based; however, to be included in the review studies only had to include one component of cognitive, or behavioural therapy. Four studies met their inclusion criteria and three of the four studies were based upon Gallagher-Thompson, Ossinalde & Thompson (1999) Coping with Caregiving. This is a manualised intervention based upon CBT and includes both elements of cognitive and behavioural therapy. The final study by Beauchamp at al. (2005) cited the Stress and Coping model (Lazarus & Folkman, 1984) as the theoretical basis for their intervention, however, it included both cognitive and behavioural methods of coping with emotions and therefore met the inclusion criteria.

Scott et al. (2015) reviewed the studies with regards to the impact they had upon care-giver depression as this was the only outcome measure that was included by all four studies. They concluded that the interventions led to a small, but significant and clinically meaningful, reduction in depressive symptomatology SMD = -0.27. However, they cautioned against drawing anything other than tentative conclusions due to the small sample sizes within each study, the small number of studies that met eligibility for inclusion in their review, and the impact of the high risk of bias.

1.5.3.2 CBT for anxiety in informal dementia care-givers.

At the time of writing the present researcher was aware of only one systematic review which focused specifically upon intervention studies for anxiety in care-givers of people with dementia. This seems at odds with the research highlighting the significant prevalence of anxiety in dementia care-givers (Joling et al., 2014; Mahoney et al., 2005; Ostojic et al., 2014). Additionally there are those who argue that anxiety and depression go hand in hand and so it is does not make sense to examine one without considering the other (Tyrer, 2001). The review by Cooper et al. (2007) aimed to bridge this gap in the research data. They identified that whilst the treatment of depression, burden, and psychological morbidity in general, had been well researched, anxiety as an outcome had been relatively neglected. Within their review they included primary research which reported the effects of a non-pharmacological intervention upon dementia care-giver anxiety. From an initial 530 references identified they found 24 that matched their search criteria. For each study included Cooper et al. (2007) grouped them into categories of interventions and gave each category an overall grade of recommendation (GR). This grade was given in accordance with the Centre for Evidence Based Medicine guidelines used to indicate the level of confidence which should be placed in an intervention's effectiveness. The grades range from A which is the highest level and means research is of a consistently high standard based on RCTs, to grade D which is studies which are inconsistent, or inconclusive.

From the included studies just three studies were based upon CBT and compared waiting list or support group to CBT group interventions for anxiety (Akkerman & Ostwald, 2004; Gendron, Poitras, Dastoor, & Perodeau, 1996; Hebert et al., 2003). Only one study was found to have a significant impact upon care-giver anxiety levels, and this was the only study whose primary focus was anxiety reduction. In particular this study included relaxation as a key component of the intervention (Akkerman & Ostwald, 2004). The other two studies included in this group of interventions did not demonstrate any difference in anxiety levels between the intervention and the control group, either immediately post intervention, or at follow up (Gendron et al., 1996; Hébert et al., 2003). This led Cooper et al. (2007) to assign a grade of D to this group of CBT interventions meaning no conclusions could be drawn with regards to their efficacy as anxiety interventions in care-givers of people with dementia, due to inconsistent findings.

More positive outcomes may have been expected for anxiety, as CBT is widely used to alleviate the symptoms of a range of anxiety disorders in the general population (Hunot, Churchill, Teixeira, Silva de Lima, 2007). However, few studies were considered in the evaluation, which may limit the interpretative accuracy of these findings. Several meta-analyses of CBT for anxiety disorders in working-age adults have been conducted. Hofmann & Smits, (2008) demonstrated the effectiveness of CBT upon anxiety and found moderate to large effect sizes favouring CBT to control conditions (Hedge's $g = 0.73$). Stewart & Chambless (2009) also concluded that CBT demonstrated both efficacy in clinical settings and effectiveness in naturalistic settings; however, they reported that the magnitude of the effect was difficult to estimate due to the lack of high quality studies.

An additional meta-analysis by Gould, Coulson & Howard (2012) investigated the efficacy of CBT for anxiety disorders in older people. They reviewed randomised controlled trials (RCTs) that had investigated the impact of CBT upon adults aged over 55 who had a diagnosis of an anxiety disorder. A total of 12 studies were included in the review and when compared to treatment as usual, or being on a waiting list, CBT was shown to be significantly more effective, with moderate effect sizes immediately post intervention (Hedge's $g = -0.66$). This significant difference was maintained at 6 month follow up, although only a small effect size was observed (Hedge's $g= -0.29$). The authors concluded that there was evidence that CBT was effective in older adults.

Vernooij-Dassen, Draskovic, McCleery & Downs (2011) aimed to address criticisms directed at care-giver research about the lack of understanding of the specific components which influenced outcomes. They completed a meta-analysis looking specifically at cognitive reframing for carers of people with dementia. Cognitive reframing is one element of CBT. Vernooij-Dassen et al. (2011) defined it as the altering, or reframing of thoughts which are maladaptive or self-defeating into thoughts which are supportive of adaptive behaviour and which are less distressing. In their review they identified research where the main goal of the intervention was to reduce care-giver difficulties by modifying all, or some, of their beliefs about their own responsibilities to the person they were caring for, their beliefs about their need for support, and the way they interpreted the behaviours of the person with dementia.

They identified eleven trials that met their inclusion criteria and of these four included measures of anxiety, with a total of 515 participants (Akkerman & Ostwald, 2004; Beauchamp et al. 2005; Chang, 1999; Hebert et al., 2003). Two of the included studies overlapped with those included by Cooper et al. (2007) (Akkerman & Ostwald, 2004; Hébert et al., 2003). An analysis of the standard mean differences in change from baseline using a fixed effects model revealed that there was a significant benefit of the intervention for the treatment of anxiety (SMD -0.21) as compared to usual care. However, the use of a fixed effects model is not recommended in psychological research where there is likely high levels of heterogeneity due to the inflated chance of Type I errors and the erroneous production of narrow confidence intervals (Borenstein, Hedges, Higgins & Rothman, 2009; Field, 2005; Hunter & Schmidt, 2000; National Research Council, 1992).

1.5.3.3 Impact of intervention characteristics.

Acknowledging the current economic situation with regards to health resources, and the practical barriers many care-givers face trying to access face to face support which may be some distance from their home, has led to the development of services via alternative means (Waller, Dilworth, Mansfield & Sanson-Fisher, 2017). By developing interventions that can be delivered over the phone, or via the internet, researchers are aiming to provide individualised support that can reach a greater number of care-givers in a timely way.

Waller et al. (2017) completed a systematic review of both telephone and computer delivered interventions with dementia care-givers. They identified 34 studies meeting their inclusion criteria; of these four studies investigated the impact of CBT delivered by telephone for dementia care-givers (Chang, Nitta, Carter & Markham, 2004; Glueckauf et al., 2007;

Wilz, Schinkothe, Soellner, 2011; Wilz & Soellner, 2016). None of the included CBT interventions assessed the impact upon anxiety, and the outcomes of the CBT interventions were not discussed in isolation. Across all types of intervention models, Waller et al. (2017) concluded that overall there was evidence to suggest that interventions delivered by telephone and/or computer had potential to be beneficial to dementia care-givers. Findings suggested some improvement for care-givers' depressive symptomology, and reduction in stress or burden levels; however, these findings were mixed and a need for studies of higher methodological quality was highlighted.

Stronger effects have been shown in interventions which have been tailored to the individual (Smits et al., 2007) and this is generally accepted to be an important consideration when designing interventions for dementia care-givers (Elvish et al., 2013; Livingston et al., 2014; Lui & Gallagher-Thompson, 2009; Zarit & Femia, 2008). However, what is less clear is the impact of delivering these interventions in groups versus individual format. Interventions delivered in group format have the potential to increase social support, but they are less easy to adapt to the needs to individual care-givers (Pinquart & Sorensen, 2006b).

A review by Selwood, Johnston, Katona, Lyketos & Livingston (2007) of psychological interventions identified individually delivered tailored therapy as effective in the reduction of burden and distress in dementia care-givers. These effects were seen both in the short-term and maintained over follow-up. However, they found that group therapy was not effective. In contrast Pusey and Richards (2001) investigated the effect of psychosocial interventions by the method of delivery, comparing individually based or group-based interventions. They concluded that the evidence of the effectiveness of both delivery formats was fairly weak due to inherent methodological weaknesses of the included studies, so they could not comment further upon the delivery format.

For psychoeducational interventions there is some evidence that group interventions are more efficacious (Dickinson et al., 2017) and one explanation for this is that they enable the development of social support. However, others have argued that delivering interventions to the individual makes them more accessible as it can be difficult to leave the person with dementia for any length of time and trying to fit in with other group members further exacerbates this difficulty (Livingston et al., 2014).

1.5.4 Summary.

In summary the evidence for CBT interventions in informal care-givers of dementia is mixed. The results are difficult to interpret due to lack of conformity in the way interventions are grouped together in reviews, and due to the small number of studies included in the analyses. However, there is evidence of moderate to large effect sizes for CBT interventions for depression in dementia care-givers (Pinquart & Sorensen, 2006b). With regard to anxiety the evidence is less clear, mainly due to the stark lack of reviews investigating anxiety outcomes. However, there is some evidence of small effect sizes when the interventions include a clear component of cognitive reframing (Vernooij-Dassen et al., 2011). There is also evidence to suggest that including relaxation in the intervention may be important if trying to reduce care-giver anxiety (Cooper et al., 2007).

1.6 Why is it Important to Complete this Review?

The quality of life of both care-givers and those with a dementia diagnosis relies upon how well the care-giver is able to adapt to the needs, and the behavioural concerns of the patient (Liu & Gallagher-Thompson, 2009). Therefore supporting care-givers not only has the potential to improve their quality of life and enable them to provide care for longer, it also ensures they are able to provide optimal care to the person with dementia, thereby ensuring their quality of life is as good as it can be.

The UK Government has outlined the importance of access to appropriate psychological support to enable care-givers to feel able to remain in their care-giving role (DoH, 2015). In line with this the National Institute for Health and Care Excellence (NICE) guidelines state that care-givers of people with dementia who are experiencing psychological distress should be offered psychological therapy and this should include offering CBT (NICE, 2006). However, it is not clear from reviewing the available literature base how strong the evidence is for the treatment of anxiety using CBT in informal care-givers and the paucity of evidence is also highlighted by NICE.

Summarising previous research with regards to the potential of CBT is a challenging task as there has been a tendency to use different categories to group interventions together (Parker et al., 2010; Steffen et al., 2008). Previous reviews which have investigated CBT as a separate category have only included a small number of studies investigating CBT, potentially missing important evidence from eligible but excluded interventions (Vandepitte et al., 2016). CBT interventions in other reviews have been grouped together with other psychotherapies or with general psychoeducation interventions. Grouping them in this way makes it difficult to separate their impact from other models (Czaja et al., 2003). Gaughler et al. (2017) highlighted the need for consistent classification of interventions by the theoretical model underpinning them in order for precise estimations of efficacy to be reached. Additionally, reviews have tended to only focus upon depression outcomes and not upon anxiety (Losada et al., 2015; Parker et al., 2010; Schulz et al., 2002), with only one review being identified which focussed specifically upon anxiety and included a separate category for CBT interventions, and this was completed some time ago (Cooper et al., 2007).

Therefore there is a need to synthesise research investigating ‘like for like’ CBT interventions with dementia care-givers using a shared theoretical framework, which is easily understood, in order for the outcomes to be of most use to decision makers in clinical practice

(Burgio, Stevens, Guy, Roth & Haley, 2003; Gaughler et al., 2017). Additionally there is a particular need to focus upon CBT interventions for anxiety in informal dementia care-givers, especially considering that prevalence of anxiety in dementia care-givers may in fact be greater than that of depression (Cooper et al., 2007).

A previous review of meta-analyses completed looking generally at care-giver interventions concluded that there has been a tendency in the past to exaggerate the impact they have had upon care-giver mental health, and recommended that subsequent meta-analyses be completed with a more careful selection of high quality randomised control trials (RCT) (DoH, 2015 see also Parker et al., 2010). This presents an opportunity to investigate whether the calls for improved methodological quality have been addressed. By focussing solely upon CBT interventions for anxiety in care-givers of people with dementia there is also the opportunity to begin to explore some of the variables or subtypes of care-givers that the intervention is most effective for and in which format (Roth et al., 2015). This has important clinical implications as it will help clinicians feel more confident identifying appropriate interventions for a given care-giver (Steffen et al., 2008).

Finally within the UK there is a government supported drive to increase access to NICE recommended and evidence based psychological therapy through the ‘Improving Access to Psychological Therapies’ (IAPT) programme (DoH, 2008). This means that there is increased familiarity with the CBT model within the NHS and therefore if CBT interventions were able to demonstrate effectiveness upon anxiety in dementia care-givers, implementing them could potentially be carried out by a range of different professionals, and not necessarily remain the responsibility of psychologists or CBT therapists (Livingston et al., 2014). This has the potential to not only increase access, but also to ensure it is delivered in the most cost effective way, in line with the current ‘stepped model of care’ (NICE, 2009).

1.7 Aims

The aims of the current study were twofold. First, to build upon the work of Cooper et al. (2007) and provide an up to date, comprehensive, systematic appraisal and summary of the literature investigating the effectiveness of CBT interventions for anxiety in informal care-givers of people with dementia in comparison to controls. Second, to explore whether care-giver, care-receiver, or intervention characteristics act as moderators upon the effectiveness of CBT. To the best of the present author's knowledge this will be the first review to focus exclusively upon CBT interventions for anxiety in dementia care-givers.

In line with the aims stated in section 1.7 the following research questions were addressed:

1.8 Research Questions

1.8.1 Primary question.

How effective is CBT, in comparison to control conditions, for anxiety in informal care-givers of people with dementia?

1.8.1.1 Exploratory questions.

The exploratory questions fall within three categories: those investigating intervention characteristics, those investigating care-giver characteristics and finally those investigating the impact of care-receiver characteristics.

1.8.1.1.1 Questions investigating intervention characteristics.

Is individual CBT with care-givers of people with dementia more effective at reducing anxiety than group CBT?

Is CBT delivered by a therapist using face to face contact more effective at reducing anxiety in informal care-givers of people with dementia than CBT interventions delivered using technology?

Is CBT which contains a relaxation component more effective than those which do not at reducing anxiety in informal care-givers of people with dementia?

1.8.1.1.2 Questions investigating care-giver characteristics.

Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by care-giver gender?

Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by relationship to care-receiver?

Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by care-givers’ anxiety levels at baseline?

1.8.1.1.3 Questions investigating care-receiver characteristics.

Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by care-receiver dementia diagnosis?

1.8.2 Secondary Question.

How effective is CBT, in comparison to control conditions, for depression in informal care-givers of people with dementia?

Chapter Two: Method

2.1 Introduction to Method Section

The methods used to address the research questions are outlined in the following chapter along with the rationale for the techniques selected. The search protocol utilised was guided by the Cochrane Collaboration Handbook (Higgins & Green, 2011) and each section of the protocol is described within this chapter. This includes the following; criteria for eligibility, strategies used for searching the literature, datum collection strategies and finally this chapter will conclude with a description of the methodology selected to facilitate the quantitative synthesis of extracted data.

2.2. Eligibility Criteria

The eligibility criteria outlines the study methodology, the population of interest and the intervention design. In order to be included in this meta-analysis both the title and abstract of potential studies were screened by the primary author. Full text articles were reviewed of all studies appearing relevant on the basis of their title and/or abstract. This was completed by the primary researcher and an independent research assistant. Articles were assessed against the criteria outlined below and inter-rater reliability was assessed using a Kappa statistic (Altman, 1991). Any disagreements about study inclusion were decided via discussion. Reasons for exclusion at the full text stage were recorded and are outlined in section 3.2.

2.2.1 Study methodologies.

Previous systematic reviews within the care-giver literature have criticised the lack of methodological quality (Burgio et al., 2001; Elvish et al., 2013, Gaughler et al., 2017). Therefore an initial decision was made to restrict study inclusion to only those studies which employed a randomised controlled methodology as this approach is generally associated with improved methodological quality (Chien et al., 2011; Higgins & Green, 2011). However, it was decided to expand this to include non-randomised controlled trials to expand the number of potentially relevant studies meeting inclusion criteria as it was expected that study numbers would be low based on previous reviews (Pinquart & Sorensen, 2006b). Additionally non-randomised controlled trials have the potential to increase the external validity of findings (Efthimiou et al., 2016; Rothwell, 2005).

Unlike past reviews (Pinquart & Sorensen, 2006b) the present synthesis did not restrict the nature of the control arm. Whilst there is an argument that comparisons with minimally active interventions can help reduce the likelihood of intervention effects being under-estimated, more recent reviews have called for comparisons with equally active control interventions in order to begin to understand how an intervention compares to other approaches (Gilhooly et al., 2016). Therefore within this meta-analysis the control arm included both non-active controls such as waiting list, treatment as usual and low level support and active control arms where an alternative intervention was provided.

Based upon guidance from the Cochrane Handbook (Higgins & Green, 2011) studies were only classified as a randomised controlled trial if an explicit statement was made by the author regarding the random allocation procedure employed.

2.2.2 Participants.

Participants were those who identified themselves as being in an informal care-giving role for someone with a formal dementia diagnosis. This could include partners, children, other family or friends who were primary care-givers for someone with any dementia diagnosis, including a diagnosis of mild cognitive impairment (MCI). The diagnosis must have been made by a qualified clinician or via the use of a standardised diagnostic assessment. The individuals receiving care were required to be living in the community and not within a professional care home environment.

If participants were taking psychotropic medication then they need to have been stable on this prior to the start of the intervention to ensure that the impact of the intervention can be distinguished.

No further restrictions were applied with regards to care-giver characteristics to ensure a broad spectrum of participants which will increase the generalisability of findings (Higgins & Green, 2011).

2.2.3 Intervention.

Only studies investigating interventions based upon cognitive behavioural therapy (CBT) were included in this review (Beck, 2011). Cognitive therapy was defined as "attempts to reduce dysfunctional emotions and behaviour by altering individual appraisals and thinking patterns" (Brewin, 1996, p. 34). Behavioural therapy was defined as "direct attempts to reduce dysfunctional emotions and behaviour by altering behaviour" (Brewin, 1996, p. 34). CBT is a talking therapy which is time-limited and structured. It uses techniques derived from cognitive and behavioural models of human behaviour to alleviate psychological distress (Laidlaw et al., 2003). CBT interventions can involve a range of elements. These can include behaviour activation, activity scheduling, cognitive restructuring through thought identification, monitoring and challenging, graded exposure tasks, emotional management strategies including relaxation, and problem solving skills training (Gallagher-Thompson & Steffen, 1994). Studies using purely cognitive or purely behavioural interventions alone were not included, neither were interventions aimed solely at one of the other elements of CBT e.g. solely problem solving or relaxation. Interventions where CBT theory and principles were used to teach behavioural management techniques, for example strategies to manage care-giving, were included providing the links to both cognitive and behavioural techniques were made explicit.

Studies which included another treatment component alongside CBT in the treatment of care-giver psychological morbidity, for example medication or respite care, were excluded as the effect of the CBT intervention could not be isolated.

No restriction was placed upon the length of the intervention or the delivery format as one of the aims of the present study was to gain further understanding of the impact that these factors may have upon the outcomes of a CBT intervention.

2.2.4 Outcome measures.

Based upon findings of a previous systematic review of care-giver interventions (Cooper et al., 2007) primary research was included if it reported the effect that the intervention had upon care-giver anxiety levels using a valid quantitative assessment tool. Measurement of care-giver outcomes were considered valid if they were based upon a standardised assessment such as a questionnaire or interview which has been assessed in terms of reliability or validity. An example of this would be the Beck Anxiety Inventory (BAI; Beck & Steer. 1993) or the Hospital Anxiety and Depression Scale (HADS; Zigmund & Snaith, 1983) both of which have been widely used and have good reliability and validity. Studies that did not include a validated measure of care-giver anxiety were excluded.

The secondary outcomes considered in this review were measures of depression. This is one of the most frequently cited care-giver outcome measures (Cooper et al., 2007) and therefore was considered to be of interest to this research. Again this outcome measure needed to be based upon standardised assessment tool, for example the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996) or the Center for Epidemiologic Studies-Depression scale (CES-D; Radloff, 1977) in order to be included in this review.

2.2.5 Summary of the eligibility criteria.

2.2.5.1 Inclusion criteria.

1. Studies must assess the impact of an intervention upon informal care-givers, including family members, spouses, children or friends,
2. Care-givers must be caring for someone with a clinician made diagnosis, or one that has been established using standardised assessment tools, of dementia or mild cognitive impairment.
3. Care-receivers must be living in the community.
4. The intervention must incorporate both behavioural and cognitive elements of CBT.
5. The studies must include an appropriate control arm which can include inactive control groups or comparison with another active intervention.
6. The participants must be randomly assigned to either the intervention or the control group
7. Studies must provide a quantitative outcome measure for participant anxiety based upon a validated and standardised anxiety measure
8. Contain data allowing for effect size calculations
9. Findings available in English language

2.2.5.2 Exclusion criteria.

The following exclusion criteria were applied:

1. Single case series, qualitative studies, meta-analysis and review articles.
2. Interventions with no reference to a CBT driven theory or only containing one element of CBT for example only behavioural activation.
3. Studies where the outcome of the CBT intervention could not be assessed in separation from other treatments. For example, multi-modal treatment packages or the administration of psychotropic medication.

4. Any study which was based on the same dataset as an already included study was excluded to ensure no datum was counted twice.

No restrictions were set with regard to date of publication or research completion due to the novelty of this review. An effort was made to include studies which had not been published in an attempt to avoid publication bias.

2.3 Search Strategy

2.3.1 Electronic searches.

A comprehensive search of key international bibliographic databases, EMBASE, MEDLINE, and PSYCHINFO and Scopus was completed between October 2016 and January 2017 to identify relevant literature with the last search date being the 20th January 2017 (see Appendix A for the sources and dates of initial searches completed). Databases were searched individually rather than via a main host such as EBSCO as searching using a main host can diminish the detection rate due to the different search terms and subject headings used by each database (Higgins & Green, 2008). Appendix B shows an example of the search strategy used for MEDLINE.

Searches were also completed using the subject specific databases of the Dementia Evidence Database via http://toolkit.modem-dementia.org.uk/ and the Rosalyn Carter care-giver intervention database via http://www.rosalynncarter.org/caregiver_intervention_database/. The former is a database designed for a range of people, both professional and family members, to enable them to search for research studies on interventions for both people with dementia and their care-givers. The latter aims to increase the use of theoretically and scientifically driven interventions with care-givers as a way of helping to improve care-givers' health and wellbeing, and provides a database detailing information about evidence based interventions.

Both these databases were reviewed to identify CBT interventions and their associated research trials.

In order to identify research that investigated the effectiveness of CBT with informal care-givers of people with dementia, a number of key terms were combined that described the target intervention and population (See Table 1 for search terms used). Although this review is interested in studies that utilised interventions driven by CBT, the intervention search terms were expansive as researchers typically use a variety of names for such interventions. No search terms were included in relation to the study design or methodology employed in order to ensure no relevant research was excluded. Truncation was used to ensure that both U.K. and U.S. variant word endings were identified. Following the initial search titles and abstracts were screened by the author and article which were clearly not relevant were excluded.

2.3.2 Ancestry method.

Sources which frequently publish intervention studies with care-givers were identified by checking reference lists of existing systematic reviews. These journals were then hand searched. Journals searched in this way included *The Gerontologist, Clinical Gerontologist, Psychology and Aging* and the *Journals of Gerontology*. This method of searching is known as the ancestry method and also included reviewing the references of previous systematic reviews for any relevant research trials (Cooke et al., 2001; Cooper et al., 2007; Dickinson et al., 2017; Elvish et al., 2013; Pinquart & Sorensen, 2006b; Vernooij-Dassen et al., 2011). The reference lists of these reviews were cross referenced with the included and excluded studies identified by the current review to ensure that no primary research had been missed. In addition this ensured that there was overlap between the studies included in the present review and those included in previous reviews, allowing for more meaningful comparison

(Gaughler, Westra & Kane, 2016; Pieper, Antoine, Mathes, Neugebauer & Eikermann, 2014).

2.3.3 Grey literature search.

Meta-analytic research is often criticised for introducing bias due to only reviewing research which has been published (Rosenthal, 1979). Research which is published is more likely to comprise those studies which have identified significant findings; these studies are likely to have larger effect sizes than comparable studies which go unpublished (McLeod & Weisz, 2004) and this can lead to an overestimation of effects in meta-analytic reviews. Therefore this review employed various strategies to identify unpublished or “grey” literature.

In the first instance a search was conducted online via http://www.opengrey.eu/. Open grey is a database which includes research from doctoral dissertations and poster presentations from conferences. In addition the Cochrane Library, which includes The Cochrane Database of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA Database) and The Database of Abstracts of Reviews of Effects (DARE) was searched alongside the specific trial register of the Cochrane Dementia and Cognitive Improvement Group. These databases were used to identify any registered trials which may be ongoing or unpublished. A request was made to authors of potentially relevant trials for a progress update and any relevant data. Dissertations and theses were searched via ProQuest Dissertation & Theses A&I. This database provides a comprehensive compilation of dissertations and theses conducted from around the world.

Formal letters were sent via email to authors who were identified as having published widely within the care-giver intervention literature asking them if they were aware of any unpublished studies. In addition any author who was contacted for further information about their study was also asked if they were aware of any other unpublished research (see Appendix C for a list of contacted authors and email correspondence).

2.3.4 Web searching.

A further search was made using the general search engine, Google Scholar, to retrieve any additional relevant studies.

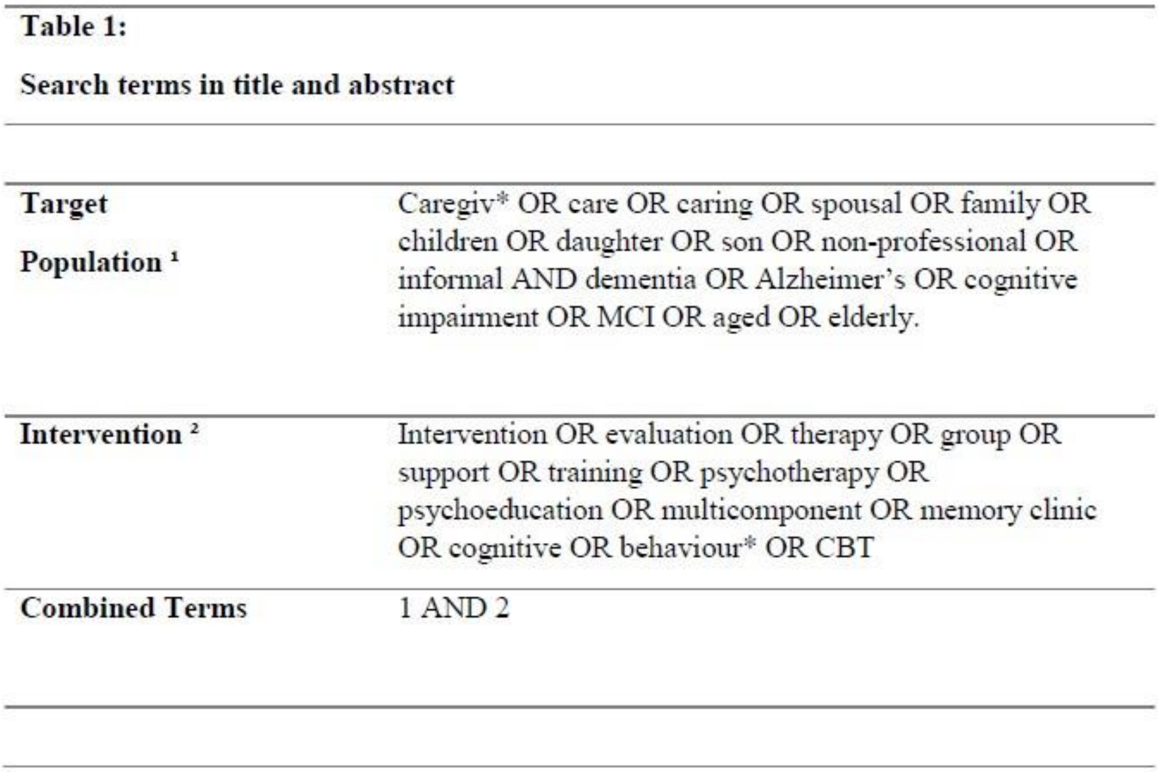


Table 1:

Search terms in title and abstract

Target Population [1]	Caregiv* OR care OR caring OR spousal OR family OR children OR daughter OR son OR non-professional OR informal AND dementia OR Alzheimer's OR cognitive impairment OR MCI OR aged OR elderly.
Intervention [2]	Intervention OR evaluation OR therapy OR group OR support OR training OR psychotherapy OR psychoeducation OR multicomponent OR memory clinic OR cognitive OR behaviour* OR CBT
Combined Terms	1 AND 2

2.4 Data Collection

2.4.1 Screening method.

Prior to screening the search results were merged using EndNote software (version X7) and all duplicate records were removed. The titles and abstracts of the remaining literature were examined and studies which were evidently irrelevant were removed. At this stage the primary researcher ensured that no potentially relevant studies were removed by being over-inclusive. This meant that any study which did not provide enough information within the abstract about the intervention, participants or design to immediately allow for conclusive exclusion were included.

