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RESEARCH ARTICLE

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Individual goal-oriented cognitive rehabilitation to improve everyday functioning for people with early-stage dementia: A multicentre randomised controlled trial (the GREAT trial)

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Objectives: To determine whether individual goal-oriented cognitive rehabilitation (CR) improves everyday functioning for people with mild-to-moderate dementia.

Design and methods: Parallel group multicentre single-blind randomised controlled trial (RCT) comparing CR added to usual treatment (CR) with usual treatment alone (TAU) for people with an ICD-10 diagnosis of Alzheimer, vascular or mixed dementia, and mild-to-moderate cognitive impairment (Mini-Mental State Examination [MMSE] score $\geq$ 18), and with a family member willing to contribute. Participants allocated to CR received 10 weekly sessions over 3 months and four maintenance sessions over 6 months. Participants were followed up 3 and 9 months post randomisation by blinded researchers. The primary outcome was self-reported goal attainment at 3 months. Secondary outcomes at 3 and 9 months included informant-reported goal attainment, quality of life, mood, self-efficacy, and cognition and study partner stress and quality of life.

Results: We randomised (1:1) 475 people with dementia; 445 (CR = 281) were included in the intention to treat analysis at 3 months and 426 (CR = 208) at 9 months. At 3 months, there were statistically significant large positive effects for participant-rated goal attainment (d = 0.97; 95% CI, 0.75-1.19), corroborated by informant ratings (d = 1.11; 95% CI, 0.89-1.34). These effects were maintained at 9 months for both participant (d = 0.94; 95% CI, 0.71-1.17) and informant (d = 0.96; 95% CI, 0.73-1.2) ratings. The observed gains related to goals directly targeted in the therapy. There were no significant differences in secondary outcomes.

Conclusions: CR enables people with early-stage dementia to improve their everyday functioning in relation to individual goals targeted in the therapy.

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activities of daily living, Alzheimer disease, disability, goal-setting, nonpharmacological intervention, person-centred, problem-solving, reablement, vascular dementia

1 | INTRODUCTION

Timely diagnosis provides an opportunity to equip people with dementia, and their family members, to manage the effects of the condition on everyday functioning and independence. Currently, however, access to nonpharmacological interventions is limited,[1] and there is a particular need for practical, evidence-based interventions that directly support the ability to function in everyday life.

People with dementia who have mild-to-moderate cognitive impairment typically have relatively preserved ability for procedural learning, and given appropriate support, there is potential to change behaviour, implement new strategies, and learn or relearn some important information[2] in order to improve everyday functioning or maintain independence. Cognitive rehabilitation (CR), an intervention that addresses the impact of cognitive impairment on functional ability,[3] has been adapted for people with dementia.[4,5] CR is a person-centred, goal-oriented, problem-solving therapy aimed at managing or reducing functional disability, mitigating excess disability,[6] and maximising engagement and social participation.

In CR, people with dementia, and where possible their family members or other supporters, work collaboratively with a therapist to choose personally relevant and meaningful goals relating to everyday activities.[4,5] The therapist identifies the person's intrinsic capacity and current level of functioning, assesses the requirements of the task or activity outlined in the goal, pinpoints areas where the two are mismatched and where problems arise, and helps devise a plan to overcome these problems using evidence-based rehabilitative methods. These methods may include the use of environmental adaptations and prompts, introduction of compensatory strategies and memory aids, procedural learning of skills, and methods for learning or relearning relevant information. The personal rehabilitation plan is put into practice over several sessions, which are conducted in the home setting to ensure that changes are directly implemented in everyday situations. Progress towards attaining the identified goals is evaluated through participant- and informant-reported levels of goal attainment.[3]

Early studies consistent with this approach demonstrated benefits for people with dementia.[7,8] These were confirmed in a series of feasibility studies[9,10] and reports from other groups,[11,12] followed by a pilot randomised controlled trial (RCT) that demonstrated superiority over an active control condition.[13] The GREAT trial was designed to provide definitive evidence about clinical effectiveness.

Key points

- Cognitive rehabilitation (CR) is an individualized problem-solving therapy that aims to manage or reduce functional disability by addressing personal goals selected by people with dementia in an everyday context.
- GREAT is the first large trial to show that CR improves participant and carer evaluations of everyday functioning in relation to specific, personally meaningful goals targeted in therapy.
- CR could be considered for inclusion in care pathways for people with mild-to-moderate dementia who require support to manage everyday life and to maintain engagement in activities and social participation.

2 | MATERIALS AND METHODS

2.1 | Design

This was a multicentre, single-blind pragmatic RCT comparing CR added to usual treatment (CR) with usual treatment alone (TAU). Outcomes were assessed 3 and 9 months post randomisation. The trial was conducted in eight centres in England and Wales. Ethical approval was given by the Wales REC 5 National Health Service (NHS) research ethics committee (Reference 12/WA/0185). Participants and study partners provided written informed consent. The trial protocol was published,[14] and the trial was registered with Current Controlled Trials, reference ISRCTN21027481.

2.2 | Participants

Participants were people of any age with an ICD-10 diagnosis of Alzheimer, vascular or mixed dementia, and mild-to-moderate cognitive impairment as indicated by a Mini-Mental State Examination (MMSE)[15] score of 18 or above. If taking dementia-specific medication, they had to have been receiving a stable dose for at least 1 month, with no expectation of change during the trial. They had to be able to give informed consent for participation and to have a family member or other supporter ("study partner") willing to contribute. Exclusion criteria were a prior history of stroke, brain injury, or other significant neurological disorder and, for practical reasons, inability to communicate in English. Any cases of uncertain eligibility were adjudicated by a panel of four clinicians.

2.3 | Sample size

Power calculations were based on the pilot trial.[13] To achieve 80% power to detect a medium effect size of 0.3, with alpha 0.05, in primary and secondary outcomes, for a two-sample comparison of means, we needed 175 people with dementia, together with their study partners, to complete the trial in each arm. Allowing for estimated potential attrition of 27%, we needed to randomise 480 people with dementia.

2.4 | Participant recruitment

Participants were recruited through NHS services, support groups, and Join Dementia Research. Recruitment was conducted by Clinical Research Network staff from April 1, 2013, to March 31, 2016.

