Cognitive Behavioural therapy (CBT) for anxiety in dementia: A pilot randomised controlled trial

Running head: CBT for anxiety in Dementia: An RCT

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Abstract

Background

Anxiety is common and problematic in dementia, yet there lacks effective treatments.

Aims

To develop a CBT manual for anxiety and dementia, and determine its feasibility through an RCT.

Methods

A ten session CBT manual was developed following literature search, expert consultation, consensus conference and field testing. Fifty participants with dementia and anxiety (and their carers) were randomly allocated to CBT plus treatment as usual (TAU) (n=25) or TAU (n=25). Outcome and cost measures were administered at baseline, 15 weeks and 6 months.

Results

At 15 weeks, there was a reduction in anxiety for CBT compared to TAU, which just lost significance after adjustment for baseline anxiety and cognition (-3.10; 95% CI -6.55, 0.34). There were significant improvements in depression at 15 weeks after adjustment (-5.37; 95% CI - 9.50, -1.25). Both improvements remained significant at six months. CBT was cost neutral.

Conclusions

CBT was feasible (in terms of recruitment, acceptability and attrition) and effective. A fully powered RCT is now required.

Declaration of Interest

None

Introduction

Anxiety in dementia is common, with prevalence estimated from 5-21% for anxiety disorders and up to 71% for anxiety symptoms [1]. Anxiety may physically present as motor restlessness, agitation, day/night disturbance and/or aggression, and often results in exacerbated symptoms of dementia due to increased dependency and behavioural problems [2,3]. Anxiety has traditionally been treated with antipsychotic medication, which has limited efficacy and devastating side-effects including sedation, depression, stroke and increased mortality [4]. Cognitive behaviour therapy (CBT) [5] is a collaborative psychological approach that addresses the interaction

between people's thoughts, feelings and behaviour. There is robust evidence that CBT is an effective first-line strategy for anxiety in older people without dementia [6]. The UK National Health Service widely endorses CBT through its "Improving Access to Psychological Therapies" (IAPT) programme [7], which supports primary care trusts in implementing CBT for depression and anxiety. There is evidence that people with dementia can learn and develop skills [8], which suggests that CBT could be used for people with dementia, as it has been in other impaired populations including learning disabilities [9]. There is some evidence for the feasibility of CBT for anxiety and depression in dementia, primarily through case studies and two small RCTs in the US [e.g. 2, 10, 11, 12]. They all concluded that larger trials are needed. This study had two phases, which correspond to phase I and II of the MRC's guidelines for developing a complex intervention and assessing feasibility [13]. They were:
(1) To develop a CBT intervention manual.
(2) To assess the feasibility of the intervention through a single-blind, pilot RCT of CBT plus treatment as usual (TAU) versus TAU for people with dementia (supported by their carers). This included an assessment of acceptability, compliance, recruitment, retention and costs.

Method

Ethics statement

Ethical approval was obtained through the 'East London 3 Research Ethics Committee' (reference number 10/H0701/124). The trial registration number is ISRCTN46521766.

Phase I: Manual development

The manual was developed in several stages, described previously [14]. Its development involved systematic literature review, expert review, a consensus conference with 30 people and field-testing with three people. The version used in this trial involved a three-phase formulation-driven therapy based on Beck and Clark's [5] cognitive model of anxiety. Phase 1 involves building a collaborative relationship, psychoeducation about CBT and the excess disability caused by anxiety in dementia, self-monitoring, developing an individualised formulation and identifying goals. During this first phase, the level of carer involvement is also established. The carer's

role is to support the person with dementia in implementing strategies, for example applying what has been discussed during sessions in everyday life. Their involvement could range from very little (e.g. attending brief parts of some sessions) to being present at all times. Phase 2 involves the application of change processes, which the therapist can adapt according to the needs and strengths of the individual. These include identifying and practicing strategies for feeling safe, identifying and challenging unhelpful cognitions, addressing 'realistic negative automatic thoughts', calming thoughts (on cue cards) and behavioural experiments. Phase 2 also had optional 'modules' for considering longstanding unhelpful 'rules for living' and for addressing interpersonal difficulties between the carer and person with dementia. Phase 3 works on ending the therapy and developing a blueprint for the future. This includes reviewing and consolidating learned skills, integration of skills into everyday life and considering the future involvement of carers and others.

