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Individual Cognitive Stimulation Therapy for dementia (iCST) Trial

Sponsor: University College London
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Study Coordinating Centre: London

Current Document: iCST Research Protocol Version 9

iCST Trial 08/116/06

Detailed Project description

1. Project title: Individual Cognitive Stimulation Therapy for dementia (iCST Trial) 08/116/06

2. Planned investigation

Research objectives

1) To investigate whether individual home-based CST benefits cognition and quality of life in people with dementia over six months relative to a control (treatment as usual group).
2) To assess the cost effectiveness of individual CST relative to treatment as usual.
3) To produce and disseminate a standardised training package and manual for individual CST.

Existing research

Dementia is a national priority, and in the UK over 700,000 older people have dementia, with an enormous social impact on health and social care services and on family carers. The cost of dementia to the UK is over £17 billion a year and family carers of people with dementia save the UK over £6 billion a year (Knapp et al., 2007). Dementia leads to progressive deterioration in cognitive functioning, activities of daily living, and social exclusion for patients, as they are often socially isolated and lacking in mental stimulation. Improving cognitive function can have a major impact on the costs of care; Jonsson et al (1999) showed that even an average 1-point difference on the MMSE was associated with a substantial reduction in the costs of caring for patients with dementia. Drug treatments for dementia such as cholinesterase inhibitors, are costly, require specialist monitoring, have a limited impact on the illness and are not suitable for all patients. Psychological therapies for dementia such as Reality Orientation (RO) have been in widespread use for several decades. However, their use has been largely unstandardised, and studies of psychological treatments have been either small, of poor methodological quality, or both (Orrell and Woods, 1996). In the UK there is growing recognition that psychological therapies for older people should be more widely available, and the National Service Framework for Older People states 'treatment for dementia always involves using non-pharmacological management strategies such as mental stimulation'. Cognitive Stimulation Therapy (CST), delivered through groups, is an evidence-based approach for people with dementia. The CST group programme was developed from a Cochrane systematic review of psychological interventions for people with dementia (Spector et al., 2000) and consists of 14, 45-minute sessions twice weekly for seven weeks for groups of five to eight people with dementia. 201 people were recruited for this multi-centre RCT from 23 centres (Spector et al., 2003) and the results showed improvements in quality of life and cognition, the economic analysis showed CST was cost-effective (Knapp et al., 2006), and in terms of Numbers Needed to Treat the results for cognition compared favourably with trials of cholinesterase inhibitors for Alzheimer's disease. CST was the only non-pharmacological therapy recommended for treating cognitive symptoms of dementia by the NICE guidelines (2006) which advised that cognitive stimulation should be available to people with dementia, regardless of medication received. With the publication of the CST manual in the UK and USA, the use of group CST is growing rapidly and a recent national report on dementia services found that group CST was used in around 30% of CMHTs for older people in England (NAO, 2007). Many services across the UK and internationally use versions of RO/CST or related activities in regular groups with people with dementia (see cst.dementia.com). An RCT of maintenance CST (Orrell et al., 2005) found a significant improvement in cognitive function for those receiving maintenance CST, compared to CST alone or no treatment and concluded that the cognitive benefits of CST could be maintained by weekly sessions for at least 6 months. Metitieri et al. (2001) and Olazaran et al. (2004) also both found that CST/RO groups had

long term cognitive benefits for people with dementia. Our recent Cochrane review has confirmed the effectiveness of cognitive stimulation approaches (Woods et al., 2009).

The need for an individualised version of CST

Around 70% of people with dementia living at home have a family carer (usually a spouse), however, many may be unsuitable (e.g. hearing/vision problems) or unwilling to participate in groups, unable to get to groups, or have no access to groups locally. In 2009 the National Dementia Strategy has also identified access to early interventions and improved home care as a priority. A programme of individual home-based CST of demonstrated effectiveness would enable centres across the UK to deliver CST locally and could enable people with dementia and their carers to feel more empowered (Moniz-Cook, 2006; Moniz-Cook et al., 2006). Individualised CST may help to delay institutionalisation, reduce associated costs of care, and provide another option for services to offer CST to people with dementia, when access to group CST is not possible due to service constraints, transport difficulties, or practical difficulties and/or reluctance regarding group participation. Family carer led individual cognitive stimulation programmes can be effective in improving cognition (Quayhagen & Quayhagen, 2001; Onder et al., 2005). In a pilot study, Moniz-Cook et al. (1998) showed that a home-based programme of individual cognitive stimulation (involving the carer) had long term benefits at 18 months follow up for; cognitive function in the person with dementia, carer mental health/wellbeing and reduced care home admissions. Quayhagen and Quayhagen (2001) found that a home based cognitive stimulation/training intervention for spousal caregivers and people with dementia improved problem solving and memory and concluded that spousal caregivers could be active participants in cognitive stimulation programmes for dementia. In a related paper, Quayhagen et al. (2000) showed that participating caregivers also had reductions in depressive symptoms. In Italy, in a 25 week study of individual RO/CST in people with Alzheimer's taking cholinesterase inhibitors, Onder et al. (2005) found that the experimental group (CST) improved relative to the control group on both the MMSE (difference 1.3 points) and the ADAS-Cog (difference 2.9 points). Onder trained family carers to deliver a standardised programme of RO/CST in the persons' own home for 30 minutes, three times per week over 25 weeks. Carers were provided with a manual and specific schedules for each session and given guidance on how to deliver the sessions. The maintenance CST programme has now been developed as part of the SHIELD study (Orrell et al., 2007) using an in depth consensus process, reference to existing manuals (e.g. Onder, Olazaran), and the results of our recent Cochrane review (Woods et al., 2009) and the RCT on maintenance CST commenced in January 2009. This means we now have a detailed and field tested CST manual comprising 38 (14 plus 24) sessions which will be adapted to form the individual cognitive stimulation programme. We propose to evaluate a home based (individual) version of CST delivered by family carers using the technology/methods from group CST and Onder's individual CST programme. If as expected individual CST leads to improvements in quality of life and cognition, this may lead to improved wellbeing for people with dementia, and economic and social benefits such as reduced costs of care and delayed institutionalisation. Individual CST could be used long-term and could rapidly become widely used as a manualised, clinically and cost-effective, standardised, and feasible intervention.