The full text articles for all studies deemed to be potentially relevant were retrieved. The primary researcher and a collaborator then applied the eligibility criteria to all full text reports independently. The collaborator was a clinical psychologist who qualified from the University of East Anglia in 2016. This process was assessed for inter-rater reliability through the use of the Kappa statistic (Altman, 1991). Any disagreements were discussed until agreement could be reached and where required study authors were contacted for further information. Before proceeding to datum collection a final decision was made about study inclusion. Reasons for the exclusion of articles at full text stage are reported in Chapter Three.

Neither the collaborator nor the primary researcher had any association or prior connections with any of the included studies, authors, or their affiliated institutions. In addition the collaborator did not have any prior interest in the literature under review. This was felt to be beneficial as familiarity has been demonstrated to have the potential to introduce bias when judging study relevance (Cooper & Ribble, 1989).

2.4.2 Data extraction.

Duplication of results within a meta-analysis can introduce significant bias (Tramer, Reynolds, Moore & McQuay, 1997). Therefore the present meta-analysis linked multiple reports from the same studies together to ensure that the datum was only entered once. If this was not clear from the information presented in the report then authors were contacted to clarify this (Higgins & Green, 2011). Data were then extracted by the primary researcher using a pre-designed datum extraction form (see Appendix D). The data extraction form was developed using the recommendations outlined in the DECiMAL guide (Pedder, Sarri, Keeney, Nunes & Dias, 2016). A sample of the data extraction forms were checked by the collaborator to ensure accuracy and completeness. Ideally both the primary researcher and the collaborator would have extracted the datum independently as this has been shown to reduce errors (Busceni, Hartling, Vandermeer, Tjosvold & Klassen, 2006), however, due to time constraints this was not possible and therefore data extraction was completed solely by the primary researcher.

Study authors were contacted via email when data were missing in an attempt to obtain said data (see Appendix E for email correspondence). Each study was assigned a unique identification number. Key data extracted from each included study are presented within a summary table in Chapter Three.

2.4.2.1 Non effect size data.

The data extracted included information required to facilitate quality appraisal and to investigate between study heterogeneity and data required for effect size calculations. The non-effect size data included details about the design, including year of publication, delivery method, and length and duration of intervention. Characteristics of both care givers and care receivers were extracted where available as these could help to explain between study heterogeneity (Pedder et al., 2016). This included details about both care recipients' and care givers' age, gender and relationship to each other, their ethnicity and the length and amount of time spent care giving. Information was also extracted for care-recipients' dementia diagnosis, including method of diagnostic assessment and the type of dementia. In order to be accepted the classification terms used needed to be those utilised within the Diagnostic and Statistical Manual of Mental Disorders – 5th addition (American Psychiatric Association, 2013).

2.4.2.2 Effect size data.

Where possible means and standard deviations were extracted directly from the research papers, or were requested from the study author via email correspondence. If this was not possible then data was extracted to allow for the mean and standard deviations to be calculated by the primary researcher. Where the standard error was reported this was converted into the standard deviation. The direction of the effect was recorded to ensure this was considered when data were entered into the meta-analysis.

2.5 Data Analysis

2.5.1 Quality assessment framework.

Causal inferences drawn from meta-analyses can be undermined by flaws in the primary studies included in the data synthesis. Such flaws can relate to the design, the procedures employed, the methods of analysis, and choice of reporting of the primary studies (Wood et al., 2008). A review of published meta-analyses was completed in 2009 by an expert group created by the UK professional association PSI (Statisticians in the Pharmaceutical Industry). The results outlined the need to improve the quality assessment of primary papers being included in data synthesis (Lane et al., 2013). Following this a new tool was created to assess the quality of meta-analyses as the existing ones did not allow for detailed evaluation of the statistical methods used. The tool designed by Higgins et al. (2013) was consulted with regards to key areas that should be taken into account when completing a meta-analysis in order to ensure that it is of high quality, in particular that it contains a section aimed at evaluating how a meta-analysis has assessed the risk of bias in included studies.

There are many tools and methods available for the assessment of risk of bias, including both checklists and scales which give each study a score (see Zeng et al., 2015 for a review). However, the Cochrane Collaboration explicitly discourages the use of tools based on a scale as they are not supported by empirical evidence or on a theoretical basis as they have been found to be inconsistent (Greenland & O’Rourhe, 2001). The studies reviewed in this meta-analysis were assessed for risk of bias following pre-defined guidelines outlined for Cochrane reviews using the Cochrane Collaboration’s tool (Higgins & Green, 2011). This tool is widely accepted and was recommended as the best tool available for quality assessment of RCTs in a recent review (Zeng et al., 2015).

The Cochrane Collaboration's tool (Higgins & Green, 2011) was applied to all included studies and allowed for a judgement to be made as to whether the study was considered to show *low risk of bias*, *high risk of bias* or *unclear risk of bias* (See Appendix F for a copy of the tool). In order to reach a judgement six domains of bias were considered for each study: selection bias, performance bias, attrition bias, detection bias, reporting bias and other bias. These domains cover (a) *random sequence generation*, (b) *allocation concealment*, (c) *blinding of participants and research personnel*, (d) *blinding of outcome assessment*, (e) *dealing with incomplete datum*, (f) *issues with selective reporting* and (g) *other sources of bias.*

Within psychological research it is often impossible for participants or personnel to be blind to the intervention; this has led some authors to exclude this from their assessment of bias. However, whilst blinding may not always be feasible, and whilst it would be unfair to consider a study as poor quality due to a lack of blinding, it is still an important consideration as it is possible that outcomes have been influenced by a participants knowledge of the intervention received and therefore the risk of bias has increased (Higgins et al., 2011b). Additionally it may be possible to blind participants if an active comparator is being utilised. Therefore it was still considered in this review but the main focus was upon blinding of outcome assessors which is something that can be achieved within intervention research and which can go some way to controlling for detection bias (Chan & Altman, 2005).

With regards to other sources of bias consideration was given to key factors identified in previous reviews (Elvish et al., 2012; Zarit & Femia, 2008) alongside the items highlighted in the Cochrane Collaboration Risk of Bias Tool (Higgins, Altman & Sterne, 2011a). These factors were used to create a series of questions which were felt pertinent to the assessment of other potential sources of bias (see Appendix G for a copy of these questions).

The primary researcher conducted the assessment of bias for each of the included studies. Each study was classified as either *low risk*, *high risk* or *unclear risk*. For the most part the information was gathered from the available trial report, however, for some studies this information was not available and so linked protocols and published comments about the trial were also considered in an attempt to gather this information. The likely impact of the risk of bias upon the results of the data synthesis were explored via sensitivity analysis.

2.5.3 Measures of treatment effect.

Primary outcome measures were validated or standardised measures of care-giver anxiety, for example Beck Anxiety Inventory (Beck & Steer, 1993). Secondary outcome of interest was validated or standardised measures of care-giver depression. The validity of the measurement scales used was assessed by the primary researcher. Anxiety is frequently measured using a series of questions, with each given an individual score, which is then summed to give a total score. These type of measurements are most commonly treated as continuous and reported as such within studies (Field & Hole, 2003). Therefore the present meta-analysis treated self-report measure data as continuous data. The outcomes used to assess care-giver anxiety were not consistent across studies and were based upon different psychometric scales. Therefore the standardised mean difference (SMD) was used to express the treatment effect (Borenstein et al., 2009; Lipsey & Wilson, 2001).

A priori it was agreed that where a study included more than one measure of anxiety only the primary measurement would be included to ensure that for each study only one treatment effect was calculated (Card, 2012). If the authors did not specify a primary measure then the intention was to choose the measure based upon the superiority of its psychometric properties. However, only one study included more than one measure of anxiety and in this case the primary measurement, as reported by the study author, was a clinician reported outcome and the secondary measurement was a self-report measure. As all other included studies were based on self-report outcomes it was decided that the self-report measure be included for the purposes of homogeneity (Field, 2013).

For each study the SMD was used to estimate the difference between intervention and the control arm and was calculated from outcomes assessed immediately post-intervention. “The standardised mean difference expresses the size of the intervention effect in each study relative to the variability observed in that study” (Higgins & Green, 2011 section 9.2.3.2). The mean post-intervention score of the control group was subtracted from the mean post-intervention score of the intervention group and the outcome was divided by the pooled standard deviation: this provided a measure known as Cohen’s *d* (Cohen, 1988). A more accurate estimation of the standard deviation is achieved by pooling the two estimates (Borenstein et al., 2009). As Cohen’s *d* can overestimate the absolute value of effect sizes in studies with small sample size, a common methodological issue in care-giver intervention research (Gallagher-Thompson & Coon, 2007), it was converted to Hedge’s *g*. Hedge’s *g* can adjust for bias resulting from small sample size (Hedges & Olkin, 1985) and the conversion is completed using the correction factor *J* (Borenstein et al., 2009). With regards to what constitutes a large or a small effect size Cohen (1988, 1992) gives some widely accepted suggestions and these were used to interpret the magnitude of Hedges *g:* “small” (0.2), “medium” (0.5), and “large” (0.8). For each study the standard error and the variance was also calculated.

2.5.4 Unit of analysis issues.

Where studies included multiple intervention groups compared to a control condition, the effect size was only calculated for the intervention that met the active arm inclusion criteria. For example, if a study compared CBT and another type of therapy to a control group only the CBT intervention was considered. However, where studies included two different types of CBT intervention in comparison to a control group a composite variable was computed which was the mean of intervention A versus control and B versus control (Borenstein et al., 2009; Scammacca, Roberts & Stuebing, 2014).

It is common for studies to contain a mixture of change-from-baseline and final value scores. However, some have criticised the use of change from baseline scores as they can be more likely to produce significant results (Fu & Holmer, 2015). Final values and change from baseline scores should not be combined as SMD (Higgins & Green, 2011): additionally the analysis of change from baseline scores can be problematic when studies report baseline and final measurements for different numbers of participants due to dropouts. Therefore where studies reported both change from baseline and final values only the final values were extracted.

2.5.5 Dealing with missing data.

The authors of any studies with missing outcome data were contacted, via email, as a first step, to request the full data. If the data remained unavailable then as discussed in the inclusion criteria, only studies which provided the necessary data to allow for effect size calculations were included in this review. The selective reporting of outcomes by any study is discussed within the review of study quality in Chapter 3. Where only standard errors (SEs) were reported, standard deviations (SDs) were calculated.

In addition this meta-analysis attempted to review the techniques used by individual study authors to deal with missing data during analysis. Any impact upon the outcomes that the missing data may have had were discussed within the assessment of risk of bias (Borenstein et al., 2009).

2.6 Data Synthesis

The Comprehensive Meta-Analysis (CMA) software, Version 3 was employed to analyse intervention effects and moderating variables. This software was chosen as it is user friendly and permits the completion of the planned analytical procedures.

2.6.1 Model.

There is a large body of evidence to suggest that real-world data collected within the social sciences are likely to be variable from study to study due to a mix of participants and the way interventions are implemented (Hunter & Schmidt, 2000; National Research Council, 1992) and that therefore there may be different effect sizes underlying each study. Due to this anticipated heterogeneity it was decided that a random-effects model would be most appropriate (Borenstein et al., 2009). The use of a random effects model also allows for inferences to be made which extend beyond the studies included in the meta-analysis as they are unconditional, allowing for generalisation of results (DeCoster, 2009; Field, 2013).

Separate random-effects meta-analyses were completed for anxiety and depression outcome measures. This review adopted a random-effects model using the DerSimonian and Laird method (1986). This approach assumes that variation observed in standard deviations is not due to variability among study populations, or the reliability of outcome measures used, but is rather due to differences in measurement scales (Borenstein et al., 2009).

A further random effects meta-analysis, following the process outlined above, was completed using follow up data for both anxiety and depression outcomes. Where studies reported more than one follow up time point the data for the longest follow was used.

2.6.2 Assessment of heterogeneity.

Each of the studies within the review were anticipated to have clinical and methodological diversity and therefore considerable heterogeneity. Factors that could be influential within participants, interventions and outcomes will be considered. Potential sources of heterogeneity included the delivery method of CBT (individual or group; therapist or via computer), the type of dementia diagnosis of the care-receiver, the relationships of the care-giver to the care-receiver, the gender of the care-giver and the anxiety symptom severity of care-givers at baseline.

Statistical heterogeneity was assessed using the I^2 statistic. This statistic allows researchers to assess the percentage of variability that is not due to chance and is rather due to heterogeneity and then calculate the strength of evidence for heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). The I^2 statistic was chosen as it allows for an estimation of the magnitude of the effect of heterogeneity, which other statistics such as Cochran's Q do not allow for (Borenstein et al., 2009). Additionally, the I^2 statistic is not dependent upon the number of studies included in the meta-analysis (Higgins et al., 2003). Some cut offs have been tentatively suggested for I^2 by Higgins et al. (2003). They propose that studies with an I^2 value around 50% are likely to represent moderate heterogeneity, studies in the order of 25% are low and 75% may be considered high (Borenstein et al., 2009).

2.6.3 Subgroup analysis.

The following subgroup analyses were planned to investigate potential causes of heterogeneity relating to intervention, care-giver, and care-receiver characteristics.

2.6.3.1 Intervention.

A subgroup analysis was completed to examine difference between individual and group delivered CBT. It was hoped that it would also be possible to explore any potential heterogeneity caused by delivery format: therapist versus technology (internet/computer only). However, this was not deemed appropriate as there was insufficient data to allow for meaningful comparison.

2.6.3.2 Care-giver characteristics

It was hoped that a subgroup analysis could be completed to examine the difference between male and female care-givers response to CBT for anxiety. However, no studies restricted participation to male care-givers only, and no studies reported data by gender subgroup. Therefore a simple meta-regression analysis was completed investigating the percentage of female participants as a moderator.

Meta-regression was also planned to investigate the impact of care-giver relationship to care-receiver and % baseline anxiety scores above cut off. This was completed for the care-giver relationship to care-receiver using the percentage of spousal care-givers as the moderator. However, the majority of studies did not report information required for the additional planned analysis. The Cochrane review does not recommend meta-regression where there are fewer than 10 studies (Deeks, Higgins & Altman, 2011). Therefore in practice there was insufficient data available to allow for baseline anxiety levels to be investigated.

2.6.3.3 Care-receiver characteristics.

A final meta-regression was planned to investigate the impact of care-receiver diagnosis upon anxiety outcomes for care-givers. As reported above this was not possible in practice due to the limited number of studies reporting this information (Deeks et al., 2011).

2.6.4 Sensitivity analysis.

Throughout the analysis a number of decisions and assumptions were made which are likely to have influenced the outcome. Whilst some decisions were straightforward others were less so due to lack of required information or consensus about statistical analysis. In order to assess how robust the findings were to these decisions, sensitivity analyses were undertaken (Higgins & Thompson, 2002). Completing such an analysis allows for conclusions to be accepted with a greater degree of certainty (Field, 2013). During the review process any issues which cast doubt upon the robustness of results and therefore may warrant sensitivity analysis, for example, the impact of control condition, were noted and a sensitivity analysis performed.

2.6.5 Estimating publication bias.

There is evidence to suggest that studies with greater effect sizes are more likely to be published and despite efforts to the contrary studies which have been published are more likely to be included in meta-analyses (Borenstein et al., 2009). In addition, alongside the traditional notion of publication bias restricting the review to English language studies and the accessibility of research can further reduce the representativeness of the included studies. If the studies included in a meta-analysis do not reflect all the available research but rather represent a biased sample then the outcomes of the data synthesis will reflect this bias (Rothstein, Sutton & Borenstein, 2005). Therefore examination of potential publication bias should be considered essential.

In order to explore potential publication bias funnel plots plotting effect size against sample size, as represented by the standard error, were produced (Light & Pillermer, 1984; Sterne & Egger, 2001). As a first step in assessing publication bias the symmetry of the funnel plot can be used as a visual indication, with asymmetrical skewed plots being suggestive of potential publication bias (Macaskill, Walter & Irwig, 2001). Larger studies tend to cluster around the mean effect size around the top of the graph. In the absence of bias smaller studies will appear towards the bottom of the graph with a wider symmetrical spread, overall resembling a funnel. Given that it is smaller studies which are less likely to be published, and if published they are likely to have larger effects, asymmetry of the funnel plot tends to be on either the left or right side at the bottom (Borenstein, 2005; Duval & Tweedie, 2000).

Although funnel plots provide a useful first step in assessing potential publication they are open to different interpretation depending on the person assessing them as they rely on visual examination (Egger, Smith, Schneider & Minder, 1997). Therefore in the presence of potential publication bias, Egger's test of the intercept was employed to provide a more objective numerical assessment as recommended within the Cochrane handbook (Egger et al., 1997; Higgins & Green, 2011). If the test result is significant then it suggests the presence of significant publication bias. As this test is said to have low power the authors recommend using $p<0.1$ as evidence of asymmetry (Egger et al., 1997).

It is possible to correct for publication bias using methods such as the trim and fill method (Duval & Tweddie, 2000). In this method the funnel plot is "trimmed" and the smaller studies, which are assumed to be causing the asymmetry are removed. Following this the estimated number of missing studies are added or "filled" to the negative side of the funnel plot and a new estimate of population effect size is calculated (Field, 2013). However, this technique can lead to over correction due to the assumptions it makes about the nature of the missing datum (Vevea & Woods, 2005). The trim and fill technique also makes the assumption that publication bias is the only explanation for the asymmetry seen in the funnel plot, it may also be that the effect size is larger in the smaller studies for other reasons which are entirely unrelated (Rothstein et al., 2005). Whilst there are other more sophisticated methods available, such as Vevea and Woods (2005) method using a weight function, their use has only been demonstrated to be effective in very large meta-analyses (Field, 2013). Therefore a decision was made not to correct for detected publication bias.

2.7 Chapter Summary

This chapter has provided detail of the methodological stages that were undertaken prior to data-synthesis and analysis. The first stage involved the development of the eligibility criteria, from this the search strategies for identifying potentially relevant studies for review could be created, and this makes up the second stage. The third stage involved following a step-wise screening process in order to select eligible studies for inclusion in the analysis. The data extraction process is described as the fourth stage. Finally, methodological considerations of data analyses are presented. This includes the process for assessing risk of bias, decisions about measures of treatment effects and processes for investigation heterogeneity via sensitivity and subgroup analyses.

Chapter Three: Results

3.1 Chapter Outline

This chapter provides a detailed review of the data collection process and the selection of studies and data analysis procedures. It begins with an overview of the process of study identification, screening and exclusion of articles. This first section includes the presentation of a PRISMA flow diagram (Moher, Liberati, Tetzlaff, & Altman, 2009). Included studies entered into the data synthesis are summarised, and presented within a table detailing their key characteristics. Those studies which were excluded from the review are also listed. The following section presents the risk of bias assessments; these are summarised descriptively, figuratively and graphically. Meta-analytic results for anxiety and depression outcomes for CBT interventions are reported and the outcomes of additionally exploratory analysis are discussed in line with the research questions. An exploration of publication bias follows. Finally, the chapter concludes with a summary of main findings and a brief discussion of these.

3.2 Search Results

The search retrieved a total of 6450 articles which were screened during the study selection process. This included 4718 that were identified using electronic searches and an additional 1732 that were retrieved through other sources such as hand searching journals, Google Scholar, sources of grey literature and contact with key authors. The authors who were contacted are listed in Appendix C.

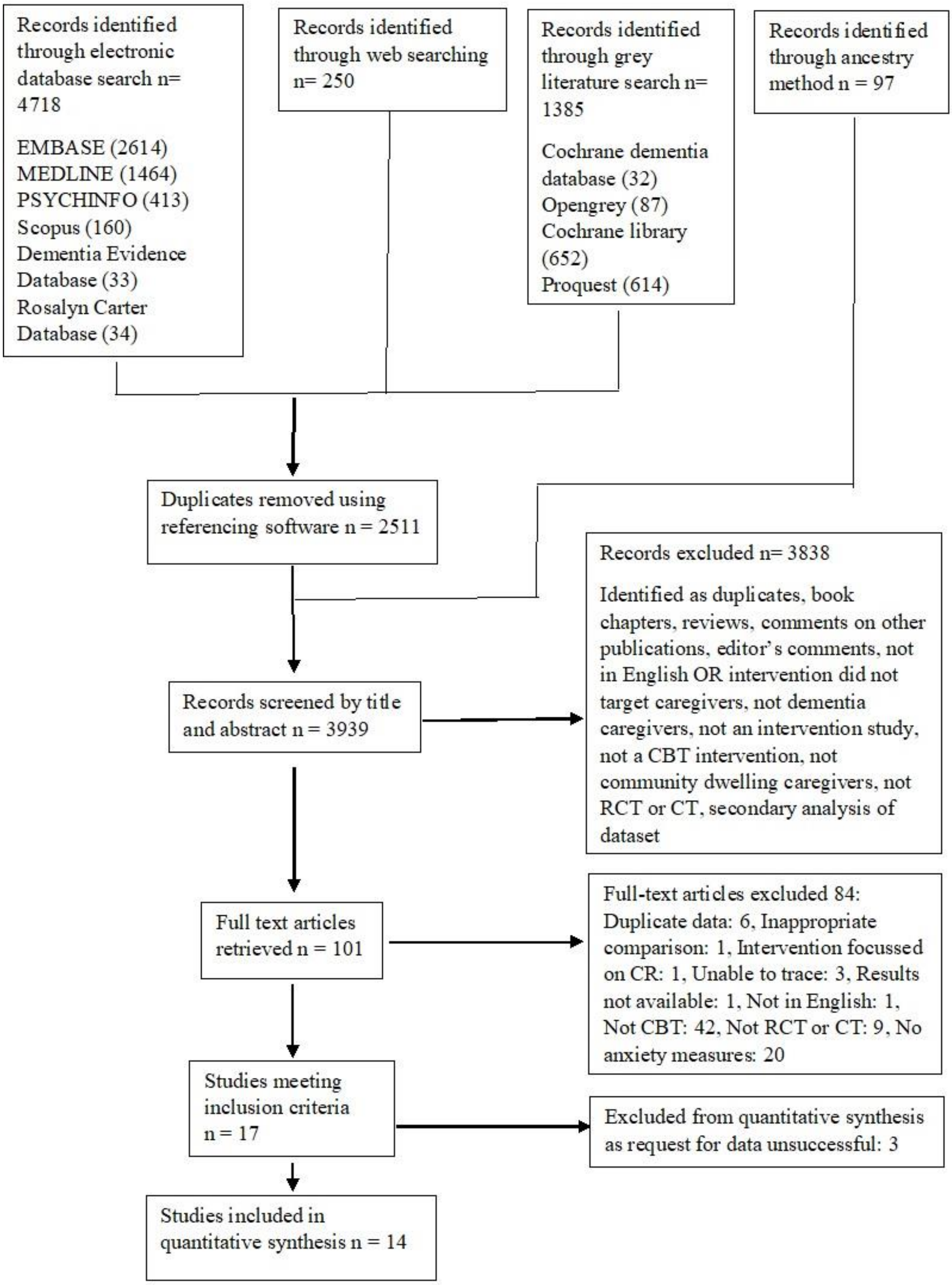
Following an initial screening of titles and abstracts 6349 articles were removed. The studies which were excluded at this stage were identified as duplicates, or did not use a control trial methodology or were unrelated to interventions for informal dementia care-givers or employed an intervention evidently not based on CBT. Records which corresponded to book chapters, editorials, or responses to other publications, as well as those publications drawing on secondary analysis were also removed at this stage. Studies were screened for duplication using Endnote software as well as hand searching as the format of some references varied depending on publication source. The large number of studies removed at this stage reflects the over inclusive search strategy employed.

One hundred and one studies were assessed in full and reviewed against the eligibility criteria. At this stage a further 84 studies were removed, all studies which were reviewed at the full text stage and excluded are presented in Appendix H in the Characteristics of Excluded Studies table alongside the reason for exclusion. Six studies were removed as they were based on duplicate data and were linked to the primary study, one study did not allow for the effects of the CBT intervention to be isolated, and a further study focussed the intervention upon the care receiver with the care-giver in attendance. Five protocols were identified during the search process and were deemed relevant, however, the contact details for two of these studies could not be found (Lancer, 2006; Topcu, Boucault, Negovanska & Hergueta, 2011). The authors of the remaining three protocols were contacted to request an update and relevant data: one did not reply (Charlesworth, 2000); one author replied to say the study had not been published and did not provide any further details (Gossink et al., 2016). The final author replied and sent through the full publication, however, this was not in English (Facal et al., 2009). Therefore all five protocols were excluded.

The remaining 71 studies were excluded as they did not satisfy the eligibility criteria. These studies were excluded on the following bases: 42 studies employed an intervention which did not use both cognitive and behavioural evidence based principles of CBT, 9 studies did not employ an RCT or CT design, and finally 20 studies did not include a validated and reliable measure of anxiety. Many of the studies that did not include anxiety outcomes were part of the Resources for Enhancing Alzheimer’s Caregiver Health (REACH) project and various authors who were part of the project were contacted to request anxiety outcomes, however, no one responded with this information.

In total 17 studies met the inclusion criteria for the study. However, three of these studies (Martin-Carrasco, Dominguez-Panchon, Gonzalez-Fraile, Munoz-Hermoso & Montorio, 2014; Rabinowitz et al., 2006; Villareal-Reyna, Salazar-Gonzalez, Cruz-Quevedo, Carrilo-Cervantes & Dimmitt-Champion, 2014) could not be included in the meta-analysis as the authors did not respond to requests for data necessary for effect size calculation. Therefore a total of 14 studies met the eligibility criteria and were included within the present review. The study selection process outlined above, along with reasons for study exclusion, is presented in a PRISMA flow diagram (Moher et al., 2009) shown in Figure 2. The agreement between the primary researcher and the collaborator regarding study inclusion was considered good (91.09%; Kappa 0.70; 95% CI 0.53 – 0.89) (See Appendix I for calculation).

Figure 2: PRISMA Flow diagram outlining study selection process



3.3 Study Characteristics

The characteristics of the studies are summarised in the sections below and in the Characteristics of Included Studies Tables. Table 2 shows the methods utilised and the participant characteristics of included studies. Table 3 shows details of the interventions employed and Table 4 shows details of the study outcomes.

3.3.1 Included studies.

A total of 14 studies were included within the review after meeting eligibility criteria. The included studies involved a total of 1701 participants, 922 assigned to CBT interventions and 779 in control conditions.

3.3.1.1 Types of studies.

The majority of studies employed a randomised parallel group design and all studies were published in peer reviewed journals in English. Two studies (Losada et al., 2015: Passoni et al., 2014) used a multi-arm trial design. For the purposes of this review only the CBT arm and the control arm were included in the review; this is discussed further below. Just over half the included studies were conducted since 2005 and therefore would not have been eligible for inclusion in the review completed by Cooper et al. (2007).

3.3.1.1.1 Sample sizes.

The smallest sample size was N=27 (Aboulafia-Brakha, Suchecki, Gouveia-Paulino, Nitrini & Ptak, 2014) ranging to the largest sample size N=299 (Beauchamp et al., 2005). Within this range seven studies had N>100 participants (Blom, Zarit, Groot-Zwaaftink, Cuijpers & Pot, 2015; Burgio et al., 2003; Hébert et al., 2003; Karagoizi et al., 2014, Livingston et al., 2014; Losada et al., 2015; Martin-Carrasco et al., 2009) and the remaining four studies had N<100 participants (Akkerman & Ostwald, 2004; Chang, 1999; Gendron et al., 1996; Gonyea, Lopez & Velasquez, 2014; Passoni et el., 2014).

3.3.1.1.2 Cultural setting.

All of the studies, except one (Aboulafia-Brakha et al., 2014 which was conducted in Brazil) were completed within Western societies. There were five studies conducted in the USA (Akkerman & Ostwald, 2004; Beauchamp et al., 2005; Burgio et al., 2003; Chang, 1999; Gonyea et al., 2014); research groups in Canada completed two studies (Gendron et al., 1996; Hébert et al., 2003); two were completed in Spain (Losada et al., 2015; Martin-Carrasco et al., 2009); one study in Greece (Karagiozi et al., 2014); one was completed by researchers in the Netherlands (Blom et al., 2015); one study was completed in Italy (Passoni, et al., 2014) and one in the UK (Livingston et al., 2014).