Phase II: Randomised Controlled Trial

Design

A single-blind, multicentre, pilot randomised controlled trial of CBT plus treatment as usual (TAU) versus TAU for people with dementia. As no trials have been done in this area, we were unable to estimate the likely effect size of this intervention. The sample size was chosen on pragmatic grounds as sufficient to demonstrate adequate recruitment and retention, although 50 participants would be sufficient to detect an effect size of 0.8 with 80% power and 5% significance. We also aimed to provide data on the possible effect size of the intervention in order to inform a power analysis for a large scale RCT.

Participants

Participants were eligible for inclusion if they (1) Met DSM-IV criteria for dementia in the mild-to-moderate range, determined by a Clinical Dementia Rating (CDR) [15] score of 0.5, 1 or 2; (2) Had clinical anxiety, as determined by a score of 11 or above on the Rating Anxiety in Dementia scale (RAID) [16], with or without co-morbid depression; (3) Lived in the community; (4) Had a carer who was willing to participate in the therapy; (5) Were able to understand and communicate in English; (6) Were willing to engage in therapy involving discussion of thoughts and feelings.

Participants were excluded if they had (1) A co-morbid psychiatric disorder (e.g. psychosis) or challenging behaviour (e.g. severe agitation), likely to prevent engagement in therapy or (2) The presence of a congenital learning disability or severe physical illness, which could impact on participation.

Procedure

Potential participants were primarily identified through NHS secondary care services within two NHS trusts. People who appeared to meet inclusion criteria were contacted by telephone or in writing by the referrer. If they chose to participate, informed consent was sought from participants and their carers using current guidance from the British Psychological Society on evaluation of capacity. Following this, people were screened for suitability and the full assessment was conducted if they were deemed suitable.

Assessments

All assessments were administered by the research assistant at week 1 (baseline), week 15 (follow-up 1) and 6 months (follow-up 2). Baseline data collected included age, gender, ethnic group, use of medication and participation in other activities.

The primary outcome was measured using the Rating for Anxiety in Dementia (RAID) [16]. This rates signs and symptoms of anxiety using interviews with carers and people with dementia. There are 18 questions in four categories: worry, apprehension, vigilance, motor tension and autonomic hypersensitivity. A score of 11 or above indicates significant clinical anxiety. It has good inter-rater and test-retest reliability and is sensitive to change.

Costs were measured using the Clinical Services Receipt Inventory (CSRI) [17], which collects information about the participant's receipt of health and social care services, equipment or adaptations, medication, accommodation (e.g. care home), income and benefits. Changes in the receipt of these services can be tracked over time, as it asks for service receipt over the previous three months each time it is administered.

Depression was measured using the Cornell Scale for Depression in Dementia [CSDD, 18]. This rates depression in five domains including mood-related signs, behavioural disturbance and ideational disturbance, using interviews with people with dementia and proxies. Good reliability and validity have been demonstrated. The mood of both the person with dementia and their carer was also measured using the Hospital Anxiety and Depression Scale (HADS) [19], a widely used measure validated for all age groups. Quality of life was measured using the Quality of Life-Alzheimer's Disease (QOL-AD) [20], a self-report measure for the person with dementia and their carer, with 13 items covering domains including physical health, energy, friends and fun. It has excellent inter-rater reliability and internal consistency, and good content, criterion and construct validity. Behavioural disturbance was measured by the Neuropsychiatric Inventory (NPI) [21]. This assesses ten areas including delusions, hallucinations, dysphoria and agitation/aggression. Content and concurrent validity, inter-rater and test-retest reliability and internal consistency are all good. Cognitive function was assessed by the Mini-Mental State Examination (MMSE) [22]. This is an internationally recognised, 11-item set of simple tasks presented to the participant including orientation to time and place, attention, recall, language and visual construction. It has a maximum score of 30 points, with 24 or less suggesting cognitive impairment. Reliability and validity are satisfactory. Person-carer relationship was assessed using the Quality of Caregiver and Patient Relationship (QCPR) [23]. This is a 14-item scale measuring relationship quality including the level of criticism and level of warmth, rated by both the person and their carer. Good reliability and validity have been demonstrated.

Randomisation procedures

Patient-carer dyads were randomly allocated to either CBT or TAU, with an allocation ratio of 1:1. The randomisation sequence was generated using Stata by an independent statistician and administered by PRIMENT Clinical Trials Unit after the participant/carer had provided consent and baseline data. A method of blocking was employed (with block sizes varying between 4 and 6) to help ensure equal numbers in the intervention and control arms. Once each individual was randomised, the Clinical Trials Unit informed the trial psychologist of allocation and the psychologist then informed the individual by telephone. Assessors were blinded to group allocation. Participants with dementia and their carers could not be blinded to group allocation,

due to the intervention being psychosocial. However, they were reminded not to disclose which arm of the study they were assigned to at the beginning of each assessment, in an attempt to minimise detection bias.