The UK Department of Health has identified improving access to psychological therapies as a priority. In recruiting for our study on reminiscence in dementia we have found that only around 20% of people with dementia and their family carers who were approached agreed to participate in the group reminiscence programme. Therefore, unless individual approaches can be adopted most people with dementia may have no access to psychological interventions. To assess the acceptability of an individualised CST programme in the UK we surveyed; 27 care staff attending CST training sessions, carers from the charity 'For Dementia', and spoke to 20 carers and people with dementia. They all thought it was very important to provide an individual form of CST; it would be feasible to carry out and acceptable, and also very

beneficial both for carers and people with dementia. They noted that not all people with dementia like group work and also transport problems may prevent people from attending. There was a consensus from people with dementia and family carers that individualised CST should be a high priority because it was likely to be very useful. Comments included 'sounds terrific', 'could bring the carer and person with dementia closer together', 'good for people who won't go out', and 'definitely needed as a useful alternative to medication'. People felt the sessions should not be too long and should be flexible to match people's abilities. Taken together the evidence suggests that a large scale trial of individual CST for dementia in the UK is feasible, likely to be effective and should be a high priority for research. Without this study it is likely that many people with dementia will have no access to any form of psychological therapy and more specifically they will be denied access to an intervention with a range of likely benefits. The potential benefits of individual CST include improved cognition and quality of life for the person with dementia leading to societal benefits such as reduced costs of care, reduced institutionalisation and improved carer quality of life and mental health. Thus, the individual CST programme has the potential to be widely used across the UK and internationally, and become the gold standard for individual cognitive stimulation based interventions in dementia.

Research methods

Study design

Multicentre, pragmatic, single blind, randomised 2 treatment arm (individual CST vs treatment as usual) controlled clinical trial over 26 weeks.

Sample

To aid generalisability participants will be from a range of community settings in the four main study sites including London/Essex, Manchester, Hull, and Bangor, and the four additional sites, Dorset, Devon, Lincolnshire and Norfolk and Suffolk. People with dementia living in the community and their carers will be recruited from a variety of settings including CMHTs, memory clinics, outpatient clinics, day centres and via existing networks including the voluntary sector e.g. Age Concern in Havering, the Alzheimer's Society in Redbridge and the Admiral Nursing services. Essential baseline information will be recorded at registration and checked for eligibility following which patients will be stratified by whether or not they are taking anticholinesterase inhibitors (no/yes), and individually randomised using an adaptive scheme. People currently on cholinesterase inhibitors would continue taking them.

Recruitment

Many participants will be recruited through contacts of the SHIELD dementia research programme which includes a project on group CST (maintenance sessions) but also through contacts identified from the REMCARE trial (also based in Manchester, Bangor and Hull). During the recruitment for REMCARE we found that on average 5 patient carer dyads needed to be approached in order to obtain 1 pair who could be recruited to the trial of reminiscence in dementia. Other REMCARE centres such as Hull and Bangor have had similar experiences and it is likely that people may well be more willing to take part in this study because of the convenience of it being based at home. The researchers will make close links with the local memory clinic and community mental health teams through attendance and regular contact. Access to patients and carers will be further facilitated by the NHS Constitution which gives patients the right to be informed about clinical research which they may wish to be involved in. For example, NELFT covers 4 boroughs in North East London with a catchment population including around 123,000 older people of who approximately 7653 have dementia. It has 3 well established memory clinics and is a member of the North Thames Dendron Hub and the North Thames Mental Health Research Network. In Hull and the East Riding of Yorkshire all patients and carers referred with dementia (and their GPs who currently have additional DENDRON support to assist with recruitment to dementia trials) are

automatically provided with 'opt in information' on current NHS Portfolio studies in dementia care, via a centralised clinical academic unit (The Hull Memory Clinical Resource Centre).

Allocation to trial groups

The North Wales Clinical Trials Unit (NWORTH) will provide trial management, data management, quality assurance and statistical assistance. Registration of patients and remote randomisation to treatment will be by an adaptive web based randomisation service managed by the North Wales Organisation for Randomised Trials in Health (NWORTH), which is an accredited trials unit with a special interest in pragmatic trials of interventions in dementia care, with core funding from the Welsh Assembly Government. Essential baseline information will be recorded at registration and checked for eligibility. Patients who have satisfied the entry criteria including informed consent/assent will be eligible. To assess generalisability a log will be maintained of patients who satisfy the entry criteria for the trial but are not randomised; this will consist of basic demographic and clinical details as well as the reasons for not consenting to randomisation.

Protection against bias

Trials of psychosocial interventions cannot be blind to therapists or participants because they are aware of which, if any, treatment they are delivering or receiving. In contrast, researchers who assess participants after randomisation should not know to which arm they belong. The data will be collected by one team of researchers whilst the training and carer support for iCST will be run by a second team of researchers. The researchers carrying out the assessments will be blind to the group that the subjects are in. The researchers providing the training and supervision, and the carers will be blind to the results of the assessments and will not have access to intervention/control lists etc. However, our experience in similar projects is that participants may occasionally and inadvertently inform researchers of the treatment they are receiving. We aim to reduce this effect by explicit reminders to participants before the assessment visit and by the use of self-report measures wherever feasible. We shall also ask all assessors to record their impression of the trial group to which each participant belongs, and their confidence in that prediction. This will enable us to conduct a retrospective estimation of the integrity of blinding, to test whether inadvertent loss of blinding leads to bias, and to adjust for any bias detected.

Adherence to treatment protocol

In order to investigate treatment process variables, and to ensure that psychosocial interventions can be replicated, it is necessary to have precise descriptions of treatment components, and to ensure that the treatment delivered was indeed the treatment intended. This has been referred to as 'treatment integrity', a concept that has been developed and expanded by Lichstein, Riedel & Grieve (1994) and applied to caregiver intervention research in the 5-year Resources for Enhancing Alzheimer's Caregivers Health (REACH) cooperative programme (Burgio et al., 2001). In the current trial, a treatment protocol, will be drafted in order to describe in detail the different treatment components of iCST, specifying and describing the treatment in detail. Lichstein et al.'s Treatment Implementation (TI) model outlines 3 treatment processes, namely delivery, receipt and enactment. Treatment delivery focuses on the interventionist's ability to present the intervention as it was intended, including ensuring the absence of aspects of other treatments. Treatment receipt focuses on the degree to which the participant has received the intended treatment and treatment enactment focuses on the extent to which the participant has made the expected changes in behaviours, for example using the skills or knowledge taught in the intervention. Two types of treatment implementation strategies are recommended: induction methods that enhance the probability that proper TI occurs, such as written manuals, and assessment methods that measure occurrence of the intended TI strategies. A diary will be kept by the carers to record their experiences, activities and impressions and also to note the views of the person with dementia. The diary would be

reviewed fortnightly with a member of the training team to improve compliance with the protocol and adherence to the intervention approach.

