Original article

Parkinson's-adapted Cognitive Stimulation Therapy: A pilot randomised controlled clinical trial

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ABSTRACT

Cognitive Stimulation Therapy (CST) is widely used with people with dementia, but there is no evidence of its efficacy in mild cognitive impairment or dementia in Parkinson's disease (PD-MCI; PDD) or dementia with Lewy bodies (DLB). We aimed to explore the impact of 'CST-PD', which is home-based, individualised CST adapted for this population. In a single-blind randomised controlled exploratory pilot trial (RCT), we randomised 76 participant-dyads (PD-MCI (n=15), PDD (n=40), DLB (n=21) and their care partners) to CST-PD or treatment-as-usual (TAU). CST-PD involves home-based cognitively stimulating and engaging activities delivered by a trained care partner. Exploratory outcomes at 12 weeks included cognition (Addenbrooke's Cognitive Evaluation; ACE-III), neuropsychiatric symptoms and function. In care partners, we assessed burden, stress and general health status. Relationship quality and quality of life were assessed in both dyad members. At 12 weeks, the ACE-III showed a non-statistically significant improvement in the CST-PD group compared to the TAU group, although neuropsychiatric symptoms increased significantly in the former. In contrast, care partners' quality of life (d = 0.16) and relationship quality ('satisfaction', d=0.01; 'positive interaction', d = 0.55) improved significantly in the CST-PD group, and care burden (d = 0.16) and stress (d = 0.05) were significantly lower. Qualitative findings in the CST-PD recipients revealed positive 'in the moment' responses to the intervention, supporting the quantitative results. In conclusion, care partner-delivered CST-PD may improve a range of care partner outcomes, which are important in supporting home-based care. A full-scale follow-up RCT to evaluate clinical and cost-effectiveness is warranted.

INTRODUCTION

Disorders of cognitive impairment within the Lewy body spectrum of diseases include mild cognitive impairment in Parkinson's disease (PD-MCI), dementia due to Parkinson's disease (PDD) and dementia with Lewy bodies (DLB). Together, DLB and PDD constitute over 15%[1] of total dementias and PD-MCI occurs in about 25% of people with Parkinson's disease (PD).[2,3] PDD and DLB are associated with significant impairments in cognition, quality of life and high levels of disability and care partner burden.[4] Treatment options focus on pharmacological approaches, which have modest effectiveness and may often not be tolerated by frail people with dementia in the context of a movement disorder. Thus, there is scope for non-pharmacological interventions that are specifically adapted for people with cognitive impairment or dementia within the Lewy body spectrum.[5] To date, only one other study of a psychosocial intervention in PDD has been conducted, and this study examined the impact of goal-oriented cognitive rehabilitation therapy.[6] This small study found positive outcomes self-rated goal attainment, mood, and quality of life in those receiving the active intervention compare to relaxation therapy and 'treatment as usual'.

Cognitive Stimulation Therapy (CST) is an evidence-based psychosocial intervention that involves engaging and cognitively-stimulating activities and discussions based on principles of errorless learning and validation.[7,8] As demonstrated by meta-analyses, CST improves cognition and quality of life in people with different forms of dementia, and improves outcomes, such as quality of life, for care partners.[9,10] In people with PDD, only one study has evaluated CST.[11] This was a small pilot cross-over trial (n=12) of people living in a care home setting. It found that group CST (offered eight weeks, twice weekly for 60 minutes), adapted for PDD, is feasible and potentially effective for cognitive and non-cognitive outcomes in PDD, compared to 'treatment as usual'.