3.3.1.2 Participants.

The participants in three of the studies were recruited solely from the general population via various media adverts (Akkerman & Ostwald, 2004; Beauchamp et al., 2005; Blom et al., 2015) and a further two studies used a combination of referrals from health care professionals and media adverts (Gonyea et al., 2014; Losada et al., 2015). Passoni et al. (2014) also recruited using media adverts, however, these were placed specifically in hospital memory clinics and the hospital newspaper. The remaining studies recruited via contacts at local Alzheimer’s Society support groups (Chang, 1999; Karagiozi et al., 2014) or through a combination of support groups, and via referrals from health professionals working with the person with dementia (Aboulafia-Brakha et al., 2014; Burgio et al., 2003; Gendron et al., 1996; Hébert et al., 2003; Livingston et al., 2014; Martin-Carrasco et al., 2009).

3.3.1.2.1 Gender and age.

Three-quarters (76%) of study participants were female and all studies reported N > 65% females in their total sample, with one study being 100% female (Chang, 1999). No study limited participation to male care-givers only. The mean age of participants was 59.55 years (SD=11.91). Across the studies the age range of care-givers was 18-89 years old.

3.3.1.2.2 Diagnostic status.

Five studies included formally assessed diagnostic criteria for care-givers in terms of their participant eligibility. Of these two studies required participants to score above cut off on the Zarit Burden Scale (Zarit, Reever & Bach-Peterson. 1980; Hébert et al. 2003; Martin-Carrasco et al. 2009). Losada et al. (2015) required participants to score above 16 on the CES-D (Radloff, 1977) and Blom et al. (2015) required scores above cut off on either the CES-D (Radloff, 1977) or the HADS (Zigmund & Snaith, 1983). Finally Akkerman & Ostwald (2004) also required care-givers to be showing some level of anxiety, however, it is unclear how this was measured.

Three studies required care-givers to report stress (Beauchamp et al., 2005) or difficulties (Burgio et al., 2003) in relation to their role as care-giver, or to want help with their care-giving role (Gendron et al., 1996). The remaining studies did not include any measures of care-giver difficulties within their inclusion criteria.

Assessing baseline anxiety was made difficult by the lack of information reported by studies regarding the cut-offs they employed. Following guidelines available for each individual anxiety assessment scale the baseline mean anxiety scores for four studies were above the cut off for clinical anxiety (Blom et al., 2015; Burgio et al., 2003; Hébert et al., 2003; Losada et al., 2015). However, scores varied widely around the mean. A further six studies had mean scores which were below the cut off point for clinical anxiety (Aboulafia-Brakha et al., 2014; Gendron et al., 1996; Gonyea et al., 2014; Livingston et al., 2014; Passoni et al., 2014). Akkerman and Ostwald (2004) reported baseline scores falling within the mild anxiety range (Beck & Steer, 1993). The remaining three studies included participants whose mean baseline anxiety scores fell within the normal range (Beauchamp et al., 2005; Karagiozi et al., 2014; Martin-Carrasco et al., 2009). It was not possible to assess baseline anxiety for the study by Chang, 1999 as it was unclear what method of scoring they had applied to their anxiety assessment.

3.3.1.2.3 Characteristics of care receiver.

Six studies focussed solely on care-receivers with a diagnosis of Alzheimer's dementia (Aboulafia-Brakha et al., 2014; Akkerman & Ostwald, 2004; Burgio et al., 2003; Gonyea et al., 2014; Martin-Carrasco et al., 2009; Passoni et al., 2014). The three other studies to report care-receiver diagnosis reported N >70% Alzheimer's dementia in their samples (Blom et al., 2015; Hébert et al., 2003; Losada et al., 2015).

With regards to gender of care-receivers six studies did not report this information (Aboulafia-Brakha et al., 2014; Akkerman & Ostwald, 2004; Beauchamp et al., 2005; Chang, 1999; Hébert et al., 2003; Karagiozi et al., 2014; Losada et al., 2015). Of those studies which did report care-receiver gender 59.17% of care-receivers were female.

3.3.1.2.4 Relationship to care receiver.

One study did not report care-giver to care-receiver relationship (Akkerman & Ostwald, 2004), all other studies reported this relationship to varying degree, with Livingston et al. (2014) and Martin-Carrasco et al. (2009) giving the most detailed breakdown. Overall, the relationship of the care-giver to the person with dementia was spouse (42.17%), adult child (37.34%), other relative (10.96%), and friend/not related (1.05%). For 7.86% of participants the relationship with the person they were caring for was not specified. Gendron et al. (1996) only looked to investigate the impact of their intervention upon spousal care-givers and therefore their sample included 100% spouses. Two other studies had N>75% spousal care-givers (Aboulafia-Brakha et al., 2014; Chang, 1999). Passoni et al. (2014) stated that the majority of their care-givers were spouses, or offspring, of the person with dementia, but they do not state the percentage of each and one care-giver was the sister of the person with dementia.

3.3.1.2.5 Time dedicated to caregiving.

The eligibility requirements with regards to the amount of time spent in the care-giving role varied between studies. Whilst four studies set no requirement for the amount of time spent care-giving (Akkerman & Ostwald, 2004; Blom et al., 2015; Chang, 1999; Karagiozi et al., 2014; Passoni et al., 2014) the other studies either required the care-givers to be the primary carer for the person with dementia (Herbert et al., 2003; Livingston et al., 2015) and/or set a minimum number of hours that needed to be spent care-giving. This ranged from at least four contacts per month (Beauchamp et al., 2005) to three studies which required the care-giver and the person with dementia to be co-habiting (Burgio et al., 2003; Gendron et al., 1996; Martin-Carrasco et al., 2009). Beauchamp et al. (2005) was the only study that required care-givers to be in employed work which presumably impacted on the amount of time they were able to dedicate to care-giving.

Five studies reported the mean number of hours spent per day care-giving and this ranged from 5.40 (SD= 2.35) hours (Aboulafia-Brakha et al., 2014) to 15.57 (SD = 8.42) (Losada et al., 2015). The mean length of time in the role as care-giver was also recorded by seven studies (Aboulafia-Brakha et al., 2014; Akkerman & Ostwald, 2004; Chang, 1999; Gendron et al., 1996; Hebert et al., 2003; Losada et al., 2014; Martin-Carrasco et al., 2009). Of the studies that recorded this information the mean length of time as a care-giver was 3.28 (SD=2.30) years.

3.3.1.2.6 Socio-demographic characteristics.

All studies, except two (Aboulafia-Brakha et al., 2014; Martin-Carassco et al., 2009), reported the education level of participants. This was either reported as the mean number of years in education, or as a percentage of participants who had completed particular levels of education. Overall for those studies reporting the mean (Akkerman & Ostwald, 2004; Burgio et al., 2003; Chang, 1999; Gendron et al., 1996; Hébert et al., 2003; Karagiozi et al., 2014;

Losada et al., 2015) the mean number of years in education for care-givers was 12.80 (SD=4.03). Blom et al. (2015) reported that just under half of the care-givers included in their study had a bachelor degree or higher (49.7%) compared to Gonyea et al. (2014) who reported that 47.5% of care-givers in their study were only educated to high school level. Passoni et al. (2014) excluded care-givers who did not have a minimum of three years education. They do not state their reason for this, however, it may be because care-givers in their intervention were required to read a manual as part of treatment.

With regards to care-giver ethnicity, seven studies did not report this demographic characteristic (Aboulafia-Brakha et al., 2014; Gendron et al., 1996; Hébert et al., 2003; Karagiozi et al., 2014; Losada et al., 2015; Martin-Carrasco et al., 2009; Passoni et al., 2014). Two studies, both set in the USA, specified ethnicity as part of their inclusion criteria. Gonyea et al. (2014) specifically focussed on care-givers who regarded themselves to be of Latino or Spanish ethnicity and recruited care-givers who were primarily Dominican (41.8%) or Puerto Rican (46.3%). Burgio et al. (2003) recruited only White (59.32%) and African Americans (40.68%) to their study. The remaining three studies set in the USA reported care-givers to be mainly Caucasian (White American >65%), with the second most commonly reported ethnicity being African American. This was similar for Livingston et al. (2015) who reported 75.38% of care-givers to be White British. Blom et al. (2015) reported that 99% of the care-givers in their study were Dutch but they do not break this down further into detailed ethnicity.

3.3.1.2.7 Co-morbidity.

Karagiozi et al. (2014) excluded any care-givers who had a psychiatric disorder according to DSM-IV (1994) criteria, or who presented with a score indicative of severe depression according to the BDI-II (Beck, Steer & Brown, 1996) due to concerns about the impact of medication upon outcomes. Akkerman & Ostwald (2004) excluded any care-givers with a history of psychiatric symptoms. Blom et al. (2015) also considered the presence of psychiatric symptoms with regards to severe anxiety, depression, or suicidal thoughts in care-givers as an exclusion criteria. However, this was not an automatic decision: care-givers were initially referred for evaluation by a physician to deem whether they needed immediate treatment elsewhere or if they could remain in the trial.

Two studies also considered care-givers' levels of cognitive functioning as assessed by the MMSE before including them in the intervention. Akkerman & Ostwald (2004) automatically excluded care-givers scoring below 23 on the MMSE and Livingston et al. (2014) referred those scoring below 24 for further evaluation and subsequently excluded those whose low scores they felt were attributable to cognitive difficulties.

3.3.1.2.8 Confounding factors.

The most commonly cited confounding factor that formed part of the exclusion criteria was current, or historic, involvement in another psychosocial, educational, or supportive group designed to help care-givers (Akkerman & Ostwald, 2004; Burgio et al., 2003; Hébert et al., 2003; Karagiozi et al., 2014; Livingston et al., 2015). Two studies excluded care-givers who regularly used alcohol or illicit substances (Aboulafia-Brakha et al., 2014; Akkerman & Ostwald, 2004) and one study excluded care-givers who were caring for someone with a history of severe psychiatric disorder or substance abuse (Gonyea et al., 2014). Four studies did not make any reference to any exclusion criteria (Beauchamp et al., 2005; Chang, 1999; Gendron et al., 1996; Passoni et al., (2014).

3.3.1.3 Types of CBT interventions

The majority of studies were delivered in a conventional format via direct contact with a therapist. However, one study was delivered solely over the internet using a multimedia programme with no therapist involvement (Beauchamp et al., 2005). A second study was predominantly delivered via a web based intervention with therapist feedback via email for homework tasks only, and one of the earliest interventions was based upon skills training delivered via a pre-recorded video with follow up phone calls from nurses (Chang, 1999).

Those interventions delivered by a therapist were predominantly delivered in a group format, with group sizes ranging from four to ten care-givers. Burgio et al., (2003) delivered the first session in a group format and this was then followed up by individual sessions at the care-giver’s home. Three studies used a solely individual intervention (Livingston et al., 2014; Losada et al., 2015; Martin-Carrasco et al., 2009) with the primary argument for this being increased opportunity to personalise the intervention (Selwood et al., 2007). Personalisation was also a key feature of the web programme developed by Beauchamp et al. (2005) as they allowed participants to choose modules that linked to their care-giving concerns and their relation to the care-recipient.

3.3.1.3.1 Theoretical model.

As expected, based on previous reviews (Kennet, Burgio & Schulz, 2000), the theoretical basis for the interventions developed by the studies included in this review was mixed. Eight studies explicitly stated that their interventions were developed from Cognitive Behavioural theory (Aboulafia-Brakha et al., 20014; Akkerman & Ostwald, 2004; Chang, 1999; Gendron et al., 1996; Gonyea et al., 2014; Karagiozi et al., 2014; Losada et al., 2105; Passoni et al., 2014). Four further studies (Blom et al., 2015; Livingston et al., 2015; Martin-Carrasco et al., 2009) were based upon the Coping with Caregiving intervention (Coon, Thompson, Steffen, Sorocco & Gallagher-Thompson, 2003; Gallagher-Thompson, Arean, Rivera & Thompson, 2001). Coping with Caregiving is a CBT intervention developed as part of the REACH programme, so whilst the researchers in the aforementioned studies did not make the link to CBT as explicit as the other studies it is clear that CBT formed the theoretical basis for these interventions.

The final three studies (Beauchamp et al., 2005; Burgio et al., 2003; Hébert et al., 2003) developed their interventions based upon the Stress and Coping model of care-giver distress (Lazarus & Folkman, 1984). This model proposes that when faced with a stressful situation care-givers make two appraisals. Within their primary appraisal the level of threat or stress is ascertained, this is followed by the secondary appraisal which is the care-givers assessment of their ability to cope. This model lends itself well to the development of a CBT based intervention (Wasilewski, Stinson & Cameron, 2017). Beauchamp et al. (2005) go on to discuss the specific elements of CBT that they used in their intervention in relation to the Stress and Coping model. Hébert et al. (2003) and Burgio et al. (2003) do not make reference to CBT as a discrete model, instead they discuss specific components of CBT.

3.3.1.3.2 Intervention components.

As per the eligibility criteria all studies included both cognitive and behavioural elements in their interventions. Every study aimed to teach care-givers cognitive restructuring skills, predominantly these were aimed at dysfunctional thoughts about care-giving but the skill was also taught to help more generally with emotional management. Nine studies claimed to use behavioural activation within their intervention, and for the most part this focussed upon increasing pleasant events and re-engaging in previously enjoyable activities. The five studies which did not employ behavioural activation used behavioural modification to assist care-givers in changing their behavioural responses to the care-receivers, and also advised them to consider how they might change some of the behaviours they found hard to cope with in the person with dementia (Akkerman & Ostwald, 2004; Beauchamp et al., 2005; Blom et al., 2015; Gendron et al., 1996; Karagoizi et al., 2014).

Psycho-education about dementia was reported as an explicit part of the majority of the interventions: only three studies did not make reference to it in their descriptions of their interventions (Akkerman & Ostwald, 2004; Burgio et al., 2003; Gonyea et al., 2014). The next most commonly taught skill fell within the category of social skills training, and this included general communication skills, such as assertiveness, as well as focussing on building social support. Only three studies did not report the inclusion of some method of social skills training (Aboulafia-Brakha et al., 2015; Akkerman & Ostwald, 2004; Gendron et al., 1996). The majority of studies also spent time helping care-givers to develop problem solving skills and five studies reported using modelling as a way of teaching new skills (Beauchamp et al., 2005; Blom et al., 2015; Chang, 1999; Gonyea et al., 2014; Hébert et al., 2003).

Akkerman & Ostwald (2004) was the only study to focus their intervention specifically upon care-giver anxiety and as such all elements of their intervention were aimed at targeting the physical, behavioural and cognitive components of anxiety. In relation to the physical components of anxiety they taught care-givers relaxation strategies. Relaxation skills were clearly reported by six further studies (Blom et al., 2015; Gonyea et al., 2014; Livingston et al., 2015; Losada et al., 2015; Martin-Carrasco et al., 2009; Passoni et al., 2014) and probably also used by Beauchamp et al. (2005) and Karagiozi et al. (2014).

There was great variation amongst studies in the level of detail provided regarding the components of the interventions employed. For example, Livingston et al. (2015) provided a full copy of their intervention at the end of their publication. In contrast Chang (1999) provided very little detail of how the components of CBT reportedly used in their intervention were actually delivered to care-givers.

3.3.1.3.3 Therapist input.

There was some variation in therapist input between studies. The majority of the studies used only direct face to face delivery by the therapist (Aboulfia-Brakha et al., 2014; Akkerman & Ostwald, 2004; Gendron et al., 1996; Hébert et al., 2003; Karagiozi et al., 2014; Livingston et al., 2014; Losada et al., 2015; Martin-Carrasco et al., 2009; Passoni et al., 2014) or face to face delivery followed up with telephone calls (Burgio et al., 2003; Gonyea et al., 2014). One study had no face to face contact with the therapist but participants received emails from the therapist in response to their homework assignments (Blom et al., 2015), and in another study the only contact with the therapist was via telephone (Chang, 1999). One intervention was delivered with no therapist contact at all and was completely delivered through a multimedia internet program (Beauchamp et al., 2005). Those interventions with limited therapist contact were delivered via videos (Chang, 1999) and via an internet program using videos and text, alongside short assessments of learning (Blom et al., 2015).

3.3.1.3.4 Intensity of interventions.

The intensity of the interventions ranged from delivery over a five week period (Gonyea et al., 2014), to a 24 week long intervention (Karagiozi et al., 2014). Only four studies reported the mean amount of therapist or intervention contact time. Burgio et al. (2003) reported the average number of home visits received was 10 (SD=2.74), with a mean duration of 50.06 minutes (SD=13.67). Akkerman & Ostwald (2004) recorded all participants to have completed all sessions of their intervention. This equates to a total of 1080 minutes of therapist contact over nine weekly sessions. Beauchamp et al. (2005) allowed for unlimited access to their internet intervention over a 30 day period and they recorded an average time of 32.20 minutes (SD=43.5) with 59% of participants visiting just once, 19% visiting twice, 11% using the program three times and 11% visiting more than three times. Blom et al. (2015) reported that 45.6% of care-givers completed all of the eight potential internet lessons within the six months, with each lesson on average taking 1.5 hours or more to complete.

Gendron et al. (1996) did not report amount of therapist contact but rather reported levels of absenteeism for their intervention group, which over the eight, 90 minute, weekly sessions was reported to be low (8.23%). However, it is not clear if this figure corresponds to the percentage of participants of who did not attend all sessions, or to the percentage of sessions missed.

3.3.1.3.5 Integrity of interventions.

The integrity or fidelity of an intervention refers to the degree to which the intervention is delivered as it was intended (Dane & Schneider, 1998). Integrity can be assessed by researchers using a range of methodological strategies, including video monitoring, manualised sessions and therapist supervision, which all aim to monitor, and improve, both the reliability and the validity (Bellg et al., 2004). Six studies did not report whether they monitored treatment integrity (Aboulfia-Brakha et al., 2014; Chang, 1999; Gonyea et al., 2014; Hébert et al., 2003; Martin-Carrasco et al., 2009; Passoni et al., 2014).

Burgio et al. (2003) assessed treatment integrity using three principles; *treatment delivery* which looks at whether the sessions were presented in the way they were intended, *treatment receipt* which measures the number and duration of therapeutic contacts to ensure delivery is in line with the protocol and *treatment enactment* which is the degree to which changes in behaviour are demonstrated by the participants outside of the intervention. To ensure treatment delivery all therapists were trained in the intervention and achieved certification by the REACH Coordinating Center in Pittsburgh prior to delivery. Additionally all contacts with participants were recorded by video and 20% were coded for accuracy in accordance with a standardised checklist, achieving mean accuracy ratings of 85% (SD=10.32) in the CBT intervention. Treatment enactment was monitored by therapists who assessed the level of between session engagement in certain activities by care givers. This was rated as good to excellent for 48% of sessions.

Losada et al. (2015) also followed the procedures outlined by Burgio et al. (2003) for assessing treatment integrity. Gendron et al. (1996) employed a similar strategy with all therapists receiving training specifically geared to the intervention protocol. Sessions were audio-taped and then reviewed by one of the study investigators and group members' engagement was monitored via therapist ratings of their participation following each session.

Hébert et al. (2003) reported the frequency of attendance by study participants as a way of monitoring treatment implementation. Of the 72 participants assigned to the CBT intervention 11% did not attend any of the sessions, 13% attended up to eight sessions, 7% attended between nine and 11 sessions and 69% of participants attended at least 12 of the 15 available sessions. Karagiozi et al. (2014) followed clinical practice guidelines for group psychotherapy created by the American Group Psychotherapy Association (AGPA) with regards to treatment implementation, however, they do not report the outcome of this. Livingston et al. (2014) selected one therapy session per participant at random to be recorded. This session was then rated by another therapist using a pre-designed fidelity checklist and given a score out of five, with five being the best. Any low scores were discussed in supervision. A similar method was employed by Akkerman & Ostwald (2004). They had a coinvestigator who assessed treatment integrity and attended 15% of the intervention groups to ensure adherence to the CBT model. If a drift from the model was observed then this was discussed with the therapist prior to the next session and a subsequent session was observed.

For the studies delivered via the internet (Beauchamp et al., 2005; Blom et al., 2015) treatment adherence was easier to monitor with regards to session structure as all sessions were standardised and therefore used an identical structure for each participant. To ensure engagement with the whole program Blom et al. (2015) sent reminders automatically via email if participants did not start a new lesson within a certain time frame, if they did not send in their homework, or if they remained inactive for a certain period of time. Beauchamp et al., (2005) reported the average amount of time and frequency with which participants accessed their intervention. However, no record was made of how many of the individual components of the intervention were accessed as they allowed care-givers to personalise their web-based programme. If some of the components of the intervention were not accessed by participants then it is unclear how consistent the intervention was with the principles of CBT. Additionally the length of time viewing the intervention ranged widely from 1 to 368 minutes.

3.3.1.3.6 Therapist qualification.

Therapist qualifications and training is also linked to treatment integrity (Bellg et al., 2004). The therapists delivering the interventions varied with regards to their qualifications and experience across the studies, and included clinical psychologists, health psychologists, psychologists with experience in delivering CBT, health professionals and social workers trained in CBT, masters level psychology graduates and nurses. One study (Burgio et al., 2003) did not report the therapist's qualifications, however, the therapist received training in the intervention prior to delivery. Seven other studies also reported therapist training (Aboulfia-Brakha et al., 2014; Akkerman & Ostwald, 2004; Blom et al., 2015; Chang, 1999; Gonyea et al., 2014; Hébert et al., 2003; Passoni et al., 2014). For Beauchamp et al. (2005) therapist training was not relevant as there was no therapist contact.

3.3.1.3.6 Comparator groups.

Four of the 14 studies used a waiting list control design (Akkerman & Ostwald, 2004; Beauchamp et al., 2005; Karagiozi et al., 2014; Passoni et al., 2014). Two studies reported using treatment as usual (TAU) as their control arm. This was described in detail by Livingston et al. (2014) as a service provided by the teaching Trusts through which participants were recruited. They expected it to be of a good standard, similar to TAU throughout the UK and based upon NICE guidelines (NICE, 2006). With regards to the care-giver TAU involved providing information and advice about dementia, and signposting and referring to local agencies for additional support. Martin-Carrasco et al. (2009) reported similar TAU involving general information about progress of Alzheimer's dementia, information that was individual to the care receiver’s diagnosis and progress, which was available when requested over the phone, and information leaflets about Alzheimer’s dementia and about local support services in the community.

Four studies employed psycho-education groups as their control (Aboulafia-Brakha et al., 2014; Gendron et al., 1996; Gonyea et al., 2014; Hébert et al., 2003). Generally these groups provided information on dementia, covering diagnosis, cognitive symptoms, disease progression and possible treatment options. Care givers were given information about interacting with the person with dementia, how to deal with challenging behaviour and keeping the care receiver safe. Time was allowed for questions and discussion at the end of the session to build upon the social support of a group intervention. Gonyea et al. (2014) had initially planned to use a wait list design but were concerned that participants would not engage. Hébert et al. (2003) referred participants in the control group to local psycho-education groups offered by the Alzheimer Society or health care organisations.

Minimal support groups were used by three studies. The information provided by these groups was not dissimilar to that covered by the psycho-education groups, however, the level of contact was far less. Blom et al. (2015) delivered their minimal support group via e-bulletins, with no direct therapist contact. The topics covered in the bulletins did not overlap with those covered by the CBT intervention. Burgio et al. (2003) provided brief and structured telephone support to care-givers in the control arm which comprised empathetic statements and active listening. They were also given written educational materials about dementia, with the aim of providing standardised information and support that were not tailored to that individual and the person they were caring for. Chang (1999) also contacted care-givers in the control group via telephone with the view to assessing care-giver wellbeing. They offered no information regarding specific strategies for caring. Those who were experiencing difficulties were referred to their health care provider or to local support groups. However, they do report on the uptake of these interventions within the control group.

Losada et al. (2015) included two comparator groups alongside a minimal support group control. The second comparator group was based upon an alternative active therapeutic model; Acceptance and Commitment (ACT) therapy (Hayes, Strosahl, & Wilson, 1999). As no other study had included an alternative active therapeutic comparison based upon an alternative theoretical model it was decided not to include data from participants in the ACT arm in the meta-analysis.

3.3.1.4 Types of outcomes.

All studies used outcome measures which were reliable and valid for use in the care-giver population. As anticipated, there was some variation in the outcome measures used for anxiety and depression across studies.

3.3.1.4.1. Anxiety.

All studies included self-report anxiety measures. Anxiety was the primary outcome for only six studies. The measures used included the following: Beck Anxiety Inventory (BAI; Beck, Epstein, Brown & Steer, 1988; Beck & Steer 1993), the Brief Symptom Inventory anxiety subscale (BSI; Derogatis, 1992), the anxiety domain from the General Health Questionnaire – 28 (GHQ-28; Goldberg and Hillier, 1979), the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A; Jorm, 1994; Zigmund & Snaith, 1983), the anxiety subscale of the Hopkins Symptom Checklist (HSCL; Derogatis, Lipman, Rickels, Uhlenhuth & Covi, 1974), and the Profile of Mood States (POMS; McNair, Lorr & Dropplemann, 1971) anxiety subscale. A number of studies used various versions of the Spielberger State Anxiety Inventory (STAI; Spielberger, Gorusch, Lushene, Vagg & Jacobs, 1983), including the shortened ten item scale in English (Spielberger, 1983; Spielberger, Gorsuch & Lushene, 1970) and translated in to Portugese (Biaggio & Natalicio, 1979), and the State Anxiety Inventory-Reduced Form (STAI-X3; Vidotto & Bertolotti, 1991).

One study (Akkerman & Ostwald, 2004) reported two primary outcome measures of anxiety: one was a self-report (BAI, Beck et al., 1988) and one was a clinician measure (HAMA, Hamilton, 1959). A priori it had been agreed that should this be the case the anxiety measure most commonly used in the other studies included in this review would be used providing the reliability and validity were comparable. In this instance this meant that only the self-report measure (BAI) was included as all other studies had used self-report measures.

3.3.1.4.2 Depression.

All studies apart from two (Akkerman & Ostwald, 2004; Hébert et al., 2003) assessed depression. Again all outcome measures were self-report and the most commonly reported measure of depression was the English and the Spanish versions of the Center for Epidemiologic Studies-Depression scale (CES-D; Radloff, 1977; Radloff & Teri, 1986; Robinson, Gruman, Gaztambibe & Blank, 2002). Other measures included the Beck Depression Inventory - Second Edition (BDI-II; Beck et al., 1996) which was also translated in to Portugese (Gorenstein & Andrade, 1998), the Brief Symptom Inventory depression subscale (BSI; Derogatis, 1992), the depression domain from the General Health Questionnaire (GHQ-28; Goldberg and Hillier, 1979), the depression subscale of the Hopkins Symptom Checklist (HSCL; Derogatis et al., 1974), the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D; Zigmund & Snaith, 1983) and the Depression Questionnaire Reduced Form (QD-R; Moroni, et al. 2006).

3.3.1.4.3. Follow-up data.

Six studies did not complete follow-up assessments (Aboulafia-Brakha et al., 2014; Beauchamp et al., 2005; Blom et al., 2015; Hébert et al., 2003; Karagiozi et al., 2014; Passoni et al., 2014. Burgio et al. (2003) completed follow up assessments but the outcomes of these assessments were not available. The rest of the studies reported follow up assessments which ranged from three months (Gendron et al., 1996; Gonyea et al., 2014) post baseline assessment to 24 months (Livingston et al., 2014).

