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RESEARCH PROTOCOL (Version 0.2)

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

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Background

The frequency of dementia will rise dramatically over the next twenty years due to increased longevity. In the UK, 700,000 people currently have dementia (>1% of the entire UK population) and this is projected to reach over a million by 2020 and double again in the subsequent 20 years (3;4). Dementia affects the person with the illness, their family and society through increasing dependence and challenging behaviour. In the UK, dementia care is currently estimated to cost £17 billion pounds per year, and this is projected to treble to £50 billion in the next 30 years as the number of older people increases (4;5); for comparison, the entire NHS budget is currently £96 billion a year. Families and individuals bear the biggest financial burden; two-thirds of people with dementia live at home, receiving most of their care from family carers, who save the public purse more than £6 billion per year. The recent Alzheimer's Society *Dementia UK* report found that current levels of services and support for people with dementia and families are inadequate (4). This impacts on the NHS, as well as patients and families, as carer psychological morbidity predicts care breakdown and therefore institutionalisation (6). There is evidence from the USA that providing specialist, individually tailored psychological support to people with dementia and their family carers can reduce rates of institutionalisation (7;8). Nationally, a reduction of this magnitude in care home placements would have huge benefits for society, because most older people want to continue living at home, and report higher quality of life when they do so, compared with those placed in care homes. There are also economic benefits; the National Audit Office recently emphasised the need to "spend to save" on dementia care. The government's 10 year plans to increase the detection of dementia (currently only 30% of cases are ever diagnosed) and improve the quality of care for people with dementia and their carers, are outlined in the National Dementia Strategy consultation document. It is projected that this huge increase in service provision will be offset by a decrease in institutionalisation rates of between 6 and 20% in ten years (5).

Evidence for a coping-based psychological therapy for carers

Our systematic review of the prevalence of mental ill-health in family carers of people with dementia has established that about 40% have psychological disorders while others have significant psychological symptoms (9;10). The coping strategies family carers use are more important than all other factors, including the cognitive and psychiatric morbidity of the person they are caring for and the hours of care they provide, in predicting their mental health. Carers who used more emotion-focussed coping strategies and fewer dysfunctional coping strategies were less anxious a year later in our recent longitudinal study (11). Such coping styles are also associated with reduced depression (12;13). These epidemiological findings accord with those from our systematic review of treatments for carer anxiety, that promoting emotion-focussed coping was one of the only interventions for which there was evidence of effect in reducing carer anxiety (14).

Coping-based therapies can also reduce carer's depression. The Coping with Caregiving programme (15;16) was developed in the USA as a group intervention, and systematic review evidence finds it has a stronger evidence base for efficacy than any other reported therapy in the field (17). It is a manual based, psychological intervention delivered in weekly group sessions. It involves promoting problem-solving and emotion-focussed strategies, and avoidance of dysfunctional coping strategies, using cognitive-behavioural methods. This programme was comprehensively evaluated in the REACH (Resources for Enhancing Alzheimer's Caregiver Health) project, which recruited carers from a range of clinical and community sources in the USA; depression scores were significantly decreased in treatment groups compared with controls in all the studies (16;18-20) and self-efficacy scores were increased (21). While the impact of this therapy programme on

rates of institutionalisation has not been tested, a recent systematic review finds that there is some evidence that carer support can reduce institutionalisation, and that therapies such as the Coping with Caregiving programme which include problem-solving strategies and offer carers a choice of support strategies which can be tailored to their individual needs are most effective (22).

Delivery of therapy

The NICE/SCIE dementia care clinical guidelines recommend that “Carers of people with dementia who experience psychological distress and negative psychological impact should be offered psychological therapy, including cognitive behavioural therapy, conducted by a specialist practitioner”. In reality, resources are not available. One of the main research recommendations made by these guidelines was that there was an urgent need for a study to answer the question “For carers of people with dementia, is a psychological intervention cost effective when compared with usual care?”. The National Dementia Strategy states there is a need “to develop practical materials for frontline staff” and to provide high quality support to carers of people with dementia. The Department of Health vision for world class commissioning is that services will be evidence-based and of the best quality (23). Although the efficacy trials discussed above have shown promising reductions in family carer morbidity, there are no manual based therapies currently available for dementia carers in the NHS, nor is there an evidence base to demonstrate whether such standardised psychological interventions can be realistically, effectively and economically delivered to family carers within NHS services. A therapy which is needed by many NHS consumers that can only be effectively implemented by clinical psychologists is unlikely to be economically viable. At the other end of the spectrum in terms of amount of professional training, Charlesworth et al (24) in the Befriending and Costs of Caring trial (an existing HTA programme) recently found that an unstructured, non-manual based befriending programme delivered by ex-carers was ineffective in reducing anxiety or depression. In 2008 the UK Department of Health unveiled plans for £170 million investment in the *Improving Access to Psychological Therapies programme* (25). This funding will be used to train an extra 3,600 psychological therapists, who will treat depression and anxiety in primary care, with training and supervision from clinical psychologists. This strategy is based on the premise that if, as anticipated, less highly trained therapists, under the supervision of clinical psychologists, can deliver manual based training that decreases morbidity, enabling people to return to work, this programme will be cost-effective and highly beneficial for society (26;27).