Planned intervention

1) The Cochrane Review on CST for dementia and the revised manual for Maintenance CST were completed in early 2009 (NIHR programme grant). The individual CST programme will be based on a modified CST manual, the updated CST review and Onder's programme, and a focus group consultation with people with dementia and their carers via Age Concern, the Alzheimer's Society and For Dementia, using the MRC guidance for the development and evaluation of complex interventions (MRC, 2008). Cognitive Stimulation Therapy (CST) as developed by this research group (Spector et al., 2003) is an effective 14 session group programme for people with dementia recommended by the NICE dementia guidelines (NICE, 2006). Maintenance CST (24 weeks) is an extended version of group CST. Individual CST would be delivered by a carer in regular contact with the person with dementia, either a family carer, a close friend, or a volunteer befriender for 30 minutes, 3 times a week over 25 weeks. The adaptation of the 38 (14 plus 24) CST sessions will take into account the feedback from our consultation with users and carers which suggested the sessions should be shorter than the CST groups and so follow the model of Onder's study which used 30 minute sessions. Each CST session will be adapted and split into two sessions with the exception of the initial session leaving 75 individual CST sessions. Each session will consist of structured cognitive stimulation. Individual CST will consist of themed activities (such as categorizing objects and word association) tailored to the ability, interests and needs of the individual. The approach focuses on implicit learning rather than explicit teaching, providing cues to aid retrieval, multi-sensory learning and using reminiscence as an aid to the here and now. All sessions will be described in the manual and an accompanying DVD with other material for each session such as music and visual cues (e.g. famous faces). The development phase of iCST comprises of three key Development Work Packages:

2) **iCST Work Package 1: User Perspective.**

The first draft of the manual ***(iCST Manual Draft 1)*** will be developed by the research team in consultation with people with dementia and their carers using focus groups and individual interviews to ensure that the manual is clear, easy to use and tailored to ensure it is appropriately focused on their abilities.

3) **iCST Work Package 2: Field Testing of iCST.**

The iCST Manual Draft 1 will be used in the feasibility study using 20 people with dementia and their carers who will be trained and then use the manual in practice. In order to reduce the development cycle we will divide the manual into 6 sections and ask carers and people with dementia to conduct 15 sessions each within a 2 month period and get continuous feedback of the sessions in practice. A researcher will attend for a maximum of 20 sessions over the time period in order to observe them being carried out in practice and identify further issues for the training. After accommodating the feedback of the field testing of the treatment, we will complete ***iCST Manual Draft 2***.

4) **iCST Work Package 3: Consensus Conference**.

After wider consultation with other experts in the field and our user and carer networks we will produce the third and final draft of the manual to be used in the full trial ***(iCST Manual Draft 3).*** This evaluation will be based on the Delphi process of consensus methodology, in line with guidelines for consensus methods for medical and health services research (Jones & Hunter, 1995).

5) In order to ensure consistency of iCST training of carers, the training model that will be used will be incorporated and described in detail, in the ***iCST Training Carers Package***. Carers will receive home based individual standardised training to deliver individual CST. The carers will be trained using a standardised manual ***(iCST Training Carers Package)***, a DVD ***(iCST DVD),*** and a standardised protocol ***(iCST Treatment Protocol).*** If homes do not have DVD players or computers to play DVDs on we will

lend DVD players to these homes for the duration of the trial. Experience in clinical practice has shown that carers sometimes 'correct' people with dementia when engaged in activities together for example looking at family photos and this can lead to a negative critical interaction. To avoid this we will ensure that the carer training involves principles of good practice in CST as set out in the CST manual (Spector et al., 2001; Spector et al., 2006). In the training sessions this will involve role play using example sessions, and the DVD showing examples of 'good' and 'bad' practice for discussion. Carers would receive a set up visit at home before the iCST programme starts which will include an appraisal of the interests of the person with dementia and their carer and the resources available at home. Carers would also receive up to ten hours support over six months including telephone support (initially weekly) and 3 visits. Simple measures of adherence will include a carer diary of monitoring of iCST sessions (reviewed by the researcher). The diary would also assess levels of engagement and enjoyment in sessions. This will enable the programme to be reproducible and widely disseminated. At the end of the trial we will liaise with an appropriate publisher to produce the manual and DVD widely. Over the course of the trial 20 in depth qualitative interviews will be conducted with the person with dementia and their carer to investigate the impact on person with dementia's experience both during the sessions and any generalised effects into everyday life, the carer role and carer relationship. A recent qualitative study of experiences of CST noted changes experienced in everyday life such as finding talking easier, improvement in memory and improvement in concentration and alertness (Spector et al., 2011).

Treatment as usual

The treatment as usual control group (TAU) will not receive any additional intervention. The control group (TAU) would be needed for a comparison with the natural progression of people with dementia. The services and interventions available to people with dementia and family carers randomised to receive usual treatment will naturally vary between and within centres and may change over time but in terms of treatment we would expect most people with mild to moderate Alzheimer's will either be on, or have been considered, for cholinesterase inhibitor medication. The CSRI will enable us to accurately record use of drugs and services across the two groups and any changes that occur. In general, the services offered to this group will also be available to those in the active treatment group, so that we will be examining the additional effects of individual CST. Many people with dementia will have access to local lunch clubs, dementia day centres (provided by organisations such as the voluntary sector), or treatment in day hospitals but the local availability of these facilities varies from area to area. However, the iCST trial will enable people who are unwilling, unable or lack access to such services to have home based therapy. Changes and developments in the availability of medications for Alzheimer's and other dementias will affect both groups equally, and will be recorded as part of the costing information collected. It is possible that participants in the usual treatment group may be involved in some form of cognitive stimulation during the 6 months of the study period. CST is a popular approach in day-care centres and CST materials are widely available but it is very unlikely that any comparable (or even any other) individual interventions for the person with dementia will be available and home based versions of CST are generally unavailable in the UK. Should these be available in a few cases this will be recorded and accounted for in our final analysis of our data set. People will not be involved in any other dementia intervention research study at the same time as the iCST trial.

Planned inclusion/ exclusion criteria

Participants meeting the inclusion criteria and who have an identified carer will be randomised between the two groups (a) treatment as usual vs (b) individual CST over 26 weeks.

Inclusion criteria

We will use the Spector, Woods Orrell et al. (2003) standardised criteria for the psychological treatment of people with dementia:

- Meet DSM IV criteria for dementia
- Score 10 or above on the MMSE
- Some ability to communicate and understand
- See/hear well enough to participate
- No major physical illness or disability affecting their participation

Additional criteria will include living in the community and regular availability of a carer (or friend or befriender) to participate in the sessions. Carer is defined as someone who has regular contact with the person with dementia (i.e. 4 hours a week), and can act as an informant. If the carer is unavailable to deliver the therapy sessions, but another person could be identified that would be willing and able to participate in the intervention with the person with dementia (i.e. deliver more than half of the sessions), then this person could deliver the intervention. This individual could be a paid carer offering support to the person with dementia at home or in another setting, should have regular contact with the person with dementia and availability in delivering the sessions. Paid carers recruited into the Trial will not substitute the carer acting as the informant for the person with dementia, as they will only contribute towards delivery of the iCST sessions.