2.5 | Randomisation and masking

Participants were individually randomised following consent and baseline assessment through secure web access to the remote randomisation centre. Randomisation was conducted by dynamic allocation[16] to protect against subversion while maintaining good balance to the 1:1 allocation ratio. Participants were stratified by centre, gender, age (under 75 vs 75 and above), and MMSE score (under 24 vs 24 and above). To maintain blinding of the trial researchers who conducted follow-up assessments, outcomes of randomisation were notified to the trial therapists only, and the trial therapists scheduled all follow-up visits by the researchers, irrespective of participants' allocation. To assess the effectiveness of blinding, at follow-up, the trial researchers indicated to which group they believed the participant was allocated.

2.6 | Intervention

The intervention consisted of 10 weekly 1-hour individual sessions of goal-oriented CR over a 3-month period followed by four 1-hour maintenance sessions over the subsequent 6 months, conducted in the participant's home. CR involved working collaboratively on up to three rehabilitation goals chosen by the participant, using a problem-solving approach. This was supplemented as needed by addressing motivational and emotional difficulties through applying emotion regulation and behavioural activation strategies, reviewing and optimising participants' existing use of strategies to manage cognitive disability, providing practice in maintaining attention and concentration, signposting to relevant services, and offering support for study partners. CR could potentially be delivered by therapists from various professional backgrounds; in this trial, the therapists were nine occupational therapists and one nurse. Therapists attended a 2-day initial training course and annual 1-day refresher training sessions and received regular centralised supervision to ensure fidelity to protocol and consistency across sites. Therapists completed therapy logs, which were reviewed by the supervisor.

2.7 | Comparator

The comparator was treatment as usual, typically consisting of medication, monitoring, and general psychosocial support.

2.8 | Outcomes

All assessments were conducted in participants' homes by trained researchers blind to group allocation.

The primary outcome was participant-rated goal attainment at 3 months, recorded using a previously validated client-centred attainment measure, a simple 0 to 10 scale that is accessible and feasible for people with cognitive impairment to complete; an improvement of 2 points in the goal attainment rating for any individual goal is considered to be clinically significant.[17-22] Participants' individual goals were collaboratively identified through a semistructured interview, the Bangor Goal-Setting Interview (BGSI).[23] All participants chose up to three goals at baseline and rated current attainment; attainment ratings were then averaged across each participant's goals to give a single summary rating. These ratings were repeated at the 3-month follow-up, providing the primary outcome. Participants also rated goal attainment at 9 months, study partners independently rated participant goal attainment at 3 and 9 months, and participants rated their satisfaction with their goal attainment at 3 and 9 months.

Other secondary outcomes for participants with dementia at 3 and 9 months were self-reported self-efficacy (Generalised Self-Efficacy Scale),[24] mood (Hospital Anxiety and Depression Scale),[25] and dementia-specific health-related quality of life (DEMQOL).[26] Participants also completed a brief cognitive test battery covering memory (story recall from the Rivermead Behavioural Memory Test),[27] attention (elevator counting and elevator counting with distraction subtests from the Test of Everyday Attention),[28] and executive function (verbal letter fluency from the Delis-Kaplan Executive Function System).[29]

Secondary outcomes for study partners at 3 and 9 months were self-reported stress (Relatives' Stress Scale),[30] quality of life (WHOQOL-BREF),[31] and health-related quality of life (EQ 5D).[32]

2.9 | Analysis

Analyses were conducted in IBM SPSS v.22 and R v.3.3.1. The main statistical analysis, conducted blind, was an intention to treat analysis. Missing data were addressed through multiple imputation of missing values using a predictive mean matching algorithm.[33] Missing outcome measure scores at baseline were imputed using centre-level factors and the participant's gender, age, and baseline MMSE score. Missing outcome measure scores at the 3- and 9-month assessments were estimated based on centre-level factors, baseline characteristics, and scores for the same outcome at the earlier time-point(s). In line with simulation-based observations of the D2 statistic's performance for pooling *P* values,[34] 25 sets of imputations were generated using the method described above. For both primary and secondary outcomes, the analysis was a mixed-effects analysis of covariance (ANCOVA) adjusted for baseline score, allocation group, and the stratification variables (age group, gender, MMSE score, and centre). Baseline score, allocation group, age group, gender, and MMSE score were treated as fixed effects and centre as a random effect. Between-group effect sizes with confidence intervals (CIs) were calculated using Cohen *d* (the mean difference between the two arms, divided by the pooled standard deviation). For the primary outcome measure, prespecified regression modelling was undertaken to identify potential effect-

modifying factors, selected on clinical and theoretical grounds. Prespecified exploratory analyses, not adjusted for multiple comparisons, examined the impact of the number of sessions received on primary and secondary outcomes at 3- and 9-month follow-up and investigated whether participants' baseline ratings of goal importance and readiness to change were associated with outcomes.

Sensitivity analyses compared the outcomes of analyses that included both imputed and complete case data with the outcomes of analyses that included complete cases only. An analysis based on treatment received irrespective of group allocation was planned, but proved unnecessary as group allocation and treatment received were 100% consistent.

Interviews were conducted with a consecutive series of participants and study partners completing the intervention in three of the trial sites by an interviewer independent of the trial. Interviews followed a semistructured schedule in which participants and study partners were asked about their experiences and perceptions of the intervention, its usefulness, the degree of effort required, and any impact on day-to-day life. Data were analysed thematically from a critical realist perspective, taking an inductive approach in identifying and exploring patterns of meaning. Initial coding of the first five transcripts was undertaken by two researchers working independently. The resulting lists of themes were compared and discussed until consensus was reached about content and organisation, after which each researcher recoded the transcripts. Related themes were clustered together, and the clusters ordered into group-level themes and subthemes, and integrated into an overall thematic map by both researchers working together. The remaining transcripts were then coded by a single researcher. Findings are presented only briefly here but will be reported more fully in a separate paper.

2.10 | Patient and public involvement

Alzheimer's Society Research Network volunteers contributed to development of the trial protocol and served as experts by experience on the Trial Steering Committee (TSC).

2.11 | Changes to protocol

The trial was initially set up with six sites, but two further sites were added to ensure recruitment targets were met. Interviews with a subset of participants and study partners were added on the recommendation of the experts by experience.

3 | RESULTS

The flow of participants through the trial is shown in Figure 1. Following baseline assessment, 475 participants were randomised to either CR (n = 239) or TAU (n = 236). One participant who did not meet diagnostic criteria was incorrectly randomised and was withdrawn from analysis. All participants received their allocated condition, and 90% of CR participants completed at least 10 sessions. Six participants in the CR group withdrew from the intervention after at least two sessions but remained in the trial to complete follow-up assessments. Retention in the trial was 94% at 3 months and 90% at 9 months. Of 36 couples invited to participate in an interview following the 9-month follow-up, 26 agreed, although in one case only the study partner completed the interview.