Table 2: *Characteristics of Included Studies: Methods and Participants*

Author year (Study ID)	Country	Design	Population Total *N*	Age CG (*M* (SD), range)	Dementia type (% AD)	Sex CG (% Fem.)	Education level *M* years (SD)	Relation to CR (%)	Time in CG role (M years (SD))	Amount of time CG (*M* hrs per day (SD))	% CG living with CR
Aboulafia-Brakha 2014	BR	CT (PG)	27	57.25 (8.68)	100*	81	NR	78 SP NR S/D	3.26 (1.79)	5.7 (2.22)	63
Akkerman 2004	US	RCT (PG)	38	58.10 (13.78) 34 - 85	100*	86	14.14 (1.96)	NR	3.57 (2.09)	15.86 (8.49)	NR
Beauchamp 2005	US	RCT (PG)	299	46.90 (12.2) 19.2 – 84.3	NR	73	NR	7 SP 67 S/D	NR	> 4 contacts per month*	NR
Blom 2015	NL	RCT (PG)	245	61.25 (12.37) 26 – 87	75	70	NR	59 SP 39 S/D	NR	NR	60
Burgio 2003	US	RCT (PG)	118	62.85 (12.33)	NR	78	13.34 (2.16)	50 SP 50 S/D	> 6 months*	> 4hrs per day*	100*
Chang 1999	US	RCT (PG)	65	66.50 (11.90)	NR	100*	14.00 (2.61)	89 SP NR S/D	3.35 (2.78)	NR	NR
Gendron 1996	CA	RCT (PG)	35	66.20 (9.50) 46 - 83	NR	66	11.80 (3.20)	100 SP*	2.21 (1.41)	NR	100*
Gonyea 2014	US	RCT (PG)	67	54.60 (3.10)	NR	96	NR	26 SP 55 S/D	NR	12 (SD NR)	63
Hébert 2003	CA	RCT (PG)	158	59.75 (12.90)	82	80	11.98 (4.09)	61 SP NR S/D	2.82 (2.12)	NR	86
Karagiozi 2014	GR	RCT (PG)	112	56.77 (14.08)	NR	77	11.30 (4.36)	30 SP 56 S/D	NR	NR	63
Livingston 2014	UK	RCT (PG)	260	62.00 (13.45) 18 - 89	NR	82	NR	42 SP 43 S/D	NR	> 1 contact per week*	63
Losada 2015	ES	RCT (MA)	90	61.82 (13.54)	76	86	NR	37 SP 54 S/D	4.36 (3.07)	14.32 (8.12)	NR
Martin-Carrasco 2009	ES	RCT (PG)	115	58.30 (13.55)	100*	69	NR	55 SP 36 S/D	3.05 (2.32)	12.05 (7.50)	100*
Passoni 2014	IT	CT (MA)	72	58.50 (12.73)	100*	79	NR	NR	NR	NR	NR

Note. BR = Brazil; CA = Canada; CG = Care-giver; CR = Care-receiver; ES = Spain; GR = Greece; IT = Italy; *M* = Mean; MA = Multiple Arm; *N* = total sample size; NL = Netherlands; NR = Not Reported; PG = Parallel Group; RCT = Randomised Control Trial; SD = Standard Deviation; S/D = Son/Daughter; SP = Spouse. *Set as inclusion criteria.

Table 3: *Characteristics of Included Studies: Interventions*

Author year (Study ID)	CBT Intervention						Control		
	Focus/Theoretical background	*N*	Dose	Delivery format	Hours treatment received (*M*, (SD))	Therapist	Type	*N*	Dose
Aboulafia-Brakha 2014	Build CH stress management and coping skills (cognitive modification/increasing pleasant activities) alongside an increase in knowledge. Direct reduction physical measure of stress and improve psychosocial wellbeing. CBT	17 (12)	8s weekly 90 mins each	Group 6-6 CGs Therapist via face to face	NR	P	Psycho-ed	18 (15)	8s weekly 60 mins each Group Up to 17 CG
Akkerman 2004	Teaching cognitive restructuring skills and behavioural skills to change responses specifically targeting CG anxiety. CBT	20	9s weekly 120 mins each	Group 4-8 CGs Therapist via face to face	18 Hours – 100% completed	CP	WL	18	NA
Beauchamp 2005	*Caregivers Friend* aimed to improve CG appraisals, increase use of coping skills and reduce depression, anxiety and burden, increase CG gain. Stress and Coping framework (Folkman, 2001)	150	Unlimited access over 30 days	Individual Via the internet	0.54 (0.72)	No therapist contact	WL	149	NA
Blom 2015	*Mastery over Dementia* aim to reduce depression and anxiety by increasing skills in beh. management and problem solving and cognitive restructuring. CBT	149	8s + Booster Completed at own pace within 5-6 mths	Individual Via the internet Therapist contact via email for homework	NR 45.6% completed all lessons	HP	MSG via e-bulletins	96	Email received every 3wks
Burgio 2003	*Skills Training Condition (STC)* targets CG beh. management techniques, problem solving and cognitive restructuring – indirectly improving CG well-being. Stress process framework.	61	1s group 180mins 9s individual 4x weekly, 2x bi-weekly, 2x bi-monthly 60 mins each + 2 f/up phone calls	Mixed Therapist via face to face and phone calls Video component	8.34 (2.28)	NR	MSG	57	Telephone contact only < 15mins each same freq. as CBT group

Chang 1999	Primary focus on CR behaviour management, specifically eating and dressing difficulties, indirectly improving CG wellbeing. CBT	34	Video viewed up to two times 8 weekly phone calls (*M = 18.3*mins)	Individual Via video Therapist contact via phone call	NR	NU	MSG	31	Telephone contact weekly to assess general wellbeing (*M* = 11.1 mins)
Gendron 1996	Focus upon cognitive restructuring and increasing skills in problem solving and communication which then reduces psychological difficulties in CG. CBT	17	8s weekly 90 mins each	Group max. 10 CGs Therapist via face to face	NR	NR	Psycho-ed	18	8s weekly 90 mins each Max. 10 CGs
Gonyea 2014	*Circulo de Cuidada* primary focus on management of CR neuropsychiatric symptoms using ABC problem solving techniques – in turn increase CG wellbeing. CBT	33	5s weekly 90 mins each + 4 f/up phone calls	Group, size NR Therapist face to face and phone calls	NR	SW	Psycho-ed	34	5s weekly group 90 mins each
Hébert 2003	Reduce CG reactions to difficult CR behaviours, indirectly reduce burden, psychological distress and anxiety. Stress and Coping Folkman (2001)	79 (60)	15s weekly 120 mins each	Group, size NR Therapist via face to face	NR	HPros	Psycho-ed	79 (56)	Group – no further details recorded
Karagiozi 2014	Develop coping skills, cognitive restructuring, and increase CG efficacy – in turn reduce depression and anxiety. CBT	58 (51)	24s weekly Psycho-ed 90 mins each 24s weekly CBT 90 mins each	Group 7–8 CGs Therapist via face to face	NR	P	WL	54 (46)	NA
Livingston 2014	*STrAtegies for RelaTives (START*) Provide info about dementia and emotional and practical coping skills to improve CG mental health. Based on Coping with Caregiving (Gallagher-Thompson, et al., 2001). CBT	173 (150)	8s freq. NR Mean 77mins each	Individual Therapist via face to face	NR 48% attended all sessions	PG	TAU	87 (75)	Ind. contact with clinician for general info as required
Losada 2015	Cognitive restructuring of negative thoughts linked to CG and increase pleasant activities to directly improve CG depression and anxiety. CBT	42	8s weekly 90 mins each	Individual Therapist via face to face	NR	CP	MSG	48	1s Group 120 mins
Martin-Carrasco 2009	*Psychoeducational Intervention Program* (PIP) teaching stress control techniques and strategies for changing CR behaviour, in turn improving CG well-being. CBT	55 (44)	8s every 1-2 weeks 90 mins each	Individual Therapist via face to face	NR	CP/NU/SW	TAU	60 (38)	Ind. contact with clinician for general info as required

Passoni 2014	*Helping Those Who Care* manual aim to increase CG knowledge about dementia to increase coping skills and reduce anxiety and depression. CBT	39	6s every 15 days 120 mins each +	Group 7–10 CGs Therapist via face to face	NR	P	WL	33	NA
			Manual only group	Individual No therapist contact	NR	NA	WL	30	

Note. CBT = Cognitive Behavioural Theory; CG = Care-giver; CP = Clinical Psychologist; CR = Care-receiver; F/up = Follow up; HP = Health Psychologist; HPros = Health Professional; MSG = Minimal Support Group; NA = Not Applicable; NR = Not Reported; NU = Nurse; P = Psychologist; PG = Psychology Graduate; s = sessions; SW = Social Worker; TAU = Treatment as Usual; WL = Waitlist; N in brackets is number of participants included in analysis.

Table 4: *Characteristics of Included Studies: Outcomes*

Author year (Study ID)	Anxiety	Depression	Additional Outcomes	Mean anxiety level at BL	Assessment	Analysis
Aboulafia-Brakha 2014	STAI-S (20 Item)	BDI	Salivary cortisol measure, PSS, ZBI	Under clinical cut off	BL, Post	CA
Akkerman 2004	BAI, HAMA		Physiological assessment of anxiety	Mild – moderate anxiety	BL, Post, FU CBT 4mths	CA
Beauchamp 2005	STAI-S (10 Item)	CES-D	Stress screening questions, self-efficacy questions, Revised Ways of Coping, CG Strain Instrument, Positive Aspects of CG	Not clinically anxious	BL, Post	CA
Blom 2015	HADS-A	CES-D	SPPIC, RMBPC, SSCQ. Pearlin Mastery Scale	Within clinically anxious range	BL, Midway, Post	ITT
Burgio 2003	STPI (Ax)	CES-D	RMBPC, PAC, LSNI, LTS	Within clinically anxious range	BL, Post, FU 12mths & 18 mths	ITT
Chang 1999	BSI (Ax)	BSI (D)	Moos Coping Scale, the CG Appraisal tool.	Within clinically anxious range	BL, Midway, Post, FU 3mths	CA
Gendron 1996	HSCL (Ax)	HSCL (D)	MBPC, ATQ, Jaloweic Coping Scale, RAI, DAS, Burden Interview Scale.	Under clinical cut off	BL, Post, FU 3 and 6mths	ITT
Gonyea 2014	STAI-S (20 Item)	CES-D	NPI-S, NPI-D, RSCSE	Under clinical cut off	BL, Post, FU 3mths	ITT
Hébert 2003	STAI-S (20 Item)		RMBPC, ZBI, Desire to institutionalise questions, BRAS, ISSB, Ilfeld Psychiatric Symptoms Scale	Within clinically anxious range	BL, Post	CA
Karagiozi 2014	BAI	BDI-II	ZBI	Not clinically anxious	BL, Post	CA
Livingston 2014	HADS-A	HADS-D	ZBI, MCTS, HSQ, EW-5D, CSRI	Under clinical cut off	BL, Post, FU 8, 12, 24 mths	CA
Losada 2015	POMS-Tension Ax	CES-D	RMBPC, LTS, Experiential Avoidance in CG scale, Dysfunctional Thoughts About CG Questionnaire.	Within clinically anxious range	BL, Post, FU 8 mths	ITT
Martin-Carrasco 2009	GHQ-28 (Ax)	GHQ-28 (D)	ZBI, SF-36	Not clinically anxious	BL, Post, FU 10 mths	CA
Passoni 2014	STAI-X3	QD-R	CNA	Under clinical cut off	BL, Post	CA

Note. ATQ = Automation Thoughts Questionnaire; Ax = Anxiety subscale; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BL = Baseline; BRAS = Bradfield Revised Affect Scale; BSI = Brief Symptom Inventory; CA = Completer Analysis; CES-D = Center for Epidemiologic Studies – Depression; CG = Care-giving;

CNA = Caregiver Need Assessment; CSRI = Client Service Receipt Inventory; D = Depression; DAS = Dyadic Adjustment Scale; EQ-5D = Europena Qulaity of Life-5 Dimensions; FU = Follow Up; HADS – A = Hospital Anxiety and Depression Scale – Anxiety; HADS-D = Hospital Anxiety and Depression – Depression; HAMA = Hamilton Anxiety Scale; HSCL = Hopkins Symptom Checklist; HSQ = Health Status Questionnaire; ISSB = Inventory of Socially Supportive Behaviour; ITT = Intention to Treat; LSNI = Lubben Social Network Index; LTS = Leisure Time Satisfaction scale; MBPC = Memory and Behaviour Problem Checklist; MCTS = Modified Conflict Tactics Scale; NPI-D = Neuropsychiatric Inventory – Distress; NPI-S = Neuropsychiatric Inventory Severity scale; PAC = Positive Aspects of Caregiving; POMS = Profile of Mood States PSS = Perceived Stress Scale; QD-R = Depression Questionnaire Reduced Form; RAI = Rathus Assertion Inventory; RCI = Reliable Change Index; RMBPC = Revised Memory and Behavioural Problem Checklist; RSCSE = Revised Scale for CG Self Efficacy; SF-36 = Health Survey Questionnaire; SPPIC = Self-Perceived Pressure from Informal Care Scale; SSCQ = Short Sense of Competence Questionnaire; STAI-S = State-Trait Anxiety Inventory State; STAI-X3 = State Anxiety Inventory-Reduced Form; STPI = State-Trait Personality Inventory; ZBI = Zarit Burden Inventory

3.4 Risk of Bias in Included Studies

The results of the risk of bias assessment completed for each study following the Cochrane Collaboration Risk of Bias Tool (Higgins et al., 2011a) are presented in the Risk of Bias tables in Appendix J. Within this table is a description of the ratings given for each of the criterion, and responses to the five follow up questions used to consider other bias, adapted from the reviews completed by Elvish et al. (2012) and Zarit & Femia (2008). A summary of the risk of bias across the included studies is presented in Figure 3 and Figure 4.

3.4.1 Selection bias.

3.4.1.1 Random sequence generation.

For six studies included in this review the risk of bias for this criterion was judged as low as the process for randomisation was clearly described, and reference was made to the use of a computer generated random number system or another appropriate technique. However, six other studies did not provide adequate information to permit a judgement. Finally, two studies were judged to be high risk, Aboulafia-Brakha et al. (2014), used a semi-random design and Passoni et al. (2014) did not randomise care-givers to the intervention group due to ethical limitations. Aboulafia-Brakha et al. (2014) reported significant differences at baseline with regards to gender and employment status. They account for this within their analysis; however, they did not examine differences in anxiety and depression outcomes at baseline.

3.4.1.2 Allocation concealment.

Half the studies did not address concealment of care-givers' group allocation and therefore were judged as unclear risk of bias for this criterion. Four studies did adequately describe allocation, which involved an independent third party (Blom et al., 2015; Livingston et al., 2014; Losada et al., 2015) or completely computerised system (Beauchamp et al., 2015), and were therefore considered low risk. The remaining three studies were judged to be high risk as little or no attempt was made to conceal allocation (Aboulafia-Brakha et al., 2014; Akkerman & Ostwald, 2004; Passoni et al., 2014).

3.4.2 Performance and detection bias.

3.4.2.1 Blinding of participants and personnel.

All studies except one (Blom et al., 2014) were judged to be at high risk of bias for this criterion. It was predicted that this would be the case as it is not really possible for both participants and therapists to be blinded to the intervention they are delivering or receiving. Additionally there was limited control for co-intervention across studies which may have further impacted upon performance bias. However, it was felt important to still consider this bias rather than remove it as lack of blinding can cause a risk of treatment effects being over-estimated (Cuijpers, Karyotaki, Andersson, Mergl & Hegerl, 2015). Blom et al. (2014) did attempt to address this risk by blinding care-givers to intervention assignment: they were not told whether it was the experimental condition or the control condition. A judgement of unclear risk was given as it seems likely that this attempt at blinding could have been broken, but no assessment of this is reported.

3.4.2.1 Blinding of outcome assessment.

To account for this criterion it is possible for all studies to ensure the outcome assessors are blind. The majority of studies adequately described their procedures for this, including using automated computer systems to collect outcomes (Beauchamp et al., 2014; Blom et al., 2015) or outcome assessors who were blinded to condition (Akkerman & Ostwald, 2004; Burgio et al., 2003; Gendron et al., 1996, Hébert et al., 2003, Karagiozi et al., 2014; Livingston et al., 2014; Losada et al., 2015; Passoni et al., 2014). The remaining four studies did not address this criterion but they employed self-report outcome measures which are not likely to be influenced by lack of blinding (Higgins & Green, 2011). Consequently all studies were judged as low risk of bias on this criterion.

3.4.3 Attrition bias.

3.4.3.1 Incomplete outcome data.

The majority of studies were deemed to be low risk of bias for this criterion as generally dropout rates were low and/or appropriate statistical analysis was completed to assess their impact upon study outcomes. Additionally two studies reported a 100% retention rate of participants (Akkerman & Ostwald, 2004; Passoni et al., 2014). However, for three studies it was not possible to allocate a judgement of either low or high risk as they provided insufficient information (Hébert et al., 2003; Karagiozi et al., 2014; Martin-Carrasco et al., 2009). Finally, the study by Chang (1999) was judged to show high risk of bias as there were significant differences between dropouts and completers, and reasons were not reported. Additionally the information needed to assess how many care-givers dropped out at each stage was not presented clearly, making it difficult to ascertain how missing data were accounted for.

3.4.4 Reporting bias.

3.4.4.1 Selective reporting.

To fully assess the extent of selection reporting it is useful to have access to study protocols. This was only possible for two studies and both of these studies were judged to be low risk as they reported all of their pre-specified outcomes (Blom et al., 2015; Livingston et al., 2014). Karagiozi et al., (2014) were also deemed to be low risk of selective reporting; whilst their protocol was not available they provided sufficient information of a convincing nature, including an explicit statement that they had completed all analyses outlined in their protocol.

Two studies were deemed to be high risk with regards to this criterion. Chang (1999) did not report all of their intended outcomes fully, and Burgio et al., (2003) fail to report follow up data and this could not be located elsewhere. The remaining studies were judged as unclear risk as whilst all expected outcomes appeared to be reported protocols were not available to ensure this.

3.4.5 Other bias.

With regards to other sources of bias consideration was given to key factors identified in previous reviews (Elvish et al., 2012; Zarit & Femia, 2008) alongside the items highlighted in the Cochrane Collaboration Risk of Bias Tool (Higgins et al., 2011). Five studies were judged to be low risk as they provided sufficient information to enable them to be considered free of other sources of bias (Akkerman & Ostwald, 2004; Blom et al., 2015; Burgio et al., 2003; Hébert et al., 2003; Losada et al., 2015).

The study by Chang (1999) was considered to be high risk with regards to other bias and this judgement was for a number of reasons. The outcomes reported were not related to the target of the intervention and it was unclear how the intervention model was actually applied as reporting was unclear and scant, and treatment integrity and exposure were not considered. Additionally, procedures in the control condition for referring care-givers elsewhere meant that it was likely they were receiving support elsewhere which had the potential to impact on their outcome ratings. Beauchamp et al. (2014) were also considered high risk of bias. Care-givers in their study were given financial rewards for completion of assessments. Financial incentives in research remains a controversial subject, as it has the potential to motivate people to take part who perhaps would not otherwise be interested (Stunkel & Grady, 2011). Additionally it has been shown to influence participants' judgement of the benefits of the intervention received (Caldwell, Hamilton, Tan & Craig, 2010). When this information was considered alongside the wide variation in both frequency (60% care-givers only accessed the intervention once), and length of time care-givers accessed the study (1-386 minutes, with average time 32mins) it was judged likely that bias was introduced.

All remaining studies were given a judgement of unclear risk as information needed to make a firm judgement of either low or high risk was felt to be missing, but there was evidence to suggest that there could potentially be bias due to problems identified.

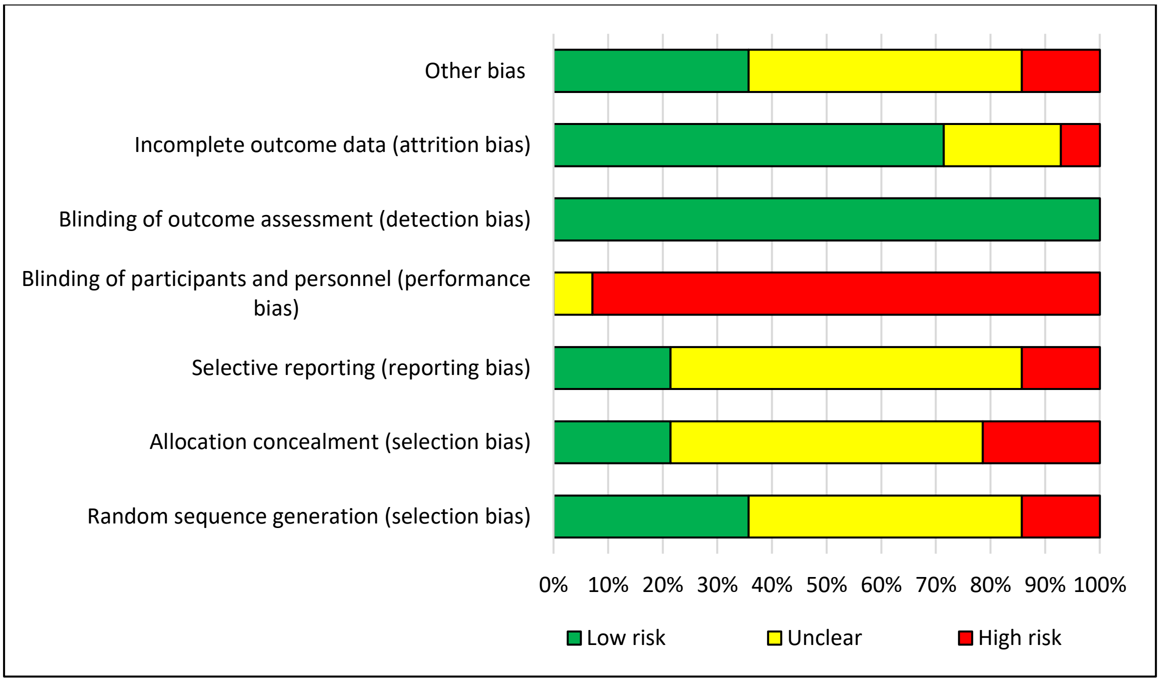
3.5 Summary of Assessment of Risk of Bias

The above outline of the assessment of risk of bias has presented all of the domains considered, however, for the purposes of an overall judgement it was decided to exclude the performance bias criterion from consideration. This was due to the fact that the blinding of participants, and study personnel, was felt to be of limited relevance to a psychological intervention. Therefore three studies were judged as high risk on one key domain (Akkerman & Ostwald, 2004; Beauchamp et al., 2014; Burgio et al., 2003), and two studies had two domains judged as high risk (Aboulafia-Brakha et al., 2014; Passoni et al., 2014) and Chang (1999) was judged high risk on three domains. Blom et al., (2015) was the only study to be judged low risk on all domains considered. The remaining studies had no high risk judgements but were all judged unclear risk on some key domains, ranging from just one (Livingston et al., 2014; Losada et al., 2015) to five domains judged as unclear risk (Martin-Carrasco et al., 2009). In summary most information was from studies judged as having an unclear risk of bias.

Figure 3: Risk of bias summary showing judgements for risk of bias for each domain for each study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants/personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aboulafia-Brakha 2014	🔴	🔴	🔴	🟢	🟢	🟡	🟡
Akkerman 2004	🟡	🔴	🔴	🟢	🟢	🟡	🟢
Beauchamp 2005	🟢	🟢	🔴	🟢	🟢	🟡	🔴
Blom 2015	🟢	🟢	🟡	🟢	🟢	🟢	🟢
Burgio 2003	🟢	🟡	🔴	🟢	🟢	🔴	🟢
Chang 1999	🟡	🟡	🔴	🟢	🔴	🔴	🔴
Gendron 1996	🟡	🟡	🔴	🟢	🟢	🟡	🟡
Gonyea 2014	🟡	🟡	🔴	🟢	🟢	🟡	🟡
Hébert 2003	🟢	🟡	🔴	🟢	🟡	🟡	🟢
Karagiozi 2014	🟡	🟡	🔴	🟢	🟡	🟢	🟡
Livingston 2014	🟢	🟢	🔴	🟢	🟢	🟢	🟡
Losada 2015	🟢	🟢	🔴	🟢	🟢	🟡	🟢
Martin-Carrasco 2009	🟡	🟡	🔴	🟢	🟡	🟡	🟡
Passoni 2014	🔴	🔴	🔴	🟢	🟢	🟡	🟡

Figure 4: Risk of bias graph showing judgements about risk of bias domains presented as percentages across all studies.



3.6 Meta-Analysis

Separate random effects meta-analyses were completed for anxiety, the primary outcome measure and depression, the secondary outcome measure. The standard mean effect sizes (reported as Hedge's g) are presented, based on weighted study effect sizes, for these outcome variables. Outcomes relating to each research question will be presented in turn, organised by outcome measure.

Throughout this section *n* refers to the number of participants included in the analyses and *k* refers to the number of studies that contributed to the analysis. Confidence intervals (CI) are reported at the 95% level for all analysis figures. For assessment of heterogeneity, to determine statistical significance, an alpha level of 0.1 was adopted due to the lack of statistical power of the chi-squared test when used in this context (Fletcher, 2007).

3.6.1 Primary question: How effective is CBT in comparison to control conditions for anxiety in informal care-givers of people with dementia?

Fourteen studies, including 1701 participants, (922 CBT, 779 control), were included in a random effects meta-analysis investigating the effectiveness of CBT for anxiety in informal care-givers of people with dementia. The study by Burgio et al. (2003) reported outcomes stratified by race, White American vs African American, and therefore these two arms were entered separately into the analysis as the control arms were also separate. A priori it was decided that where studies included two different CBT interventions in comparison to a control group a composite variable would be computed, for entry into the main analysis, using the mean of intervention A versus control and B versus control (see section 2.5.4 of method) (Borenstein et al., 2009). This technique was applied to Passoni et al. (2014) to create a single pair-wise comparison for the main analysis (Higgins & Green, 2011).

A random-effects meta-analysis of posttreatment anxiety outcomes for CBT interventions indicated a significant “small” effect favouring CBT over waiting-list, treatment as usual, and minimal support groups for anxiety as reported by care-givers (g = -0.15, 95% CI [-0.15, 0.00], z = 1.94, p = 0.05, k = 14, n = 1600) (Figure 5). Results indicate a moderate level of heterogeneity (I^2 = 52%) and this was significant (X^2 = 29.29, df = 14, p = 0.01) suggesting that the variability in estimated treatment effect was due to heterogeneity rather than chance fluctuations.

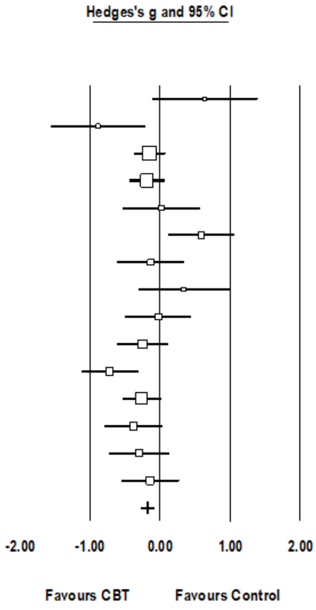
The study by Akkerman & Ostwald (2004) and the study by Karagiozi et al. (2014) were identified as having a SMD considerably higher (g = -0.88, g = -0.72 respectively) than the other included studies (g ranged from -0.38 to 0.64). Therefore a sensitivity analysis was completed removing these outliers. Their exclusion resulted in no significant treatment effect (k = 12, n = 1468, g = -0.10, 95% [-0.23, 0.04], z = 1.42, p = 0.16) and reduced heterogeneity to 32% (p = 0.12). This indicates that the inclusion of these studies had an impact upon the pooled SMD. Of note the study by Akkerman & Ostwald (2004) was the only study whose intervention was designed with the sole focus of reducing care-giver anxiety. The study by Karagiozi et al. (2014) included an intervention that was almost twice as long as all other interventions, and involved two session of 90 minutes each week.

A further sensitivity analysis was completed to remove those studies deemed to be at high risk of bias (Akkerman & Ostwald, 2004; Aboulafia-Brakha et al., 2014; Beauchamp et al., 2014; Burgio et al., 2003; Chang, 1999; Passoni et al., 2014). Exclusion of these studies resulted in a “small” but non-significant effect size favouring CBT over the control comparators (k = 8, n =956, g = -0.25, 95% CI [-0.41, -0.10], z = 3.15, p = 0.22). The level of heterogeneity was no longer statistically significant and reduced to a level which may not be important (X^2 =9.45, df = 7, p = 0.22, I^2 = 26%), suggesting that these studies had a considerable impact on the consistency of outcomes.

A third sensitivity analysis was conducted investigating the impact of comparator condition upon treatment outcome. Three comparators were considered; waiting list, minimal support group which included treatment as usual, and psychoeducation. Results indicate that CBT is associated with “small” significant treatment effect, in favour of CBT ($g = -0.40$, 95% CI [-0.75, -0.06], $z = 2.29$, $p = 0.02$, $k = 4$, $n = 533$) when compared to waiting list control conditions only. This analysis is associated with moderate heterogeneity ($I^2 =$ 66%). No treatment effect was found when CBT was compared to minimal support control conditions, or to an active comparator suggesting that comparator condition has an impact upon treatment effect outcomes. The difference between comparator groups did not reach statistical significance but the analysis indicated a moderate level of heterogeneity ($X^2 = 3.51$, df = 2, p = 0.17, $I^2 = 43.1\%$). However, this comparison should be treated with caution as there were only a small number of studies in each comparison, and the studies comparing CBT to waiting list contained both the Akkerman & Ostwald (2004) and the Karagiozi et al. (2014) study, both of which had SMD higher than other included studies.