Exclusion criteria
People with dementia not meeting the criteria for individual work (living in a care home, no available family carer to deliver the sessions and act as an informant).

Ethical arrangements
The study will be approved through the appropriate multicentre research ethics application and local research governance procedures. We will use the SHIELD Trial Steering Committee (TSC) with an independent chairperson and a Data Monitoring and Ethics Committee (DMEC) reporting to the TSC. All researchers will receive training in the Good Clinical Practice guidelines. In accordance with good practice the trial will be registered with www.controlledtrials.com and allocated an ISRCTN number. This trial is not covered by the Medicines for Human Use (Clinical Trials) Regulations 2004 since it is a psychological intervention, but trial sites are all up to date with best practice GCP training. The data will be collected and managed through MACRO, which is an electronic data capture system which meets regulatory compliance for designing electronic case report forms, data entry, data monitoring and data export, and good practice guidelines. MACRO has built in systems for keeping an audit trail and quality assurance.

Risks and anticipated benefits for trial participants
There appear to be no documented harmful side-effects from participating in CST or Maintenance CST groups, and no adverse reactions were apparent in the CST or REMCARE studies. Benefits are consistently reported by participants in the groups, including enjoyment, feelings of validation and self-worth. The desire of participants to continue meeting following the sessions provides an indication of the value placed on the benefits. Prospective participants will be fully informed of the potential risks and benefits of the project. Moreover after the end of the trial all participants will receive a copy of the DVD and the manual to enable them to repeat and continue the sessional programme.

Consent
Participants will be in the mild to moderate stages of dementia, and therefore would generally be expected to be competent to give informed consent for participation, provided that appropriate care is taken in explaining the research and sufficient time is allowed for them to reach a decision. It is helpful for a family member or other supporter to be involved, and we would aim to ensure that this is done wherever

possible. It will be made clear to both participants and family carers that no disadvantage will accrue if they choose not to participate. In seeking consent, we will follow current guidance from the British Psychological Society on evaluation of capacity. In this context, consent has to be regarded as a continuing process rather than a one-off decision, and willingness to continue participating will be continually checked through discussion with participants during the assessments. Where the participant's level of impairment increases, so that they are no longer able to provide informed consent, the provisions of the Mental Capacity Act will be followed. The initial giving of informed consent provides a clear indication of the person's likely perspective on continuing at this point, and the family carer will be consulted in this regard. At any point where a participant with dementia becomes uncomfortable with the assessments they will be discontinued.

Confidentiality

The research will follow the Data Protection Act 1998 guidance. Only members of the research team will have access to the original data. Participants' personal details will be stored separately from the data, and will be kept in a separate file on a password protected computer at the University College London. Each participant will be assigned an identification code, which will be used in all data storage files; these will not contain names or any other means of personal identification. All personal details will be deleted on completion of the study.

Retention of trial documentation

In line with UCL data protection policy anonymous data and trial documentation will be kept securely for a period of 10 years following the completion of the trial.

Proposed sample size

The main analysis will be based on intention to treat for the primary outcome ADAS-Cog. Our group CST study (Spector et al., 2003) had an effect size (SMD) of 0.32. Our Cochrane review of RO (Spector et al., 2001) found a SMD of 0.58, the maintenance group CST study found an SMD of 0.68 compared to TAU. Onder's individual RO/CST study found a SMD of 0.41. Taking a conservative approach we estimate the SMD relative to TAU to be 0.35. A sample size of 260 will have 80% power to detect a SMD of 0.35 using a two group t-test with a 0.05 (two sided) significance level comparing the individual CST and the TAU groups. Assuming 15% attrition we propose to recruit 306 people with dementia. Based on our experience in three previous dementia trials; the CST trial, the needs in care homes trial (Orrell et al., 2008), and the activities in care homes trial (Wenborn et al., 2009), we predict a 12-15% loss to follow up (7-10% excluding deaths). To safeguard loss to follow up we will apply standard procedures to maximise follow up used successfully in our earlier studies. Over the 20 month recruitment period we intend to recruit a minimum of 9 dyads per month over 20 months from the London/Essex site and 4 dyads per month over 15 months from each of the Manchester, Hull, and Bangor sites. The additional sites of Dorset, Devon, Lincolnshire, Norfolk and Suffolk will recruit a total of 2 dyads per month over a recruitment period of 10 months. This is entirely feasible as in London we recruited on average of 8 people per month for the REMCARE trial and 12 people per month for the MCST trial with both trials completed to schedule.

Statistical analysis

We shall analyse by intention to treat, in that all available data will be included, however methods of imputation such as LOCF are of limited utility in dementia, where the expectation is decline for the usual treatment group, and participants will be lost through death and illness. A method of multiple imputation using a linear regression model will be used where needed. Our sample size calculations are based on the numbers estimated to be available at the study end-point, 6 months after randomisation. We shall use

analysis of covariance to adjust for baseline differences in outcome variables. Variables to be considered in the model will include among others gender and age. Analyses will consider the evaluation 6 months after randomisation as the primary end-point in evaluating whether the intervention has had a substantive effect on the person with dementia. Further model definition will be provided in the statistical analysis plan.

The trials will be subject to the usual monitoring by TSC and DMEC. Interim analyses will not be conducted unless requested by the DMEC. Qualitative data including transcripts of focus groups and interviews would be subjected to thematic analysis using the Nvivo software.

Health economic evaluation

The primary evaluation will be a cost-effectiveness analysis (CEA) from (a) a health and social care perspective, and (b) a societal perspective. Service use data, user charges and information on unpaid carer support will be collected using an adapted CSRI. The primary CEA will measure effectiveness using the ADAS-Cog; further analyses will look at other outcomes (particularly QoL-AD and QALYs generated from the DEMQOL with societal weights, built on a currently underway HTA-funded study). Cost-effectiveness acceptability curves will be plotted, generated from the net benefit approach and using bootstrap regression for a range of values of willingness to pay for incremental primary outcome measure changes and QALY gains. Unit costs will be estimated to be nationally generalisable. CEACs have been widely adopted as a method to quantify and graphically represent uncertainty in economic evaluation studies of health-care technologies (Fenwick, O'Brien, & Briggs, 2004). The economic evaluation will be fully integrated into the main outcome evaluations. The interventions received will be fully costed from the perspective of local dementia services to generate a total programme cost and cost per participant or per participant-carer pair. We will also conduct a cost-consequences analysis (CCA) to which all these outcomes will contribute, and examining resource impacts across different budgets (e.g. dementia services, primary care, secondary care, local government, patient and family). This trial is not a head to head comparison with maintenance group CST (six months) however as the designs, duration, and data collected are very similar we will be able to make comparisons between individual and maintenance group CST in terms of costs and benefits.