We undertook an iterative development process to adapt the individualised form of CST (iCST) specifically for people with PD-MCI/PDD/DLB to be delivered by their care partners at home (PD-CST).[12] PD-CST differs from professionally delivered group-based CST, in that PD-CST can be delivered at home by a trained care partner and can be tailored more easily to the specific needs and capabilities of the recipient. Here we report the results of an exploratory pilot study of the impact of PD-CST on recipients of the intervention and their care partners. In addition, we evaluated the acceptability of the intervention and the feasibility of conducting a full-scale

RCT. We found that PD-CST was well tolerated and acceptable, with certain modifications, by people with PD-MCI/PDD/DLB and their care partners, and that the trial design was feasible (reported elsewhere).[13]

PARTICIPANTS AND METHODS

The full protocol is published in detail elsewhere.[14]

Standard protocol approvals, registrations, and patient consents

The study received favourable ethical opinion from Yorkshire & Humber – Bradford Leeds Research Ethics Committee (reference: 15/YH/0531) and was performed in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice. The study was registered at isrctn.com (registration number ISRCTN11455062). All participants were volunteers and provided written informed consent or consultee agreement to participate in the study.

Study design and participants

The INVEST study was a single-blind parallel arm RCT, conducted at seven sites in the UK, to explore the impact of CST-PD compared to treatment-as-usual (TAU) on cognitive, behavioural, care partner and other dementia-related outcomes in people with PD-MCI/PDD/DLB and their care partners. Since this was the first time home-based CST adapted for this population had been tested and we had no *a priori* evidence of how the intervention would be received, we specifically included participants with different levels of cognitive impairment, ranging from MCI to moderate-stage dementia.

We recruited people with PD-MCI/PDD/DLB and their care partners as participant-dyads if they met the following inclusion criteria: (1) diagnosis of PD-MCI (Level 1), PDD (probable or possible) or DLB (probable or possible) according to standard clinical diagnostic criteria;[15-17] (2) willing and able to participate in the intervention; and (3) on stable medication for at least four weeks prior to study entry. Exclusion criteria were: (1) unwilling or unable to participate; (2) contact with a care partner three times or less per week; (3) no care partner or companion able to participate; (4) living in residential care; (5) unable to understand conversational English; and (6) neuropsychiatric complications too severe (i.e. depression, psychosis or fluctuating levels of cognitive impairment/delirium) to enable participation in the study (as per expert clinicians' judgement). Care partners were included if they provided care or support for

the participant with cognitive impairment and were well enough to be trained to deliver the intervention. Care partners were excluded if they were unable to understand conversational English, were non-literate or had severe physical illness or dementia (as per self-report and performance on the Montreal Cognitive Assessment).[18] All PD-MCI/PDD/DLB participants (n=76) had the capacity to consent to participation at the start of the trial. During the trial, four participants lost the capacity to consent, thus a nominated consultee was appointed enableing all four to continue in the study.

Randomisation and blinding

The Manchester Academic Health Science Centre Clinical Trials Unit, as an independent arbiter applied a single-strata, blocked randomisation to CST-PD or TAU at a 1:1 level by participant-dyad. Due to the nature of the intervention, dyads were not blind to treatment allocation but procedures were in place to conceal the allocation from the independent, blinded outcome raters. Following randomisation, the distribution of the tree diagnostic sub-groups (PD-MCI, PDD and DLB) was balanced across the two arms with respect to MCI and dementia.

Intervention

The details of the intervention and how we adapted it to the specific needs of people with PD-MCI, PDD or DLB is outlined in McCormick et al. 2017a.[12] The adaptation process took account of several factors, including the cognitive profile (e.g. particular challenges with executive function, recall and visuospatial deficits), fatigue and apathy, fluctuating levels of attention, motor and general physical frailty of this population. The adapted intervention, CST-PD, entailed care partner-delivered manual-based individualised CST-based therapy sessions, delivered at home for 30 minutes per session, two to three times per week. The activities varied in theme and complexity and could be tailored to suit individual needs. The adapted therapy manual comprised over 60 topics categorized into nine different themes, with each topic containing several cognitively stimulating activities such as discussion topics, word association games, and creative tasks. Activities varied in complexity and were matched and adapted to suit the needs of the recipient. The manual itself was paper-based, easy to handle and had large accessible print. It was indexed to enable ease of use. All care partners were trained to deliver the therapy as intended. The TAU group, which received no additional intervention, provided a comparison with the CST-PD group. Any additional non-pharmacological interventions that the participants in the TAU group might have received following randomization (e.g. physiotherapy, occupational therapy, speech therapy) were noted by the research team.