In our proposed study, we would use similar delivery infrastructure; we anticipate that a psychological therapy specifically tailored to the emotional, practical and information needs of carers could have significant population benefits, including greater carer and care recipient wellbeing and decreased statutory care costs. Our therapy will be delivered by Graduate Mental Health Workers (GMHW), trained and supervised by the co-applicant experts in psychology, carer involvement, nursing and psychiatry, who all work in the NHS. The therapy will be manual based and our system of training and regular supervision will aim to ensure a high degree of fidelity to the programme manual. Plans to restructure community mental health teams, outlined in *New Ways of Working*¹, include the development of GMHW posts within teams in future

The need for an effective individual manual based therapy

Through our clinical and personal involvement in caring for people with dementia, we are aware of the difficulties carers face in attending a group intervention, as it can be very difficult to make alternative care arrangements and to be available at a pre-specified time. Individual therapy also has the advantage that it can be tailored to the specific problems faced by the carer. There is evidence from systematic reviews that therapies individualised to the carer receiving them were most effective in delaying institutionalisation (29), and that individual behavioural therapies are more effective

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than group interventions in reducing carer morbidity (30). We have adapted the above programme, *Coping with Caregiving*, with the authors' agreement, for NHS use, as an individual therapy. As individual therapies are quicker to deliver, because in groups time is needed for all group members' problems to be discussed, this has decreased the number of weekly sessions required. During piloting of the therapy, we found that our therapy took eight sessions to deliver.

Summary

Family carers of people with dementia are a group at high risk of mental health problems. As they provide most of the care received by people with dementia in this country, and the number of people with dementia is projected to increase substantially, there is an urgent need within society to develop ways to decrease their distress. The UK government has recognised that family dementia carers need dedicated psychological therapies, and that this should be a key component of high quality dementia care, but in practice resources are not available. The only randomised controlled trials that have demonstrated efficacy of a manual based psychological therapy in this group were carried out in the USA and the therapy was conducted by clinical psychologists. Clinical psychologists are a highly trained and finite resource within the NHS. Programmes of stepped care, in which mental health workers deliver therapy supervised by clinical psychologists, have been devised to widen availability of psychological therapies. We plan to test the feasibility, efficacy and cost-effectiveness of an individual psychological manual based intervention for family carers, delivered by GMHW as part of NHS care. This would be the first study to test a manual based therapy for dementia carers in an Randomised Controlled Trial (RCT) in the UK, and the first study worldwide to test the effectiveness of GMHWs delivering therapy to this group.

Aims and objectives

Primary objective: To determine (1) the (short and long term) clinical and (2) the cost-effectiveness of eight sessions of manual based coping strategy therapy, delivered over 8-14 weeks by supervised graduate mental health workers to family carers, compared to usual service provision. We will determine these from the perspective of family carers of people with dementia living at home, and from a societal and National Health Service (NHS) perspective. Our primary short term clinical outcomes will be at measured at 4, and 8 months with longer term outcomes including 12 and 24 month measurements,

Secondary objectives:

- (1) To determine the effect of the intervention on time to institutionalisation of the person with dementia, strategy use (coping and abusive behaviour) and the quality of life of the carer and person with dementia.
- (2) To consider whether the effect of therapy depends on: coping style, baseline burden; type of relationship (spouse versus non-spouse); whether the carer is living with the patient; the severity of the patient's dementia and associated neuropsychiatric symptoms; and centre.

This study would enable the translation of our epidemiological and systematic review research findings about carers' anxiety and depression and its management into clinical practice. We want to determine whether our evidence based psychological treatment package would deliver significant clinical benefits if offered to all family members providing regular care to people with dementia referred to specialist care. If such benefits are demonstrated this package could be implemented throughout NHS dementia services as the initial part of a stepped care programme. There would also be scope for considering the adaptation of the programme for other chronic illnesses.

Methods

Study design

This is a pragmatic multi-centre randomised controlled trial.

Recruitment

Setting and infrastructure

As most people identified in primary care with possible dementia are now referred to a specialist service for diagnosis we intend to recruit through: two mental health trusts (North Essex Foundation Partnership Trust, Camden and Islington Foundation Trust and); and the Dementia Research Centre- National Hospital for Neurology and Neurosurgery (DRC-NHNN), a tertiary service whose referrals include a high rate of people with young onset dementia. Consultants from all these recruiting centres are co-applicants. We will also recruit from the North East London and Essex Admiral Nurse service, covering Barking, Dagenham, Redbridge, Havering and Waltham Forest, to include those who use this growing resource. This service is led by Juanita Hoe (nurse practitioner and co-applicant). Our sampling frame encompasses urban, suburban and rural areas and ethnic and social class diversity, ensuring results will be generalisable to the UK. Our recruitment will be assisted through adoption of the project by North Thames DeNDRoN. Neurology (CM) and psychiatry (GL) leads for North Thames DeNDRoN, and the national lead for neurology (MR) are co-applicants.