Intervention and control conditions

CBT plus TAU: The patient-carer dyads participated in up to ten weekly sessions, each lasting approximately one hour. This number was determined on the basis of the published literature, the team's experience and patient and carer feedback during field testing. Sessions were shortened and breaks taken as required to maintain attention. Sessions were delivered by four Clinical Psychologists with experience of working with people with dementia. Participants receiving CBT were permitted to utilise any standard treatment available for anxiety if required.

Treatment as usual (TAU): This was defined as the standard treatment available to people with anxiety and dementia, which was most likely to include medication or no treatment.

Statistical methods

Data were analysed using the intention to treat principle. Baseline summary statistics by randomised group were calculated. Outcomes at 15 weeks and six months were modelled separately using linear regression, with coefficients and 95% confidence intervals presented (see statistical appendix). Results for the participants with dementia are presented unadjusted and adjusted for baseline anxiety (score on the RAID) and baseline cognition (score on the MMSE). Analyses on the carer scales were adjusted for the value of the scale at baseline. It was agreed a priori that the adjusted analysed would be the primary analyses. All analyses were carried out using Stata version 12.1.

Cost analysis

The cost analysis adopted a health and social care (HSC) perspective, which considers only costs incurred by organisations providing health and social care services. Unit costs were obtained from the PSSRU compendium for 2011 [24] where possible. It was decided a priori that cost differences at both follow-up points would be compared after adjusting for pre-baseline HSC costs, baseline MMSE score and baseline RAID score, using multiple regression. To minimise the effect of skewness, 95% bias-

corrected confidence intervals for between-group mean costs were estimated using non-parametric bootstrapping techniques (re-sampling with replacement; 1000 repetitions). Missing values within the main cost analysis were addressed through imputing mean values. For each variable used in the cost analysis, missing values accounted for fewer than 15% of total responses. Two sensitivity analyses were conducted. The first used no imputations (costs that could not be calculated due to missing data were excluded) and the second excluded outliers (individuals with abnormally high costs in one or more cost categories- e.g. accommodation costs).

Results

Sample

Tables 1 and 2 show the characteristics of the sample; table 1 for the people with dementia and table 2 for the carers. There were 20 males and 30 females aged between 63 and 98 years. Randomised groups were balanced in terms of gender, mean age and ethnicity of the patient (Table 1). In the CBT plus TAU group, all carers were family members, whereas this was the case for 80% in the TAU group. This might explain the much higher median hours spent a week caring in the CBT versus the TAU group (61 versus 15), with family carers generally describing their care as 24/7 (Table 2). The median MMSE was 23 for both groups. However, the median RAID was lower in the CBT plus TAU group compared to the TAU group (17; IQR 14, 21 versus 22; IQR 17, 24 respectively) (Table 1). There was also a lower use of anxiolytic medication in the CBT plus TAU group (8%) compared to the TAU group (24%).

[Table 1 here: Baseline summary statistics for the participant by randomised group]
[Table 2 here: Baseline summary statistics for the carer by randomised group]

Recruitment and Retention

Figure 1 shows the flow of participants through the trial. 153 participants were referred to the study, of which 93 came from secondary care services (Memory clinics, Admiral nursing), 26 through searches of case notes by the researcher, 22 from voluntary services, 7 via other research studies and 5 via other routes (e.g. self-referral). 103 dyads were screened out as they did not meet eligibility criteria (63), refused participation (34), person with dementia passed away (4) or became ill (2). 50

participant carer dyads were randomised to either CBT plus TAU (*n*=25) or TAU only (*n*=25). Nine participants withdrew from the trial at first follow up. Two participants were unable to be assessed at first follow up but were assessed for second follow up. Another three withdrew from the trial at second follow up. Primary outcome data were available for all participants who were assessed at the first follow up.

[Figure 1: Consort Diagram here]

Feasibility

It was possible to recruit the required number within the given timeframe (14 months), with approximately one in three referrals recruited into the trial. Attrition was acceptable: 39 of the 50 dyads were retained at 15 weeks and 38 at 6 months. Generally, people took up the intervention when offered it. Of the 25 participants allocated to CBT plus TAU, four dropped out, three due to the person or carer withdrawing and one due to death. Of the remaining 21, 14 people attended all ten sessions. Seven people felt they had achieved their treatment goals sooner and finished early after six (n=2), seven (n=2), eight (n=2) and nine sessions (n=1). Of the 25 allocated to TAU, eight dropped out of the research, four due to carer stressors, two due to dissatisfaction of allocation, one due to stress in the person with dementia and one where contact was lost. There was a significant difference in gender between those who were retained and dropped out. Of those retained, 48% were male and of those who dropped out, 9% were male. A greater percentage of participants with moderate dementia dropped out (36%) compared with those retained in the study (10%). There were no reported adverse effects or side effects of the intervention.