Procedure

Following consent, participant-dyads underwent a screening period to ensure eligibility. Participants meeting inclusion criteria received two to three care partner-delivered CST-PD sessions of 30 minutes each or TAU for 12 weeks. Prior to the intervention being delivered, care partners in the intervention arm received a two-hour protocol-guided training session of CST-PD, delivered in their own homes by a member of the research team. Training included a researcher-guided therapy session with the person with PD-MCI/PDD/DLB. The researcher completed a protocol training checklist and provided additional training and telephones support as needed, based on a skills' checklist. Assessments took place at baseline and 12-weeks. Participants who withdrew from the study before their scheduled assessment visits received an early termination assessment. Those experiencing a serious adverse event withdrew from the study. Feasibility, acceptability and tolerability evaluations were also undertaken (reported in McCormick et al.).[13] Assessments for people with PD-MCI/PDD/DLB included: cognition, neuropsychiatric symptoms, quality of life, functional ability, relationship satisfaction and resilience (Table 1). Care partner assessments were: quality of life, health ratings, relationship satisfaction, burden and resilience (Table 1). Care partners in the CST-PD group used diaries to report adherence of sessions and 11 participant-dyads completed a semi-structured interview to elicit their views and experiences of the intervention.

Outcome measures

The primary outcomes of the overall INVEST study were tolerability, acceptability and feasibility (reported in McCormick et al.).[13] Here we report a range of exploratory participant and care partner outcomes (see Table 1) including cognition, behaviour, function, quality of life and care partner burden and stress. We also examined aspects of the dyadic relationship, resilience and empathy. All rated outcomes were undertaken by highly trained research nurses with extensive experience in dementia and PD-related research. Additionally, qualitative outcomes using observational data from participant-dyad diaries, completed after each therapy session, and semi-structured interviews, in a sub-sample of the CST-PD group were also included.

'Feasibility' included a detailed evaluation of eligibility, recruitment and retention rates, overall trial design (the degree to which the protocol balanced scientific and practical considerations), willingness to be randomised, blinding procedures and data collection (i.e.

timing, quality, acceptability). ‘Acceptability’ was the extent to which the participant-dyads considered the intervention ‘appropriate’ (i.e. care partner’s perceptions of the recipient’s interest, motivation and sense of achievement following each therapy session) and the ability of recipients endure the intervention (i.e. adverse event rate).

Table 1 Outcome measure descriptions.

			Respondent	
Outcome domain	**Specific measurement tool**	**Description of the tool**	**Person with PD-MCI/PDD /DLB**	**Care partners**
Cognition	**The Addenbrooke's Cognitive Examination** (ACE-III) [a 19]	Global cognition (total score) and cognitive sub-domains of memory, attention, verbal fluency, language and visuospatial function.	✓	
	The Dementia Cognitive Fluctuation Scale (DCF) [b 20]	Fluctuations in person with PD-MCI/PDD/DLB cognition reported by the care partner.	✓ (proxy)	
Functional ability	**The Pill questionnaire** [b 21]	The ability to undertake a specific activity of daily living (i.e. medication intake).	✓	
Quality of life	**The Parkinson's Disease Questionnaire-39** (PDQ-39) [b 22]	Parkinson's-specific quality of life.	✓	
	The EuroQoL-5D (EQ5D) [a 23]	Health-related quality of life.	✓	✓
Neuropsychiatric symptoms (NPS)	**The Neuropsychiatric Inventory** (NPI) [b 24]	Presence and magnitude of 'clinically significant' (frequency x severity ≥4) of NPS sub-domains reported by the care partner.	✓ (proxy)	
	The Hospital Anxiety and Depression Scale (HADS) [b 25]	Self-rated anxiety and depression.	✓	✓
	The Lille Apathy Rating Scale (LARS) [b 26]	Self-rated apathy.	✓	
Health	**The Short Form-12 Health Survey** (SF-12) [a 27]	General physical and mental health.		✓
Relationship quality	**The Relationship Satisfaction Scale** (RSS) [a 28]	Satisfaction with the dyadic relationship.	✓	✓
	The Dyadic Relationship Scale (DRS) [a,b 29]	Positive dyadic interaction and negative strain.		✓