Recruitment plans

We will use the recruitment process streamlined during previous and current large studies in this population. The Admiral Nursing service, Camden and Islington Foundation Trust and Dementia Research Centre-NHNN all have anonymised databases of existing clients who have agreed to be approached for research and these will be searched. The DRC-NHNN is a national referral centre, so we will approach all London and Essex carers who meet criteria. When potential participants are identified on these databases their current suitability will be checked with clinicians currently seeing them.

Research Assistants who will all have contracts with the participating trusts, with the additional help of DeNDRoN clinical research officers (CROs), will identify potential participants from the mental health trusts through discussion with clinicians when attending weekly team community mental health or memory clinic meetings. They will have their suitability confirmed by a clinician and initially will be approached by the clinician and only if they agree to the research will notes be read. Appropriate patients will be notified of opportunities to join in, and will be free to choose whether they wish to do so, after a full explanation. We would expect, extrapolating from previous figures, that from the three mental health trusts we would approach at least 20 carers of people with young onset dementia.

Family carers who provide emotional or practical support at least weekly and identify themselves as the primary carer of someone with dementia living at home, will be sent a standard letter from the treating clinician together with an information sheet inviting them to participate. The content of this letter will be agreed with the clinician at the start of the project, then, as participants are identified, we will seek the clinician's agreement to send out the letter. The research assistants and manager will complete this for them. Clinicians may also invite people to participate and directly give them the information sheet. The standard letter will explain that a research assistant will call the carer in about a week to answer questions and, if the carer agrees, arrange an interview to obtain informed consent. The carer will also be given a contact telephone number for the clinician, and invited to ring them if they do not wish to be contacted by the researchers. Research assistants will have logistic support (mobile phone, availability of one of the coapplicants) to enable some of the interviews to take place in the evening, to be inclusive of all carers, including those who are in paid employment.

The assessment

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Interviews of carers will take place at baseline, 4, 8, 12 and 24 months. The interviews will take between forty minutes and one and a half hours. The longer time will be when the carer is unable to read (eyesight or literacy), or wishes to widen the discussion.

At baseline, carers will be asked about sociodemographic details for the carer and the person with dementia (including age, gender, ethnicity, relationship (e.g. spouse, child), level of education, last occupation and their living situation.

At baseline, 4, 8, 12 and 24 months, the carers will be asked about their psychotropic medication. They will also complete: Hospital Anxiety and Depression Scale (HADS) (31): this is validated for all ages and settings in people who are physically well or ill (32), and in one Asian and one African ethnic group. There are three validation studies in community samples (as opposed to solely, for example, people with cancer) (32). The largest of these included 6163 participants, more than five times the sum of the other validation studies, and include random samples of adults throughout the age group and groups of people with psychiatric and physical illnesses (32a). While the HADS is usually used to generate scores and caseness for the two subscales of clinically significant anxiety and depression separately, this study found that the total HADS score (HADS-T) had better sensitivity and positive predictive value than either of the individual scales in identifying cases when validated against International Classification of Diseases Criteria (ICD). The authors comment that their results are in line with previous smaller studies. Our pilot data shows that carers' psychological symptoms worsen over 6 months even in those initially reporting no symptoms and those who were "cases" did not improve over time. In addition, emotion-focussed coping strategy use prevented future carer psychological morbidity as well as treating it. We have therefore not specified a minimum HADS score for carer inclusion. Carers will also complete the Brief Coping Orientation to Problems Experienced scale (COPE) to measure coping strategy use (33); the Zarit Burden Interview (34) a 22-item self-report questionnaire, the most consistently used measure of carer burden and the Modified Conflict Tactics Scale (35).

We will use the Mini Mental State Examination (36), at baseline only, the most widely used measure of cognitive impairment, to give the level of cognitive impairment in carers aged >60 to ensure they themselves do not have dementia. This will be so that we exclude carers with dementia. If they score <24 the carer will be discussed with a supervising clinical applicant to see whether this is related to cognition or education. The Health Status Questionnaire (HSQ) (37) and the Euroqol EQ5D (38), both quality of life measures, will also be completed by the carers. The EQ5D is a generic measure to generate QALYs (quality of life adjusted health years); societal weights will be applied.

Regarding the patient, the carer will complete the Neuropsychiatric Inventory (NPI) (39): a validated instrument with 12 domains, included as neuropsychiatric symptoms are associated with carer psychological morbidity and the Quality of Life for patients with Alzheimer's Disease (QoL-AD(40)). The QoL-AD has proven reliability and validity when completed by the carer. The Client Service Receipt Inventory (CSRI; (41)) will be used to collect service use information about the carer and the patient (including institutionalisation, extra patient care during therapy), unpaid carer support and other aspects relevant to health economics. We will measure the use of institutional care by collecting information from carers at each interview and making sure we use the CSRI (Client Service Receipt Inventory) to collect accurate and sufficiently disaggregated data to capture the growing variety of placement types. We will define "institutional or 24-hr care" to mean residential, nursing and continuing care placements. We will use the CSRI to give us measures of number of days living in each of a number of different settings over the course of the research period.

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When we consider date of entry to 24 hour care settings, we will include any time people were in hospital awaiting placement to 24 hour care.