Proposed outcome measures

Cognitive function is a key outcome and we have selected the ADAS-Cog as the standard measure used in such studies. QoL-AD is the European standard measure of quality of life in dementia (Moniz-Cook et al., 2008). The CSRI is a standardised measure of health/social and formal/informal costs. Service use data will be collected using an adapted version of the CSRI. Primary outcomes: cognition, quality of life, and cost-effectiveness. Assessments will be: baseline (pre-CST); 13 weeks (to safeguard loss to follow-up) and 26 weeks. This is long enough to allow for measurable deterioration in dementia and assess the impact on overall costs of care.

Primary outcomes

ADAS- Cog, (Rosen et al., 1984)

ADAS-Cog was designed to measure the severity of the most important cognitive symptoms of Alzheimer's disease (AD). The ADAS-Cog is the most popular cognitive testing instrument used in clinical trials of drug treatments for dementia. It consists of 11 tasks measuring the disturbances of memory, language, praxis, attention and other cognitive abilities which are often referred to as the core symptoms of AD. This is a brief, widely used test of cognitive function, with good reliability and validity (Weyer et al., 1997).

Quality of Life-Alzheimer's disease Scale (QoL-AD; Logsdon et al., 1999)

This widely used brief, self-report questionnaire has 13 items covering the domains of physical health, energy, mood, living situation, memory, family, marriage, friends, chores, fun, money, self and life as a whole. It has been recommended in a European consensus statement on outcome measures for dementia (Moniz-Cook et al., 2008). The QoL-AD has good internal consistency, validity and reliability (Logsdon et al., 1999; Thorgrimsen et al., 2003).

Secondary Outcomes

Client Service Receipt Inventory (Beecham & Knapp, 1992)

The CSRI will be adapted for the study. It will be completed by the person's carer before the intervention, 13 weeks after the intervention, and at the end of the intervention period. The CSRI has been extensively used in studies of mental health care. The inventory uses information about the service user's background, and comprehensively gathers information about accommodation, medication profile and services used. It provides the data from which to estimate the costs of dementia care, unpaid carer inputs and wider carer impacts. It provides the data from which to estimate costs.

DEMQOL (Smith et al., 2005)

The DEMQOL scale measures five domains of quality of life; health and well-being, cognitive functioning, social relationships and self-concept. The scale uses self-rated reports of quality of life administered to the person with dementia by a trained interviewer. This measure can also be administered to the family carer to provide the DEMQOL-proxy. It has high internal consistency (0.87) and acceptable inter-rater reliability (ICC 0.84) and good concurrent validity with the QoL-AD and DQoL scales. It is included as a quality of life scale and a utility measure since there is a HTA funded study underway which will enable the DEMQOL to be converted to utility scores.

Neuropsychiatric Inventory (NPI) (Cummings et al., 1994)

The NPI assess 10 behavioural disturbances occurring in dementia patients: delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, and aberrant motor activity. The NPI uses a screening strategy to minimize administration time, examining and scoring only those behavioural domains with positive responses to screening questions. Both the frequency and the severity of each behaviour are determined. Information for the NPI is obtained from a caregiver familiar with the patient's behaviour. Studies reported here demonstrate the content and concurrent validity as well as between rater, test-retest, and internal consistency reliability; the instrument is both valid and reliable (Cummings et al., 1994).

Bristol Activities of Daily Living Scale (BADLS) (Bucks et al., 1996)

The BADLS is carer rated instrument consisting of 20 daily-living abilities. The scale has face validity; assessing items rated as important by and using levels of ability generated by carers; construct validity as demonstrated by principal components analysis; and concurrent validity as it correlates well with observed task performance. It has good test-retest reliability as measured by Cohen's Kappa. Carers report that it is easy to use and it is relatively short. The BADLS also shows sensitivity to change in people with Alzheimer's disease receiving anticholinesterase medication and significantly correlates with changes in the Mini-Mental State Examination and the ADAS-Cog (Byrne et al., 2000).

Geriatric Depression Scale (GDS-15) (Sheikh & Yesavage, 1986)

The Geriatric Depression Scale (GDS) is one of the most commonly used self rating depression scales in geriatric populations. The shorter version of the GDS (GDS-15), comprises of 15 easy to use items, with answers in yes/no format, and is designed to exclude those somatic symptoms of depression that are also seen in non-depressed elderly people. The GDS-15 is principally a self-rating scale but may be used

partly as an observer-administered scale, where the questions are read aloud to the patient who is instructed to answer either yes or no to the questions. Previous studies have shown that the GDS-15 has acceptable sensitivity and specificity when used with people with mild to moderate dementia (Lach et al., 2010).

Quality of the Carer Patient Relationship (QCPR) (Spruytte et al., 2002)
The QCPR is a measure of relationship quality, which is applicable to parent- as well as partner- or child-carers. Originally developed in the Netherlands this scale comprises 14 items (with 5 point Likert-type scales) designed to assess the warmth of the relationship and the presence or absence of conflict and criticism. The QCPR will be completed by both the person with dementia and carer. Previous studies have shown that the QCPR has good internal consistency for carers and concurrent validity with other measures of relationship quality and carer distress (Spruytte et al., 2002). In the trial platform of the REMCARE study, the QCPR, showed good internal consistency for people with dementia (Woods et al., 2009).

Mean number of days in institutional care at 6 month follow up
This information will be incorporated in the CRSI.

Carers' primary outcome measures
SF-12 (Ware, Kosinski, and Keller, 1996)
The Short Form-12 Health Survey measures generic health concepts relevant across age, disease, and treatment groups. It provides a comprehensive, psychometrically sound, and efficient way to measure health from the patient's point of view by scoring standardized responses to standard questions. The SF-12 (questions #32-38 on the Patient Form) is designed for self-administration, reducing the burden of data collection for health care providers. Most people can complete the SF-12 in less than 3 minutes without assistance. The SF-12 was designed to measure general health status from the person's point of view. The SF-12 includes 8 concepts commonly represented in health surveys: physical functioning, role functioning physical, bodily pain, general health, vitality, social functioning, role functioning emotional, and mental health. Results are expressed in terms of two meta-scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). The SF12 has been widely used with carers and the mental component summary provides a good proxy for mental health and emotional status. The SF12 can generate the SF6D, a utility measure which can be used to obtain quality adjusted life years (QALYs).