	The Family Caregiving Role Scale (FCR) [a,b 30]	Specific feelings associated to care provision.		✓
Burden	**The Zarit Burden Interview** (ZBI) [b 31]	Burden related to care provision.		✓
	The Relatives' Stress Scale (Rel.SS) [b 32]	Stress related to care provision.		✓
Resilience	**The Brief Resilience Scale** (BRS) [a 33]	The ability to bounce back in stressful situations.	✓	✓
Empathy	**The Interpersonal Reactivity Index** (IRI) [a 34]	Empathic tendencies and perspective taking.	✓	

Notes: [a] Higher scores better; [b] Higher scores worse.

Sample size

We based our sample size calculation on previous studies,[35] and took a conservative approach, estimating the standardised effect size on cognition to be 0.4. As this was a pilot feasibility trial, we chose a one-sided test and a less stringent significance level of 0.2 to avoid missing a promising effect. Thus, assuming 80% power and a correlation coefficient of 0.5 between baseline and endpoint on cognitive outcomes, the required sample size was 27 completers per group. By enrolling 32 dyads per group, it allowed for a 15% attrition rate. For the secondary, exploratory outcomes, the proposed sample size of 27 per group was within the recommended guidelines (24–50 participants[35,36]) required to estimate the SD for a sample size calculation. Since the attrition rate was higher than expected during the first year of recruitment (28%), we obtained ethical approval to enrol 38 dyads per group to maintain the target number of completers.

Data analysis

Since this was an exploratory trial of a new complex intervention, we agreed *a priori* to interpret the results with caution. Thus, although we undertook initial inferential statistics and hypothesis testing, our goal was to uncover any important potential associations in the study variables.[37] For this reason, we evaluated statistical significance at the 0.2 level using a one-sided test. Specifically, we explored changes in measures between the two groups (CST-PD and TAU) over time using ANCOVA, controlling for baseline values. All analyses were conducted on an intention-to-treat basis, on complete case data. For the *qualitative analysis*, using NVivo 11 software[38], data from participant-dyad diaries, researcher field notes, and semi-structured interviews were used. We triangulated the results of our quantitative findings with thematic analysis.[39] Using an inductive process, we systematically extracted codes from each data source to derive key themes; these were subsequently triangulated with the quantitative outcome to establish correspondence between the qualitative and qualitative data. We arrived at the final themes by consensus of five INVEST investigators (IL, SV, SM, SS and BK).

RESULTS

The 76 recruited participant-dyads were randomised to either the CST-PD (n=38) or the TAU group (n=38) following randomisation (Figure 1). Characteristics of participant-dyads are outlined in Table 2. Twenty-one per cent (n=16) of participants with PD-MCI/PDD/DLB were female and all were native English speakers. Diagnoses included 19.8% (n=15) PD-MCI,

52.6% (n=40) PDD, and 27.6% (n=21) DLB. Of the care partners, 89% (n=68) were female, and 77.6% (n=59) were spouses or live-in partners and 17.1% (n=13) were adult children. The remaining four care partners included a grandchild, a friend, a live-in carer and a divorcee. Of those randomised, 72% completed the full study protocol.

Baseline demographics revealed a relatively good case mix between the two arms, with only education and diagnosis seeing a slight imbalance (see Table 2). Descriptive statistics of the outcome measures at baseline are presented in Table 2. There were also some imbalances in baseline outcome scores between the two arms, suggesting randomisation was not fully successful, possibly due to the small sample size. We avoided any potential bias by controlling for baseline scores in the analysis. No cognitive enhancing medications were changed during the course of the study.

