

Goal-oriented cognitive rehabilitation for early-stage Alzheimer's and related dementias: the GREAT RCT

Linda Clare,^{1*} Aleksandra Kudlicka,¹ Jan R Oyebode,² Roy W Jones,³ Antony Bayer,⁴ Iracema Leroi,⁵ Michael Kopelman,⁶ Ian A James,⁷ Alison Culverwell,⁸ Jackie Pool,⁹ Andrew Brand,¹⁰ Catherine Henderson,¹¹ Zoe Hoare,¹⁰ Martin Knapp,¹¹ Sarah Morgan-Trimmer,¹² Alistair Burns,⁵ Anne Corbett,¹ Rhiannon Whitaker¹³ and Bob Woods¹⁴

¹Centre for Research in Ageing and Cognitive Health, University of Exeter, Exeter, UK

²School of Dementia Studies, University of Bradford, Bradford, UK

³Research Institute for the Care of Older People (RICE), Bath, UK

⁴Division of Population Medicine, University Hospital Llandough, Cardiff University, Cardiff, UK

⁵Department of Neuroscience and Experimental Psychology, University of Manchester, Manchester, UK

⁶Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, St Thomas' Hospital, King's College London, London, UK

⁷Centre of the Health of the Elderly, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK

⁸Kent and Medway NHS and Social Care Partnership Trust, St Martin's Hospital, Canterbury, UK

⁹Dementia Pal Ltd, Southampton, UK

¹⁰North Wales Organisation for Randomised Trials in Health, Bangor University, Bangor, UK

¹¹Personal Social Services Research Unit, London School of Economics and Political Science, London, UK

¹²Institute of Health Research, University of Exeter Medical School, Exeter, UK

¹³Whitaker Research Ltd, Bangor, UK

¹⁴Dementia Services Development Centre, Bangor University, Bangor, UK

*Corresponding author l.clare@exeter.ac.uk

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Scientific summary

The GREAT RCT

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Scientific summary

Background

Cognitive rehabilitation (CR) is an individualised, goal-oriented, problem-solving approach aimed at managing or reducing functional disability and maximising engagement and social participation. This intervention is intended to support everyday functioning by addressing the impact of cognitive impairment on functional ability. People with dementia and their family members or other supporters (here referred to as 'carers') work together with a CR therapist to identify personally relevant and meaningful goals relating to their everyday activities. The therapist identifies the person's intrinsic cognitive and functional capacity and current level of functioning, assesses the requirements of the task or activity outlined in the goal, pinpoints areas in which the two are mismatched and problems arise and helps to devise a plan to overcome these problems using evidence-based rehabilitative methods. Participants and carers work together with the therapist to implement this plan over several sessions conducted in the home setting. Progress towards attaining the identified goals is evaluated through participant- and carer-reported levels of goal attainment. Building on a series of feasibility studies and a successful pilot trial, the multicentre Goal-oriented cognitive Rehabilitation in Early-stage Alzheimer's and related dementias: multicentre single-blind randomised controlled Trial (GREAT) aimed to provide definitive evidence about the clinical and cost-effectiveness of CR for people with mild to moderate dementia.

Methods

Trial design

The trial design was a two-arm, single-blind, pragmatic randomised controlled trial comparing CR added to usual treatment with usual treatment alone. Participants were assessed at baseline and at 3 and 9 months post randomisation.

Participants

Participants were individuals of any age with an *International Classification of Diseases*, Tenth Edition (ICD-10), diagnosis of Alzheimer's disease, vascular dementia or mixed Alzheimer's disease and vascular dementia, and in the relatively early stages, as indicated by a Mini Mental State Examination (MMSE) score of ≥ 18 points. If taking dementia-specific medication, the participants had to be receiving a stable dose for at least 1 month before joining the trial, with no expectation of a change in dose during the course of the trial. Participants had to have a carer who was willing to take part and provide collateral information, and had to be able to give informed consent. The exclusion criteria were people with a prior history of stroke, brain injury or other neurological disorder and an inability to communicate in English.

Participants were recruited in eight centres in England and Wales through NHS and voluntary sector services and Join Dementia Research over a 36-month period from 1 April 2013 to 31 March 2016. All assessments and intervention sessions were conducted in participants' own homes.

Sample size

To achieve 80% power to detect a medium effect size of 0.3 with alpha 0.05 in the primary and secondary outcomes, 175 people with dementia, together with their carers, were needed to complete the trial in each arm. Allowing for a potential attrition of 27%, it was necessary to randomise 480 people with dementia, each with a carer.

Randomisation

Participants were individually randomised following consent and baseline assessment, through the online randomisation centre that was managed by the Clinical Trials Unit. Randomisation was stratified by centre, sex, age (< 75 years vs. ≥ 75 years) and MMSE score (< 24 points vs. ≥ 24 points).