Figure 5. Forest plot showing estimated treatment effect of CBT for anxiety outcomes in informal dementia care-givers.

Study name	Statistics for each study						
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
ABOULAFIA-BRAKHA 2014	0.638	0.385	0.149	-0.117	1.394	1.656	0.098
AKKERMAN 2004	-0.883	0.347	0.120	-1.563	-0.203	-2.545	0.011
BEAUCHAMP 2005	-0.149	0.116	0.013	-0.376	0.077	-1.292	0.196
BLOM 2015	-0.186	0.131	0.017	-0.442	0.070	-1.424	0.154
BURGIO 2003 AA	0.016	0.284	0.081	-0.541	0.573	0.056	0.956
BURGIO 2003 W	0.592	0.242	0.058	0.118	1.065	2.447	0.014
CHANG 1999	-0.133	0.246	0.060	-0.614	0.349	-0.540	0.589
GENDRON 1996	0.340	0.333	0.111	-0.312	0.993	1.022	0.307
GONYEA 2014	-0.024	0.242	0.058	-0.498	0.449	-0.101	0.920
HEBERT 2003	-0.249	0.185	0.034	-0.613	0.114	-1.346	0.178
KARAGIOZI 2014	-0.718	0.208	0.043	-1.126	-0.310	-3.447	0.001
LIVINGSTON 2014	-0.261	0.141	0.020	-0.538	0.016	-1.845	0.065
LOSADA 2015	-0.380	0.211	0.045	-0.794	0.034	-1.798	0.072
MARTIN-CARRASCO 2009	-0.295	0.221	0.049	-0.728	0.137	-1.340	0.180
PASSINI 2014	-0.141	0.210	0.044	-0.553	0.272	-0.669	0.504
	-0.178	0.051	0.003	-0.277	-0.078	-3.499	0.000



3.6.2 Exploratory questions.

The following analyses fall into three categories; those investigating in: What impact does the intervention format have upon the effectiveness of Cognitive Behavioural Therapy (CBT) for anxiety in informal dementia care-givers?

3.6.2.1 Questions investigating intervention characteristics.

3.6.2.1.1 Is individual CBT with care-givers of people with dementia more effective at reducing anxiety than group CBT?

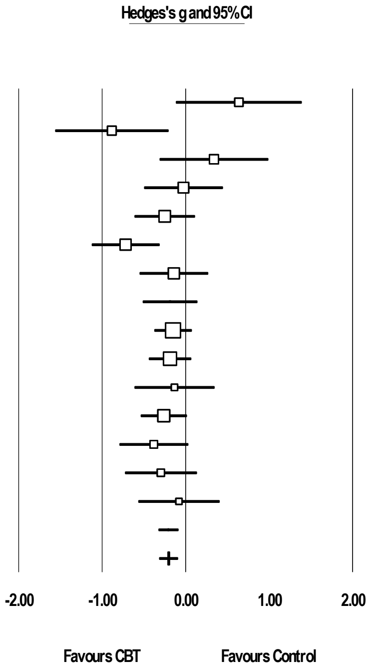
A subgroup analysis was completed to investigate the impact of intervention delivery format upon anxiety in informal dementia care-givers. The study by Burgio et al. (2003) was excluded from the planned subgroup analysis as the intervention employed a mixed approach, including both individual and group CBT. The study by Passoni et al. 2014 was included in both the group comparison and the individual comparison as their trial included two CBT arms, one delivered in a group format and one delivered to the individual. As this meant entering the control data twice a sensitivity analysis was completed investigating the impact of this and it was deemed to have little or no importance.

Subgroup analysis of studies employing individual CBT versus those using group CBT indicated there were no significant statistical differences between them. A “small” effect size was found for both group (g=-0.19) and individual (g=-0.21) CBT, favouring CBT over comparators. This was statistically significant for individual CBT interventions (p = 0.001), but not for group CBT interventions (p = 0.27). The results suggested high levels of heterogeneity for the group CBT interventions (I^2 = 74%).

Visual analysis of the forest plot represented in Figure 6 indicated both Akkerman & Ostwald (2004) and Karagiozi et al. (2014), group CBT interventions, were outliers. Akkerman & Ostwald (2004) is the only study which was specifically designed with the exclusive aim of reducing anxiety in care-givers, and Karagiozi et al. (2014) was by far the most intensive and longest intervention. Exclusion of both these studies though sensitivity analysis resulted in no significant treatment effects for group CBT over comparators and reduced heterogeneity (I^2=32%).

Figure 6. Forest plot showing estimated treatment effect of CBT for anxiety in dementia care-givers: delivery format subgroup analysis.

Group by Delivery format	Study name	Statistics for each study						
		Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Group	ABOULAFIA-BRAKHA 2014	0.638	0.385	0.149	-0.117	1.394	1.656	0.098
Group	AKKERMAN 2004	-0.883	0.347	0.120	-1.563	-0.203	-2.545	0.011
Group	GENDRON 1996	0.340	0.333	0.111	-0.312	0.993	1.022	0.307
Group	GONYEA 2014	-0.024	0.242	0.058	-0.498	0.449	-0.101	0.920
Group	HEBERT 2003	-0.249	0.185	0.034	-0.613	0.114	-1.346	0.178
Group	KARAGIOZI 2014	-0.718	0.208	0.043	-1.126	-0.310	-3.447	0.001
Group	PASSONI 2014	-0.141	0.210	0.044	-0.553	0.272	-0.669	0.504
Group		-0.186	0.168	0.028	-0.515	0.143	-1.109	0.267
Individual	BEAUCHAMP 2005	-0.149	0.116	0.013	-0.376	0.077	-1.292	0.196
Individual	BLOM 2015	-0.186	0.131	0.017	-0.442	0.070	-1.424	0.154
Individual	CHANG 1999	-0.133	0.246	0.060	-0.614	0.349	-0.540	0.589
Individual	LIVINGSTON 2014	-0.261	0.141	0.020	-0.538	0.016	-1.845	0.065
Individual	LOSADA 2015	-0.380	0.211	0.045	-0.794	0.034	-1.798	0.072
Individual	MARTIN-CARRASCO 2009	-0.295	0.221	0.049	-0.728	0.137	-1.340	0.180
Individual	PASSONI I 2014	-0.079	0.249	0.062	-0.568	0.410	-0.317	0.751
Individual		-0.205	0.062	0.004	-0.327	-0.084	-3.304	0.001
Overall		-0.203	0.058	0.003	-0.317	-0.089	-3.483	0.000



3.6.2.1.2 Is CBT delivered by a therapist using face to face contact more effective at reducing anxiety in informal care-givers of people with dementia than CBT interventions delivered using technology?

A priori it was decided that a subgroup analysis would be conducted investigating the impact of mode of delivery, therapist vs technology. However, only two studies were identified for inclusion that used technology to deliver their intervention (Beauchamp et al., 2014; Blom et al., 2015). These two studies varied greatly with regards to both clinical and methodological factors, consequently it was decided that synthesising these data was not considered appropriate.

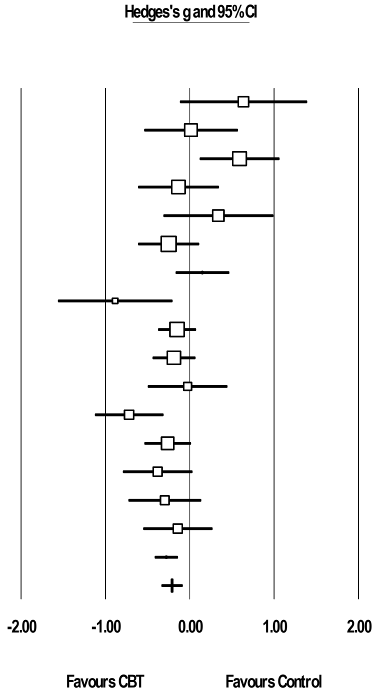
3.6.2.1.3 Is CBT which contains a relaxation component more effective than those which do not at reducing anxiety in informal care-givers of people with dementia?

A “small” and significant effect size was found in favour of CBT interventions which contained a relaxation component over comparators for anxiety not including a relaxation component (*g* = -0.28, 95% CI [-0.42, -0.14], *z* = 3.90, *p*<0.0001). The level of heterogeneity was low and not significant (I^2 = 25%, *p* = 0.22***)***. For those studies which did not include a relaxation component the results indicated a “small” effect favouring comparators over CBT (*g* = 0.15, 95% CI [-0.17, 0.47]). This was not statistically significant (*p*= 0.35) and there was a moderate level of heterogeneity (I^2 = 54%). The difference between studies with a relaxation component and those without did not reach statistical significance.

Visual analysis of the forest plot represented in Figure 7 again identified both Akkerman & Ostwald (2004) and Karagiozi et al. (2014) as outliers. A sensitivity analysis was completed and the effect sizes were maintained despite their exclusion.

Figure 7. Forest plot showing estimated treatment effect of CBT for anxiety in dementia care-givers: relaxation component subgroup analysis.

Group by Relaxation	Study name	Statistics for each study						
		Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
NO	ABOULAFIA-BRAKHA 2014	0.638	0.385	0.149	-0.117	1.394	1.656	0.098
NO	BURGIO 2003 AA	0.016	0.284	0.081	-0.541	0.573	0.056	0.956
NO	BURGIO 2003 W	0.592	0.242	0.058	0.118	1.065	2.447	0.014
NO	CHANG 1999	-0.133	0.246	0.060	-0.614	0.349	-0.540	0.589
NO	GENDRON 1996	0.340	0.333	0.111	-0.312	0.993	1.022	0.307
NO	HEBERT 2003	-0.249	0.185	0.034	-0.613	0.114	-1.346	0.178
NO		0.151	0.163	0.027	-0.168	0.470	0.927	0.354
YES	AKKERMAN 2004	-0.883	0.347	0.120	-1.563	-0.203	-2.545	0.011
YES	BEAUCHAMP 2005	-0.149	0.116	0.013	-0.376	0.077	-1.292	0.196
YES	BLOM 2015	-0.186	0.131	0.017	-0.442	0.070	-1.424	0.154
YES	GONYEA 2014	-0.024	0.242	0.058	-0.498	0.449	-0.101	0.920
YES	KARAGIOZI 2014	-0.718	0.208	0.043	-1.126	-0.310	-3.447	0.001
YES	LIVINGSTON 2014	-0.261	0.141	0.020	-0.538	0.016	-1.845	0.065
YES	LOSADA 2015	-0.380	0.211	0.045	-0.794	0.034	-1.798	0.072
YES	MARTIN-CARRASCO 2009	-0.295	0.221	0.049	-0.728	0.137	-1.340	0.180
YES	PASSINI 2014	-0.141	0.210	0.044	-0.553	0.272	-0.669	0.504
YES		-0.277	0.071	0.005	-0.416	-0.138	-3.899	0.000
Overall		-0.208	0.065	0.004	-0.336	-0.081	-3.205	0.001



3.6.2.2 Questions investigating care-giver characteristics.

3.6.2.2.1 Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by care-giver gender?

Subgroup analysis was planned to investigate whether the effectiveness of CBT with care-givers is influenced by care-giver gender. However, none of the included studies had restricted eligibility to male care-givers and none had reported subgroup analysis by gender. Therefore simple meta-regression was used to evaluate the impact of care-giver gender on effect sizes for CBT for anxiety at post-assessment. The percentage of female participants reported by each study was entered as the co-variate. The results indicated that the percentage of female care-givers reported by studies did not significantly predict the study effect sizes for the impact of CBT upon care-giver anxiety, $ß = -0.01$, $SE = 0.01$, $Z = -1.68$, $p = 0.09$.

3.6.2.2.2 Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by relationship to care-receiver?

Two studies did not report the relationship of care-giver to care-receiver (Akkerman & Ostwald, 2004; Passoni et al., 2014) and therefore could not be included in this analysis. For all other studies ($k= 12$) a simple meta-regression analysis indicated that the percentage of spousal care-givers reported by studies did not significantly predict the study effect sizes for the impact of CBT upon care-giver anxiety, $ß = 0.005$, $SE = 0.003$, $Z = 1.57$, $p = 0.12$.

3.6.2.2.3 Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by care-givers' anxiety levels at baseline?

It was planned to complete further analysis investigating the impact of baseline anxiety scores using the percentage of care-givers reaching above clinical cut off for anxiety as the covariate. However, this information was not reported clearly by the majority of included studies. The Cochrane review does not recommend meta-regression when there are fewer than ten studies (Deeks et al., 2011). Therefore in practice there was insufficient data available and it was decided that conducting this analysis was not appropriate.

3.6.2.3 Questions investigating care-receiver characteristics.

3.6.2.3.1 Is the effectiveness of CBT for anxiety in informal care-givers of people with dementia moderated by care-receiver dementia diagnosis?

A priori it had been planned to investigate the impact of care-receiver diagnosis upon effect sizes for CBT for anxiety in informal dementia care-givers. However, it was not possible to conduct planned meta-regression analysis by percent of Alzheimer's diagnosis of person with dementia as the majority of studies did not report dementia diagnosis (k =7) (Deeks et al., 2011).

3.6.3 Secondary Question: How effective is CBT, in comparison to control conditions, for depression in informal care-givers of people with dementia?

The studies by Akkerman & Ostwald (2004) and Hebert et al. (2003) did not include a measure of care-giver depression. Therefore only 12 studies were entered in the analysis for depression (N= 1452, 812 CBT: 640 Control). The study by Burgio et al. (2003) reported outcomes stratified by race, African American vs White care-givers, so these were entered into the analysis as two separate arms.

A random effects meta-analysis of posttreatment depression outcomes for CBT interventions indicated a significant "small" effect favouring CBT over waiting list, treatment as usual, and minimal support groups for depression as reported by care-givers (g = -0.21, 95% CI [-0.39, -0.02], z = 2.19, p = 0.03, k = 12, n = 1600) (Figure 8). Results indicate a moderate level of heterogeneity (I^2 = 62%) and this was significant (X^2 = 31.89, df = 12, p = 0.001) suggesting that the variability in estimated treatment effect was due to heterogeneity rather than chance fluctuations.

Two studies (Karagiozi et al., 2014; Losada et al., 2015) were identified as having a SMD considerably higher (*g* = -0.99, *g* = -0.78 respectively) than the other included studies (*g* ranged from -0.43 to 0.38). Therefore a sensitivity analysis was completed removing these outliers. Their exclusion resulted in a reduced “small” significant treatment effect (*g* = -0.12, 95% [-0.23, -0.00], *z* = 2.00, *p* = 0.05, *k* = 10, *n* = 1265) and reduced heterogeneity to 0% (*p* = 0.51). This indicates that the inclusion of these studies had an impact upon the pooled SMD.

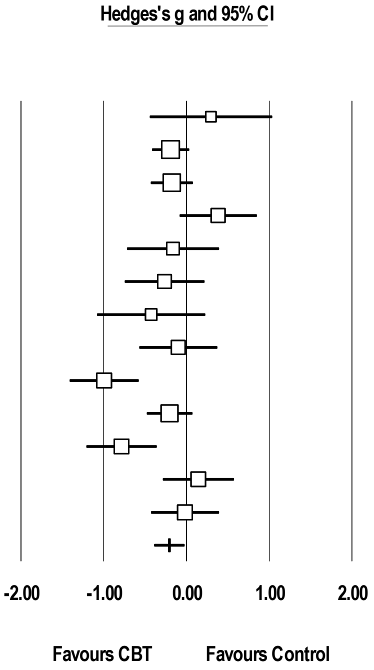
As per the meta-analysis for anxiety outcomes a further sensitivity analysis was completed to remove those studies deemed to be at high risk of bias (Aboulafia-Brakha et al., 2014; Beauchamp et al., 2014; Burgio et al., 2003; Chang, 1999; Passoni et al., 2014). Exclusion of these studies resulted in an increased “small” significant effect size favouring CBT over the control comparators (*g* = -0.35, 95% CI [-0.63, -0.07], *z* = 2.45, *p* = 0.01, *k* = 7, *n* =841). The level of heterogeneity was statistically significant and represents a level approaching high (I^2 = 72%), suggesting that the removal of these studies had a considerable impact on the consistency of outcomes.

A third sensitivity analysis was conducted investigating the impact of comparator condition upon treatment outcome for depression. Results indicate that CBT is associated with a “small” but non-significant treatment effect, in favour of CBT (*g* = -0.39, 95% CI [-0.90, 0.13], *z* = 1.47, *p* = 0.14, *k* = 3, *n* = 298) when compared to waiting list control conditions only. This analysis is associated with high heterogeneity (I^2 = 85%). When CBT was compared to minimal support control conditions a “small” significant treatment effect was found in favours of CBT (*g* = -0.16, 95% CI [-0.40, 0.08], *z* = 1.47, *p* = 0.02, *k* = 6, *n* = 825), this was associated with moderate heterogeneity (I^2 = 61%). No significant treatment effect was found when CBT was compared to psycho-education comparator groups. The test for subgroup differences was not significant and indicated a level of heterogeneity that may not be important ($I^2 = 0\%$).

Figure 8. Forest plot showing estimated treatment effect of CBT for self-report depression outcomes in dementia care-givers.

Statistics for each study

Study name	**Hedges's g**	**Standard error**	**Variance**	**Lower limit**	**Upper limit**	**Z-Value**	**p-Value**
Aboulafia-Brakha 2014	0.298	0.378	0.143	-0.443	1.038	0.788	0.431
Beauchamp 2005	-0.190	0.116	0.013	-0.417	0.036	-1.647	0.100
Blom 2015	-0.176	0.131	0.017	-0.432	0.080	-1.344	0.179
Burgio 2003 W	0.384	0.239	0.057	-0.083	0.852	1.610	0.107
Burgio 2003 AA	-0.161	0.285	0.081	-0.719	0.397	-0.566	0.571
Chang 1999	-0.263	0.246	0.061	-0.746	0.220	-1.066	0.286
Gendron 1996	-0.425	0.334	0.112	-1.080	0.230	-1.271	0.204
Gonyea 2014	-0.098	0.242	0.058	-0.571	0.376	-0.404	0.686
Karagiozi 2014	-0.993	0.214	0.046	-1.412	-0.574	-4.641	0.000
Livingston 2014	-0.203	0.141	0.020	-0.480	0.074	-1.435	0.151
Losada 2015	-0.783	0.217	0.047	-1.209	-0.357	-3.601	0.000
Martin-Carrasco 2009	0.145	0.220	0.048	-0.286	0.575	0.659	0.510
Passoni 2014	-0.016	0.210	0.044	-0.428	0.395	-0.078	0.938
	-0.206	0.094	0.009	-0.391	-0.021	-2.184	0.029



3.6.4 Follow up data.

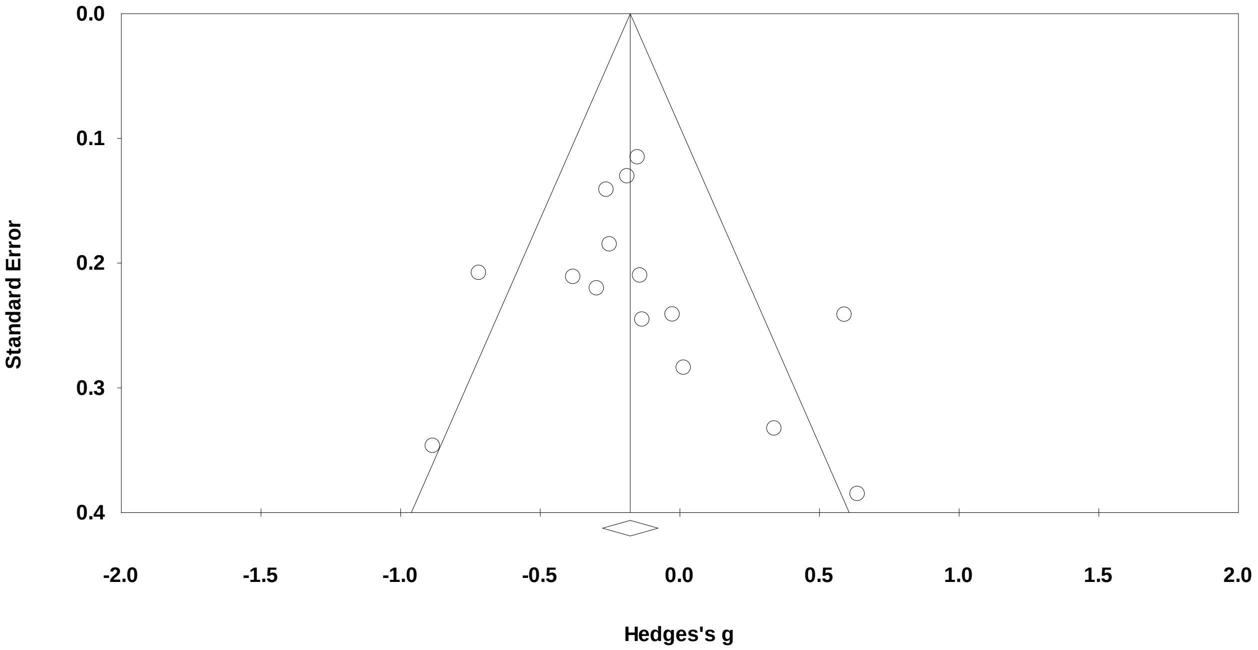
A further random effects meta-analysis was conducted using follow up data for both anxiety and depression outcomes. For studies that reported more than one follow up time point the data for the longest follow up time point was used. Data at follow up was only available for five studies (Chang, 1999; Gonyea et al., 2014; Livingston et al., 2014; Losada et al., 2015; Martin-Carrasco et al., 2009) (k=5, n=303). Three studies which reported assessing care-givers at follow up could not be included because they did not report these outcomes (Burgio et al., 2003; Gendron et al., 1996). The final study employed a methodology which meant that outcomes were not available for the control group (Akkerman & Ostwald, 2004).

A significant “small” effect was found favouring CBT over comparators for anxiety and depression outcomes as reported by care-givers at follow-up (*g* = -0.31, 95% CI [0.51, -0.12], *z* = -3.13, *p* = 0.002, and *g* = 0.31, 95% CI [-0.49, -0.13], *z* = -3.43, *p* = 0.001 respectively). The magnitude of the effect was slightly increased in comparison to post-intervention outcomes. Results for both analyses indicated low levels of heterogeneity.

3.7 Publication Bias

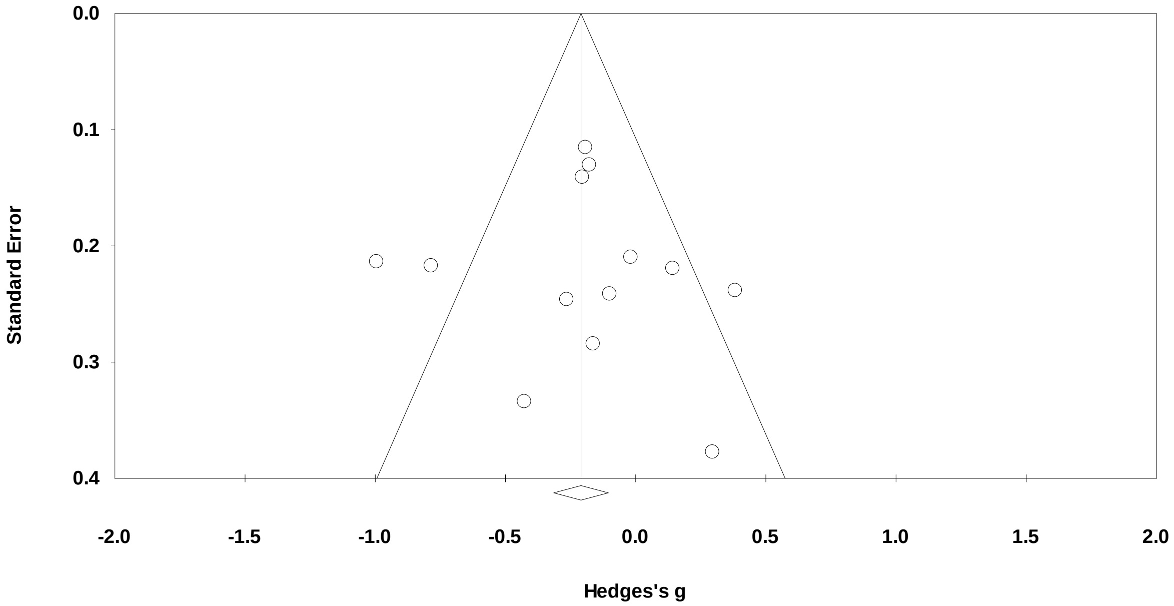
A funnel plot was used to graphically assess publication bias for both anxiety and depression outcomes by plotting the summary effect size against the standard error (Light & Pillemer, 1984). The symmetry of the funnel plots were assessed visually in the first instance. The plot for anxiety outcomes (Figure 9) is reasonably symmetrical but suggests that small scale studies with small effect sizes are missing. The significance of this was assessed using Egger’s test of the intercept with Hedge’s g as the standard difference. This was not significant (*t* = 0.83, *df* = 13, *two tailed p* = 0.42) suggesting insufficient evidence to indicate the presence of publication bias.

Figure 9. Funnel plot of standard error by Hedge’s g: CBT versus control for anxiety.



Visual inspection of the funnel plot for depression outcomes (Figure 10) showed reasonable symmetry with the presence of two outliers. Egger's test of the intercept showed that there was no significant asymmetry, again suggesting that there was insufficient evidence to indicate the presence of publication bias (*t* = 0.16, *df* = 11, *two tailed p* = 0.87).

Figure 10. Funnel plot of standard error by Hedge's g: CBT versus control for depression.



3.8 Chapter Summary

A total of 6450 articles were screened during the study selection process. Studies were screened based on the inclusion criteria and reasons for excluding studies were reported within this chapter. A total of 14 studies investigating the impact of CBT interventions upon anxiety in informal dementia care-givers were included in the data synthesis. The included studies involved a total of 1701 participants, 922 assigned to CBT interventions and 779 in control conditions. These studies used a mixture of waiting list, minimal support and psychoeducation as comparators and the majority were randomised controlled trials. Two studies delivered the CBT intervention via the internet, whilst all other studies used CBT delivered in a traditional format by therapists. Most of the information included in this review was from studies deemed to be at an unclear risk of bias.

Quantitative synthesis of post treatment data suggest that CBT for anxiety in dementia care-givers is associated with a “small” effect with the presence of significant and clinical heterogeneity. A small effect was also indicated for symptoms of depression in care-givers post treatment. These effects were maintained to follow up. Sensitivity analysis indicated that the type of comparator contributed to the effect size for anxiety outcomes, with CBT being favoured over waiting list conditions but demonstrating no treatment effects when compared to minimal support groups and psychoeducation.

Planned subgroup analysis investigating the impact of delivery format upon anxiety outcomes suggested that there was no significant difference between individual and group CBT formats. Excluding studies which did not include a relaxation component within their intervention slightly increased the magnitude of the effect in favour of CBT over all comparators. An investigation of care-giver gender suggested that this care-giver characteristic did not impact upon outcomes. However, limitations with subgroup analyses mean they should be treated with caution. Additional planned subgroup analyses to investigate other care-giver characteristics and to investigate care-receiver characteristics were not possible due to the small numbers of studies reporting these outcomes.

Chapter Four: Discussion

4.1 Chapter Outline

The primary aim of the current meta-analysis was to systematically appraise the available research investigating the use of CBT interventions for anxiety in informal care-givers of people with dementia. CBT has shown potential with this client group; however, to date there has been little systematic appraisal of CBT interventions in isolation from other interventions. Additionally, the available appraisals have mostly focussed upon other care-giver outcomes and not upon anxiety. Within this chapter, the main findings of the review are summarised in relation to the research questions and the available background literature. The clinical implications of the findings are discussed, as are the theoretical implications, and recommendations for future research are outlined (Schünemann et al., 2011). Finally the chapter concludes with a review of the strengths and limitations of the current research and an overall summary.

4.2 Summary of Main Findings

4.2.1 Primary research question: How effective is CBT in comparison to control conditions for anxiety in informal care-givers of people with dementia?

A total of 14 studies were identified that investigated the impact of a CBT intervention upon informal care-givers' anxiety levels in comparison to a control condition, as measured by self-report outcomes. These interventions all included both cognitive and behavioural components of CBT (Laidlaw et al., 2003). The results indicated that at post intervention, CBT is associated with a "small" effect ($g = -0.15$) and is favoured over controls. The magnitude of the effect increased slightly at follow-up ($g = -0.31$) and was again in favour of CBT interventions; however, only five studies reported follow up data. The magnitude of this effect was maintained when studies deemed to be of high risk of bias were removed, but it was no longer statistically significant.