Preliminary analysis compared the effect of treatment allocation and baseline characteristics of subjects with and without complete data at follow-up using a logistic model for each outcome. Differential missingness was observed in the treatment arms, with a higher proportion of missing data in the intervention arm. For the primary outcome, data were missing for 21 individuals, 6 (29%) in the control arm and 15 (71%) in the intervention arm. We found no differential missingness conditional on the participant characteristics; thus, we proceeded with the main analysis under the 'missing at random' assumption.

A total of 56 participant-dyads completed the study, 24 in the CST-PD group and 32 in the TAU group. Using ANCOVA to model group differences of change in cognition at 12 weeks by adjusting for baseline scores, global cognition (ACE-III) improved by 1.7 on average in the CST-PD group compared to the TAU group; however, this difference was not statistically significant [Adjusted mean difference (AMD) = 1.7, Cohen's d = 0.38, p = 0.227]. The results of the exploratory measures revealed a number of potential changes in outcomes for both intervention recipients and care partner groups and are presented in Table 3. For intervention recipients, the CST-PD group had statistically lower scores on the verbal fluency sub-scale of the ACE-III (AMD = -0.74, d = 0.35 , p = 0.134), higher scores on the Neuropsychiatric Inventory (NPI) total signalling greater symptoms (AMD = 4.46, d = 0.42, p = 0.049), as well as the proportion of 'clinically significant' (FxS score $\geq$ 4) and 'clinically present' NPI (FxS score >1) scores (AMD = 0.05, d = 0.35, p = 0.078; AMD = 0.05, d = 0.25, p = 0.173, respectively), the Brief Resilience Scale (AMD = -1.17, d = 0.12, p = 0.174), and the

Perspective Taking subscale of the Interpersonal Reactivity Index (AMD = -1.32, d = 0.03, p = 0.082). Conversely, for the care partner sample, CST-PD resulted in statistically significant *improvements* compared to TAU on quality of life [EuroQol index (AMD = 0.08, d = 0.16, p = 0.048) and visual analogue scale measures (AMD = 4.76, d = 0.07, p = 0.104)], burden and stress [Zarit Burden Interview (AMD = -2.24, d = 0.16, p = 0.193), and the Relatives' Stress Scale (AMD = -1.75, d = 0.05, p = 0.160), respectively] and relationship quality [Relationship Satisfaction Scale (AMD = 3.46, d = 0.01, p = 0.020), and the Dyadic Relationship Scale positive interaction subscale (AMD = 1.76, d = 0.55, p = 0.015)]. In contrast, care partners in the CST-PD group reported a significant increase in anxiety symptoms measured by the HADS (AMD = 1.03, d = 0.30, p = 0.112). Adherence data, retention and integrity of blinding (for details see elsewhere)[13] revealed that over two thirds of participants in the CST-PD group received the recommended dose of at least 60 minutes of therapy per week.