The trial therapists were asked to consider each person with dementia's 'suitability for cognitive therapy'. This provided a systematic approach to identifying those areas where 'pre-therapy' techniques may be required, for example strategies to expand emotional vocabulary or increase awareness of the link between cognitions, actions and emotions. Memory and language problems could be compensated for in most cases except where the degree of severity was such that the person with dementia was unable to 'hold in mind' the presence of the therapist during sessions and was continuously surprised by their presence, or in circumstances where the ability to have meaningful verbal exchanges was severely compromised. The therapy was least

feasible in cases where there were significant and longstanding interpersonal difficulties between the person with dementia and their family carer or where there was no consistent family carer and the person with dementia needed a high level of in-session support.

Adherence

All four CBT therapists received a two-hour training session on the manual by GC, a Clinical Psychologist with 15 years experience of using CBT for older people. The same psychologist also provided clinical supervision. Sessions were recorded where possible and one session per dyad was coded by an independent Psychologist for adherence to CBT using the Cognitive Therapy Scale - Revised (CTS-R) [24]. Six cases were excluded from rating due to requests not to be recorded (n=4), technical problems (n=1) and work primarily involving the carer (n=1). Of the 15 recordings rated, an average score in the "competent" range was achieved. There was a range in scores, largely due to the range of therapist expertise and extent to which participants met 'suitability for Cognitive Therapy' criteria.

Main Clinical Outcomes

Table 3 shows that, using RAID, anxiety was significantly lower in the CBT plus TAU group at 15 weeks (-4.32; 95% CI -8.21, -0.43). This lost statistical significance when adjusted for baseline anxiety and cognition (-3.10; 95% CI -6.55, 0.34). Depression, as measured by the CSDD was also significantly lower in the CBT plus TAU group and remained following adjustment (-5.37; 95% CI -9.50, -1.25). There were no significant differences or notable trends in quality of life, cognition, anxiety and depression (measured by the HADS) or the quality of caregiver patient relationship from the carer or patient perspective.

[Table 3 here: Outcomes at 15 weeks, coefficients for CBT]

The advantage shown by the CBT plus TAU group over the TAU group with regard to anxiety was maintained at six months, with those in the CBT group scoring on average 4.59 points lower than the TAU group although this fell a little short of statistical significance after adjustment (95% CI-9.34, 0.15). The difference in depression score on the CSDD was similar to that at 15 weeks and was also

statistically significant after adjustment (-5.08; 95% CI -9.25, -0.92). As at 15 weeks, there were no statistically significant differences in any other variables.

[Table 4 here: Outcomes at 6 months, coefficients for CBT]

Cost analysis

Cost per session for the intervention was £114.36. This included the average time spent by the therapist administering the intervention (including planning), therapist training, travel and equipment. Average session attendance per person was 8.8, hence average total intervention cost per person was £1002. The CBT plus TAU group had higher pre-baseline mean total cost from a HSC perspective compared to TAU, with a mean difference of £834.27 (Table 5). Although this difference was not significant (with a 95% bias-corrected confidence interval of -£285.77, £3069.38), it needs to be taken into account when comparing post-randomisation costs, and was controlled for.

Table 6 shows costs incurred between baseline and follow-up 1. While the costs (from a HSC perspective) are significantly lower for the CBT plus TAU group (unadjusted mean difference -£680.04; adjusted mean difference -£564.38), this was not enough to offset the intervention cost. Including the cost of the intervention, total costs were higher for the CBT plus TAU group compared to TAU, although this difference was not significant, with an unadjusted mean difference of £321.97 (95% bias corrected confidence interval of -£345.94, £946.85), and adjusted mean difference of £769.80(95% bias-corrected confidence interval of -£121.99, £1697.38).

Between the first and second follow-up, mean costs were again higher for the CBT plus TAU group compared to TAU, although this difference was not significant, with an unadjusted mean difference of £1085.02, (95% bias-corrected confidence interval of -£354.81, £4078.64), and an adjusted mean difference of £256.12, (95% bias-corrected confidence interval of -599.05, 1506.23) (Table 7). The first sensitivity analysis (which used no imputations) found no deviations from the main analysis with regards to trends or significance of any findings. The second sensitivity analysis (which removed high cost outliers) found no significant difference in costs from a HSC perspective at first follow-up, which was not surprising as sample size was reduced.