Two studies (Akkerman & Ostwald, 2004; Karagiozi et al., 2014) were identified as outliers and a subsequent analysis was completed with them removed. The removal of these studies resulted in a reduction in the effect size (*g* = -0.10). Of note, the study by Akkerman & Ostwald (2004) was the only study with an intervention designed with the sole focus of reducing care-giver anxiety. The systematic review completed by Cooper et al. (2007) also singled out this study as being the most effective at reducing care-giver anxiety out of the three CBT interventions reviewed. Possible explanations for this are discussed later in this chapter. The study by Karagiozi, et al. (2014) included an intervention that was almost twice as long as all the other interventions, suggesting that perhaps the length of intervention has an impact upon intervention effectiveness.

A final analysis investigated the effectiveness of CBT for anxiety in informal care-givers in comparison to each type of control condition in isolation. The magnitude of the effect size for CBT at post-intervention was increased when compared to waiting list only (*g* = -0.40); however, no significant treatment effects were found when CBT was compared to minimal support group or to psychoeducation.

Overall, the findings suggest that CBT is more effective than no treatment at reducing anxiety in informal care-givers of people with dementia when considering self-report measures. The results are less clear when comparing CBT to minimal support groups or to more active control conditions employing psychoeducation. The effect sizes reported by the present review are not dissimilar to those reported by the Vernooij-Dassen et al. (2011) meta-analysis of interventions for care-givers that included cognitive reframing, an element of CBT. They also reported “small” effect sizes in favour of CBT interventions (SMD = -0.21) over controls; however, they do not explore the impact of type of control upon outcomes so no further comparisons could be made.

4.2.1.1 Exploratory questions.

The present review completed exploratory analysis with the aim of investigating the impact of intervention characteristics, care-giver characteristics and care-receiver characteristics upon the effectiveness of CBT for anxiety in informal care-givers of people with dementia. However, these planned subgroup analyses were restricted to a degree by a lack of studies reporting the necessary information (Deeks et al., 2011).

Previous research suggests some differences between the type of dementia the care-receiver is diagnosed with and the impact this has upon care-givers (Diehl et al., 2003). For example, there is evidence that frontotemporal dementia can cause higher levels of distress in informal care-givers (Nicolaou et al., 2010) and it was hoped that the present study might have investigated whether this also has an impact upon the effectiveness of CBT interventions. However, this was not possible due to the limited number of studies reporting this information (k=7). For similar reasons it was also not possible to investigate the impact of mode of delivery upon outcomes as only two studies used technology (Beauchamp et al., 2014; Blom et al., 2015), as opposed to face to face therapist contact, to deliver their interventions. These studies were felt to vary greatly both clinically, and methodologically, therefore is was not considered appropriate to synthesise this data. Finally, it was also hoped that an analysis to investigate the impact of the percentage of participants scoring above clinical cut-off for anxiety at baseline could be completed. Unfortunately this was not possible, again due to the lack of studies reporting this information. The possible impact of this will be discussed in section 4.3.

4.2.1.1.1 Questions investigating intervention characteristics.

Subgroup analysis investigating the impact of CBT interventions upon anxiety in informal care-givers of people with dementia indicated no significant difference in effect between individual and group based CBT. Both individual and group CBT achieved “small” effect sizes (*g* = -0.20 and *g* = -0.21 respectively). However, the two studies identified as outliers (Akkerman & Ostwald, 2004; Karagiozi et al., 2014) both fell within the category of group CBT interventions and their exclusion resulted in no significant treatment effects for group CBT. An earlier review completed by Sorensen, Pinquart & Duberstein (2002) found that group interventions were also less effective at reducing symptoms of burden in care-givers and that individual interventions were better placed to increase care-giver wellbeing. Direct comparison to the present review cannot be made as Sorensen et al. (2002) did not investigate anxiety as an outcome and they also included different models of care-giver interventions; however, it may be that working at an individual level has the potential to improve outcomes.

The previous review by Cooper et al. (2007) highlighted the potential importance of including a relaxation component in interventions aiming to reduce anxiety in informal care-givers of people with dementia. The subgroup analysis investigating this within the present study lends some support to this conclusion. Whilst the difference between those CBT interventions which contained a relaxation component and those that did not did not reach statistical significance with regards to the impact they had upon anxiety in informal care-givers at post intervention, the results suggest some differences. Subgroup analysis including only CBT interventions which contained a relaxation component increased the overall magnitude of the effect size, although still “small”, in favour of CBT over control (g= -0.27). This effect was maintained when the two studies identified as outliers (Akkerman & Ostwald, 2004; Karagiozi et al., 2014) were removed. In comparison the analysis for CBT interventions without a relaxation component found a “small” non-significant effect size in favour of control conditions (g = 0.15).

4.2.1.1.2 Questions investigating care-giver characteristics.

The included studies did not evaluate the impact of CBT upon care-giver anxiety according to care-giver gender, therefore it was not possible to conduct the planned subgroup analysis on this variable. Instead a regression analysis was completed using the percentage of female participants reported by the study. The results suggested that care-giver gender did not have an impact on the effectiveness of CBT interventions. However, generally, the included studies recruited very few male participants and it is possible that male care-givers would be less likely to show a decline in negative symptomatology associated with care-giving due to their reluctance to disclose negative feelings (Pinquart & Sorensen, 2006a). Therefore unless differences between males and females were particularly significant the method of analysis is likely to have masked any discrepancies and as such this conclusion should be regarded as tentative.

A further analysis also suggested that the relationship to care-receiver did not significantly predict the outcome of CBT interventions for anxiety outcomes. However, caution must be applied again to this finding as no study reported outcomes by care-giver to care-receiver relationship, therefore the present review used the percentage of spousal care-givers in this analysis. Subsequently it is possible that the impact of other relationships were masked.

It was not possible to investigate the impact of baseline anxiety scores upon outcomes. It was hoped that the percentage of care-givers scoring above cut off for anxiety could be used as a covariate, however the majority of studies did not report this information.

4.2.2 Secondary Question: How effective is CBT, in comparison to control conditions, for depression in informal care-givers of people with dementia?

The secondary aim of the present review was to synthesise the research investigating the effectiveness of CBT interventions in the reduction of depression in informal care-givers of people with dementia. The results of this analysis indicated a “small” significant effect favouring CBT over control conditions (*g* = -0.21) at post-intervention. Removal of studies deemed to be high risk of bias increased the magnitude of this effect size slightly. A further analysis was completed removing two studies which were identified as outliers (Karagiozi et al., 2014; Losada et al., 2015). This reduced the effect size and also the heterogeneity between studies suggesting that these studies had an impact on the variability seen. When CBT was compared to waiting list and minimal support group controls in isolation the favourable effects of CBT upon depression outcomes were maintained. However, when compared to psychoeducation controls, no significant treatment effect was found. At follow up, the magnitude of the effect size for CBT interventions was increased slightly (*g* =-0.31) and again this favoured CBT over control conditions. However, this analysis only contained a small number of studies (*k*= 5) due to the lack of studies reporting follow-up outcomes.

The results of the present study contrasts with a previous review completed by Pinquart & Sorensen (2006b) who found significant “medium” effects for the impact of CBT on care-giver depression (Cohen’s *d* = -0.70) at post-intervention. However, it is not clear exactly what methodology the included studies employed, nor is it clear which studies were included in this review or their quality; this makes further exploration of this difference challenging.

4.3 Theoretical Implications

The most frequently cited model of care-giver distress is that proposed by Lazurus & Folkman’s (1984) Transactional Theory (Levesque et al., 2002). This model draws on the ideas of stress and coping and identifies care-giver distress as being due to the appraisals care-givers make about how difficult or threatening the care-giving situation is, and their assessment of their ability to cope. Put simply if the situation outweighs the care-givers perceived ability to cope then they will become distressed (Folkman, 1997). Subsequently interventions have been developed based upon this idea with the aim of increasing a care-givers' skills and ability to cope and helping them to more realistically appraise their situation. The CBT model lends itself well to this approach and more recently Losada et al. (2006) have proposed a cognitive model to explain exactly how CBT driven interventions with care-givers might work.

Losada et al. (2006) state that early experiences shape a care-givers beliefs about their care-giving role and these in turn lead to the development of either helpful or unhelpful automatic thoughts. Such thoughts then create a range of physiological, behavioural and emotional responses in the care-giver, which again are either helpful or lead to psychological distress. Therefore CBT interventions should focus upon care-givers' core beliefs and automatic thoughts helping them to develop cognitive flexibility and more realistic thoughts. Interventions should also include strategies to assist care-givers to manage their behavioural responses to care-giving as well as considering the link between their behaviour and their emotions, for example, withdrawing from enjoyable social activities and decreased mood (Au et al., 2015).

The current review only included CBT interventions which included both a cognitive component and a behavioural component and therefore targeted all the elements identified by Losada et al. (2006). In support of this model the review found overall effects in favour of CBT for both anxiety and depression in care-givers of people with dementia. However, these effects were "small" for both outcomes, much lower than would be expected given the suggested effectiveness of CBT for anxiety in both the adult and older adult population (Butler et al., 2006; Hofmann & Smits, 2008; Laidlaw & Kishita, 2017) and for depression in care-givers (Pinquart & Sorensen, 2006b). Additionally the findings for anxiety were not robust to all subgroup analyses. Whilst this could be taken to suggest that the CBT model proposed by Losada et al. (2006) does not fully explain care-giver anxiety the “small” effect sizes may also be due to methodological issues with the included studies.

Exploring the literature looking at CBT interventions for anxiety disorders in adults more generally Yulish et al. (2017) proposed that the different findings of RCTs are determined by the degree to which the intervention is focused upon the target problem being presented by the participant. They completed a meta-analysis investigating the impact of focussing upon the participants’ problems on outcomes of CBT treatments for anxiety disorders and concluded that more specific problem focused interventions achieved better outcomes. The primary aim of the present review was to investigate the impact of CBT interventions upon anxiety in informal care-givers of people with dementia. However, in light of the aforementioned study it may be that in order to be particularly effective, first the care-givers would need to identify anxiety as a problem, and secondly the intervention would need to focus upon the target problem of anxiety.

Considering these factors in light of Losada et al. (2006) model of CBT interventions, an intervention focussing specifically on anxiety in care-givers would focus its energy on teaching care-givers to identify anxiety provoking thoughts and to learn strategies for challenging these specifically, and for using behavioural skills to reduce the physiological symptoms of anxiety. However, if the intervention’s primary aim is, for example, to reduce burden in the care-giver or to increase care-giver skills in providing care for someone with a dementia diagnosis the primary focus is very different. Intuitively one would expect the former intervention to have a greater impact upon anxiety. Within this review anxiety was specified as the primary outcome for under half of the included studies, and for all bar one this was in combination with other primary outcomes, such as depression or burden, meaning the intervention had multiple aims. For the rest of the studies included in this review anxiety was a secondary outcome as they focused upon increasing knowledge and skills more generally or reducing behavioural difficulties in the care-receiver rather than upon directly addressing care-giver anxiety. This lack of focus upon anxiety may explain the “small” effect sizes observed.

A similar criticism was levelled against the care-giver intervention research more generally by Knight, Lutzky & Macofsky-Urban (1993) in what is often cited as one of the first meta-analyses of care-giver interventions. They reviewed a wide range of care-giver interventions in an aim to dispel a previous claim that care-giver interventions were ineffective (Callahan, 1989). Whilst Knight et al. (1993) also only observed small to moderate effect sizes they identified that the interventions and the outcomes used were often not appropriately matched. For example, if a study employed a psychoeducation intervention then it would be appropriate to expect strong effects on care-giver knowledge but less so to expect a reduction in care-giver burden as a primary outcome. Within the present review those studies which did identify anxiety as a primary outcome mostly included relaxation as a component to help to manage the behavioural symptoms. Including specific skills to target anxiety should provide the intervention with a better match to the outcomes being assessed. When an analysis was completed with only those studies the effect size increased, thus interventions with a specific focus upon anxiety may achieve larger effect sizes.

Returning to the point raised by Yulish et al. (2017) that in order to be most effective the intervention should focus upon the problem being presented by the care-giver, we must consider that the majority of studies within this review included participants who were not showing difficulties with anxiety at baseline. This means that they were unlikely to identify anxiety as a problem they needed support with. This has the potential to impact upon the results in two ways. First focusing on the care-givers’ identified problem may have important implications for change as it sets the care-giver up to focus on that target problem, and engages them in the intervention actively thinking about the outcome they have identified

(Wampold & Budge, 2012). If care-givers included in the studies in this review did not think that they were anxious they were unlikely to attend to, or notice, any change in anxiety and as anxiety was only measured through self-report the care-givers' perceptions were key (Yulish et al., 2017).

Secondly, if baseline anxiety levels are low then the intervention may suffer from the floor effect and it would be unlikely to demonstrate a significant reduction in anxiety (Brodaty & Gresham, 1989; Zarit & Teri, 1991). When meta-analyses suggest overall small effect sizes it is possible that this result may obscure more significant outcomes for a subgroup of patients. For example, Lorenzo-Luaces, Derubeis van Staten, & Tiemens (2016) analysed data investigating the impact of CBT for depression in a community sample. The overall finding was a very small and statistically non-significant advantage for CBT over a TAU control condition. However, when this was investigated further using "Patient Response Patterns" as a subgroup, they found that outcomes for those patients who were deemed to be hard to treat were significantly more positive when treated with CBT as opposed to TAU. This result was over-shadowed by the majority of patients, who fell within the easy to treat category, for whom there was no difference in response to CBT over TAU. The present study had hoped to investigate the impact of anxiety diagnosis at baseline, as it is possible that those who were presenting as more anxious at baseline may have shown more favourable response to CBT (Yulish et al., 2017). However, the studies included in the present review made the assessment of baseline anxiety levels challenging as they commonly did not report cut offs or details of the scores for the scales used. This made such an analysis untenable and possibly meant that results of those care-givers who were anxious at baseline were overshadowed by the majority who were not.

There was only one study which included an intervention which was solely designed with the aim of reducing anxiety. This study also included care-givers who were exhibiting levels of anxiety and therefore were more likely to identify anxiety as a problem (Akkerman & Ostwald, 2004). This intervention focused specifically upon targeting dysfunctional thoughts that gave rise to anxiety and introduced specific skills for managing the behavioural symptoms of anxiety. Of note, this study was identified as an outlier as it found much larger effect sizes in favour of CBT than the other included studies. Considered in light of the above this may further support the hypothesis that CBT has the potential to be more effective than seen in this meta-analysis in the treatment of informal care-giver anxiety. However, that the effectiveness is dependent upon the intervention being focused upon anxiety and the care-givers identifying anxiety as a problem (Yulish et al., 2017).

4.4 Clinical Implications

This review aimed to build upon the work of Cooper et al. (2007) and provide an up to date, comprehensive, systematic appraisal and summary of the literature investigating the effectiveness of CBT interventions for anxiety in informal care-givers of people with dementia in comparison to controls. From a clinical point of view the findings of the present study are not as clear as one might have hoped.

The findings suggest that CBT has potential in the treatment of both anxiety and depression in informal care-givers of people with dementia. This is especially true when compared to no intervention indicating that care-givers who are given access to a CBT intervention are more likely to show lower levels of depression and anxiety than those who are not provided with any support. It may also be that if the care-giver is presenting as clinically anxious then a CBT intervention specifically targeting anxiety has the potential to be effective. This is important clinically as anxiety has been shown to be prevalent amongst this population (Cooper et al., 2007; Dura et al., 1991; Joling et al., 2015; Ostojic et al., 2014) and if not treated can lead to a breakdown of the care-giving situation leading to a potential admission to an institution for the care-receiver and poor outcomes for the care-giver (Prince et al., 2014; Spijker et al., 2008).

When compared to more active control groups, in particular psychoeducation, the effects of CBT upon anxiety were reduced. Again there are a number of possible explanations for this, including methodological weakness. However, it may also be that CBT and psychoeducational groups are comparable in terms of their effectiveness. Indeed there are a number of overlaps between the two approaches as both interventions seek to provide care-givers with increased knowledge about dementia, and general care-giving skills, and past reviews have grouped these interventions together (Gallagher-Thompson & Coon, 2007). It is possible that such education is in itself effective in producing change; however, more systematic appraisals of the literature are needed to address this question. Clinically this has the potential to be important as psychoeducation groups are already established within the charity sector (Hebert et al., 2003) and it may be that there is no justification for clinicians in memory clinics, or mental health settings, to offer additional interventions for care-givers if they can receive such interventions in a more accessible and less costly setting.

Should services provide specific interventions for informal care-givers of dementia the present review has identified relaxation as a potentially important component to consider when working with care-givers who appear anxious. This is in line with the recommendations made by Cooper et al. (2007). This is useful information for clinicians to keep in mind as it may be that they are able to introduce some elements of relaxation techniques even if a full CBT intervention is not available. However, again further research is needed and this will be highlighted in the following section.

Finally it is generally accepted in the literature that individually tailoring interventions to care-givers is beneficial (Elvish et al., 2013; Livingston et al., 2014; Lui & Gallagher-Thompson, 2009; Smits et al., 2007; Zarit & Femia, 2008). This has led some to argue that an individual format is preferable because it makes such tailoring easier to organise (Livingston et al., 2014; Losada et al., 2015; Selwood et al., 2007). The present study did not find a vast difference between those interventions that were delivered in an individual format and those delivered in a group format with regards to anxiety outcomes. From a clinical perspective this may allow clinicians more freedom to choose an intervention that best fits with their service. However, it is important to keep in mind that nearly all the studies included in this review allowed for individualisation to some degree within their interventions and therefore any intervention should look to maintain this (Noar, Benac & Harris, 2007; Yulish et al., 2017). Additionally it will be important to take the individual care-giver into consideration as for some care-givers the idea of joining a group setting may in itself be anxiety provoking and subsequently prevent them from engaging (Butler et al., 2006).

Within the UK the CBT model is already well established within a range of care settings, therefore, there are a range of staff familiar with its delivery. This potentially provides an opportunity for easier translation from research to practice (Livingston et al., 2014). This is important as reviews have highlighted successful interventions with care-givers but despite this they are not widely known about by clinicians or widely available in services (Banerjee, 2014; Maslow, 2012). From a clinical point of view ease of translation to clinical settings could mean increased accessibility and cost-effective delivery should CBT interventions be recommended as effective for anxiety in informal care-givers of people with dementia. However, the findings of the present review do not lend themselves easily to such firm recommendations for clinical practice and call for further research.

4.4 Future Research

This meta-analysis has perhaps generated more questions than it has answered and this lends itself to a number of recommendations for future research. With regards to further CBT intervention research for anxiety in dementia care-givers these recommendations broadly fall into two categories; research investigating the gaps highlighted by the present review, and research to address methodological concerns raised by the present review. Whilst perhaps premature to be making such recommendations, as outlined below, both of these areas will be discussed in turn in section 4.5.1 and 4.5.2. The decision to include these recommendations was in recognition of the pressure being applied, by researchers and policy makers alike, to provide effective support to dementia care-givers meaning further intervention research is likely already underway (DoH, 2015; Laver et al., 2016; Zarit, 2018). However, before considering these areas it is impossible to ignore some gaps, highlighted by this review, in the care-giving literature more generally which should take precedent.

Best practice guidelines for developing complex interventions recommend that a systematic approach is applied, whereby the evidence base and theory practice links are established as a primary step (Craig et al., 2008). In line with this one would assume that there was a clear evidence base highlighting both the need for anxiety interventions, and an understanding of factors causing anxiety in dementia care-givers. Whilst a comprehensive search of the literature is beyond the scope of this paper the research reviewed suggests that neither of these primary steps have been met.

There are multiple reports highlighting anxiety as prevalent in the dementia care-giver population (Dura et al., 1991; Kessler et al., 2002; Ostojic et al., 2014; Sallim et al., 2015). However, as discussed earlier in section 4.3, the majority of studies included in this review contained care-givers who were not presenting as clinically anxious. Whilst this may be due to challenges associated with recruiting care-givers who meet the criteria for DSM-IV anxiety diagnosis (see Wiprzycka, Mackenzie, Khatri & Cheng, 2011), it may also be that care-givers do not want help with anxiety and therefore those with anxiety are not coming forward to partake in research. A recent review of the care-giver literature identified a paucity of research investigating, and understanding, care-giver needs with regards to both their support needs and their mental health needs (Bangerter, Griffin, Zarit & Havyer, 2017; see also McCabe, You & Tatangelo, 2016). Bangerter et al., (2017) suggested that a hierarchy of care-giver needs should be developed in a similar way to the model that exists for individuals with dementia (Schölzel-Dorenbos, Meeuwsen & Olde Rikkert, 2010). This apparent lack of understanding of dementia care-givers' needs is further highlighted by the lack of reliable, comprehensive, and consistent tools for completing such an assessment (Mansfield, Boyes, Bryant & Sanson-Fisher, 2017). If there is not a clear understanding of care-giver wants and needs then it will likely be very challenging to design care-giver interventions which are meaningful, and this appears true not only for anxiety but for all difficulties faced by dementia care-givers (Bastawrous, 2013; Chou, Chu, Tseng & Lu, 2003). Therefore a primary step within the dementia care-giver research should be to address this critical gap in the literature.

If it is established that care-givers do want help with anxiety then there is a need for a better understanding of the mechanisms underpinning this anxiety. This is an area which also appears to have been overlooked (Zarit, 2018), something which similarly appears true within other care-giver populations (see Woodford, Farrand, Watkins & Llewellyn, 2018). Losada et al., (2006) proposed the CBT model of care-giver distress in an attempt to address the need for interventions to be theoretically underpinned. This model proposes that dysfunctional thoughts play a central part in the development of care-giver distress. Whilst there is some limited research investigating links between dysfunctional thoughts and care-giver depression (Losada et al., 2011; McNaughton, Patterson, Smith & Grant, 1995), and dysfunctional thoughts and care-giver physical health (Ali & Bokharey, 2015b), there appears to be a need for this link to be explored with regards to anxiety.

There are now studies looking at the relationships between care-giver and care-receiver characteristics and anxiety (Covinsky et al., 2003; Sallim et al., 2015) and also investigating the impact of care-giver coping styles on anxiety (Li, Cooper, Bradley, Shulman & Livingston, 2012). However, if CBT interventions are to be successful there is a need to understand whether anxiety is being driven by dysfunctional thoughts. If anxiety in dementia care-givers is in fact being driven by unalterable aspects, such as concerns for the future of the care-receiver, then this requires a very different approach (Greenwood & Mackenzie, 2010; Greenwood, Mackenzie, Wilson & Cloud 2009). Likewise if dysfunctional thoughts are linked to anxiety for dementia care-givers then there is a need to better understand these specific thoughts, as would happen within CBT interventions for anxiety in other populations (Hofmann & Smits, 2008; Laidlaw & Kishita, 2017), rather than treating care-giving itself as a disease (Zarit, 2018).

4.5.1. Gaps in the CBT intervention literature.

Ideally the aforementioned points will be addressed before further intervention research is completed. Should anxiety be identified as something dementia care-givers want help with, and should it be linked to dysfunctional thoughts and therefore suited to the CBT model, then the following recommendations should be considered.

One aim of this research was to identify whether anxiety outcomes for informal care-givers of people with dementia have remained overlooked (Cooper et al., 2007). This review identified 34 studies which evaluated CBT in informal care-givers of individual with dementia using a RCT or a CT design. However, 20 of these were excluded from the present review as they did not include a validated measure of anxiety, suggesting that anxiety outcomes continue to be overlooked (Cooper et al., 2007; Joling et al., 2015; Elvish et al. 2013; Losada et al. 2015). To highlight this point further this review could only identify one study which formed part of the REACH program which reported anxiety outcomes.

The REACH program was a large scale program conducted over 5 years, sponsored by the National Institute on Aging and the National Institute for Nursing Research, with the aims of designing and investigating the impact of specific interventions across a range of different sites and for a number of different care-givers (Burgio et al., 2001). This has been cited as one of the largest bodies of care-giver research to date and is praised for including large sample sizes, methodologically strong research studies and a large number of carers from ethnic minorities (Maslow, 2012). Despite contacting a number of authors involved in the REACH project the present author could only find one study reporting anxiety outcomes for the CBT intervention included as part of the study (Burgio et al., 2003). Future studies investigating CBT interventions for informal care-givers of people with dementia should therefore look to reflect care-giver needs rather than solely focusing on depression.

Should anxiety be identified as a problem for dementia care-givers then there is a need for studies to investigate CBT interventions which have been designed with care-giver anxiety in mind. Care-giving is often associated with psychological distress which may lead to difficulties such as anxiety and depression, but it is not a “disorder” therefore interventions should focus upon the specific difficulty being presented by the care-giver as opposed to the care-giving experience in general (Schulz et al., 2002). The present study could only identify one such intervention, and this was the same one that Cooper et al. (2007) identified ten years ago. Such studies should look to design interventions based upon Losada et al. (2006) CBT model with the focus at each stage being upon anxiety. This would provide a better match between intervention and outcome and would therefore be expected to achieve effects similar to those of CBT interventions for anxiety in the general population (Butler et al., 2006; Kishita & Laidlaw, 2017; Yulish et al., 2017).

The above suggestions are not new and are not specific to care-givers. Reviewing the literature for older adults more broadly some have claimed that it is common place for anxiety to be overlooked, and not just a problem specific to care-giver research (Ballenger et al., 2001; Bryant, Jackson & Ames, 2008). Anxiety may also be more likely to be misdiagnosed or go untreated than depression and this seems particularly likely when other co-morbid difficulties are present (Durham, 2007). It seems that for the past two decades there have been calls for more research focussing on interventions for anxiety disorders in older adults, where the tendency has been to focus on depression or dementia (Beekman et al., 1998; Kishita & Laidlaw, 2017).

Additionally it is evident that more consideration should be given to baseline anxiety levels, at the very least these should be reported clearly in future studies. Including care-givers with sub-threshold anxiety may be important because this may prevent an escalation of symptoms, and prevention is better than cure (Joling, et al. 2015). However, in order to reach firmer conclusions there needs to be further investigation with much clearer reporting of baseline anxiety.

The results of the present review revealed a slight increase in the magnitude of effect size at follow up. One possible explanation may be that CBT interventions have an initial impact upon outcomes such as knowledge of illness and increased care-giving skills due to the large psychoeducational component included in many of these interventions. This in turn has an impact upon a care-giver’s anxiety levels but this may not be seen until follow up once care-givers have had the opportunity to apply their new knowledge and skills to their situation (Mittelman, 2008). Future research should therefore look to include follow-up assessment as understanding the long term impact will be an important consideration for care-givers who have to give up time, which is already limited, to partake in interventions (Ory et al., 1999; Dupuis et al., 2004). This will also be an important factor for decision makers when deciding what interventions to offer within a service, as the effects need to be sustainable as dementia is a long-term condition which can lead to long-term care-giving for family members (Alzheimer’s Association, 2010). Within the present review less than half the included studies provided sufficient follow up data to allow for them to be included in the data synthesis, thus restricting the conclusions that can be drawn regarding the longevity of reported treatment effects.

In addition further research investigating CBT interventions should look to explore the relative effects of different components of CBT interventions for anxiety in informal care-givers. The design and implementation of such studies will be informed by a better understanding of the mechanisms underpinning anxiety in care-givers, but they will also lend themselves to developing that understanding. The present author identified one study which has started to investigate this with regards to the specific CBT components of cognitive restructuring (Vernooij-Dassen et al., 2011). However, the findings of this review suggest that studies which look to compare CBT interventions with a relaxation component to the relaxation component in isolation are warranted. It may be that relaxation delivered in isolation is as effective in reducing care-giver anxiety as relaxation in combination with CBT. A relaxation intervention has the potential to be delivered in a wider range of settings as it would not require clinicians to have experience of the CBT model (Peters et al., 2011). Relaxation instructions can readily be presented via an audio-tape. This could increase accessibility for care-givers. In line with this the present study also highlights the need for further interventions addressing anxiety in informal care-givers which rely on non-traditional methods for delivery, such as the internet, as again these have the potential to increase accessibility.

Finally if future studies are warranted for care-giver anxiety then they should look to compare CBT interventions for anxiety in care-givers to interventions drawing on different psychological models. Within the present review only one study had completed such an analysis (Losada et al., 2015) which highlights a further gap in the literature. Whilst comparisons between different theoretical models of therapy have been criticised under the finding of the “Dodo bird’s verdict” (see Rosenzweig 1936; Luborsky et al., 2002) such a standpoint should not be assumed, and therefore further investigation within the informal care-giver population is justified. Such comparisons have potential to answer questions that a clinician has about what type of intervention will be most effective for the individual care-giver in front of them (Shadish & Sweeney, 1991) and it may be that anxiety in care-givers is underpinned by mechanisms which are better targeted by interventions other than CBT.