We will also use the CDR (Clinical Dementia Rating) as an informant instrument to grade the level of impairment of the individual with dementia(40a)

We will keep anonymised data on the gender and relationship (eg partner or non-partner) of those carers invited to participate who did not respond, to assess the generalisability of our findings. The study recruitment criteria are very inclusive to ensure generalisability within the UK.

Feasibility of recruitment

In our recent (2007-8) non-intervention study, we completed recruitment and interview of family carers of people with dementia living at home without inducement (CC, GL, SN, ZW, RB), ahead of schedule. We achieved a recruitment rate of 18 carers per centre per quarter, and recruited from North Essex Partnership, and Camden and Islington Foundation Trusts, recruiting only carers of newly referred patients with dementia. In the proposed study, we will also be approaching all carers who have been referred in the last year to these trusts, so will be recruiting from a larger pool and have also added more services (DRC). We think that more carers may be interested, as we are offering the possibility of an additional service. However, as the amount of time we are asking carers to dedicate to this study is greater, we have predicted a modest total recruitment rate of 9 carers per centre per quarter (over 6 quarters). As we are aware that recruitment is labour intensive, we have projected that each research assistant will be required to recruit and complete the baseline interview on 2 carers a week. This estimate is based on previous experience of employing Research Assistants of the same grade for similar work.

Allocation to trial groups

Randomisation to group allocation, and to therapist, will be undertaken by Institute of Psychiatry (CTU), by means of an online computer generated randomisation system. They will use individual randomisation and stratify by centre with random permuted blocks (so numbers are balanced even in the early stages of the trial but of random size blocks so it is difficult to determine the allocation sequence). Use of an automated randomisation system will ensure concealment of allocation.

Blinding

We cannot blind participants to treatment group, but outcome assessors will be blinded. Assessors will ask participants at the beginning of each rating session not to disclose their allocation group; we will ask the rater to guess the allocation group for each participant at the end of each assessment to detect whether unblinding occurs and to specify if they have been unblinded. Six FTE GMHWs will work as therapists and assessors, but they will not fulfill these roles at the same centre, to ensure they remain blinded to allocation. The therapists will work in two teams of three, housed in separate offices. When researchers leave they will be replaced (currently 10 therapists have been involved in the study). The trial manager will allocate each carer to a group, and allocate one of the two groups to complete baseline and follow-up assessments for each carer, and allocate the other group as therapist for those in the intervention arm. This will ensure that, in the intervention arm, the assessor is not the therapist, or working in the same team as the therapist. We have used self-report measures for our main outcome measures as another means of reducing the potential for bias.

Co-carers

Occasionally, two family members share caring responsibilities equally, so there are two primary carers. Where this has occurred in previous studies, we have found that

families select one person to take part. For one of the intervention sessions in which information about care and legal planning is imparted, the participating carer is invited to bring another family member along if they share caring responsibility, but the research outcome is measured only with the pre-agreed main participant.

Planned intervention

Therapy intervention

The Coping with Caregiving programme ^{2,3} was developed as a group intervention programme for USA carers, and systematic review evidence finds it has a stronger evidence base for efficacy than any other reported therapy in the field ⁴. It uses the stress appraisal and coping response model, and principles from cognitive behavioural therapy ⁵. With the author's permission, we have developed and piloted an individual therapy programme based closely on this original therapy, adapted for NHS use. The therapist has a manual and the carer is also given written information and guidance. The intervention is designed to be delivered in eight sessions over 8-14 weeks. The therapy will take place where the carers prefers, we anticipate this will usually be at their home. The therapy will be carried out with an interpreter if the carer does not speak English fluently.

The sessions cover 1: Introduction: learning about dementia, carer stress and understanding behaviours of the person cared for; 2-6: Discussion of problems that the carer finds difficult, incorporating behavioural management techniques; skills to take better care of themselves, including changing unhelpful thoughts, assertive communication, relaxation and planning pleasant activities; increasing communication; promoting acceptance; where to get emotional support and positive reframing. 7: Future needs of the patient, with psychoeducation about care and legal planning, specifically adapted to the UK 8: Maintaining the skills learned over time. Carers are given homework tasks to complete between sessions, including identifying triggers and reactions to challenging behaviours, and identifying and challenging negative thoughts.

Training and delivery

Graduate Mental Health Workers (GMHW) will be employed to deliver the intervention. We envisage recruiting psychology assistants, who have a degree in psychology but without clinical psychology training. Job descriptions will specify evidence of listening skills, empathy and clinical experience. This level of expertise will ensure breadth of skills (to impart information, knowledge of dementia, mental health & knowing when more support is needed). During recent recruitment, we advertised a research assistant post at the same level, received 86 applications despite advertising for less than a week, and identified seven out of eight shortlisted applicants at interview with this level of experience who would be appropriate to appoint to such a post. A short training programme will be delivered by the psychologist, medical, and nursing co-applicants. There will be a strong practical focus on how to deliver the therapy, empathic listening skills, effective use of supervision and when to ask for help. They will also have teaching sessions dedicated to working with interpreters and cultural sensitivity. As the manual will be delivered by English speaking researchers with an interpreter it will not be translated but the interpreters will be asked to translate the homework material as the sessions progress. Training will emphasise the need to operate from an inclusive values base and to respect diversity. Knowledge will be acquired through a combination of seminars, discussion groups, reflective learning and guided reading. Skills-based competencies will be learnt through clinical simulation in small groups. In devising our training programme, we will draw on the curriculum for psychological therapists devised by the Department of Health for their improving access to psychological therapies programme ⁶.