[Table 5 here: Participant pre-baseline costs (£) by service group with mean imputations]
[Table 6 here: Participant costs (£) between baseline and first follow-up (15 weeks) by service group with mean imputations]
[Table 7 here: Participant costs (£) between first follow-up (15 weeks) and second follow-up (6 months) by service group with mean imputations]

Power calculation for a full trial

For an unadjusted analysis, to detect a difference of four points on the RAID at 15 weeks (14 versus 18 in the CBT versus TAU groups respectively), both with a standard deviation of 6 and 90% power, 48 people would be needed in each group to provide data on the RAID at the primary end point (15 weeks).

Discussion

Summary of results

This trial demonstrated that formulation-based cognitive behavioural therapy (CBT) is feasible for people with mild to moderate dementia and clinically significant anxiety. At 15 weeks, there were differences in anxiety which approached significance, and these improvements remained at six months. Although the CBT intervention was targeted at the thoughts, feelings and behaviours characteristic of anxiety, the more significant finding was the difference in depression as measured by the CSDD at both 15 and 26 week follow-up. CBT led to a short-term reduction in health and social care costs (by 15 weeks), although this reduction was not enough to outweigh the cost of the intervention itself. In other words, CBT was cost-neutral. There were no significant changes in any other outcomes.

Acceptability and feasibility of CBT

The therapy was acceptable to people with dementia and their family carers as demonstrated by their willingness to participate, uptake of the intervention and low level of withdrawal from the intervention. The intervention was feasible for those with mild to moderate dementia (MMSE scores ranging from 25 to 16), although greater scaffolding by the therapist, a slower pace, greater repetition, increased emphasis on behavioural rather than cognitive techniques and a higher degree of

involvement from family carers was necessary with people in the more moderate stages of dementia. A challenge for this research was creating a manualised approach with enough built in flexibility to cover a variety of clinical presentations, both in terms of the profile of cognitive deficits and the nature and duration of the anxiety. One method for providing flexibility is to have a range of 'modules' within the manual, an approach used both here and in the 'Peaceful Mind' CBT studies in the US [11,12].

Strengths and limitations

There were a few limitations to this study. Firstly, there was a significant difference in baseline anxiety on the RAID, with the TAU group being significantly more anxious. It is therefore hard to know how effective CBT might have been for a more anxious group and one would hope for a more balanced sample in a larger trial. One therapist saw the majority of patients (18 cases), with only four cases seen by the three other therapists (one of whom treated two cases and two who treated one case each). This could imply that the effects were largely due to the therapist rather than the intervention. However, the strength of this approach is that there was limited therapist variability, hence interpretations of the manual will have predominantly been the same.

There was no measureable impact of the therapy on anxiety measured using the HADS. This may be due to the differences in content between the RAID and the HADS anxiety scale, or due to the differences in methods of administration. Both the CSDD and the RAID take into account the carer's and rater's view of presenting symptomatology rather than relying on self-report by the person with dementia alone. Finally, in a full trial we could do a full cost-effectiveness analysis, looking at trade-offs between better outcomes and higher costs. This was not feasible with this small sample pilot, which only considered costs from a health and social care perspective. It may be hypothesised, for example, that CBT might lead to reduced carer costs if outcomes are better for the people with dementia. Our analysis of costs from an HSC perspective was a strength in that it is of relevance to decision-makers considering whether their organisation should implement CBT.

Implications for research and practice

The results suggest that a larger, fully powered RCT is now required to assess the effectiveness of CBT for anxiety in dementia. The data from this trial have been used to provide a power calculation for a full RCT, suggesting that a minimum of 96 participants (48 in each group) would be required prior to inflation for drop out and additional inflation using the intra-class correlation associated with clustering by therapist. The manual is written for use by therapists who already have a good knowledge of using CBT and experience of work with people with dementia, although prior experience of carrying out CBT with people with dementia was not required. Future research may be required in evaluating the effectiveness of the therapy delivered by non-specialists. The manual developed for this trial will be published, enabling others to use it.

Conclusion

This pilot trial demonstrates that a full RCT of CBT for anxiety in people with dementia is feasible and that the manualised intervention is acceptable to people with dementia and their carers. The data arising from the feasibility trial also suggest that the intervention leads to reductions in anxiety, depression and potentially short-term costs of other HSC services, and that further investigation into the use of CBT for depression in dementia is also warranted.