4.5.2. Methodological issues.

One aim of the current review was to assess if earlier methodological criticisms levelled at the care-giving intervention research had been addressed (DoH, 2015; Parker et al., 2010). Analysing the studies included in the current review it is apparent that some criticisms have not been adequately addressed. Almost half the studies included in this review were deemed to be at high risk of bias due to methodological concerns, and these concerns largely centred on a lack of clear reporting, making it difficult to fully assess the processes used to protect against bias. For example, hardly any of the included studies detailed their randomisation procedures making it challenging to fully assess the extent to which the authors achieved allocation concealment.

The studies included in this review did not always make it easy to follow the flow of participants through the trial, making it difficult for the reader to be sure how many care-givers had completed the intervention. Additionally, less than half of the included studies provided intention to treat (ITT) analyses despite the now largely accepted recommendation to do so (Abraha et al., 2015; Schulz, Altman, & Moher, 2010). ITT analysis provides a more realistic reflection of clinical practice, as all participants that started the intervention are included in the analysis. This reflects real life situations where only some care-givers fully adhere to the intervention they are receiving. Failure to complete ITT analysis can introduce further bias to studies and in turn this bias may have been carried through to the present meta-analysis (Gupta, 2011; White, Carpenter & Horton, 2012). Therefore future research should look at addressing these methodological limitations, and in particular include clearer reporting of methodological procedures (Schulz et al., 2010).

Studies should be rigorous with regards to both design and delivery. In particular, employing methods to monitor treatment integrity and ensuring standardisation of the treatment received. The failure to monitor treatment implementation has been highlighted in past reviews of the care-giving literature (Burgio et al., 2001), but despite this the present review still found many studies did not pay attention to this factor. This criticism is particularly true for the study by Beauchamp et al. (2005). A potential strength of their study was that it was delivered via the internet and allowed for complete personalisation of the modules accessed; however, the authors did not report which components were accessed by care-givers. This makes replication challenging.

Additionally, given the small effect sizes seen in the present review, studies should ensure that they are sufficiently powered to detect small effect sizes. The majority of studies in this review did not have sufficient sample sizes to detect such effects (Borenstein et al., 2009; Cooke et al., 2001; Schulz et al., 2010). Well-designed studies of this nature would allow for clearer appraisal and interpretation of results, allowing any outcomes to be more confidently attributed to intervention effects as opposed to methodological weaknesses.

4.5 Strengths of Current Study

To best of the author’s knowledge this is the first quantitative review focussing exclusively upon CBT interventions for anxiety in informal care-givers of people with dementia, and this is a notable strength of this research. Previous reviews of interventions with care-givers have been criticised for grouping interventions from different theoretical backgrounds, using terms which have rarely been explicitly defined (Gaughler et al., 2017; Gilhooly et al., 2016; Parker et al., 2010). For example, CBT interventions have been included in categories of psychoeducational interventions in some studies (Gallagher-

Thompson & Coon, 2007) but others have included them with psychosocial interventions (Cooke et al., 2001). For clinicians reviewing the literature to understand which intervention would be most efficacious such broad categories are unhelpful (Burgio et al., 2001). The present study addressed this criticism by focussing exclusively upon CBT interventions for informal care-givers of people with dementia.

Categorising studies by the theoretical model underpinning them provides the opportunity to increase understanding of how the interventions may be affecting change (Elvish et al. 2013). It also has the potential to provide much clearer recommendations for clinicians. Without informal care-givers providing support to family members the care system in the UK would likely be placed under such strain that it would collapse (Banerjee, 2014). This has been recognised by the Government and there is a drive to increase support for care-givers (DoH, 2015). However, the services available to care-givers of people with dementia vary throughout the U.K. and often care-givers do not have access to the support required (Banerjee, 2014; Maslow, 2012). Therefore it is crucially important to synthesise the evidence base in a way that is clear and that also enables those commissioning services to be able to clearly identify which interventions will be most helpful to the care-givers presenting in their services.

The present study used predefined criteria which clearly specified what would be considered a CBT intervention. A thorough and over-inclusive search strategy was then employed to ensure that all studies using such an approach were identified (Borenstein et al., 2009). This was challenging as studies often do not make explicit reference to the theoretical model driving them. For example, the study by Livingston et al. (2014), which was generally thought to be high quality, based their study upon the Coping with Caregiving intervention by Gallagher-Thompson et al. (1996). However, at no point in their extensive write up do they make explicit reference to CBT. This was verified through additional contact. By employing an over-inclusive search criteria at the initial stages it is considered likely that all relevant studies were identified. Consequently, this meant that to the best of the present author's knowledge the largest number of CBT interventions for informal care-givers were combined in one review thus ensuring a larger empirical base from which to draw conclusions (Wampold et al., 2017).

Additionally this is thought to be the first meta-analysis to focus primarily upon anxiety outcomes in informal care-givers of people with dementia, which have been largely overlooked by the research (Cooper et al., 2007; Losada et al., 2015). This presented an opportunity to begin to investigate outcomes for different subgroups, which remains a strength of this study despite not being able to complete all of the planned subgroup analyses. Understanding the specific intervention, care-giver and care-receiver characteristics that might moderate the effects of CBT interventions for anxiety is important to enable care-givers to gain access to interventions that will be most appropriate given their specific situation. A "one size fits all" approach is not likely to be effective given the heterogeneity in the care-giver population, therefore identifying information which can guide the decision making process is crucially important (Parker et al., 2010).

Methodologically the present meta-analysis followed best practice guidelines in line with current recommendations set by the Cochrane review where possible (Higgins & Green, 2011). The study selection process was completed by two assessors working independently. These strategies were employed in an attempt to reduce the impact of potential biases and to enable a full review of CBT interventions. The current review also attempted to ensure that all included studies were subjected to a full and transparent analysis of bias, helping to ensure that findings were robust to possible sources of bias. Consequently all decisions made that might have impacted upon findings were subjected to sensitivity analysis so that any potential impact could be fully understood (Borenstein et al., 2009).

4.6 Limitations of Current Study

Despite the strengths outlined in section 4.5 the present review should be interpreted in light of its limitations. As already mentioned some of the planned subgroup analyses were restricted by the limited number of studies reporting necessary information. This meant that some sources of heterogeneity could not be explored. For example, it was not possible to explore the impact of care-receiver diagnosis and this has been shown to have an impact upon care-giver wellbeing (Nicolaou et al., 2010). It may also have been useful to consider the effect that the intervention intensity had upon outcomes. There was some evidence that this could be a potential moderator and there was considerable variation between studies with regards to this factor. Additionally there was some evidence within the available studies to suggest that care-giver ethnicity may be an important variable to consider (Burgio et al. 2003) and future studies should consider this. Within this review, as in past reviews, certain groups of care-givers were likely over-represented as those coming forward for research trials typically tended to be white, well educated, female, spousal care-givers (Gallagher-Thompson et al., 2007; Pinquart & Sorensen, 2006b; Vernooij-Dassen et al., 2011).

Whilst study inclusion was decided by two independent assessors, data extraction relied solely upon one author and to a large extent relied only upon the information reported in the published article. On occasion this information may not have adequately represented all components of the delivered intervention. Attempts were made to gain further information via subsequent publications or via contact with the primary researchers, but this was not always possible. The analysis of study bias was also not counter-verified by a second author. However, it was completed following a well-established and outlined procedure and so this would not be expected to affect the results. Finally the protocol for this study was not registered or published. However, again this would not be expected to affect the results as approach followed was fixed during the study.

In order to investigate anxiety outcomes for informal care-givers it was necessary to pool outcomes from different patient-reported outcomes. This is widely practised but could lead to an increase in between-study heterogeneity and biased results (Puhan, Soesilo, Guyatt & Schunemann, 2006). To reduce this bias it is important that the outcome measures correlate strongly, which indicates they are measuring similar constructs. It is also important that their ability to detect important changes, particularly small changes, should be similar (Dennis, Boddington & Funnell, 2007). The most frequently used method for combining different outcomes is to use standardised mean differences, and this was the method employed in this review. However, there are critics of this method who argue that when effects are transformed in this way heterogeneity is introduced (Cummings, 2004). One way to explore this may be to investigate the outcome instrument as a variable within the meta-analysis (Puhan et al., 2006); however this was not possible here due to the small number of studies employing each instrument. Therefore appropriate caution should be used when interpreting the results and future research could investigate the similarities in responsiveness between the anxiety outcomes commonly used in the care-giver intervention research.

Finally the present review did not investigate acceptability. Whilst it may not have been possible to complete a detailed analysis of care-givers who did not complete their assigned interventions due to lack of available detail in the included studies, considering dropout rates and any additional assessments of acceptability is important. There is research suggesting that care-givers, even those with mental health difficulties meeting the criteria for clinical diagnosis, do not identify themselves as needing a psychotherapeutic intervention (Burgio, Hardin, Sinnott, Janosky & Hohman, 1995). Additionally care-givers tend to be time poor and overburdened and this may cause them to be less likely to engage with interventions, especially as those care-givers who are distressed are often found to hold beliefs that they should put the care-receivers' needs before their own (Arai et al., 2000). Understanding how care-givers view interventions could help to ensure they are designed in a way that increases engagement and facilitates easy access; there is little point investing time and energy in designing effective interventions if those care-givers who most need them do not view them as acceptable.

4.7 Conclusion

This review aimed to build upon the work of Cooper et al. (2007) and provide an up to date, comprehensive, systematic appraisal and quantitative summary of the literature investigating the effectiveness of CBT interventions for anxiety in informal care-givers of people with dementia, in comparison to controls. Fourteen studies were identified as eligible and were included in the quantitative synthesis. The findings revealed "small" effect sizes in favour of CBT over control conditions for the treatment of anxiety in informal care-givers. Similar findings were identified for the secondary outcome of care-giver depression. To a degree these effects were dependent on the type of control, with the effects diminishing when CBT interventions were compared to psychoeducation control groups. Preliminary evidence suggests that including a relaxation component may be important to achieve positive outcomes with regards to care-giver anxiety. However, the overall conclusions were limited by the lack of included studies reporting the necessary detail to allow for subgroup analysis and by some key methodological weaknesses identified in the literature.

The tendency to overlook anxiety outcomes within the care-giver literature remains. In particular this review highlights the need for a greater understanding of the needs of dementia care-givers, specifically if anxiety is something they would like support with. And is the anxiety driven by elements which can be explained by the CBT model or are they related to realistic unalterable concerns about their care-giving role? Should the answer to both these questions be “yes”, then more research looking to investigate CBT interventions which have been designed specifically with care-giver anxiety in mind are needed. These interventions should look to provide a clear theoretical link between the intervention and the outcomes being assessed, and then include care-givers who identify themselves as having difficulties with the target problem addressed by the intervention. There is of course no “one size fits all” intervention for care-givers which is why it is particularly important to develop interventions which are designed for, and effective with, care-givers who are experiencing anxiety. Subsequent clinical trials need to be larger in scale, with processes for adequate randomisation and allocation concealment, and clear reporting of baseline symptomatology, care-giver characteristics, treatment integrity and acceptability.

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Appendices

Appendix A: Web Links for Search Sources and Dates of Initial Searches

Web links for search sources	Date of initial search
Cochrane Library: http://www.cochranelibrary.com	27/10/2016
Cochrane Dementia Database: http://www.cochranelibrary.com/review-group/Dementia%20and%20Cognitive%20Improvement%20Group/	15/01/2017
Dementia Evidence Database: http://toolkit.modem-dementia.org.uk/	14/01/2017
EMBASE: https://www.elsevier.com/solutions/embase-biomedical-research	17/11/2016
Google Scholar: http://scholar.google.co.uk	10/12/2016
MEDLINE: http://www.ncbi.nlm.nih.gov/pubmed	17/11/2016
Open Grey: http://www.opengrey.eu/	24/11/2016
PsychINFO: http://www.apa.org/pubs/databases/psycinfo/	5/11/2016
ProQuest Dissertation & Theses A&I: http://www.proquest.com/products-services/pqdtglobal.html	5/11/2016
Rosalyn Carter care-giver intervention database: http://www.rosalynncarter.org/caregiver_intervention_database/	10/01/2017
Scopus: https://www.scopus.com/search/form.uri?display=basic	31/10/2016

Appendix B: Sample search strategy for MEDLINE

1. (carer or care?giv* or caregiv* or care giv*).ti,ab.

2. (caretak* or care tak* or care?tak*).ti,ab.

3. informal care.ti,ab.

4. children caring.ti,ab.

5. (children provid* adj3 care).ti,ab.

6. ((son? or daughter? or friend?) adj2 (care or caring)).ti,ab.

7. ((husband? or wives or wife or spouse? or relatives) adj2 (care or caring or support or supporting)).ti,ab.

8. ((family or families) adj2 (caring or support)).ti,ab.

9. exp caregivers/

10. or/1-9

11. (Dementia or Alzheimer* or elderly or aged or (cognitive) adj2 (impairment) or MCI

12. exp dementia/ or alzheimer disease/ or *COGNITION DISORDERS/

13. 11 or 12

14. 10 and 13

15. (Intervention* or evaluation or psycho?social or support or training or therapy or (multi-component adj4 support) or (carer* adj2 support*) or counsel?ing or psycho?educational or education or (emotional adj2 support) or cognitive or behavio?r or CBT or (behavio?r adj3 manag*) or (multi-component adj3 training) or peer group* or support group* or memory clinic af.

20. 14 and 15

Appendix C: List of authors contacted via email in search of additional studies and copy of email template.

The following researchers who had published widely in the field of dementia caregiver research were contacted to request information about any ongoing studies. The following researchers were contacted; Rhonda Akkerman, Louis Burgio, Claudia Cooper, Dolores Gallagher-Thompson (REACH project), Gill Livingston (START project), Andres Losada, Penny Rapaport (START project).

Email Template

Dear *[author name]*

I am a Trainee Clinical Psychologist at the University of East Anglia, UK, and I am currently conducting my doctoral thesis. I am investigating the use of Cognitive Behavioural Therapy for anxiety in informal caregivers of people with dementia. I am being supervised by Professor David Peck and Dr. Imogen Rushworth (University of East Anglia). I am conducting a meta-analysis on the effectiveness of CBT in informal caregivers and during my literature search I have identified several studies you have completed with care-givers of people with dementia.

I am asking all authors who have made significant contributions to this area of research if they are aware of any further ongoing or unpublished trials investigating the effectiveness of CBT with informal caregivers of people with dementia. There is no restriction on age range of participants, or the relationship between them and the individual with dementia as long as they are not in a professional caregiving role and the study includes a validated measure of care-giver anxiety.

Thanks very much in advance for your help,

Lauren Staples

Appendix D: Data Extraction Form

Code items with missing data as 99. Code items that are deemed as non-applicable as 11.

General

1. **Study ID**: Assign an identification number

2. **Reference:** Text; Document full reference in APA format

3. **Country of origin**: Text

4. **Type of report**: Circle
    1. Journal article
    2. Book chapter
    3. Thesis or doctoral dissertation
    4. Conference paper
    5. Other (+specify)

5. Confirm eligibility: *Circle*
  1. Included
  2. Excluded (*give reason for exclusion)*

Methods

1. Method of randomisation: *Text*

** Following guidance from the Cochrane Handbook (Lefebvre, Manheimer, Glanville, 2011) if the author of the study states explicitly that a random allocation procedure was used then the trial will be classified as a RCT. If no explicit statement regarding randomisation is included, but its use as a procedure cannot be ruled out, or the trial uses a quasi-method of allocation, it will be classified as a CCT.*

2. Number of control groups: *Digits*

3. Format of Control group/s: if more than one control group, code separately in additional columns
  1. Treatment as usual
  2. Wait list
  3. Supportive Counselling
  4. Psychoeducation
  5. Active intervention based on different psychological model
  6. Other *(please state)*

4. Control group description: *Text* (Sufficient for replication, if feasible)

Control 1	Control 2	Control 3

5. Baseline group differences: *Circle*

1. Not assessed
2. Assessed, negligible differences
3. Assessed, some difference, judged unimportant
4. Assessed, some difference, judged important (e.g. significant differences between multiple variables or on one major variable such as baseline anxiety scores).

6. Length of follow up: *Text*

<u>Intervention design</u>

1. Intervention description: *Text* (Sufficient for replication, if feasible)

2. Setting: *Text*

3. Was anxiety the primary target of the intervention? *Circle*

1. Yes
2. No
3. Unclear

4. If anxiety was not the primary target of the intervention what was? *Text*

5. Was the CBT intervention based on a manual? *Circle*

1. Yes
2. No
3. Unclear

6. CBT Format: *Circle*

1. Individual
2. Group
3. Other: please give description

7. Direct therapist contact: *Circle*

1. Yes
2. No
3. Unclear

8. If answer yes to question 7 in what format was the therapist contact? *Circle*

1. Email
2. Telephone call
3. Skype
4. Face-to-face
5. Letters
6. Other *(please specify)*

9. Therapist qualifications and training: *Circle*

1. Clinical Psychologist
2. CBT therapist
3. Mental Health Practitioner
4. Counsellor

5. Student
6. Other *(please specify)*

10. Length of each treatment session: *in minutes*

11. Number of treatment sessions offered: *Digits*

12. Mean number of treatment session attended: *Digits*

13. Total length of intervention: in minutes

14. Mean total length of treatment received: *Digits*

15. Additional comments regarding therapist input: *Text (e.g. therapist supervision, evidence that specified intervention components were delivered as described)*

Participants

1. Total sample size (at baseline): *Digits*

2. Size of intervention group (at baseline): *Digits*

3. Sample size of control group (at baseline): if more than one control group, code separately in additional columns, ensuring that the columns correspond to those used in item….

4. Number of dropouts from intervention group: *Digits (please give information regarding stage of dropout)*

Control 1	Control 2	Control 3

5. Number of dropouts from comparator group: *Digits (please give information regarding stage of dropout)*

	Control 1	Control 2	Control 3
Mean age			
Age range			

6. Completers' characteristic in comparison to dropouts' characteristic: *Text*

7. Reasons for dropouts: *Text*

8. Recruitment method: *Text* (Sufficient for replication, if feasible including inclusion and exclusion criteria)

10. Was a diagnostic criteria set for the caregiver? *Circle*
1. Yes

2. No
3. Unclear

If yes please describe: *Text*

11. Mean age of total sample: an average may be used if only an age range is documented

12. Age range of total sample: *Digits*

13. Mean age of CGs in intervention group: an average may be used if only an age range is documented

14. Age range of CGs in intervention group: *Digits*

15. Mean age of CGs in control group: an average may be used if only an age ranged is documented. If more than one control group, code separately in additional columns, ensuring that the column numbers correspond to those used in items ……

16. Age range of CGs in control group: an average may be used if only an age range is documented

15. Mean age of care-receiver in intervention and control group: an average may be used if only an age range is documented.

16. Age range of care-receiver in intervention group: *Digits*

17. Mean amount of time spent care-giving per week: in hours

18. Range of time spent care-giving per week: in hours

19. Mean length of time in care-giving role: in years

20. Range of time in care-giving role: in years

21. Relationship to care-receiver: *Digits*

	Spouse	**Child**	**Sibling**	**Friend**	**Other**
Intervention					
Percentage					
Whole Count					
Control					
Percentage					
Whole Count					

22. Dementia diagnosis of care-receiver: *Digits*

	Alzheimer's	**Vascular**	**Fronto-temporal**	**Mixed dementia**	**Lewy Bodies**	**MCI**	**Other**
Intervention							
Percentage							
Whole count							

Control							
Percentage							
Whole count							

23. Sex of care receiver: *Digits*

	Male	**Female**
Intervention		
Percentage		
Whole count		
Control		
Percentage		
Whole count		

24. Sex of care-givers in intervention group: *Digits*

	Male	**Female**
Percentage		
Whole count		

25. Sex of care-givers in control group: if more than one control group code in separate tables

1	**Male**	**Female**	**2**	**Male**	**Female**	**3**	**Male**	**Female**
Percentage			**Percentage**			**Percentage**		
Whole count			**Whole count**			**Whole count**		

26. Socio-demographics of care-givers (e.g. Education level, Income level, Occupation, Religion, Ethnicity): *Text & Digits*

Outcomes

1. Outcome measure for Anxiety symptoms: *Circle*

1. BAI
2. GAD-7
3. STAI
4. HADS-A
5. Other *(please specify and check validity)*

2. Outcome measure for depressive symptoms: *Circle*

1. BDI
2. PHQ-9
3. HADS-D
4. CES-D

5. Other *(please specify and check validity)*

Outcome data key: recorded in table below

1. Effect size type
   1. Immediately post intervention
   2. Follow up

2. Outcome descriptor: text; description of outcome variable e.g. anxiety, depression, burden

3. Outcome report type
   1. Self report
   2. Clinician report
   3. Informant report

4. **Cut off scores/ severity thresholds included:**
   1. No
   2. Yes
   3. Unclear

5. **Unit of measurement:**
   1. Continuous
   2. Dichotomous

6. **Upper limit of measure:** *Digits*

7. **Lower limit of measure:** *Digits*

8. **Is a low score favorable?**
   1. No
   2. Yes
   3. Unclear

9. Analysis
   1. Completion
   2. Intention to treat

10. Intervention group mean

11. Control group mean: if more than one control group, code separately in different rows, ensuring that the row number corresponds to the column numbers used in items …..

12. Intervention group standard deviation

13. Control group standard deviation: if more than one control group, code separately in different rows, ensuring that the row number corresponds to the column numbers used in items…..

14. Direction of effect
   1. Favours treatment
   2. Favours control
   3. Neither

	ES1	**ES2**	**ES3**	**ES4**	**ES5**	**ES6**
1. ES type						
2. Outcome descriptor						
3. Outcome report type						
4. Cut off scores included?						
5. Unit of measurement						
6. Upper limit measure						
7. Lower limit measure						
8. Low score favourable?						
9. Analysis						
10. Intervention group mean						
11. Control group mean (1)						
Control group mean (2)						
12. Intervention group standard deviation						
13. Control group SD (1)						
Control group SD (2)						
14. Direction of effect						

Risk of bias

1. **Random sequence generation (selection bias):** *Circle*
Low
Unclear

High
Support for judgement: *Text (include quotes and comments)*

2. **Allocation concealment (selection bias):** *Circle*
Low
Unclear
High
Support for judgement: *Text (include quotes and comments)*

3. **Blinding of participants and personnel (performance bias):** *Circle*
Low
Unclear
High
Support for judgement: *Text (include quotes and comments)*

4. Blinding of outcome assessment (detection bias): *Circle*
Low
Unclear
High
Support for judgement: text (include quotes and comments)

5. Incomplete outcome data (attrition bias): *Circle*
Low
Unclear
High
Support for judgement: Text (include quotes and comments)

6. Selective reporting (reporting bias): *Circle*
Low
Unclear
High
Support for judgement: Text (include quotes and comments)

7. Other bias: *Circle*
Low
Unclear
High
Support for judgement: Text (include quotes and comments

Appendix E: Details of individual requests for data

In the event of missing or unclear information needed to calculate effect sizes, corresponding authors were contacted via email to request the information needed.

Email Template

Dear *[author name]*

I am a Trainee Clinical Psychologist at the University of East Anglia, UK, and I am currently conducting my doctoral thesis. I am investigating the use of Cognitive Behavioural Therapy for anxiety in informal caregivers of people with dementia. I am being supervised by Professor David Peck and Dr. Imogen Rushworth (University of East Anglia). I would like to include your *[year of study]* trial *([title of study]*) in a meta-analysis that I am conducting on the effectiveness of CBT in informal caregivers.

In order to include your study in the meta-analysis, I would require some additional information and I was wondering if you could help me with this please? I require *[details of missing data]*. I would be very grateful if you would be able to share this data to enable me to include your paper in my study.

Additionally, I am asking all authors of included studies if they are aware of any further ongoing or unpublished trials investigating the effectiveness of CBT with informal caregivers of people with dementia. There is no restriction on age range of participants, or the relationship between them and the individual with dementia as long as they are not in a professional caregiving role and the study includes a validated measure of care-giver anxiety.

Thanks very much in advance for your help,

Lauren Staples

Trainee Clinical Psychologist

Details of correspondence

This list also includes authors contacted at the data searching stage to request further information to decide upon study eligibility for inclusion.

Study	Author Contacted	Data Received (Y/N)
Blom et al (2015)	Anne Pot	Y
Buchanon et al (2003)	Jeremy Buchanon	Y
Charlesworth et al (2009)	Georgina Charlesworth	N
Facal et al. (2009)	Igone Etxeberria	Y
Forstmeier et al. (2015)	Simon Forstmeier	Y
Gendron et al. (1996)	Carole Gendron	N
Kilimann (2016)	Ingo Kilimann	Y
Lancer (2006)	Kevin Lancer	N
Lane (2003)	Geoffrey Lane	N
Mackenzie (2008)	Corey Mackenzie	Y
Martin-Carrasco et al. (2014)	Manuel Martin-Carrasco	N
Passoni et al. (2014)	Serena Passoni	Y

Rabinowitz et al. (2006)	Yaron Rabinowitz	N
Livingston et al. (2014)	Penny Rappaport	Y
REACH studies various	Dolores Gallagher-Thompson Louis Burgio Richard Schulz	N
Villareal-Reyna et al. (2012)	Jane Dimmitt Champion	N

Appendix F: The Cochrane Collaboration's Risk of Bias Tool (Higgins & Green 2011)

Accessed: http://handbook-5-1.cochrane.org/chapter_8/table_8_5_d_criteria_for_judging_risk_of_bias_in_the_risk_of.htm

Home > Part 2: General methods for Cochrane reviews > 8 Assessing risk of bias in included studies > 8.5 The Cochrane Collaboration's tool for assessing risk of bias > Table 8.5.d: Criteria for judging risk of bias

Table 8.5.d: Criteria for judging risk of bias in the 'Risk of bias' assessment tool

<table>
<tr><td colspan="2">RANDOM SEQUENCE GENERATION
Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.</td></tr>
<tr><td>Criteria for a judgement of 'Low risk' of bias.</td><td>The investigators describe a random component in the sequence generation process such as:
• Referring to a random number table;
• Using a computer random number generator;
• Coin tossing;
• Shuffling cards or envelopes;
• Throwing dice;
• Drawing of lots;
• Minimization*.
*Minimization may be implemented without a random element, and this is considered to be equivalent to being random.</td></tr>
<tr><td>Criteria for the judgement of 'High risk' of bias.</td><td>The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example:
• Sequence generated by odd or even date of birth;
• Sequence generated by some rule based on date (or day) of admission;
• Sequence generated by some rule based on hospital or clinic record number.
Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorization of participants, for example:
• Allocation by judgement of the clinician;
• Allocation by preference of the participant;
• Allocation based on the results of a laboratory test or a series of tests;
• Allocation by availability of the intervention.</td></tr>
<tr><td>Criteria for the judgement of 'Unclear risk' of bias.</td><td>Insufficient information about the sequence generation process to permit judgement of 'Low risk' or 'High risk'.</td></tr>
<tr><td colspan="2">ALLOCATION CONCEALMENT
Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.</td></tr>
<tr><td>Criteria for a judgement of 'Low risk' of bias.</td><td>Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation:</td></tr>
</table>

	• Central allocation (including telephone, web-based and pharmacy-controlled randomization); • Sequentially numbered drug containers of identical appearance; • Sequentially numbered, opaque, sealed envelopes.
Criteria for the judgement of 'High risk' of bias.	Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: • Using an open random allocation schedule (e.g. a list of random numbers); • Assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); • Alternation or rotation; • Date of birth; • Case record number; • Any other explicitly unconcealed procedure.
Criteria for the judgement of 'Unclear risk' of bias.	Insufficient information to permit judgement of 'Low risk' or 'High risk'. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement – for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.
BLINDING OF PARTICIPANTS AND PERSONNEL **Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.**	
Criteria for a judgement of 'Low risk' of bias.	Any one of the following: • No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; • Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
Criteria for the judgement of 'High risk' of bias.	Any one of the following: • No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; • Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
Criteria for the judgement of 'Unclear risk' of bias.	Any one of the following: • Insufficient information to permit judgement of 'Low risk' or 'High risk'; • The study did not address this outcome.
BLINDING OF OUTCOME ASSESSMENT **Detection bias due to knowledge of the allocated interventions by outcome assessors.**	
Criteria for a judgement of 'Low risk' of bias.	Any one of the following: • No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; • Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
Criteria for the judgement of 'High risk' of bias.	Any one of the following: • No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding;

	• Blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
Criteria for the judgement of ‘Unclear risk’ of bias.	Any one of the following: • Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’; • The study did not address this outcome.
INCOMPLETE OUTCOME DATA **Attrition bias due to amount, nature or handling of incomplete outcome data.**	
Criteria for a judgement of ‘Low risk’ of bias.	Any one of the following: • No missing outcome data; • Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); • Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; • For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; • For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; • Missing data have been imputed using appropriate methods.
Criteria for the judgement of ‘High risk’ of bias.	Any one of the following: • Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; • For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; • For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; • ‘As-treated’ analysis done with substantial departure of the intervention received from that assigned at randomization; • Potentially inappropriate application of simple imputation.
Criteria for the judgement of ‘Unclear risk’ of bias.	Any one of the following: • Insufficient reporting of attrition/exclusions to permit judgement of ‘Low risk’ or ‘High risk’ (e.g. number randomized not stated, no reasons for missing data provided); • The study did not address this outcome.
SELECTIVE REPORTING **Reporting bias due to selective outcome reporting.**	
Criteria for a judgement of ‘Low risk’ of bias.	Any of the following: • The study protocol is available and all of the study’s pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; • The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).