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All therapists will be trained to adhere to the manual. They will be required to demonstrate, by role-play, competence in delivering the intervention before recruitment commences; this will be assessed by our clinical psychologist (Dr Penny Rapaport). Dr Rapaport will meet with each of the teams (two teams of three therapists) on alternate weeks for 1.5 hours for group supervision. She will also have available an hour of dedicated time for individual consultation as needed by the therapists. These individual meetings will be initiated either by the therapists or by the research team as needed. Therapists will, with the carer's permission, record one therapy session per participant. They will use this in supervision, and they will submit a random sample of recordings for monitoring by two researchers not involved in the therapy, who will independently rate fidelity to the manual using a standard checklist.

This will score adherence to the manual text and leader instructions for each of the subsections of the session recorded. After 12 sessions have been recorded we will calculate the interrater reliability by using the kappa statistic. Inter-rater agreement can be interpreted in accordance with Landis and Koch's (1977) classification (0.41 – 0.60 = moderate; 0.61 – 0.80 = substantial; ≥ 0.81 = almost perfect agreement). If satisfactory we will then use only one rater.

Supervision will be in a group format to enable effective learning from the experiences of others and to facilitate a professional network for the workers of peer support. All participants will have been seen by clinicians before the trial and most will have been seen at home and risks will have been assessed as part of clinical work.

Safety

The trial manager will have an online diary detailing where the workers are so this can be accessed from home. All workers will carry mobile phones and will have telephone access to a named co-applicant involved in the training and supervision during working hours and in the evening if they are delivering therapy then. Workers will call another member of their team when they finish if not returning to the office. We will have addresses, phone numbers and next of kin details of all workers.

Treatment as Usual (TAU)

As several teaching trusts are involved we expect the TAU to be similar to good "TAU" throughout the UK. We will adjust for centre in analyses, as TAU may differ between them. Most existing services are based around the person with dementia. Treatment is medical, psychological and social. Thus it will consist of assessment, diagnosis and information; practical support; treatment of neuropsychiatric and cognitive symptoms and carer support. There will be no restrictions on treatment options for carers as this would be unethical, and we are proposing a pragmatic trial to assess the benefits of this treatment package in addition to usual care. Few carers were receiving psychology input (<1%) in our previous carer study, so we do not expect this to influence the outcome.

Planned inclusion/ exclusion criteria

Inclusion criteria

- Family carers who provide emotional or practical support at least weekly and identify themselves as the primary carer of someone with dementia not living in 24 hour care.
- We will only recruit carers of patients referred in the last year, as early mental health interventions work best, and this is the intended point of delivery within the NHS.
- We will use interpreters to ensure our recruitment strategy is inclusive.

Exclusion criteria

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- Carers who are unable to give informed consent to the trial, for example because they have dementia themselves or unable to participate because of dementia. (assessed using Mini Mental state examination)
- Carers who are currently taking part in a randomised clinical trial in their capacity as a family carer.
- Carers who live more than 1.5 hours from the researchers' base.

Outcome measures

Assessors will be blinded to randomisation group. Outcomes will be measured at 4, 8, 12 and 24 months.

Our primary outcome measures are:

1. Carer HADS-T score (31) (measured at 4 and 8 months for the short term analysis and including 12 and 24 months for long term analysis).
2. Cost-effectiveness over 24 months: Cost of care for each group will be measured using the Client Service Receipt Inventory (CSRI). The EQ5D is a generic measure to generate QALYs (quality of life adjusted health years); societal weights will be applied.

Our secondary outcome measures are:

1. Time to entry of the person with dementia to 24-hr care
2. Carer (HSQ) and care recipient (QoL-AD) quality of life
3. COPE
4. MCTS
5. HADS-A & HADS-D

We will also describe changes in depression and anxiety caseness on the HADS but as many people will not reach "caseness" prior to the trial we do not expect it to reach significance.

We envisage that while the majority of the participants will be of white European ethnicity there will also be significant numbers from Black and minority ethnic groups. No measure of depression in older people is validated across all the ethnic groups from whom we plan to recruit. Screening measures for mental illness have been found to be valid in UK black older populations and attempts to construct a culturally specific instrument have not improved on their psychometric properties. Current expert consensus is that the cultural sensitivity of researchers is the most important factor in cross-ethnic validity and that generic measures should be used (46). Our primary outcome measure, the Hospital Anxiety and Depression Scale (HADS) has been validated in one Asian and one African group but not all ethnic groups (47).

Very long term outcome

After 24 months we will ask carers to re-consent and will ask if we can follow them up every six months with a phone call while they are caring for the person with dementia at home to ask them if we can post/email them the HADS to fill in (details below) and tell us whether and when the person they care for has entered 24 hour care. This is to consider the long term effect of the therapy on institutionalization and carer mood.