Declaration of interests

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Aimee Spector: Conception and design of study, led initial draft of article and oversaw revisions.

Georgina Charlesworth: Conception and design of study, critical revision of article.

Michael King: Conception and design of study, critical revision of article.

Miles Lattimer: Contributed to initial draft of article and revisions.

Susan Sadek: Contributed to initial draft of article and revisions.

Louise Marston: Led statistical analysis, critical revision of article.

Amritpal Rehill: Led economic analysis, critical revision of article.

Juanita Hoe: Conception and design of study, critical revision of article.

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Statistical appendix

We checked the distribution of all outcome measures. Some of these were skew; hence medians (interquartile range) and means (standard deviation) are presented in Table 1. After linear regression, we checked the assumption of normality of the residuals for each model by plotting them on a histogram. Some were Normally distributed, despite the outcome variable not being Normal. Where the residuals were deviant from Normal, we transformed the outcome using the most appropriate transformation to make the outcome Normally distributed (or very close to Normal) and then repeated the linear regression. For some outcomes there was not a transformation that made the outcome near Normal. Where this was the case, we did not attempt to fit a model with a transformed outcome. Where transformation occurred, the models with the transformed and untransformed outcomes were compared using Akaike Information Criteria (AIC). In the majority of cases, the models with the untransformed outcome were the best using this criterion. For others, there was little difference between them so we have presented results from the untransformed models in Tables 2 and 3.

Table 1: Baseline summary statistics for the participant by randomised group

Variable	CBT and TAU		TAU	
Socio demographics	**Mean or n/N**	**(SD) or %**	**Mean or n/N**	**(SD) or %**
Age	78	(7)	79	(7)
Male	10/25	40	10/25	40
Non-white ethnicity	0/25	0	1/25	4
Years in education, median (IQR)	9	(9, 10)	10	(9, 11)
Use of Anxiolytic medication (Lorezapam, Diazepam, Buspirone)	2/25	8	6/25	24
Standardised scales				
Participant				
MMSE median (IQR)	23	(19, 24)	23	(16, 25)
MMSE mean (SD)	21	(5)	20	(6)
QOL AD median (IQR)	35	(30, 38)	34	(32, 38))
QOL AD mean (SD)	34	(5)	35	(6)
QCPR median (IQR)	61	(57, 63)	61	(56, 65)
QCPR mean (SD)	59	(5)	60	(6)
HADS total median (IQR)	12	(9, 18)	14	(9, 23)
HADS total mean (SD)	14	(7)	16	(9)
HADS Anxiety median (IQR)	7	(5, 12)	8	(6, 11)
HADS Anxiety mean (SD)	8	(4)	9	(5)
HADS Depression median (IQR)	5	(4, 6)	6	(3, 12)
HADS Depression mean (SD)	5	(3)	7	(4)
RAID median (IQR)	17	(14, 21)	22	(17, 24)
RAID mean (SD)	18	(6)	21	(6)
CSDD median (IQR)	13	(11, 17)	19	(13, 22)
CSDD mean (SD)	14	(5)	18	(7)
NPI total median (IQR)	22	(13, 31)	27	(22, 39)
NPI total mean (SD)	24	(17)	28	(12)
NPI total carer distress median (IQR)	10	(7, 16)	13	(9, 18)
NPI total carer distress mean (SD)	12	(7)	14	(6)
CDR questionable/mild dementia	21/25	84	21/25	84
CDR moderate dementia	4/25	16	4/25	16

Abbreviations: RAID Rating anxiety in dementia; MMSE Mini mental state examination; QOL AD Quality of life Alzheimer's Disease; QCPR Quality of Caregiver-Patient Relationship; HADS Hospital Anxiety and Depression Scale; CSDD Cornell Scale for Depression in Dementia; NPI Neuropsychiatric Inventory; CDR Clinical Dementia Rating

Table 2: Baseline summary statistics for the carer by randomised group

Variable	CBT and TAU		TAU	
	Mean or n/N	(SD) or %	Mean or n/N	(SD) or %
Socio demographics				
Age, median (IQR)	69	(62, 80)	66	(51, 74)
Male	11/25	44	9/25	36
Non-white ethnicity	0/25	0	0/25	0
Relationship to participant				
Spouse/ partner	18/25	72	11/25	44
Son/ daughter	7/25	28	9/25	36
Other	0/25	0	5/25	20
Time spent as a carer (months), median (IQR)	24	(18, 48)	24	(18, 36)
Hours a week spent caring, median (IQR)	61	(10, 168)	15	(6, 80)
QOL AD median (IQR)	33	(31, 35)	32	(27, 37)
QOL AD mean (SD)	32	(5)	32	(6)
QCPR total median (IQR)	57	(54, 61)	52	(48, 61)
QCPR total mean (SD)	57	(7)	54	(8)
HADS total median (IQR)	9	(4, 12)	9	(6, 13)
HADS total mean (SD)	10	(6)	9	(5)
HADS Anxiety median (IQR)	6	(2, 8)	5	(3, 9)
HADS Anxiety mean (SD)	6	(4)	6	(4)
HADS Depression median (IQR)	3	(1, 7)	4	(2, 4)
HADS Depression mean (SD)	4	(4)	4	(2)