3.1 | Sample characteristics

Demographic and clinical characteristics of the participants with dementia and study partners are summarised in Table 1. There were 111 serious adverse events reported during the trial, affecting 68 participants and 26 study partners and mostly involving hospitalisation; blinded assessors judged that none were related to trial participation.

3.2 | Numbers analysed

The intention to treat analysis included data from 474 participants at baseline (CR n = 238; TAU n = 236), 445 participants at 3 months (CR n = 218; TAU n = 227), and 426 participants at 9 months (CR n = 208; TAU n = 218).

3.3 | Main outcome analyses

The primary outcome was participants' goal attainment ratings on the BGSI at 3 months. Participant attainment and satisfaction ratings and study partner attainment ratings across all time points, and details of the statistical analyses, are summarised in Table 2. According to these participant-reported outcomes, CR was effective in improving functioning in the targeted areas at 3 months from the perspective of both participants and study partners, and this improvement was maintained at 9 months. Note that the analyses reported in Table 2 cover all goals that were identified at baseline, and for the CR group, this included a number of goals that were not addressed in the intervention. The CR group participants identified 679 goals and worked on 481 (71%) of these with the therapists. Taking just the 481 goals that were addressed in therapy, the mean change in participants' goal attainment ratings was an improvement of 2.84 points (SD 2.84) at 3 months and 2.77 points (SD 3.18) at 9 months, while study partners' ratings showed an improvement of 3.09 points (SD 2.73) at 3 months and 2.76 points (SD 3.14) at 9 months.

For the primary outcome measure at 3 months, linear mixed-effects models examining participant (centre, MMSE score, diagnosis, medication use, education, socio-economic status, and blinding effectiveness) and study partner (centre, gender, age, education, hours spent helping the participant, and type of relationship with the participant) factors predicting change in participants' goal attainment ratings from baseline to follow-up in the CR group were not statistically significant apart from socio-economic status, where higher socio-economic status was associated with better outcomes; see Supporting Information Table S1. Participants' baseline ratings of the importance

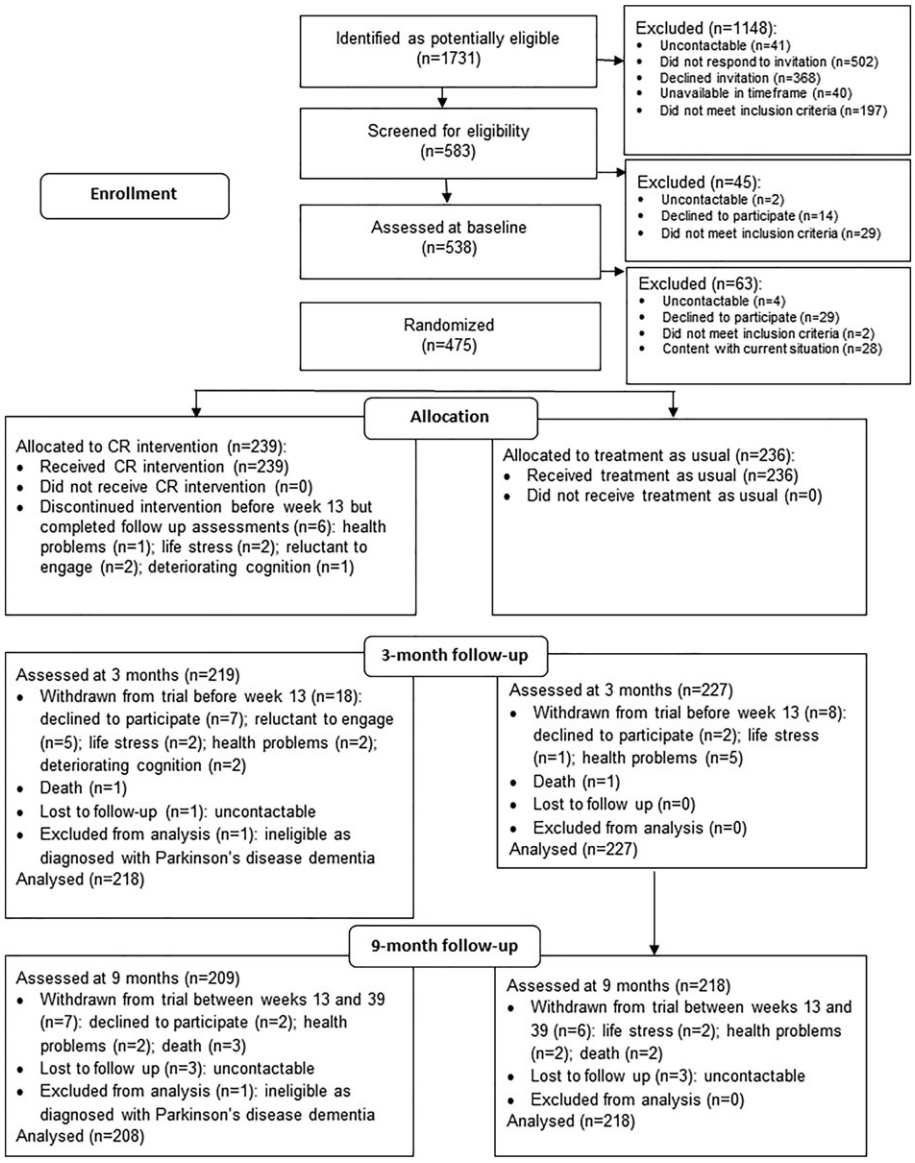

FIGURE 1 Participant flow through the GREAT trial

of each goal did not predict improvement. Ratings of readiness to change in relation to the goal were significantly associated with improvement in attainment ratings (t_{403} = 2.66, r = 0.13, P = 0.008), as was adherence, defined as number of CR sessions completed (b = 0.17; SE = 0.09; t_{215} = 2.01; P = 0.046; 95% CI, 0-0.34).

Scores on secondary outcome measures at all time-points, and ANCOVA analyses, are presented in Table 3. Following Bonferroni correction, there were no significant differences. Effect sizes were small to negligible, although in some cases with wide confidence intervals.

3.4 | Sensitivity analyses

Results from the analysis of complete case data were very similar to those of the multiple imputation analysis and did not alter the pattern of findings; see Tables S2 and S3. The difference in attrition between CR and TAU was minimal, and no statistically significant differences were observed in baseline characteristics or in primary and secondary outcomes for participants who withdrew and remained in the study; see Tables S4 and S5. Consequently, multiple imputation did not need to be modified.