Sample size and Power

This trial was originally powered for a primary outcome of HADS anxiety score. The required sample size for this outcome was calculated to be 90 in the TAU group and 168 in the intervention group. For the reasons given (see page 5) previously, it has been agreed that the primary outcome should now be changed to HADS-T. As

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recruitment is complete the sample size available for analysis is fixed with achieved numbers of 87 in the TAU group and 173 in the intervention group. The following power calculation justifies that this achieved sample size will be adequate to address the new objectives based on the HADS-T outcome.

This power calculation initially considers the short term primary analysis of HADS-T score using repeated measurements at 4 and 8 months with an adjustment (using analysis of covariance) for baseline score. With 87 carers in the control group and 173 in the intervention group we effectively have a sample size of 78 versus 111 for calculating power. This effective sample size has factored in adjustments for 10% dropout and a design effect of 1.4 for clustering in the intervention arm (the revised design effect has been calculated using a reduced average cluster size, now known to be 15 carers per therapist, but assuming an ICC of 0.03 as in the original calculation). Our cross-sectional pilot study data shows the mean HADS-T for family carers in a representative sample from secondary care was 12.2 with a standard deviation (SD) of 7.4. We would consider a decrease of 2.4 points in this mean to be a clinically significant improvement.

The calculations assume a HADS-T standard deviation of 7.4 (as from the pilot data), correlation between baseline and follow-up scores of 0.5 and a correlation between repeated follow-up measurements of 0.7 (both chosen as conservative estimates). Based on these values with the current sample size we will have 80% power to detect a difference of 2.4 points on the HADS-T scale, and 90% power to detect a 2.7 point difference, both consistent with differences considered to be clinically important. Longer term analysis incorporating 12 and 24 month measurements are also planned. Although in this case further attrition may be expected, the extra repeated measurements should ensure that power remains adequate to detect important treatment effects. For example assuming an average of 3 follow up measurements per carer and assuming 20% dropout at 24 months, the sample size remains adequate to detect a difference in means of 2.4 with 80% power (other assumptions remain as before).

Statistical analysis

We have a statistician as a co-applicant in our research team who has retired. Statistical collaboration is now provided by PRIMENT statistician Dr Julie Barber supported by Philip Prah.

Our health economic analysis will be led by our health economist PI Prof Knapp who will supervise Dr Romeo's work on the project. Our analytic strategy is based around the two primary main study objectives.

Carer health component: The short term analysis using 4 and 8 month outcome data will be undertaken soon after the 8 month data is finalised. Long term outcome analysis incorporating all repeated measurements up to 24 months will be analysed at a later date when these data are finalised. Similar approaches to analysis will be used in both cases and will be detailed in statistical analysis plans written prior to commencing each analysis.

In brief we will test our main hypotheses that HADS-T score will be significantly lower in the intervention compared with usual care group using a multilevel mixed model to take account of the partially clustered design, repeated measurements and to adjust for baseline covariates (41a). We will also use similar models to address the secondary outcomes. Sensitivity analyses will be used to consider the impact on conclusions of missing data, non compliance, baseline imbalances and other

assumptions. We will investigate whether there is a differential effect of treatment for predefined subgroups by extending models to include treatment interactions.

Health economic component: Cost comparisons will be made between the groups, adjusted for baseline differences, and any non-normality of data (transformation or non-parametric test). Cost-effectiveness analyses combine costs generated from the CSRI with (a) HADS-T score and with secondary outcomes at the same time points as outcome analyses. (b) QALY measures generated from the EQ-5D, allowing comparison with other health care interventions. Cost-effectiveness acceptability curves will be plotted using bootstrap analyses to locate the findings of the economic evaluation in their wider decision-making context. Sensitivity analyses will examine the consequences of key assumptions. Study perspectives will be (1) health and social care system; (2) societal.

Ethical arrangements

We will apply for multi-centre research ethics approval (MREC) and obtain local research governance approval for the study, as appropriate. The study personnel, co-investigators as the management group and independent Trial Steering Committee (TSC) will ensure that the study is conducted within appropriate NHS and professional ethical guidelines. All the information will be kept strictly confidential and held in accordance with the principles of the Data Protection Act (1998). Each participant will be assigned a research number and all data will be stored without subject name or address. Data will be held on a secure database on a password-protected computer at University College London. Access to data will be restricted to the research team, and research assistants' access will be limited as far as possible. In order to enable follow-up contacts, it will be necessary to identify the patients, but access to contact details (e.g. name and address) will be restricted to key members of the research team. Audio-tapes of interviews for training and fidelity monitoring (using a digital voice recorder) will be destroyed once the main study is complete. The people with dementia will not be interviewed nor will their medical notes be accessed.

Carers will be sent a standard letter from, or approached in person by the treating clinician, and provided with an information sheet with full study details including possible benefits and risks. They will then be contacted, unless they have declined, and offered the opportunity to ask questions and make a date for the interview. Their written informed consent will be obtained prior to commencing the baseline assessment for the trial and at least 24 hours after they have received the information sheet. When asking for consent, the researcher will explain that, as this is a clinical trial, they cannot choose which group they are allocated to, and that whilst we hope that the therapy will be beneficial this cannot be guaranteed. Patients and carers will continue to have usual care in both groups. Carers who do not have capacity to consent to take part in the trial will not be included.