Abbreviations: QOL AD Quality of life Alzheimer's Disease; QCPR Quality of Caregiver-Patient Relationship; HADS Hospital Anxiety and Depression Scale;

Table 3: Outcomes at 15 weeks, coefficients for CBT

Outcome	Unadjusted		Adjusted*	
Participant	**Coefficient**	**95% CI**	**Coefficient**	**95% CI**
RAID	-4.32	(-8.21, -0.43)	-3.10	(-6.55, 0.34)
MMSE	1.45	(-2.58, 5.49)	0.21	(-1.72, 2.15)
QOL AD	1.44	(-2.24, 5.12)	0.70	(-2.85, 4.26)
QCPR total	0.49	(-3.53, 4.50)	0.58	(-3.64, 4.80)
HADS total	-0.75	(-5.09, 3.59)	0.02	(-3.89, 3.94)
HADS Anxiety	0.47	(-1.89, 2.83)	0.90	(-1.10, 2.90)
HADS Depression	-1.22	(-3.96, 1.52)	-0.88	(-3.63, 1.88)
CSDD	-6.34	(-10.60, -2.08)	-5.37	(-9.50, -1.25)
NPI total	-7.90	(-18.43, 2.63)	-7.19	(-18.21, 3.82)
NPI total carer distress	-2.37	(-6.81, 2.06)	-2.61	(-7.18, 1.97)
Carer				
QOL AD	2.61	(-1.52, 6.74)	1.00	(-1.85, 3.85)
QCPR total	3.88	(-2.08, 9.85)	-0.32	(-4.88, 4.24)
HADS total	-0.60	(-4.27, 3.06)	0.07	(-2.62, 2.76)
HADS Anxiety	-0.80	(-3.34, 1.74)	-0.28	(-2.01, 1.44)
HADS Depression	0.20	(-1.50, 1.90)	0.38	(-0.92, 1.67)

Abbreviations: RAID Rating anxiety in dementia; MMSE Mini mental state examination; QOL AD Quality of life Alzheimer's Disease; QCPR Quality of Caregiver-Patient Relationship; HADS Hospital Anxiety and Depression Scale; CSDD Cornell Scale for Depression in Dementia; NPI Neuropsychiatric Inventory; CDR Clinical Dementia Rating

*Participant outcomes control for baseline MMSE and baseline RAID. Carer outcomes control for the outcome at baseline.

Table 4: Outcomes at 6 months, coefficients for CBT

Outcome	Unadjusted		Adjusted*	
Participant	**Coefficient**	**95% CI**	**Coefficient**	**95% CI**
RAID	-5.47	(-10.67, -0.27)	-4.59	(-9.34, 0.15)
MMSE	0.86	(-2.75, 4.48)	-0.06	(-1.94, 1.81)
QOL AD	-0.85	(-4.49, 2.79)	-0.90	(-4.52, 2.71)
QCPR total	-2.53	(-6.86, 1.81)	-2.81	(-7.15, 1.52)
HADS total	-0.05	(-5.60, 5.50)	0.22	(-4.88, 5.31)
HADS Anxiety	0.30	(-2.75, 3.35)	0.43	(-2.35, 3.21)
HADS Depression	-0.35	(-3.56, 2.86)	-0.22	(-3.33, 2.90)
CSDD	-5.46	(-9.62, -1.31)	-5.08	(-9.25, -0.92)
NPI total	-10.06	(-20.63, 0.51)	-9.42	(-20.10, 1.27)
NPI total carer distress	-3.25	(-8.41, 1.91)	-2.85	(-8.06, 2.36)
Carer				
QOL AD	2.41	(-1.88, 6.69)	1.08	(-1.81, 3.97)
QCPR total	5.24	(-0.39, 10.87)	1.27	(-2.38, 4.92)
HADS total	0.25	(-3.78, 4.27)	0.93	(-2.06, 3.91)
HADS Anxiety	0.06	(-2.68, 2.79)	0.70	(-1.60, 2.99)
HADS Depression	0.19	(-2.11, 2.49)	0.16	(-1.64, 1.96)

*Participant outcomes control for baseline MMSE and baseline RAID. Carer outcomes control for the outcome at baseline.