Blinding

The trial researchers were blind to the participants' group allocation.

Intervention

The intervention was 10 sessions of CR over 3 months, followed by four maintenance sessions over the next 6 months. This was provided in addition to usual treatment. The intervention was delivered by trained therapists (nine occupational therapists and one nurse) who received regular individual and group supervision to ensure fidelity to the protocol.

Comparator

The comparator was treatment as usual (TAU).

Outcomes

The primary outcome was participant rating of goal attainment at the 3-month follow-up. All participants identified up to three goals at baseline. Goals were elicited using the Bangor Goal-Setting Interview (BGSi), with goal attainment rated using a previously validated simple and accessible rating scale on which a 2-point improvement is considered to be clinically significant. This measure also yielded secondary outcomes, as attainment ratings were made independently by participants and carers at each time point and participants rated their satisfaction with goal attainment at each time point.

Other secondary outcomes were participant self-efficacy [Generalized Self-Efficacy Scale (GSES)], depression and anxiety (Hospital Anxiety and Depression Scale), cognition (story recall from the Rivermead Behavioural Memory Test), elevator counting from the Test of Everyday Attention, letter fluency from the Delis–Kaplan Executive Function System, quality of life [DEMENTIA Quality Of Life questionnaire (DEMQOL)], service utilisation (Client Services Receipt Inventory), carer stress (Relatives' Stress Scale), health status [EuroQol-5 Dimensions (EQ-5D)] and quality of life (World Health Organization's Quality of Life Instrument – brief version).

Participant goals were recorded. Therapists recorded the per cent attainment for all goals addressed in therapy. Therapists completed therapy logs with details of each session and contributed to a focus group discussion about perceived influences on outcome.

Participant and carer experience of the intervention was explored through interviews with a subset of participants and carers. These were a consecutive series of participants completing the trial in three sites. Interviews were conducted and the data were analysed by researchers who were not otherwise involved in the trial.

Analyses

A statistical analysis was conducted as an intention-to-treat analysis. The main analysis for the primary outcome was an analysis of covariance (ANCOVA) adjusted for baseline score, allocation group and stratification variables (age, sex, MMSE score and centre), which were treated as random effects. The analysis used a mixed-effects model. Additional regression modelling was undertaken to identify factors that could be important in attaining and maximising the observed effects. This was done separately for people with dementia and carers. The analyses for the secondary outcomes used the ANCOVA adjusted for baseline score, allocation group and stratification variables.

Goals identified by participants were categorised descriptively. Therapists recorded the extent of attainment for all goals addressed in therapy as a percentage score using criteria identified at the outset. Data from the therapy logs and focus group were examined in relation to factors perceived as affecting progress.

Participant and carer interviews were analysed thematically to identify key features of their experience of the intervention.

The main economic evaluation was a cost-effectiveness analysis, conducted, first, from a health and social care perspective and, second, from a societal perspective.

Changes to protocol

There were two changes to the protocol. The trial was initially set up in six centres, but two more centres were added in June 2015 to ensure that recruitment targets were met. Interviews with participants and carers were added to the protocol following discussion with the trial steering group, which included experts by experience.

Results

Recruitment

A total of 583 participants were screened, of which 475 were randomised to receive either CR ($n = 239$) or TAU ($n = 236$). One participant in the CR group was incorrectly included and was removed from the analyses. At the 3-month follow-up, 219 CR participants and 227 TAU participants were reassessed. At the 9-month follow-up, 209 CR participants and 218 TAU participants were reassessed. Retention in the trial was 94% at 3 months and 90% at 9 months.

The mean age of the participants was 78.56 years (range 53–95 years) and the mean MMSE score was 23.82 points (range 18–30 points). The majority of participants (59.5%) had a diagnosis of Alzheimer's disease. Carers were mainly spouses or partners (69.8%).

Primary outcome

For the CR group, participant attainment ratings improved at the 3-month follow-up by 2.57 points on average, and this improvement was maintained at 9 months. Average ratings in the TAU group showed a negligible improvement of less than 1 point at 3 months. The ANCOVA indicated that the differences between CR and TAU groups were significant at both 3 and 9 months, with large effect sizes of 0.81 and 0.8, respectively.

The same pattern was observed for informant attainment ratings, with the CR group improving by an average of 2.7 points and maintaining the improvement at 9 months; however, the TAU group ratings showed a negligible improvement of < 1 point. The ANCOVA indicated that the differences between the CR and TAU groups were significant at both 3 and 9 months, with large effect sizes of 0.93 and 0.79, respectively.