3.5 | Qualitative evaluation

Participants and study partners who were interviewed after completing the trial responded positively to the intervention, although for some study partners this was tempered by the knowledge that dementia would continue to progress. Participants and study partners valued the relationship with the therapist, both for the specific focus on developing and personalising strategies and for the more general information and support provided. Interviewees said that

TABLE 1 Demographic and clinical characteristics of the participants and study partners

Measure	Whole Sample n = 474	CR n = 238	TAU n = 236
(a) Participants with dementia[a]			
Age, mean (SD), range	78.56 (7.07); 53 to 95	78.25 (7.13); 53 to 95	78.87 (7.01); 55 to 95
Sex (male), n (%)	248 (52.3)	124 (52.1)	124 (52.5)
Ethnicity, n (%):			
White	457 (96.4)	226 (95.0)	231 (97.9)
Mixed/multiple ethnic group	2 (0.4)	2 (0.8)	0 (0)
Asian/Asian British	6 (1.2)	3 (1.3)	3 (1.3)
Black/African/Caribbean/black British	7 (1.5)	5 (2.1)	2 (0.9)
Other ethnic group	2 (0.4)	2 (0.8)	0 (0)
First language (English), n (%)	445 (93.9)	222 (93.3)	223 (94.5)
Marital status (married), n (%)	330 (69.6) n = 474	167 (70.2) n = 238	163 (69.1) n = 236
Years of education	12.57 (3.37); 5 to 33 n = 471	12.57 (3.33); 6 to 24 n = 236	12.58 (3.42); 5 to 33 n = 235
Occupational status, n (%):			
I Professional	52 (11.0)	23 (9.7)	29 (12.3)
II Managerial/technical	157 (33.1)	81 (34.0)	76 (32.2)
III N Skilled, nonmanual	103 (21.7)	54 (22.7)	49 (20.8)
III M Skilled, manual	80 (16.9)	41 (17.2)	39 (16.5)
IV Partly skilled	50 (10.5)	24 (10.1)	26 (11.0)
V Unskilled	32 (6.8)	15 (6.3)	17 (7.2)
Diagnosis, n (%):			
Alzheimer's disease	284 (59.9)	139 (58.4)	145 (61.4)
Vascular dementia	74 (15.6)	43 (18.1)	31 (13.1)
Mixed	116 (24.5)	56 (23.5)	60 (25.4)
MMSE score, mean (SD), range	23.82 (3.02); 18 to 30	23.89 (3.04); 18 to 30	23.75 (3.02); 18 to 30
Charlson comorbidity index weighted score, mean (SD), range	2.52 (1.47); 1 to 11	2.49 (1.47); 1 to 11	2.55 (1.48); 1 to 10
Subjective rating of health, n (%):			
Excellent	39 (8.2)	20 (8.4)	19 (8.1)
Very good	125 (26.4)	65 (27.3)	60 (25.4)
Good	159 (33.5)	77 (32.4)	82 (34.7)
Fair	121 (25.5)	61 (25.6)	60 (25.4)
Poor	30 (6.3)	15 (6.3)	15 (6.4)
DEMQOL, mean (SD), range	92.30 (12.33); 39 to 112; n = 472	92.00 (12.90); 39 to 112; n = 237	92.61 (11.75); 39 to 112; n = 235
GSES, mean (SD), range	30.94 (5.09); 11 to 40; n = 469	30.75 (4.81); 13 to 40; n = 237	31.13 (5.35); 11 to 40; n = 232
HADS, mean (SD), range:	n = 472	n = 238	n = 234
Depression	3.77 (2.79); 0 to 14	3.87 (2.83); 0 to 12	3.67 (2.75); 0 to 14
Anxiety	5.14 (3.64); 0 to 16	5.29 (3.67); 0 to 16	4.98 (3.62); 0 to 16
RBMT, mean (SD), range:	n = 473	n = 237	n = 236
Immediate recall	2.66 (2.11); 0 to 11.5	2.58 (2.10); 0 to 9.5	2.73 (2.12); 0 to 11.5
Delayed recall	0.38 (1.96); −1 to 9	0.39 (1.94); −1 to 8	0.37 (1.97); −1 to 9
TEA, mean (SD), range:			
Elevator counting	6.39 (1.16); 0 to 7 n = 463	6.35 (1.27); 0 to 7 n = 232	6.42 (1.05); 1 to 7 n = 231
Elevator counting with distraction	4.55 (2.72); 0 to 9; n = 448	4.39 (2.68); 0 to 9; n = 223	4.72 (2.75); 0 to 9; n = 225
DKEFS verbal fluency, mean (SD), range	26.27 (11.82); 2 to 64; n = 470	25.78 (11.61); 2 to 64; n = 235	26.77 (12.03); 3 to 58; n = 235
Medication use, n (%) reporting use of:	n = 438	n = 215	n = 223
Dementia medications	332 (75.8)	157 (73.0)	175 (78.5)
Hypnotics and anxiolytics	3 (0.7)	1 (0.5)	2 (0.9)
Anti-psychotic medication	6 (1.4)	2 (0.9)	4 (1.8)
Antidepressants	98 (22.4)	57 (26.5)	41 (18.4)
Anti-epileptics	2 (0.5)	1 (0.5)	1 (0.5)

(Continues)

TABLE 1 (Continued)