Abbreviations: RAID Rating anxiety in dementia; MMSE Mini mental state examination; QOL AD Quality of life Alzheimer's Disease; QCPR Quality of Caregiver-Patient Relationship; HADS Hospital Anxiety and Depression Scale; CSDD Cornell Scale for Depression in Dementia; NPI Neuropsychiatric Inventory

Table 5: Participant pre-baseline costs (£) by service group with mean imputations

	CBT (N=25)		TAU (N=25)		Difference (unadjusted)	
Service group	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**95% bias-corrected CI**
Accommodation	492.77	2349.54	-	-	492.77	(20.05, 1706.41)
Hospital services	614.32	742.16	558.10	961.47	56.22	(-435.97, 499.06)
Community services	744.66	1458.53	565.47	715.84	179.19	(-311.87, 997.75)
Equipment/ adaptations	26.13	62.33	29.59	92.07	-3.47	(-54.12, 35.33)
Day-services	88.79	217.52	44.52	135.72	44.28	(-52.80, 146.21)
Medication	296.98	193.85	231.70	162.26	65.28	(-31.04, 175.57)
Total (Health and social care perspective)	2263.65	3937.53	1429.38	1342.21	834.27	(-285.77, 3069.38)

Table 6: Participant costs (£) between baseline and first follow-up (15 weeks) by service group with mean imputations

	CBT (N=21)		TAU (N=18)		Difference (unadjusted)		Difference (adjusted*)	
Service group	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**95% bias-corrected CI**	**Mean**	**95% bias-corrected CI**
Accommodation	17.85	81.79	48.58	206.12	-30.74	(-140.22, 78.75)	-4.88	(-96.86, 61.03)
Hospital services	244.10	277.36	460.17	526.09	-216.07	(-510.82, 36.41)	-146.34	(-446.93, 55.91)
Community services	321.60	427.14	767.40	930.73	-445.80	(-978.57, -2.00)	-417.19	(-980.13, -95.35)
Equipment/ adaptations	20.94	76.73	32.30	90.14	-11.37	(-64.85, 36.68)	-11.84	(-78.66, 42.95)
Day-services	111.53	332.36	70.30	152.85	41.23	(-80.77, 250.47)	20.15	(-90.11, 223.48)
Medication	266.55	170.47	283.85	176.08	-17.3	(-128.48, 90.49)	-4.27	(-115.26, 106.71)
Total (Health and social care perspective)	982.56	823.55	1662.61	1170.58	-680.04	(-1401.91, -67.46)	-564.38	(-1252.08, -112.85)
CBT intervention cost	1002.01	222.65	-	-	1002.01	(892.01, 1086.42)	1010.96	(898.46, 1102.99)
Health and social care plus CBT cost	1984.58	841.02	1662.61	1170.58	321.97	(-345.94, 946.85)	769.80	(-121.99, 1697.38)

*Adjusted for baseline HSC costs, baseline MMSE and baseline RAID.

Table 7: Participant costs (£) between first follow-up (15 weeks) and second follow-up (6 months) by service group with mean imputations

	CBT (N=21)		TAU (N=17)		Difference (unadjusted)		Difference (adjusted*)	
Service group	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**95% bias-corrected CI**	**Mean**	**95% bias-corrected CI**
Accommodation	113.63	520.73	-	-	113.63	(76.98, 280.74)	19.08	(-94.02, 129.03)
Hospital services	448.84	650.05	296.68	345.75	152.16	(-152.81, 493.88)	79.05	(-175.83, 334.93)
Community services	1396.37	4067.95	623.30	832.37	773.07	(-401.88, 3117.64)	85.67	(-627.76, 1102.29)
Equipment/ adaptations	2.34	6.51	3.80	7.66	-1.47	(-5.74, 3.38)	-2.25	(-6.42, 2.03)
Day-services	84.99	144.45	61.29	84.25	23.70	(-44.42, 105.85)	16.37	(-55.33, 95.59)
Medication	297.56	179.77	273.65	160.45	23.91	(-92.28, 129.09)	58.20	(-36.01, 151.23)
Total (Health and social care perspective)	2343.73	5072.26	1258.72	971.47	1085.02	(-354.81, 4078.64)	256.12	(-599.05, 1506.23)

*Adjusted for baseline HSC costs, baseline MMSE and baseline RAID.