In the CR group, the average satisfaction ratings improved by 2.7 points at 3 months and increased further to give a 3-point improvement over baseline at 9 months. The average satisfaction ratings for the TAU group improved by 1.2 points at 3 months with a further slight increase at 9 months. The ANCOVA indicated that the differences between CR and TAU groups were significant at both 3 and 9 months, with large effect sizes of 0.7 and 0.67, respectively.

Few predictors were identified to indicate which participants were most likely to benefit, but more positive participant baseline ratings of readiness to change and a higher number of sessions completed were associated with greater gains, and at the 9-month follow-up, participants with higher MMSE scores had better outcomes.

Secondary outcomes

Following correction for multiple comparisons, there were no significant changes in any secondary outcome measures following intervention. Effect sizes were small to negligible, although in some cases with wide confidence intervals (CIs). Exploratory analyses examining whether or not benefits were seen for particular subgroups yielded no statistically significant models.

Process evaluation

Participants and carers engaged well in therapy, with 89% of CR participants completing at least 10 sessions.

The goals addressed in therapy related to engaging in activities, managing everyday tasks and situations, using appliances and devices, being well oriented, retaining or keeping track of information and events, locating belongings, recognising, identifying and naming people and objects, engaging in conversation, keeping in contact with family and friends, being organised, managing emotions and basic self-care. Therapists rated the per cent attainment for each goal addressed; 54.8% of goals were rated as being at least 75% attained, and 79.8% were rated as being at least 50% attained. Only 5% of goals showed no progress towards attainment. The therapists' perception was that the degree of impairment or dementia severity was the main determinant of progress.

Participants and carers were uniformly positive about the intervention and felt that they experienced improvements in the activities of daily living and in well-being. They found that the intervention helped with the process of psychological adjustment to living with dementia, leading to feelings of greater confidence, less anxiety and better coping skills. The relationship they built up with the therapist was important, both as a vehicle for providing information, education and support and as the means by which rehabilitative strategies were developed, accepted and personalised.

Economic analyses

Cost-effectiveness analyses

The cost of an increase of 1.32 points in the BGSi attainment rating was £1296 from the health and social care perspective and –£9 from the societal perspective. The cost of attaining an increase of 1.53 points [incremental cost-effectiveness ratio (ICER) point estimate] on the GSES was £4470 from the health and social care perspective and –£2961 from the societal perspective.

Cost-utility analyses

The cost per DEMQOL utility score (DEMQOL-U)-derived quality-adjusted life-year (QALY) was £1,110,000 from the health and social care perspective. The ICER was negative (–£1,052,000) from the societal perspective, the cost being somewhat lower in the CR group than that in the TAU group (by £526, 95% CI –£3108 to £1927). There were no differences between the groups in terms of QALYs derived from the DEMQOL-U. It was not possible to be certain that either strategy (CR or TAU) is cost-effective at any level of willingness to pay. The cost-per-carer QALY (from the EQ-5D) was £632,000 from the health and social care perspective. The ICER was negative (–£902,000) from the societal perspective, with costs being somewhat lower in the CR group than those in the TAU group (by £902, 95% CI –£3616 to £1705); there were no differences in the EQ-5D-derived QALYs between the groups.

Thus, there was no evidence for cost-effectiveness in terms of gains in the person-with-dementia QALY (DEMQOL-U) or in the carer QALY (EQ-5D, three-level version) from either study perspective. By reference to the primary outcome of participant-rated goal attainment, CR was cost-effective from both the health and social care and societal perspectives at willingness-to-pay values of £2500 and above for improvement in the goal attainment measure equivalent to the standardised mean difference (1.32). There was no evidence for cost-effectiveness on the self-efficacy (GSES) measure from either cost perspective.

Conclusions

Cognitive rehabilitation is clinically effective in enabling people with early-stage Alzheimer's disease or vascular or mixed dementia to improve their everyday functioning in relation to individual goals targeted in the therapy. CR was not cost-effective when gauged against QALY gains for either participants with dementia or carers, but would be cost-effective by reference to the primary outcome (goal attainment) if decision-makers were willing to pay for gains in participant-rated goal attainment. The results showed improved functioning in the targeted areas in the CR group at the 3-month follow-up, and this improvement was maintained at the 9-month follow-up. Participants in the CR group were more satisfied with their ability to carry out the everyday activities targeted in the intervention, and participants and carers felt that the intervention helped them to develop and implement strategies and adjust to the challenges of living with dementia. CR may be a useful addition to care pathways for those people with mild to moderate dementia who would benefit from developing strategies to manage their everyday activities and maintain their engagement in life, and may be particularly valuable if offered in the months following a dementia diagnosis.

Future research will aim to provide evidence on the longer-term outcomes of CR and to extend the approach to people with rarer forms of dementia. The next steps will be to implement CR into health and social care services.

Trial registration

This trial is registered as ISRCTN21027481.

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