Measure	Whole Sample n = 474	CR n = 238	TAU n = 236
(b) Study partners[b]			
Relationship to participant with dementia, n (%):			
Spouse/partner	331 (69.8)	167 (70.2)	164 (69.5)
Adult child (including in-law)	118 (24.9)	58 (24.3)	60 (25.4)
Other	25 (5.3)	13 (5.5)	12 (5.1)
Age, mean (SD), range	68.74 (13.01); 17 to 92	68.45 (13.76); 17 to 92	69.04 (12.24); 23 to 92
Sex (male), n (%)	142 (30.0)	75 (31.5)	67 (28.4)
Ethnicity, n (%):			
White	449 (94.7)	224 (94.1)	225 (95.3)
Mixed/multiple ethnic group	5 (1.1)	4 (1.7)	1 (0.4)
Asian/Asian British	10 (2.1)	4 (1.7)	6 (2.5)
Black/African/Caribbean/black British	8 (1.7)	6 (2.5)	2 (0.8)
Other ethnic group	2 (0.42)	0 (0)	2 (0.9)
First language (English), n (%)	443 (93.5)	222 (93.3)	221 (93.6)
Marital status (married), n (%)	393 (82.9)	187 (78.6)	206 (87.3)
Years of education, mean (SD), range	13.49 (3.52); 4 to 26; n = 472	13.67 (3.45); 5 to 25; n = 237	13.32 (3.58); 4 to 26; n = 235
Occupational status, n (%):			
I Professional	49 (10.3)	30 (12.6)	19 (8.1)
II Managerial/technical	158 (33.3)	74 (31.1)	84 (35.6)
III N Skilled, nonmanual	137 (28.9)	64 (26.9)	73 (30.9)
III M Skilled, manual	47 (9.9)	24 (10.1)	23 (9.7)
IV Partly skilled	55 (11.6)	27 (11.3)	28 (11.9)
V Unskilled	20 (4.2)	14 (5.9)	6 (2.5)
NA	8 (1.7)	5 (2.1)	3 (1.3)
Stress (RSS), mean (SD), range	n = 471; 18.96 (9.44); 0 to 52	n = 236; 18.85 (9.04); 2 to 46	n = 235; 19.08 (9.83);0 to 52
WHOQOL domains, mean (SD), range:			
Physical	n = 470; 15.34 (2.95); 5 to 20	n = 237; 15.30 (3.00); 5 to 20	n = 233; 15.37 (2.90); 7 to 20
Psychological	n = 470; 15.14 (2.15); 8 to 20	n = 237; 15.13 (2.19); 8 to 20	n = 233; 15.15 (2.10); 8 to 20
Social	n = 468; 15.13 (2.66); 5 to 20	n = 235; 15.19 (2.67); 5 to 20	n = 233; 15.07 (2.66); 7 to 20
Environmental	n = 470; 16.43 (2.15); 10 to 20	n = 237; 16.35 (2.30); 10 to 20	n = 233; 16.52 (1.99); 10 to 20
EQ 5D3L, mean (SD), range:			
Index	n = 468; 0.78 (0.25); −0.18 to 1	n = 235; 0.77 (0.25); −0.18 to 1	n = 233; 0.79 (0.24); −0.07 to 1
VAS	n = 467; 74.48 (19.95); 0 to 100	n = 234; 73.52 (20.95); 1 to 100	n = 233; 75.44 (18.90); 0 to 100

[a]Data are mean (SD) range, or n (%). CR, cognitive rehabilitation; TAU, treatment as usual; MMSE, Mini–Mental State Examination (higher scores indicate better performance); DEMQOL, people with dementia quality of life questionnaire (higher scores indicate better quality of life); GSES, Generalized Self-Efficacy Scale (higher scores indicate stronger sense of perceived self-efficacy); HADS, Hospital Anxiety and Depression Scale (higher scores indicate higher levels of anxiety and depression); RBMT, Rivermead Behavioural Memory Test (higher scores indicate better performance); TEA, Test of Everyday Attention (higher scores indicate better performance); D-KEFS, Delis-Kaplan Executive Function System (higher scores indicate better performance).

[b]Data are mean (SD) range, or n (%). CR, cognitive rehabilitation; TAU, treatment as usual; RSS, Relatives' Stress Scale (higher scores indicate higher levels of caregiving-specific stress); WHOQOL-BREF, World Health Organisation Quality of Life Instrument—brief version (higher scores indicate better quality of life); EQ 5D3L, European Quality of Life 5 Dimensions questionnaire Level version (higher score indicates higher health status); VAS, Visual Analogue Scale (higher score indicates higher health status).

the therapy had been effective in supporting engagement in everyday activities and had improved their adjustment to living with dementia, resulting in less anxiety, better coping skills, feelings of empowerment, and improved well-being and quality of life. Some commented that the intervention increased their problem-solving ability and enabled them to develop new strategies for different situations.

4 | DISCUSSION

The GREAT trial demonstrates that individualised, goal-oriented CR is an effective intervention for people with early-stage Alzheimer disease and vascular or mixed dementia wishing to improve aspects of their everyday functioning. Outcomes elicited from participants and study partners indicated that CR improved functioning in the areas targeted in the therapy

TABLE 2 Goal attainment ratings at baseline, 3-month and 9-month follow-up, and statistical comparisons

(a) Goal attainment ratings[a]

Measure	CR			TAU		
	Baseline (n = 238)	3 mo (n = 218)	9 mo (n = 205)	Baseline (n = 236)	3 mo (n = 227)	9 mo (n = 211)
Participant rating of attainment	3.53 (1.74)	6.10 (1.99)	6.05 (2.21)	3.55 (1.59)	4.41 (1.84)	4.22 (2.00)
Participant rating of satisfaction	3.76 (1.76)	6.47 (1.88)	6.75 (1.97)	3.86 (1.49)	5.05 (1.94)	5.26 (2.05)
Study partner rating of attainment	2.76 (1.43)	5.46 (1.94)	5.21 (2.33)	2.72 (1.32)	3.55 (1.73)	3.31 (1.96)

(b) Statistical comparison at 3-month follow-up[b]

Measure	*P*	Bonferroni Adjusted *P*[c]	Mean Difference	95% CI for Mean Difference	*d*	95% CI for *d*
Participant rating of attainment	<0.001	NA	1.58	1.27 to 1.90	0.81	0.62 to 1
Participant rating of satisfaction	<0.001	<0.001	1.34	1.01 to 1.66	0.7	0.51 to 0.88
Study partner rating of attainment	<0.001	<0.001	1.75	1.42 to 2.07	0.93	0.74 to 1.12

(c) Statistical comparison at 9-month follow-up[d]

Measure	*P*	Bonferroni Adjusted *P*[e]	Mean Difference	95% CI for Mean Difference	*d*	95% CI for *d*
Participant rating of attainment	<0.001	<0.001	1.71	1.35 to 2.08	0.8	0.61 to 0.99
Participant rating of satisfaction	<0.001	<0.001	1.36	1 to 1.73	0.67	0.49 to 0.86
Study partner rating of attainment	<0.001	<0.001	1.70	1.32 to 2.09	0.79	0.60 to 0.97

[a]Data are mean (SD). CR, cognitive rehabilitation; TAU, Treatment as usual.

[b]Analysis of covariance (ANCOVA) adjusted for baseline score, allocation group and stratification variables, age, gender, MMSE score and site. CI, confidence intervals. NA, not applicable, as no correction was planned for the primary outcome. The *d* effect size estimates were based on a fixed effect size model as they cannot be derived directly from the mixed-effects model and were calculated by converting eta squared to *r*, and then converting *r* to *d*.

[c]Nineteen adjustments in total to adjust for all the participant and carer outcome measure comparisons, except for the primary outcome.