Carers' secondary outcome measures
Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983)
HADS is a self completed measure, consisting of 14 questions, seven for anxiety and seven for depression. The two seven-item subscales, each score 0–3, which generate scores for generalised anxiety and depression (0–21). The HADS is a widely used measure of anxiety and depression validated for all age groups which identifies caseness for clinically significant depression and anxiety (Mykletun et al., 2001).

EQ-5D (EuroQol group, 1990)
EQ-5D is a standardized instrument for use as a measure of health outcome. Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status. EQ-5D was originally designed to complement other instruments but is now increasingly used as a 'stand alone' measure. EQ-5D is designed for self-completion by respondents and is ideally suited for use in postal surveys, in clinics and face-to-face interviews. It is simple to use taking only a few minutes to complete. Instructions to respondents are included in the questionnaire. A recent randomised

controlled trial by Charlesworth et al. (2008) used the EQ-5D to evaluate quality of life in carers of people with dementia and to derive utilities for the calculation of QALYs. Given recent studies reporting that the EQ5D and SF6D can lead to different health-related utility scores but it is not clear why these differences arise and how they may affect cost utility analysis results (Grieve et al., 2009), both scales need to be included.

Resilience Scale (RS-14) (Wagnild, 2009)
The Resilience Scale was developed based on qualitative work with women who experienced a major life event (Wagnild & Young, 1993). In the shorter version of the original scale (RS-14) participants are asked to respond to each item by either agreeing or disagreeing with each statement, on a scale of 1 (disagree) to 7 (agree). The responses are summed and higher scores indicate stronger resilience. Previous studies have shown that the measure demonstrates high internal consistency, test – retest reliability, and construct validity with measures of life satisfaction, morale and depression (Wagnild, 2009).

Research governance
University College London is the nominated sponsor for the project. As an extension to the SHIELD programme we propose to use the same established Trial Steering Committee and the Data Monitoring & Ethics Committee (DMEC) as a sub-committee. Membership and terms of reference for the TSC and DMEC have been drawn up and agreed.
Trial Steering Committee Members
Prof James Lindesay (Chair) Professor of Psychiatry for the Elderly, Leicester University
Dr Vincent Kirchner, Consultant Psychiatrist OPMHS, Camden
Dr Jan Oyebode, Consultant Clinical Psychologist, Older Adults, Birmingham
Rachel Thompson, Lead Practice Development Admiral Nurse, for dementia
Catherine Crombie, Clinical Lead Occupational Therapist, Hammersmith
Elayne Dunn, 'CHAT' (cognitive help and therapy), Sussex
Prof Martin Orrell (PI, SHIELD, NELFT/UCL)
U Hla Htay, Family Carer, Uniting Carers for dementia (Ukfd)
Prof Bob Woods (SHIELD, Bangor University)
HTA representative (to be added)
DMEC Committee Members
Prof Jill Manthorpe (Chair), Professor of Social Work, King's College London
Jennifer Hellier, Statistician, King's College London
Dr Ciaran Regan, Consultant Psychiatrist, WLMHT
David Prothero, Family Carer, Uniting Carers for dementia (UKfd)
Trial Statistician (in attendance)

Quality control
Compliance to GCP standards is now a requirement of all MRC and NHS R&D funded clinical trials NHSE, 1999) and this trial will be conducted according to GCP standards as interpreted by MRC guidelines, giving particular credence to guidance on multi-centre trials. Accurate records will be kept, in accordance with the protocol laid out in the investigator's manual for recruitment, randomization and data collection. Data will be collected and managed in a systematic and verifiable manner. Research associates will be trained, supervised and supported. Data collection will be ongoing with a database designed at the outset, to expedite reporting and enable data quality control. Compliance to GCP, protocol and trial processes will be monitored monthly in the first year and quarterly subsequently. The PI will ensure that careful records of randomisation are maintained via a trial register and that subject confidentiality is assured. Quality control will be applied to a sample of key data items both at study sites and during data

entry. Project management methods will be used including detailed work plans, quarterly meetings of the applicants, monthly local management meetings, and regular supervision sessions. Teleconferences will be used to coordinate progress across the eight sites.

4. Project timetable and milestones

Original Timetable	**Revised Timetable**	**Milestones**
April 2010-June 2010	April 2010-June 2010	Prepare job descriptions, obtain ethics approval, appoint to trial coordinator post.
July 2010	July 2010	Project start, trial coordinator in post
September 2010	September 2010	Adaptation of CST manuals into individual format
November 2010	November 2010	Consultations with users and carers Set up database with NWORTH
January 2011	January 2011	First draft Individual CST manual, expert/network consultations
March 2011	March 2011	Second draft of manual, field testing of manual
July 2011	July 2011	Report on field testing, final draft of manual
September 2011	March 2012	Recruitment/trial commences London/Essex site
December 2011	June 2012	Recruitment/trial commences Hull, Bangor/ Manchester Recruitment/trial commences Additional Sites
January 2012	July 2012	Submit papers: CST trial protocol, individual CST development
March 2012	July 2012	Commence follow up assessments London/Essex site
June 2012	September 2012	Commence follow up assessments Hull, Bangor/ Manchester
	October 2012	Commence follow up assessments Additional Sites
June 2012	November 2012	Recruitment target 50% (76) London/Essex site
September 2012	December 2012	Recruitment target 50% (76) Hull, Bangor/ Manchester Recruitment target 50% Additional Sites
April 2013	April 2003	Recruitment complete 4 Additional Sites
July 2013	May 2013	Recruitment complete (153) Hull, Bangor/ Manchester
	June 2013	Recruitment complete (153) London/Essex site
October 2013	February 2014	Complete Follow up assessments Hull, Bangor/ Manchester and Additional Sites Submit paper on baseline data
January 2014	February 2014	Complete Follow up assessments London
March 2014	March 2014	All data entered and preliminary analyses Submit paper on baseline data
April 2014	April 2014	Complete analyses and draft RCT paper
May 2013	May 2013	Submit RCT paper, submit final HTA report
June 2013	June 2013	Submit health economics paper Publish and disseminate individual CST manual

5. Expertise

Our team includes expertise in old age psychiatry (MO/AB), clinical psychology (BW/EMC/AS), trial methodology/statistics (IR) and health economics (MK). The applicants and collaborators have a long and successful record of working together. BW and MO have worked together for 12 years including developing the CANE. Also the MRC trial platform of reminiscence in dementia (BW, IR, MO); the HTA REMCARE trial (BW, MO, EMC, IR, NWORTH); the CST trial (MO, BW, MK, AS); the Wellcome study of dementia in care homes (BW, MO, MK); INTERDEM (BW, EMC, MO), and the SHIELD and CHALLENGE-DEMCARE NIHR research programmes (MO, BW, EMC, IR, MK, AS, NWORTH). We have planned recruitment to this study should it be funded, to complement rather than compete with the above mentioned studies in dementia Bangor (BW), Hull (EMC) and London (MO).