The anticipated benefits for trial participants are significant improvement in carer mental health and quality of life. We do not anticipate any risks for trial participants. Although talking about the problems of coping with caring could be upsetting, in our experience carers do not find it distressing and usually find it helpful. Although the graduate mental health workers may not have worked previously in a clinical setting, evidence of listening skills will be a criterion for recruitment and they will be trained and well supervised. The potential benefits for society are the development of a cost-effective therapy that will reduce distress of carers of people with dementia that is widely deliverable within the NHS. As well as reducing distress at a population level, there is evidence that carer mental ill health predicts institutionalisation (45) and elder abuse (46), and that carer support can decrease care home placements (47). Thus there will be benefits to people with dementia and economic benefits.

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If information disclosed by a carer leads us to believe that a patient or carer is at significant risk, the researcher will discuss this with their supervisor. If appropriate they will approach the participant and seek their consent for disclosure to the referring clinician. The information sheet will specify that “we respect confidentiality but cannot keep it a secret if anyone is being seriously harmed or is at high risk of serious harm”. If there is reason to believe that harm is occurring or there is a high risk it is likely to occur, we will report this to the referring clinician without consent if this is refused. In our recent study of 220 carers of people with dementia, in which we specifically asked about abusive behaviour, we judged it necessary to ask the carers permission to disclose information to the treating clinician in five cases, and permission was granted in four cases. In the fifth case, after discussion of the situation with the project supervisors, it was not deemed necessary or appropriate to disclose information against the carer’s wishes. As a psychological intervention, this trial is exempt from registration under the Medicines for Human Use (Clinical Trials) Regulations 2004. We will however ensure that the trial is registered with the appropriate body (www.controlledtrials.com) and assigned an ISRCTN number in accordance with good practice. In line with UCL data protection policy, we will retain relevant trial documentation for 10 years.

Research governance

University College London will act as nominated sponsor for the project. We will form a Data Monitoring Committee and Trial Steering Committee.

Data Monitoring Committee (DMC)

We will set up a Data Monitoring Committee (DMC) that will have access to the comparative data. The DMC will consider whether any interim analysis is necessary, review data from any analysis and consider requests for data release. The members will monitor these data and make recommendations to the Trial Steering Committee (TSC) on whether there are any ethical or safety reasons why the trial should not continue with the safety, rights and well-being of the Trial Participants being paramount. Membership of the DMC will be completely independent, and comprise three members (a consumer, a clinician with experience in the relevant area and a trial statistician). We propose and have approached, as chair, Professor Cornelius Katona, a clinician experienced in dementia research; a carer, U Hlay Hty (a carer representative with experience of working with mental health researchers) and a statistician (from PRIMENT). They will meet before the trial starts, for an interim analysis and annually or as needed after that. The chief investigator will arrange the meetings with the chair of the DMC. The project team will provide the DMC with a comprehensive report, the content to be agreed in advance by the Chair of the DMC and they will feed this into the TSC.

Trial Steering Committee (TSC)

The TSC will have an independent Chair and the following proposed membership.

Name	Affiliation	Role
Dr Joanna Murray	Institute of Psychiatry	Independent chair/ psychologist
Dr Kate Maxmin	North East London Foundation Trust	Independent psychiatrist/member
Dr TBS Baamurali	East London Foundation Trust	Independent member/psychiatrist
Professor Gill Livingston	University College London	Lead investigator/ psychiatrist
Lynne Ramsey		Independent carer representative

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HTA representative	HTA	
Membership as appropriate: trial statistician, trial coordinator	University College London	Trial coordinator and co-applicants

The TSC will meet annually and more often if indicated. The role of the TSC is to provide overall supervision for the trial, concentrate on the progress of the trial and adherence to the protocol and provide advice through its independent Chairman. The ultimate decision for the continuation of the trial lies with the TSC. The TSC will report to the sponsors (University of College London) and the HTA.

4. Project timetable and milestones

We will start pre-trial work by 15-4-09. This will include obtaining ethics and local trust research governance approvals, finalising our training programme, arranging adoption of study by DeNDRoN, and advertising for and recruiting research staff. We will start the trial on 1-8-09.

Time Milestones

Time	Milestones		
	Management	Recruitment and therapy delivered (n)	Follow-up (n)
First 3 months (1-9-09 – 1-11-09)	trial manager start one month earlier Orientate and train staff Set up database First meeting of TSC		
3 months – 6 months (1--12 – 31-3-09)	Begin fortnightly therapist supervision meetings Begin therapy fidelity monitoring process	Begin recruitment Control arm: 16 Intervention arm: 26 Therapy sessions:208	
6– 12 months (1-4-09 – 31-9-10)		Recruitment Control arm: 30 Intervention arm: 54 Therapy sessions:432	4 months: 84 8 months: 42
Year 2 (1-10-10 – 30-09-11)	Continue fortnightly therapist supervision meetings and therapy fidelity monitoring process	Finish recruitment by beginning of 4 th quarter Control arm: 44 Intervention arm: 88 Therapy sessions:704	4 months: 142 8 months: 150 1 year: 126
Year 3 (1-10-11 – 31-9-12)	Analyse short term outcomes. Discuss with stakeholders dissemination policy. Complete data entry, lock data and analyse; write up project, publish in high impact international journal; implement dissemination policy (if successful).		4 months: 32 8 months: 66 1 year: 132 2 years: 126
Year 4	Complete data entry, lock		2 years: 132