[d]ANCOVA adjusted for baseline score, allocation group and stratification variables, age, gender, MMSE score and site. CI, confidence intervals. The *d* effect size estimates were based on a fixed effect size model as they cannot be derived directly from the mixed-effects model and were calculated by converting eta squared to *r*, and then converting *r* to *d*.

[e]Twenty adjustments in total to adjust for all the participant and carer outcome measure comparisons.

at 3 months, and this improvement was maintained at 9 months. When considering the goals actually addressed in therapy, improvements met criteria for clinical significance. High levels of adherence and low attrition indicated that the intervention was acceptable to participants and study partners. Participants and study partners interviewed in depth viewed the intervention positively and felt that it was beneficial.

4.1 | Strengths and limitations

A key strength is that the intervention targeted real-life situations and aimed to improve participants' functioning in areas that were meaningful to them, avoiding any problems relating to lack of transfer or generalisation of effects. The primary outcome was a proximal measure, directly evaluating perceptions of change in the areas targeted in the intervention. No trial-related adverse events or harms were identified.

There are several limitations to consider. Due to the constraints of trial design, the goal-setting interview was conducted by researchers not involved in delivering therapy, whereas in clinical practice, the goal-setting process would be undertaken by the therapist and might be more efficient. While participants were invited to select up to three goals, on average, the therapists were able to address two goals per participant. The primary outcome was based on ratings of progress with all goals identified at baseline, rather than just those goals that were actually addressed; therefore, the overall estimate of improvement in goal attainment is a conservative one. Ratings for the goals that were directly addressed showed a clinically meaningful degree of change. The trial design did not allow us to conclusively demonstrate that benefits were due to the specific effects of CR rather than nonspecific effects of contact with a therapist; however, the observed gains related specifically to improvements in functional ability for goals directly targeted in the therapy, and in the pilot trial, CR demonstrated benefits over an active control condition. In selecting secondary outcome measures, it would have been useful to include a measure of functional ability.

4.2 | How the findings relate to other evidence

The results confirm the finding from our pilot trial[13] that CR is effective in improving those aspects of everyday functioning targeted in the intervention. A different, but related, approach to improving everyday functioning involves structured training in completing selected activities of daily living. Two recent trials[35,36] found that performance on trained tasks improved, although there was no evidence of generalisation to everyday situations[35] or improvement in secondary outcomes such as quality of life. The only other large-scale trial

TABLE 3 Scores on secondary outcome measures at baseline, 3-month and 9-month follow-up, and statistical comparisons

(a) Scores for participants with dementia[a]

Measure	CR			TAU		
	Baseline	3 mo	9 mo	Baseline	3 mo	9 mo
DEMQOL	n = 237 92.00 (12.90) 39 to 112	n = 218 92.79 (11.95) 51 to 112	n = 204 92.36 (12.00) 54 to 112	n = 235 92.61 (11.75) 47 to 111	n = 227 93.20 (12.00) 51 to 111	n = 213 92.25 (12.82) 45 to 112
GSES	n = 237 30.75 (4.81) 13 to 40	n = 215 30.98 (4.62) 18 to 40	n = 194 30.76 (4.91) 15 to 40	n = 232 31.13 (5.35) 11 to 40	n = 224 30.59 (5.61) 11 to 40	n = 207 30.62 (5.60) 10 to 40
HADS depression	n = 238 3.87 (2.83) 0 to 12	n = 218 3.90 (2.86) 0 to 15	n = 194 4.19 (3.23) 0 to 17	n = 234 3.67 (2.75) 0 to 14	n = 226 3.74 (2.69) 0 to 12	n = 210 3.83 (2.82) 0 to 17
HADS anxiety	n = 238 5.29 (3.67) 0 to 16	n = 216 5.13 (3.66) 0 to 17	n = 193 5.63 (3.83) 0 to 18	n = 234 4.98 (3.62) 0 to 16	n = 226 4.61 (3.41) 0 to 15	n = 210 4.88 (3.37) 0 to 20
RBMT immediate recall	n = 237 2.58 (2.10) 0 to 9.50	n = 218 2.88 (2.16) 0 to 10	n = 200 2.34 (2.09) 0 to 10	n = 236 2.73 (2.12) 0 to 11.50	n = 226 2.79 (2.12) 0 to 11	n = 211 2.37 (1.96) 0 to 10
RBMT delayed recall	n = 237 0.39 (1.94) −1 to 8	n = 217 0.94 (2.31) −1 to 8.50	n = 200 0.23 (1.97) −1 to 8.50	n = 236 0.37 (1.97) −1 to 9	n = 225 0.66 (2.16) −1 to 11	n = 210 0.36 (1.97) −s1 to 9.50
TEA elevator counting	n = 232 6.35 (1.27) 0 to 7	n = 210 6.31 (1.23) 0 to 7	n = 191 6.21 (1.41) 0 to 7	n = 231 6.42 (1.05) 1 to 7	n = 219 6.36 (1.22) 0 to 7	n = 206 6.24 (1.32) 1 to 7
TEA elevator counting with distraction	n = 223 4.39 (2.68) 0 to 9	n = 198 4.62 (3.08) 0 to 10	n = 177 4.66 (3.11) 0 to 10	n = 225 4.72 (2.75) 0 to 9	n = 208 4.90 (3.15) 0 to 10	n = 193 4.52 (3.07) 0 to 10
DKEFS verbal fluency	n = 235 25.78 (11.61) 2 to 64	n = 217 26.29 (12.56) 0 to 58	n = 198 26.30 (13.32) 0 to 62	n = 235 26.77 (12.03) 3 to 58	n = 227 26.80 (12.38) 3 to 68	n = 211 25.90 (12.36) 1 to 67

(b) Scores for study partners[b]