MO is an old age psychiatrist specialising in psychosocial interventions and health services research for dementia. A joint paper with BW set out a manifesto for developing a rigorous evidence-based approach to the evaluation of psychological approaches in dementia care, which has resulted in a number of Cochrane reviews and a recently published RCT of a cognitive stimulation approach in dementia, including a health economics evaluation. He will lead and coordinate the study and manage the researchers based in London and the North East London Foundation Trust.

BW is a clinical psychologist, who has been developing and evaluating psychological approaches in dementia care, including reminiscence therapy, since 1977; he is amongst the pioneers of an evidence-based approach in this field, and is a co-author of three Cochrane systematic reviews. He will be responsible for the management of the project and the research staff at Bangor. He leads the Neurodegenerative & Dementia Research Network (NEURODEM) of the Clinical Research Collaboration Cymru/Wales (CRCC – the Welsh arm of UKCRC), and is the Acting Director of N-WORTH.

AS is an academic clinical psychologist who was the key researcher on the original CST study, developing CST and running the RCT. She co-authored the manual and has developed the CST training programme.

IR is a clinical trialist/methodologist who specialises in designing and conducting pragmatic RCTs, and developing patient-assessed measures of health outcomes for RCTs. He was founding director of the North Wales Organisation for Randomised Trials in Health (& social care) (NWORTH – an accredited trials unit) and, having moved to Swansea University, continues to collaborate with NWORTH on a number of trials). He will advise on the statistical, design, randomisation and data management aspects of the project.

EMC is a clinical psychologist who has been a pioneer of psychosocial interventions, in a variety of settings including primary care and care homes. She brings access to the Yorkshire and Humberside area through her position in the Humber Mental Health Teaching NHS Trust. She will manage the researchers based in Hull and the East Riding of Yorkshire.

MK is an economist and social policy analyst most of whose work is in the mental health and social care fields. He has professorial positions in social policy (LSE) and health economics (KCL), and directs the NIHR School for Social Care Research.

AB is a leading expert in dementia research and clinical trials at the University of Manchester, he is closely linked with clinical services in the Manchester area will be able to guide the implementation of the project in this large centre of population. He will manage the researcher based in Manchester.

GVL has been the carer of her mother with dementia for the past 4 years. This project is particularly close to her way of thinking in dementia care. She is involved in many of the organisations which offer support to carers and people with dementia in North East London and Essex. She is an experienced Teacher/Trainer in English Language Teaching with experience in developing teaching materials and course design, as well as evaluating the effectiveness of both. Her personal experience and teaching expertise will make her invaluable in the design of the manual and the training.

The programme benefits from access to the NWORTH Clinical Trials Unit which provides expertise in the evaluation of complex interventions and pragmatic randomised trials in health and social care. N-WORTH will support the proposed trial, both methodologically and technically. In particular N-WORTH will adapt its trial software and Standard Operating Procedures (SOPs) to the trial, and contribute to the technical training and supervision of all researchers.

The application also benefits from close links with Dementia Services Development Centres in London, Wales and North West England and with the regional dementia networks (Dendron: North Thames and North West, and NeuroDem Wales/Cymru as well as two year time limited funding of 5 staff for recruitment to dementia trials in Hull and the East Riding of Yorkshire via DENDRON/CLRN support.

6. Service users

Gillian Lasocki a family carer is a coapplicant. Carers will be involved in the research process as consultants (e.g. opinions on patient information sheets and consent forms) and collaborators (e.g. involvement in pilots of training packages & in training project personnel). In terms of user involvement, people with dementia will be involved in the research process as consultants (e.g. focus groups on HTP for dementia, focus groups on MCST programme). For the consultation and development work we will involve the Alzheimer's Society, Age Concern, the charity For Dementia, and Alzheimer's Concern Ealing (because of their expertise in ethnic minority) issues and carer representatives from the London Centre for Dementia Care. Voluntary sector and carer representatives have a direct role in the management of the trial through the TSC and the DMEC.

7. Justification of Support Required

Clinical Trials Unit

This is a complex project which requires excellent trial management and we will be working with NWORTH a well established Clinical Trials Unit which is building a portfolio in psychological interventions in dementia research. We have been working with NWORTH on a number of related dementia projects already including the MRC trial platform on reminiscence in dementia, the REMCARE trial, and the SHIELD NIHR research programme. This means that we already have an established relationship with NWORTH which this study will further consolidate.

An experienced Trial Manager (Rhiannon Whitaker 0.1 FTE) from the NWORTH team will oversee the management of the trial, and will support the Trial Coordinator (based at UCL) in day-to-day trial management. The experienced trial statistician (Dr Zoe Hoare 0.1 FTE) will be responsible for overseeing the randomisation procedures, data analysis, and preparing reports for the DMEC. She will be supported by NWORTH IT (20% initially reducing to 10% after 12 months), a data manager who will set up and manage the MACRO database and other expertise as required from the NWORTH team. A trial secretary

(0.1 FTE) will provide administrative support and a quality control and compliance officer (0.05 FTE) will provide advice and support in relation to quality assurance matters.

Research staff
The Trial Coordinator (1 FTE) will be based at UCL and responsibilities will include the development of the individual CST manual and training, organisation of consultation process, day to day coordination of the trial across the 4 centres, recruitment, data collection, and the trial completion and write up. This wide range of responsibilities requires a level of expertise and experience and this post has therefore been costed at Grade 7 for the full duration of the study. In addition, administrative support has been costed at 0.4 FTE for the study duration for tasks including the preparation of data packs, photocopying, meeting organisation, and liaison between researchers and centres.