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(1-10-12 – 31-9-13)	data and analyse; write up project, publish in high impact international journal; implement dissemination policy (if successful); submit final report to HTA		
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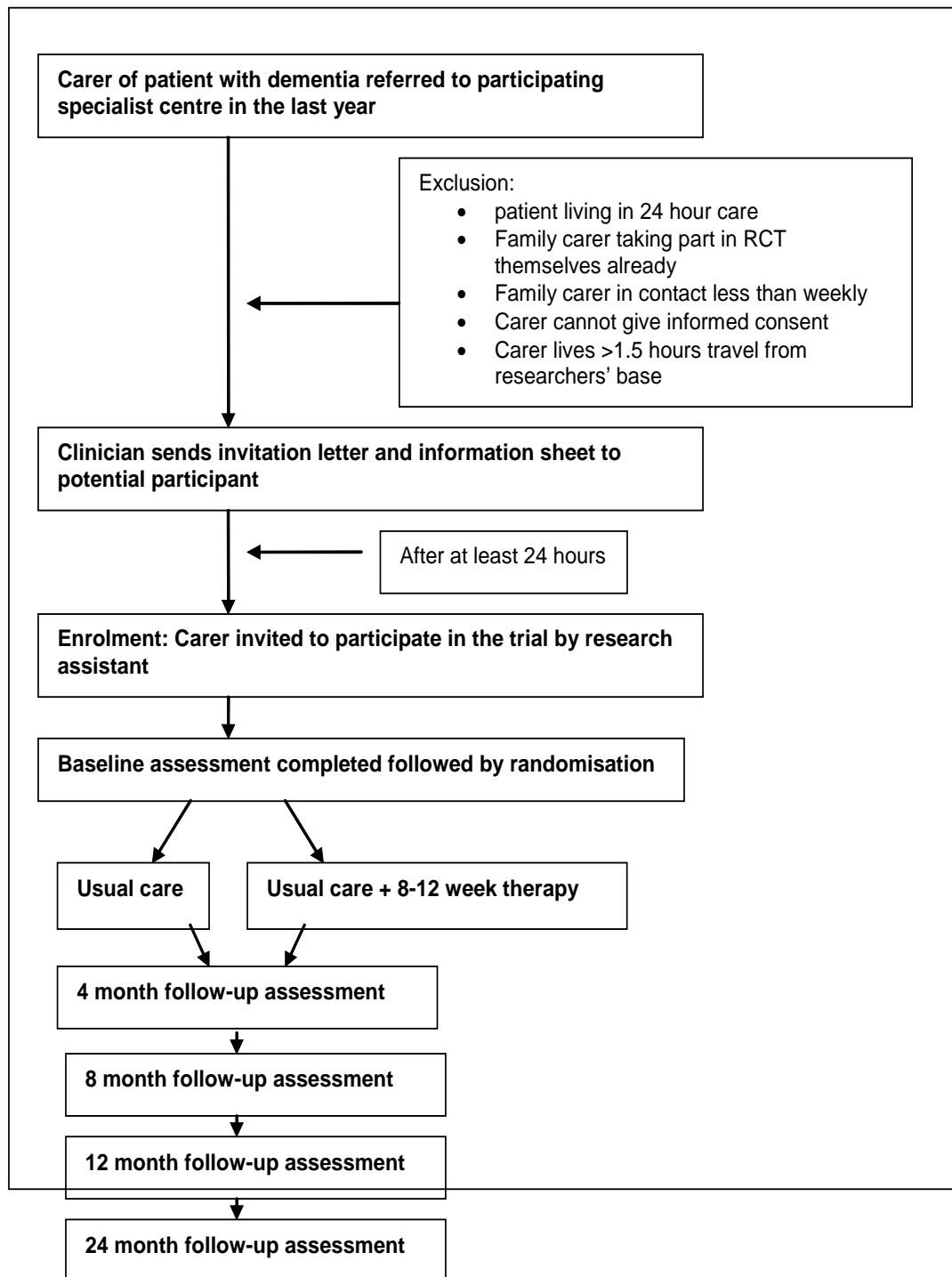
Dissemination

We will provide a summary sheet of the findings or let participants know where they can access the results. We will also discuss with stakeholders (academics clinicians, carers representatives) the dissemination policy depending on results

Service users

SN (co-applicant) is an ex-carer whose expertise within the group is the carer perspective. She has worked with our groups on previous large studies and has been involved in the development and design of this study proposal. *For Dementia*, a voluntary organisation dedicated to training and development of dementia services including Admiral Nurses, is supportive of this application. We have agreement from an independent user representative to join our DMC and will invite an independent user representative to join our TSC.

CONSORT Flow Diagram



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