Measure	CR			TAU		
	Baseline	3 mo	9 mo	Baseline	3 mo	9 mo
RSS	n = 236 18.85 (9.04) 2 to 46	n = 212 19.42 (9.62) 2 to 46	n = 200 21.23 (9.92) 2 to 51	n = 235 19.08 (9.83) 0 to 52	n = 221 20.42 (10.33) 1 to 54	n = 211 21.65 (10.74) 2 to 50
WHOQOL physical	n = 237 15.30 (3.00) 5 to 20	n = 212 15.20 (2.93) 5 to 20	n = 199 14.95 (3.14) 6 to 20	n = 233 15.37 (2.90) 7 to 20	n = 220 15.07 (2.86) 6 to 20	n = 210 14.78 (2.97) 6 to 20
WHOQOL psychological	n = 237 15.13 (2.19) 8 to 20	n = 212 14.98 (2.21) 7 to 20	n = 199 14.74 (2.41) 7 to 20	n = 233 15.15 (2.10) 8 to 20	n = 220 14.74 (2.20) 7 to 20	n = 210 14.53 (2.38) 7 to 20
WHOQOL social	n = 235 15.19 (2.67) 5 to 20	n = 211 15.03 (2.47) 7 to 20	n = 197 15.04 (2.72) 8 to 20	n = 233 15.07 (2.66) 7 to 20	n = 219 14.80 (2.58) 7 to 20	n = 210 14.51 (2.83) 5 to 20
WHOQOL environmental	n = 237 16.35 (2.30) 10 to 20	n = 212 16.33 (2.26) 9 to 20	n = 199 16.00 (2.40) 9 to 20	n = 233 16.52 (1.99) 10 to 20	n = 220 16.18 (2.04) 10 to 20	n = 210 16.04 (2.05) 11 to 20
EQ 5D3L index	n = 235	n = 209	n = 196	n = 233	n = 217	n = 211

(Continues)

TABLE 3 (Continued)

	0.77 (0.25) −0.18 to 1	0.75 (0.24) −0.18 to 1	0.73 (0.27) −0.18 to 1	0.79 (0.24) −0.07 to 1	0.74 (0.25) −0.24 to 1	0.75 (0.23) −0.07 to 1
EQ 5D3L VAS	n = 234 73.52 (20.95) 1 to 100	n = 208 74.13 (18.92) 0 to 100	n = 198 74.14 (19.16) 10 to 100	n = 233 75.44 (18.90) 0 to 100	n = 217 73.14 (18.95) 0 to 100	n = 211 72.42 (19.13) 0 to 100
(c) Statistical analyses at 3-month follow-up[c]						
Measure	***P*[d]**	**Bonferroni Adjusted *P***	**Mean Difference**	**95% CI for Mean Difference**	***d***	**95% CI for *d***
Participants with dementia						
DEMQOL	0.738	1.000	0.24	−1.27 to 1.75	0.02	−0.16 to 0.20
GSES	0.126	1.000	0.58	−0.16 to 1.32	0.11	−0.07 to 0.29
HADS depression	0.861	1.000	0.00	−0.42 to 0.41	0.02	−0.16 to 0.20
HADS anxiety	0.478	1.000	0.17	−0.30 to 0.65	0.06	−0.12 to 0.24
RBMT immediate recall	0.189	1.000	0.19	−0.10 to 0.48	0.10	−0.08 to 0.28
RBMT delayed recall	0.096	1.000	0.24	−0.04 to 0.52	0.12	−0.06 to 0.30
TEA elevator counting	0.799	1.000	0.01	−0.19 to 0.21	0.02	−0.16 to 0.20
TEA elevator counting with distraction	0.784	1.000	0.01	−0.45 to 0.47	0.03	−0.15 to 0.21
DKEFS verbal fluency	0.794	1.000	0.15	−1.12 to 1.41	0.02	−0.16 to 0.20
Study partners						
RSS	0.382	1.000	−0.50	−1.61 to 0.62	0.05	−0.13 to 0.23
WHOQOL physical	0.431	1.000	0.12	−0.18 to 0.42	0.04	−0.14 to 0.22
WHOQOL psychological	0.214	1.000	0.18	−0.10 to 0.47	0.08	−0.10 to 0.26
WHOQOL social	0.572	1.000	0.10	−0.25 to 0.45	0.05	−0.13 to 0.23
WHOQOL environmental	0.050	0.947	0.26	0 to 0.51	0.13	−0.06 to 0.31
EQ 5D3L index	0.295	1.000	0.02	−0.01 to 0.05	0.07	−0.11 to 0.25
EQ 5D visual analogue scale	0.286	1.000	1.58	−1.31 to 4.47	0.09	−0.09 to 0.27
(d) Statistical analyses at 9-month follow-up[e]						
Measures	***P*[f]**	**Bonferroni Adjusted *P***	**Mean Difference**	**95% CI for Mean Difference**	***d***	**95% CI for *d***
Participants with dementia						
DEMQOL	0.215	1.000	1.08	−0.62 to 2.78	0.09	−0.09 to 0.27
GSES	0.38	1.000	0.37	−0.45 to 1.18	0.07	−0.11 to 0.25
HADS depression	0.614	1.000	0.12	−0.35 to 0.6	0.05	−0.13 to 0.23
HADS anxiety	0.334	1.000	0.26	−0.26 to 0.77	0.08	−0.1 to 0.26
RBMT immediate recall	0.496	1.000	0.10	−0.19 to 0.4	0.06	−0.12 to 0.24
RBMT delayed recall	0.466	1.000	−0.10	−0.37 to 0.17	0.06	−0.12 to 0.24
TEA elevator counting	0.718	1.000	−0.01	−0.27 to 0.25	0.04	−0.14 to 0.22
TEA elevator counting with distraction	0.334	1.000	0.23	−0.23 to 0.69	0.09	−0.09 to 0.27
DKEFS verbal fluency	0.342	1.000	0.71	−0.75 to 2.16	0.06	−0.12 to 0.24
Study partners						
RSS	0.808	1.000	0.08	−1.09 to 1.25	0.02	−0.16 to 0.2
WHOQOL physical	0.399	1.000	0.14	−0.19 to 0.47	0.05	−0.13 to 0.23
WHOQOL psychological	0.346	1.000	0.15	−0.16 to 0.45	0.06	−0.12 to 0.24
WHOQOL social	0.049	0.93	0.41	0 to 0.81	0.15	−0.03 to 0.33
WHOQOL environmental	0.371	1.000	0.13	−0.15 to 0.4	0.06	−0.12 to 0.24
EQ 5D3L index	0.547	1.000	−0.01	−0.04 to 0.02	0.04	−0.14 to 0.22
EQ 5D visual analogue scale	0.071	1.000	2.60	−0.22 to 5.42	0.14	−0.04 to 0.32

[a]Data are mean (SD) range. CR, cognitive rehabilitation; TAU, treatment as usual; DEMQOL People with DEMentia Quality Of Life questionnaire (higher scores indicate better quality of life); GSES, Generalized Self-Efficacy Scale (higher scores indicate stronger sense of perceived self-efficacy); HADS, Hospital Anxiety and Depression Scale (higher scores indicate higher levels of anxiety and depression); RBMT, Rivermead Behavioural Memory Test (higher scores indicate better performance); TEA, Test of Everyday Attention (higher scores indicate better performance); D-KEFS, Delis-Kaplan Executive Function System (higher scores indicate better performance).