The research assistants will be responsible for recruitment, data collection, and training & support for carers. Based on our previous experience in the REMCARE study for recruitment we would expect to need to screen around 3 patient/carer dyads for each one recruited making 900 assessments. In addition, we would need to conduct 3 assessments (including baseline, intermediate and follow up assessments) for each of the 306 people initially recruited and taking into account attrition this is approximately 900 in all. This approximates to 750 work days of RA time. If between 150 and 160 pairs are randomised into the treatment arm and each of these requires 10 hours support and another 10 hours coordinating the support and receiving supervision plus 2 to 3 hours training. This means each pair requires 3 work days equivalent to around 500 days of RA time in total. Time is also needed to set up the project in each area, attend meetings/conferences, annual leave, and to input and check data. Based on 40 weeks this means that in London we require 0.6 FTE over 30 months, in Hull and Bangor we require 0.7 FTE over 24 months and in Manchester 1 FTE over 24 months. Additional time is needed in Manchester as AB is not linked with either the REMCARE, or SHIELD programmes.

The CST supervision of the RAs will be by Dr Aimee Spector, a clinical psychologist and one of the originators of CST who will spend 2 hours per week on the study including meeting attendance.

Other costs
Travel and Subsistence: Travel expenses are required for visits to participants' homes costed at £8 per visit by car/public transport (900 for screening, 900 for assessments and 500 for carer support). Travel and subsistence are also required for conference attendance/presentation, attendance at quarterly project meetings, and biannual TSC and DMEC meetings. Also attendance at welcome meeting at HTA.

Other: This includes photocopying, laser toner cartridges, and production of the DVD and the manual to publication standard.

Equipment: Each of the researchers responsible for data collection will be provided with a laptop computer, to assist in data entry and management and each site will have a laser printer. Mobile phones are also needed to be able to contact researchers and for personal safety.

Voluntary sector: This is required for travel expenses of carers and people with dementia, and payments for time, including for GL for attendance at meetings and assistance in manual development. GL is costed at £20 per hour for 500 hours over the duration of the study.

Health Economics: The complexity of the cost data and the need for appropriate analyses necessitates the involvement of a health economist supervised by MK.

IR is required to provide overall statistical and methodological expertise for the study. BW, EMC and AB will require time to coordinate the sites and attend meetings. MK will supervise the health economics component of the study. MO will require time to coordinate the study and attend meetings.

Excess Treatment Costs

NHS Excess Treatment Costs are associated with this proposal are strictly limited since the carer manual and DVD would be expected to be complete in itself and specifically designed to be used by family carers. Having said this many services may consider it worthwhile to provide training sessions for carers and access to advice via the local voluntary sector organisations. In view of this we have calculated excess treatment costs on the assumption that each carer may receive an average of 2 hours of training/support time from a member of the local community mental health team. This means Excess Treatment Costs have been calculated as approximately £14,100 over the duration of the trial.

Service Support Costs

On the assumption that each screening (900) takes one hour of staff time and each recruited participant (300) requires another two to three hours (e.g. contacts with researcher, meetings, checking clinical records, advice, discussions with staff). Service support costs have thus been calculated as £45540 over the course of the trial.

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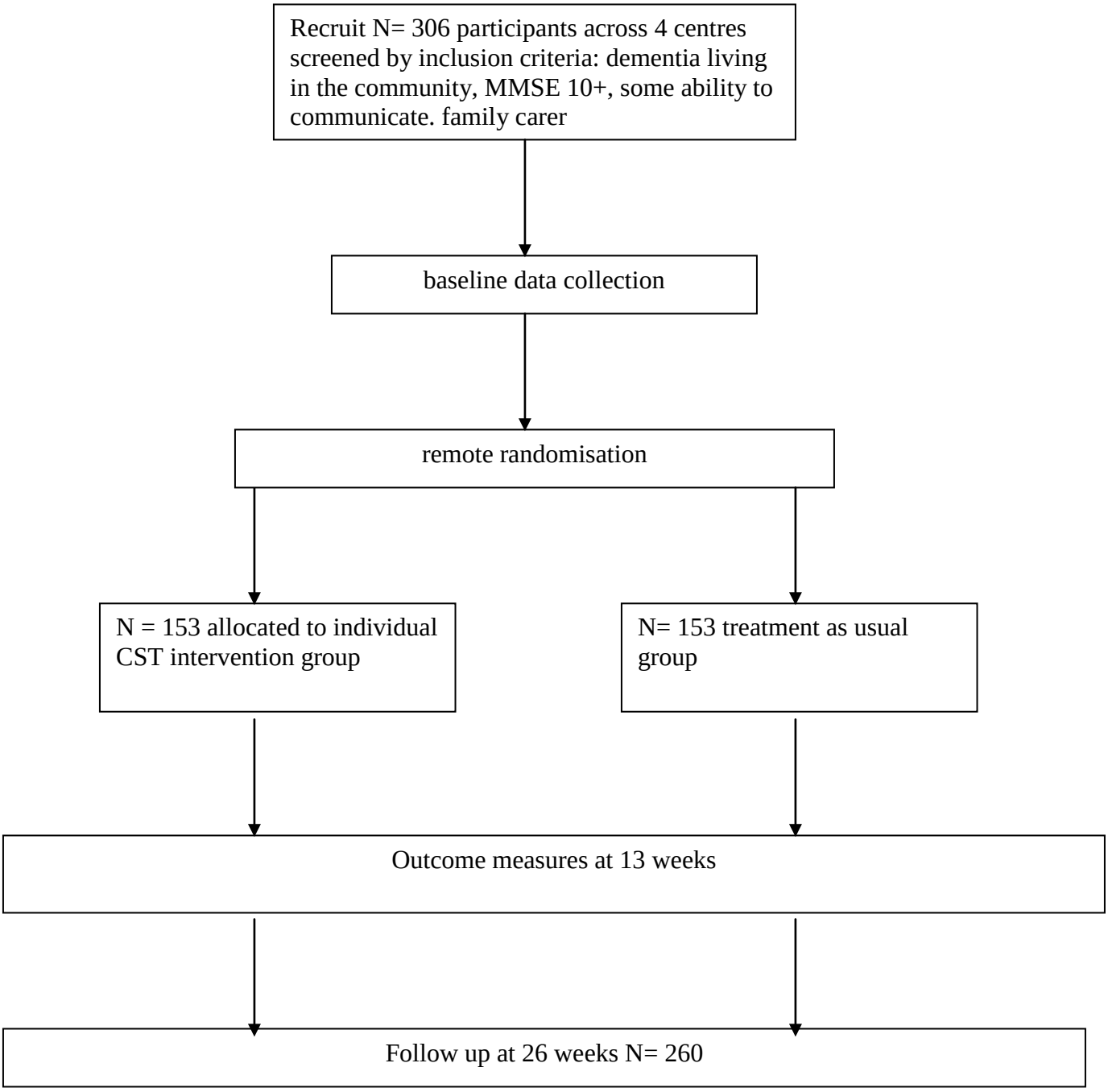

Figure 1. Flow of participants through the individual CST randomised controlled trial.