Criteria for the judgement of 'High risk' of bias.	Any one of the following: • Not all of the study's pre-specified primary outcomes have been reported; • One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; • One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); • One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; • The study report fails to include results for a key outcome that would be expected to have been reported for such a study.
Criteria for the judgement of 'Unclear risk' of bias.	Insufficient information to permit judgement of 'Low risk' or 'High risk'. It is likely that the majority of studies will fall into this category.
OTHER BIAS **Bias due to problems not covered elsewhere in the table.**	
Criteria for a judgement of 'Low risk' of bias.	The study appears to be free of other sources of bias.
Criteria for the judgement of 'High risk' of bias.	There is at least one important risk of bias. For example, the study: • Had a potential source of bias related to the specific study design used; or • Has been claimed to have been fraudulent; or • Had some other problem.
Criteria for the judgement of 'Unclear risk' of bias.	There may be a risk of bias, but there is either: • Insufficient information to assess whether an important risk of bias exists; or • Insufficient rationale or evidence that an identified problem will introduce bias.

Appendix G: Questions considered as part of the assessment of “other” bias

The following questions were developed based on reviews by Elvish et al. (2013) and Zarit & Femia (2008) and were answered for each study to assist in the assessment of other factors that may be associated with bias. The answers to these questions were considered alongside the items identified in the Cochrane review as important to assessing “other” sources of bias.

- Are care-givers exhibiting symptoms at baseline of the primary outcome the intervention is being assessed by?
- Are care-givers asking for help? And do they want help with a problem addressed by the intervention?
- Is the intervention based on a clear theoretical model? Are the outcomes being assessed clearly linked to the domains targeted by that model?
- Is treatment delivered as planned? How is this assessed?
- Is the control arm assessed for integrity? i.e. are steps taking to ensure care-givers in the control arm are not seeking help elsewhere?

Appendix H: Characteristics of Excluded Studies Table

Study	Reason for Exclusion
Ali 2015	Not RCT or CT
Au 2015	Did not employ both cognitive and behavioural techniques in the intervention
Au 2015	Did not employ both cognitive and behavioural techniques in the intervention
Banningh 2013	Not RCT or CT
Belle 2006	No anxiety outcome measurement
Blom 2013	Duplicate data linked to original
Bourgeois 2002	Did not employ both cognitive and behavioural techniques in the intervention
Bruvik 2013	Did not employ both cognitive and behavioural techniques in the intervention
Buchanan 2003	No anxiety outcome measurement
Buckwalter 1999	Did not employ both cognitive and behavioural techniques in the intervention
Burns 2010	Did not employ both cognitive and behavioural techniques in the intervention
Callan 2016	Not RCT or CT
Chang 1999	No anxiety outcome measurement
Charlesworth 2000	Protocol available – contacted author but no reply
Chen 2015	Did not employ both cognitive and behavioural techniques in the intervention
Cheng 2016	Did not employ both cognitive and behavioural techniques in the intervention
Cheung 2015	Did not employ both cognitive and behavioural techniques in the intervention
Chiu 2015	Did not employ both cognitive and behavioural techniques in the intervention
Coon 2003	No anxiety outcome measurement
Cristancho-Lacroix 2015	Did not employ both cognitive and behavioural techniques in the intervention
Cummings 1999	No anxiety outcome measurement
Czaja 2008	Did not employ both cognitive and behavioural techniques in the intervention
Dias 2008	Did not employ both cognitive and behavioural techniques in the intervention
Donaldson 1999	Care receiver was the primary focus
Durcharme 2012	Did not employ both cognitive and behavioural techniques in the intervention
Elliot 2010	Did not employ both cognitive and behavioural techniques in the intervention
Elmstahl 2008	Not RCT or CT
Facal 2009	Protocol available, author contacted and replied but study not in English
Forstmeier 2015	No anxiety outcome measurement

Gallagher-Thompson 1994	Not RCT or CT
Gallagher-Thompson 2001	Not RCT or CT
Gallagher-Thompson 2003	No anxiety outcome measurement
Gallagher-Thompson 2007	No anxiety outcome measurement
Gallagher-Thompson 2008	No anxiety outcome measurement
Gallagher-Thompson 2010	No anxiety outcome measurement
Gallagher-Thompson 2015	Did not employ both cognitive and behavioural techniques in the intervention
Garand 2013	Did not employ both cognitive and behavioural techniques in the intervention
Garand 2006	Did not employ both cognitive and behavioural techniques in the intervention
Gaugler 2015	Did not employ both cognitive and behavioural techniques in the intervention
Glueckauf 2012	Inappropriate control so effect of CBT could not be isolated
Gonyea 2012	Duplicate data linked to original
Gonyea 2013	Duplicate data linked to original
Gonyea 2014	Did not employ both cognitive and behavioural techniques in the intervention
Gossink 2016	Protocol available, author contacted, replied but no further information provided as awaiting publication
Graham-Philips 2016	Did not employ both cognitive and behavioural techniques in the intervention
Hatch 2014	Did not employ both cognitive and behavioural techniques in the intervention
Hauck 2003	Did not employ both cognitive and behavioural techniques in the intervention
Hengudomsub 2016	No anxiety outcome measurement
Hepburn 2001	Did not employ both cognitive and behavioural techniques in the intervention
Hepburn 2005	Did not employ both cognitive and behavioural techniques in the intervention
Hicken 2016	Did not employ both cognitive and behavioural techniques in the intervention
Jang 2004	Did not employ both cognitive and behavioural techniques in the intervention
Kajiyama 2013	No anxiety outcome measurement
Kilimann 2016	Did not employ both cognitive and behavioural techniques in the intervention
Lancer 2006	Protocol available, unable to trace further information
Lane, 2003	No anxiety outcome measurement
Livingston 2013	Duplicate data linked to original
Losada 2014	Duplicate data linked to original
Losada 2015	Duplicate data linked to original
Knapp 2013	No anxiety outcome measurement
Kuo 2013	No anxiety outcome measurement

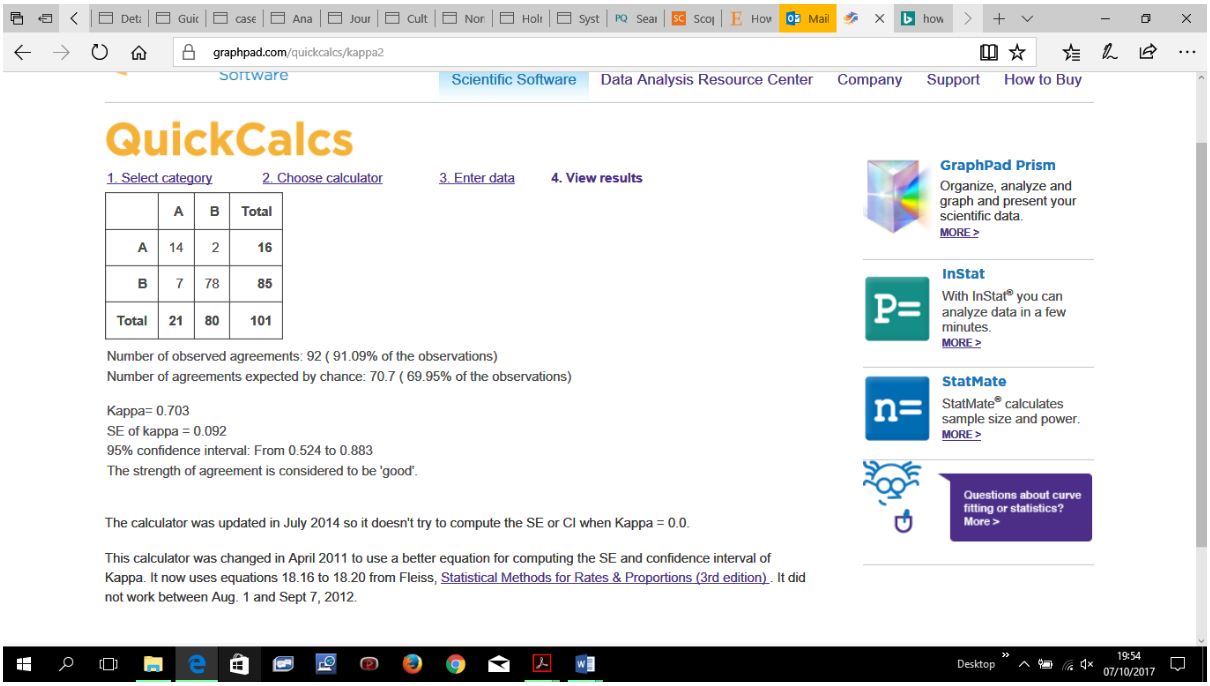
Kwok 2013	Did not employ both cognitive and behavioural techniques in the intervention
Lane 2003	Data not available to calculate effect size
Lee 2010	Did not employ both cognitive and behavioural techniques in the intervention
Lewis 2009	Did not employ both cognitive and behavioural techniques in the intervention
Losada 2011	No anxiety outcome measurement
Mackenzie 2008	Not RCT or CT
Mahoney 2003	Did not employ both cognitive and behavioural techniques in the intervention
Marriot 2000	No anxiety outcome measurement
Martin-Carrasco 2014	Data not available to calculate effect size
Marquez-Gonzalez 2007	No anxiety outcome measurement
McGinnis 2015	Did not employ both cognitive and behavioural techniques in the intervention
McKinnon 2012	No anxiety outcome measurement
Meichsner 2016	No anxiety outcome measurement
Mittelman 2004	Did not employ both cognitive and behavioural techniques in the intervention
Moore 2013	Did not employ both cognitive and behavioural techniques in the intervention
Nichols 2011	Did not employ both cognitive and behavioural techniques in the intervention
Ostwald 1999	Did not employ both cognitive and behavioural techniques in the intervention
Rabinowitz 2006	Data not available to calculate effect size
Schinkothe 2015	Not RCT or CT
Steffen 2000	No anxiety outcome measurement
Steffen 2016	Did not employ both cognitive and behavioural techniques in the intervention
Topcu 2011	Protocol available, unable to trace further information
Ulstein 2007	Did not employ both cognitive and behavioural techniques in the intervention
Villareal-Reyna 2012	Data not available to calculate effect size
Winter 2006	Did not employ both cognitive and behavioural techniques in the intervention
Wilz 2011	Not RCT or CT
Yeon 2007	Did not employ both cognitive and behavioural techniques in the intervention

Appendix I: Kappa calculation for study inclusion

Kappa calculations were completed using an online calculator

http://graphpad.com/quickcalcs/kappa1.cfm

1) Kappa calculation for study inclusion



	A	B	Total
A	14	2	16
B	7	78	85
Total	21	80	101

Number of observed agreements: 92 (91.09% of the observations)
Number of agreements expected by chance: 70.7 (69.95% of the observations)

Kappa= 0.703
SE of kappa = 0.092
95% confidence interval: From 0.524 to 0.883
The strength of agreement is considered to be 'good'.

The calculator was updated in July 2014 so it doesn't try to compute the SE or CI when Kappa = 0.0.

This calculator was changed in April 2011 to use a better equation for computing the SE and confidence interval of Kappa. It now uses equations 18.16 to 18.20 from Fleiss, Statistical Methods for Rates & Proportions (3rd edition) . It did not work between Aug. 1 and Sept 7, 2012.

Appendix J: Risk of bias assessment tables for each included study

Study ID: Aboulafia-Brakha, et al. 2014

Type of bias	Entry	Judgement	Support for judgement
Selection bias	Random sequence generation	High risk	Quote (from report) "The assignment to each group was done during the first contact by phone, in alternating order".
Selection bias	Allocation concealment	High risk	Comment: randomisation based upon alternation. Significant differences in baseline gender and work status. N
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Comment: Four participants dropped out of the treatment group, three participants dropped out of the control group. Quote: "reasons mentioned by participants for discontinuing interventions included lack of availability, lack of interest in the programme and not feeling concerned by the topic" Comment: missing data balanced between groups, with similar reasons for discontinuation.
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. There is no inclusion criteria addressing cortisol levels – an assumption is made that cortisol levels will be raised in caregivers.
2. Caregivers were contacted based on the fact that their relative had been diagnosed with ADRD and not because they had requested help/support.
3. Theoretical framework linked to stress reduction which was the primary outcome.
4. No assessment made of treatment adherence/fidelity
5. Information about concurrent treatment not recorded/monitored for control group, however, they were given 8 weekly group sessions making it less likely they would seek help elsewhere.

Study ID: Akkerman & Ostwald, 2004

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Unclear risk	Comment: insufficient information about the randomisation process to permit judgement of "low" or "high" risk.
Selection bias	Allocation concealment	High risk	Quote: "the principle investigator randomised participants….after completion of a brief telephone screen".
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: "A trained assessor (a Master's prepared clinical social worker, masked to condition) administered all subsequent assessments…." Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Quote: "Three participants dropped out prior to completing their randomised interventions (two were in the CBT intervention)" Comment: missing data balanced between groups.
Other bias	Bias due to problems not covered elsewhere in the table	Low risk	Comment: any potential sources of bias are not thought to be important and are discussed within the narrative section within the results.

1. Caregivers had to exhibit some level of anxiety at baseline, however, unclear how this was assessed.
2. Participants were recruited from general population through media advertising, it is unclear whether they were approaching for help with a certain problem.
3. A clear theoretical model was used to drive the intervention to target anxiety.
4. Treatment integrity was assessed and any drift from the proposed model was monitored.
5. Those on the waitlist were subsequently enrolled onto the programme which reduced the likelihood of them seeking alternative support. Those involved in any alternative psychotherapy were excluded at baseline.

Study ID: Beauchamp, et al. 2005.

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Unclear risk	Comment: insufficient information about the randomisation process to permit judgement of "low" or "high" risk.
Selection bias	Allocation concealment	Unclear risk	Comment: method of concealment is not described therefore insufficient information to permit judgement of "low" or "high" risk.
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Comment: measures were completed online Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Quote: "comparisons between those who dropped out and those who completed the study yielded no significant differences on demographic characteristics and bassline measures. Thus there were no apparent biases that were due to attrition". Comment: missing data balanced between groups.
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. Caregivers had to report experiencing stress in their caregiving role – however, baseline scores suggested very low mean stress levels.
2. Caregivers were required to report stress in relation to their caregiving role. There is also an element of personalisation to the intervention allowing them to select areas for help that match their need.
3. Based on a theoretical model of stress and primary outcome assesses domains specifically targeted by the model.
4. Satisfaction with the program was assessed for all participants, however, all completers were given financial rewards which may have biased responses. Treatment components were selected by individual participants and so cannot be sure that all participants received all elements of the program. This was not monitored.

5. Participants in the control arm were given access to the program after just 30 days reducing the likelihood of accessing support elsewhere, this was not monitored. In discussion section the authors discuss possibility that program motivated those in the intervention arm to seek further online support, again this is not monitored.

Study ID: Blom, et al. 2015.

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Low risk	Quote: "… a computerised random-number generator for block randomisation…".
Selection bias	Allocation concealment	Low risk	Quote: "A researcher not connected to the study…..". Comment: randomisation was completed by a researcher independent to the study using a computerised programme.
Reporting bias	Selective reporting	High risk	Comment: The study protocol is available and all expected outcomes are reported.
Performance bias	Blinding of personnel and participants	Unclear risk	Quote: "Participants did not know whether the intervention they received was the experimental or the comparison intervention". Comment: Blinding of key study participants attempted but it is possible that the blinding could have been broken.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: "The data were collected via the internet with no intermediary interviewer"
Attrition bias	Incomplete outcome data	Low risk	Quote: "Three participants dropped out prior to completing their randomised interventions (two were in the CBT intervention)" Comment: missing data have been imputed using appropriate methods.
Other bias	Bias due to problems not covered elsewhere in the table	Low risk	Comment: any potential sources of bias are not thought to be important and are discussed within the narrative section within the results.

1. Caregivers had to have some level of anxiety or depression to be included in the study.
2. Caregivers had to approach researchers expressing interest in taking part in the study suggesting they were seeking help in their caregiving role, however, it is not clear whether they were told that the intervention was designed to help with depression and anxiety.

3. The intervention was based upon research investigating interventions that successfully reduced psychiatric symptoms in caregivers.
4. Treatment is delivered via an internet program so is standardised and requires participants to access all elements. Participants received feedback on homework from a coach and the nature of this feedback was not monitored, although the coach received prior instruction to report in exercises only and not to provide any additional help.
5. Participants were blind to the condition, and those in the control condition received e-bulletins every three weeks. There was no assessment as to whether they were seeking help elsewhere.

Study ID: Burgio, et al. 2003

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Low risk	Quote (from report) “Dyads being minimized to the STC or the MSC”. Comment: minimisation is considered to be the equivalent to being random.
Selection bias	Allocation concealment	Unclear risk	Comment: Not explicitly stated how the procedure was completed.
Reporting bias	Selective reporting	High risk	Comment: not all outcomes reported. Follow up data not reported and not available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “for bias to be minimized intervention and assessment of a dyad were never conducted by the same individual” Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Quote: “there were no significant differences in discontinuation rate between the two groups” Comment: missing data balanced between groups, with similar reasons for discontinuation.
Other bias	Bias due to problems not covered elsewhere in the table	Low risk	Comment: any potential sources of bias are not thought to be important and are discussed within the narrative section within the results.

1. Caregivers had to report at least three problem behaviours in the CR to meet eligibly requirements. One of the outcomes measured was CR problem behaviour. None of the other outcome measurements were included in the eligibility criteria.
2. Caregivers could self-refer suggesting they were seeking help, they also had to report problem behaviours in the CR.
3. Intervention is based on stress process framework and outcomes appear to be related to theoretical model.
4. Treatment implementation is assessed using specific model: treatment delivery, treatment receipt and treatment enactment.
5. The control group had contact that mirrored the frequency of the intervention group, which reduced likelihood of them seeking help elsewhere but this was not officially monitored.

Study ID: Chang, 1999

Type of bias	Entry	Judgement	Support for judgement
Selection bias	Random sequence generation	Unclear risk	Comment: insufficient information about the sequence generation to permit judgment of “low” or “high” risk.
Selection bias	Allocation concealment	Unclear risk	Comment: not described within the report.
Reporting bias	Selective reporting	High risk	Comment: one of more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Unclear risk	Comment: significant differences between dropouts and completers reported on some domains but no assessment of differences in dropout reasons between conditions. Quote: “MMSE scores were significantly different between completers and dropouts indicating greater deterioration of the person with dementia in the dropout group” Comment: Reason for missing outcome potentially linked to intervention assignment, not clear how many participants dropped out and how the intervention effects were calculated.
Other bias	Bias due to problems not covered elsewhere in the table	High risk	Comment: it is not clear which elements of CBT were delivered to caregivers

1. Caregivers had to report significant eating and dressing problems in the CR but changes in this domain are not the primary outcome measure.

2. Participants were approached for inclusion rather than seeking inclusion. They did have to report difficulties in the CR but it is unclear if they wanted to help with this.

3. Intervention is based upon CBT but it is unclear how this model is applied within the intervention.

4. The intervention was partly delivered via video which was standardised. Phone calls were also made and these ranged in length from 5 mins to 90 mins and there is no report of assessment of treatment adherence and it is not clear what elements of CBT were received.

5. Caregivers in the control condition were referred to other sources of support, uptake/specific details of these sources of support are not reported.

Study ID: Gendron, et al. 1996

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Unclear risk	Comment: insufficient information about the sequence generation to permit judgment of “low” or “high” risk
Selection bias	Allocation concealment	Unclear risk	Comment: not described within the report
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “Data were collected……by one interviewer who was blind as to subject assignment and objectives of research”. Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Comment: no missing outcome data.
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. The primary aim of the intervention was to teach assertiveness but levels of assertiveness did not form eligibility criteria, and baseline measures suggest caregivers were just below the average range.

2. Caregivers had to be requesting help to cope with their situation.

3. The intervention is based on CBT model and the elements of the intervention are clearly linked to the outcomes being assessed.

4. Treatment integrity is not reported.

5. The control group received the same number of contacts as the control group which may have been enough to stop them seeking support elsewhere but this was not assessed.

Study ID: Gonyea, et al. 2014

Type of bias	Entry	Judgement	Support for judgement
Selection bias	Random sequence generation	Unclear risk	Comment: insufficient information about the sequence generation to permit judgment of “low” or “high” risk
Selection bias	Allocation concealment	Unclear risk	Comment: not described within the report
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Comment: missing data were imputed using appropriate methods.
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. Eligibility criteria did not include any assessment of caregiver wellbeing even though this was a primary outcome measure.
2. The majority of participants were referred into the programme by professionals – it is not clear if this is because they were requesting help or because the professional felt they would be eligible.
3. The intervention is based on trans-diagnostic CBT and there are links between the structure of the intervention and the outcomes measures used.
4. The intervention was manualised but no measure was reported for treatment integrity.
5. Control condition was also manualised with the same frequency of contact as the intervention condition. The active engagement aimed to reduce the likelihood of participants seeking support elsewhere but this is not recorded.

Study ID: Hebert, et al. 2003

Type of bias	Entry	Judgement	Support for judgement
Selection bias	Random sequence generation	Low risk	Quote: “randomization was performed within each centre and wave using the minimization technique”
Selection bias	Allocation concealment	Unclear risk	Comment: not described within the report
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “….by trained interviewers blinded to the group assignment of the participants”. Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Unclear risk	Comment: insufficient reporting of reasons for attrition to permit judgement.
Other bias	Bias due to problems not covered elsewhere in the table	Low risk	Comment: any potential sources of bias are not thought to be important and are discussed within the narrative section within the results.

1. Participants had to be exhibiting moderate to severe burden to be eligible for inclusion.
2. Caregivers had to report at least one problem behaviour per week but recruitment strategy does not specify if they were self-referring. They also had to be reporting high levels of burden but again it is unclear whether they were requesting help with this.
3. The intervention is based upon transactional theory of stress and coping and the primary aims were to reduce stress reactions to difficult behaviours. Secondary aims were to indirectly reduce burden and psychological distress and the links between the model and the outcome aims are explained.
4. The intervention was manualised which would help to ensure standardisation. The authors state that the program was implemented as planned but do not report how this was assessed.
5. Part of the inclusion criteria required participants not to engage in any other psychotherapy or support group during the application of the intervention/control group. Previous attendance in therapy was recorded.

Study ID: Karagiozi et al. 2014

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Unclear risk	Comment: insufficient information about the sequence generation to permit judgment of “low” or “high” risk
Selection bias	Allocation concealment	Unclear risk	Comment: not described within the report
Reporting bias	Selective reporting	Low risk	Quote : “the data were analysed on a per-protocol basis” Comment: all expected outcomes were reported.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “Each participant was assessed….. by the same trained psychologist who was blind to the allocation of groups”. Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	High risk	Comment: majority of drop outs from control condition did so because of lack of interest. Comment: imbalance in reasons for missing data across intervention groups.
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. Excluded participants with psychiatric diagnosis or severe depression as required urgent attention. There was no inclusion criteria regarding caregivers to have certain levels of burden, anxiety or depression which were primary outcomes.
2. It is not clear if caregivers were requesting help for any of the primary outcomes, but they were interviewed before participation to identify individual targets – these are not reported.
3. Intervention is based on CBT model and appears to use idea that improve interpretation of caregiving will reduce burden, anxiety and depression.
4. Guidelines were used to monitor treatment delivery but there is no record of how this was assessed.
5. The control was waitlist for 6 months and there is no report of whether their involvement in other programs was assessed.

Study ID: Livingston, et al. 2014

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Low risk	Quote: “randomisation to intervention was carried out using an online computer-generated randomisation system”
Selection bias	Allocation concealment	Low risk	Comment: randomisation was completed using central allocation
Reporting bias	Selective reporting	Low risk	Comment: all expected outcomes were reported. Protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “Outcome assessors were blinded to randomisation status”. Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Comment: missing data have been imputed using appropriate methods
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. Caregivers were not required to reach certain levels of symptom severity to meet eligibility.
2. Caregivers were referred to the study by their clinicians, there is no mention of whether they were requesting help or how the decision was made to refer them.
3. The intervention is based on a pre-existing caregiver intervention and whilst not made explicit it is based on CBT. There is some explanation of how the intervention is expected to impact on the primary outcomes.
4. Treatment integrity is closely assessed and interventionists all have clinical supervision.
5. The control group was TAU and what this involved is well explained but it was not recorded exactly what participants accessed.

Study ID: Losada, et al. 2015

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Low risk	Quote: “participants were randomised …..using computer-generated random numbers”
Selection bias	Allocation concealment	Low risk	Comment: central allocation via a web-based system.
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “all the assessments were done by psychologists …..who were blind to treatment conditions and the main hypotheses of the study”. Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Comment: missing outcome data balanced across intervention groups with similar reasons for missing data.
Other bias	Bias due to problems not covered elsewhere in the table	Low risk	Comment: any potential sources of bias are not thought to be important and are discussed within the narrative section within the results.

1. Caregivers had to have a certain level of depression at baseline to be included in the study.
2. Recruitment was via clinician referral and out of 377 possible participants 242 did not meet eligibility criteria and this was in part due to not having significant levels of depression suggesting that participants put forward were not ones who had been identified as needing help with depression.
3. Intervention is based upon CBT with a link between the theory and the outcomes being assessed.
4. Treatment integrity was assessed using same methods as Burgio, et al. 2001 and deemed to be acceptable.
5. Participants in control group had minimum contact and no assessment was made as to whether they accessed additional support.

Study ID: Martin-Carrasco, et al. 2009

Type of bias	**Entry**	**Judgement**	**Support for judgement**
Selection bias	Random sequence generation	Unclear risk	Quote: "randomised assignment was performed by centre and in blocks of four" Comment: insufficient information about the sequence generation to permit judgment of "low" or "high" risk
Selection bias	Allocation concealment	Unclear risk	Comment: not described within the report
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Unclear risk	Comment: insufficient reporting of attrition to permit judgement of "low" or "high" risk.
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. Caregivers had to have a certain level of burden to be eligible for inclusion and burden was one of the primary outcome measures.
2. Caregivers were referred by their clinicians, it is unclear how they were selected or whether they had requested help.
3. There is no explicit discussion of the main theoretical model. It is based on CBT techniques but these are not clearly linked to the outcomes measured.
4. Investigators received training in how to deliver the intervention and it was manualised. There is no record of how treatment integrity was monitored.
5. It is not clear how or if integrity of the control condition was assessed.

Study ID: Passoni, et al. 2014

Type of bias	Entry	Judgement	Support for judgement
Selection bias	Random sequence generation	High risk	Quote: “we could only randomise the control versus OM conditions between caregivers who did not join the CBT meetings” Comment: allocation to the CBT group was based on preference of the participant. Although the groups that were randomised were randomised by means of computer generated random numbers.
Selection bias	Allocation concealment	High risk	Comment: caregivers in the CBT group were not randomised.
Reporting bias	Selective reporting	Unclear risk	Comment: all expected outcomes were reported. No protocol available.
Performance bias	Blinding of personnel and participants	High risk	Comment: Blinding of participants and personnel not possible for studies of psychological intervention.
Detection bias	Blinding of outcome assessment (self-report measures)	Low risk	Quote: “baseline and follow up data are gathered by independent and blinded interviewers for OM and CO groups”. Comment: self-report measures are unlikely to be influenced by lack of blinding.
Attrition bias	Incomplete outcome data	Low risk	Comment: no missing outcome data
Other bias	Bias due to problems not covered elsewhere in the table	Unclear risk	Comment: insufficient evidence that identified problem will introduce bias

1. No assessment of anxiety levels as part of eligibility assessment.
2. All CG in control conditions were asked about participation during routine appointments at dementia hospital. CG in the CBT condition had referred themselves after seeing adverts in hospital waiting room, suggesting they were looking for extra support.
3. The intervention is clearly based upon CBT model with links to outcomes described.
4. The intervention was based upon a manual and delivered by therapists experienced in CBT, however, there is no record of monitoring of adherence to manual.
5. The control group were on a waitlist for three months when they then had access to TAU which included group CBT this may have increased the likelihood of them waiting and not seeking help elsewhere, however, this was not assessed.