[b]Data are mean (SD) range. CR, cognitive rehabilitation; TAU, treatment as usual; RSS, Relatives' Stress Scale (higher scores indicate higher levels of caregiving-specific stress); WHOQOL-BREF, World Health Organisation Quality of Life Instrument—brief version (higher scores indicate better quality of life); EQ 5D3L, European Quality of Life 5 Dimensions questionnaire Level version (higher score indicates higher health status); VAS, Visual Analogue Scale (higher score indicates higher health status).

[c]DEMQOL, People with DEMentia Quality Of Life questionnaire (higher scores indicate better quality of life); GSES, Generalized Self-Efficacy Scale (higher scores indicate stronger sense of perceived self-efficacy); HADS, Hospital Anxiety and Depression Scale (higher scores indicate higher levels of anxiety and depression); RBMT, Rivermead Behavioural Memory Test (higher scores indicate better performance); TEA, Test of Everyday Attention (higher scores indicate better performance); D-KEFS, Delis-Kaplan Executive Function System (higher scores indicate better performance). RSS, Relatives' Stress Scale (higher scores indicate higher levels of caregiving-specific stress); WHOQOL-BREF, World Health Organisation Quality of Life Instrument—brief version (higher scores indicate better quality of life); EQ 5D3L, European Quality of Life 5 Dimensions questionnaire Level version (higher score indicates higher health status); VAS, Visual Analogue Scale (higher score indicates higher health status). The *d* effect size estimates were based on a fixed effect size model as they cannot be derived directly from the mixed-effects model and were calculated by converting eta squared to *r*, and then converting *r* to *d*.

[d]Nineteen adjustments in total to adjust for all the participant and carer outcome measure comparisons, except for the primary outcome.

[e]DEMQOL People with DEMentia Quality Of Life questionnaire (higher scores indicate better quality of life); GSES, Generalized Self-Efficacy Scale (higher scores indicate stronger sense of perceived self-efficacy); HADS, Hospital Anxiety and Depression Scale (higher scores indicate higher levels of anxiety and depression); RBMT, Rivermead Behavioural Memory Test (higher scores indicate better performance); TEA, Test of Everyday Attention (higher scores indicate better performance); D-KEFS, Delis-Kaplan Executive Function System (higher scores indicate better performance). RSS, Relatives' Stress Scale (higher scores indicate higher levels of caregiving-specific stress); WHOQOL-BREF, World Health Organisation Quality of Life Instrument—brief version (higher scores indicate better quality of life); EQ 5D3L, European Quality of Life 5 Dimensions questionnaire Level version (higher score indicates higher health status); VAS, Visual Analogue Scale (higher score indicates higher health status). The *d* effect size estimates were based on a fixed effect size model as they cannot be derived directly from the mixed-effects model and were calculated by converting eta squared to *r*, and then converting *r* to *d*.

[f]Twenty adjustments in total to adjust for all the participant and carer outcome measure comparisons.

of CR[37] reported that, compared with usual treatment, CR participants showed less functional decline at 24 months, a 6-month delay in institutionalisation and lower overall rates of institutionalisation, but no significant differences mood or quality of life. The CR intervention in that trial was poorly described, and goal attainment was not directly measured.

These findings taken together indicate that it is possible to promote improved functional ability through both CR and structured training. In CR, this improvement directly benefits targeted areas of everyday life, whereas the improvements observed following structured task-specific training may not generalise to real-life situations. Other benefits resulting from CR or structured training are not captured by available standardised outcome measures. In GREAT, there are several possible explanations for the lack of change in secondary outcomes. The finding of no differences in cognitive test scores was unsurprising as the intervention does not directly seek to improve cognitive function. As only a small proportion of participants reported clinical levels of depression or anxiety at baseline, there was little scope for the intervention to demonstrate improvements in these domains. The absence of reduction in stress for study partners might be explained by the fact that the intervention did require effort from them, both to engage when they may feel they have already tried various strategies without success and to support the implementation of strategies through the therapy. However, the qualitative findings were at odds with the results from secondary outcome measures. The intervention may therefore have provided wider benefits that were not detected by available standardised measures.

4.3 | Implications

The study shows that people with dementia are able to identify key goals and are motivated to address them. Readiness to make changes in these areas predicts outcome and is an important factor for practitioners to consider at initial assessment. However, only those provided with structured support are able to make demonstrable progress in attaining their goals. Engagement in this process is crucial for progress to be made and is facilitated through the positive relationship with the practitioner and the encouragement and support the practitioner provides. The findings demonstrate the potential of practical interventions to enable people with dementia to function better in areas that are important to them and that can make a difference to their lives. While GREAT followed a structured protocol, CR is not a fixed intervention and can be adapted to different contexts to meet a variety of needs.[5] If CR can be delivered in real-world practice in a cost-effective manner, it could form a component of postdiagnostic care pathways for those recently diagnosed who would welcome support to develop strategies for living with dementia, or of community reablement or home care packages for those with more complex needs.

5 | CONCLUSIONS

Individual, goal-oriented CR enables people with dementia to function better and more independently in relation to goals targeted in the therapy. This personalised approach addresses individual concerns in the home setting and can be applied flexibly to meet different kinds of need. Enablement is an appropriate objective for services that support people with dementia, and the application of CR provides a means of translating this objective into practical support in a way that is acceptable and relevant to people with dementia and their families. CR can potentially contribute to improving the choice of interventions available to people living with dementia who have mild-to-moderate cognitive impairment, helping to address the current gap in provision of psychosocial interventions.[1]

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CONFLICT OF INTEREST

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, and no other relationships or activities that could appear to have influenced the submitted work.

AUTHOR CONTRIBUTIONS

L.C., B.W., J.O., R.W.J., A.Ba., M.Ko., M.Kn., and J.P. conceived the study, wrote the protocol, and obtained funding. L.C. led the trial. A. Ku. managed the day-to-day running of the trial. B.W., J.O., R.W.J., M.Ko., I.L., I.A.G., and A.C. were local principal investigators responsible for the running of the trial at each site. Z.H., A.Br., and C.H. planned and conducted statistical analyses. L.C. drafted the article and is the guarantor. All authors contributed to the interpretation of the results and reviewed and approved the final manuscript. This report represents independent research commissioned by the NIHR. The views and opinions expressed by the authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme, or the Department of Health.

DATA SHARING

Requests to access the full quantitative dataset may be directed to the lead author (L.C.).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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