Figure 1 CONSORT 2010 Flow Diagram

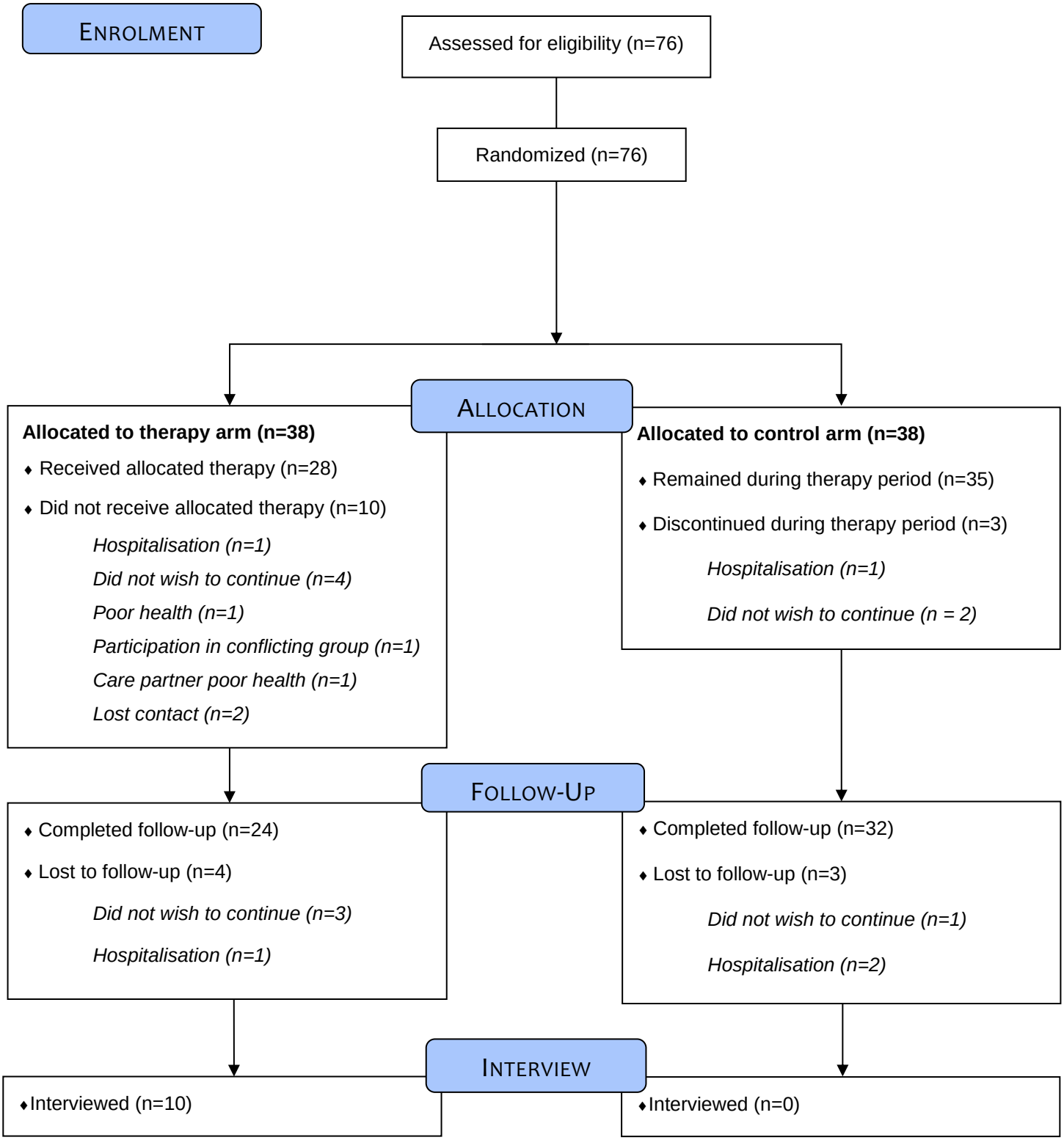

Table 2 Baseline demographic and clinical variables in the active intervention (CST-PD) and control (TAU) groups.

Demographics and other variables		**People with PD-MCI/PDD/DLB (n = 76)**				**Care partners (n = 76)**			
		Control		**Intervention**		**Control**		**Intervention**	
Categorical variables		**n**	**%**	**N**	**%**	**n**	**%**	**n**	**%**
Gender	Female	8	21.05	8	21.05	35	92.11	33	86.84
	Male	30	78.95	30	78.95	3	7.89	5	13.16
Ethnicity	White	35	92.11	36	94.74	35	92.11	35	92.11
	Non-white	2	5.26	2	5.26	2	5.26	3	7.89
	Did not specify	1	2.63	0	0.00	1	2.36	0	0.00
Education level	Up to 18 year old schooling	22	57.89	18	47.37	20	52.63	17	44.74
	Further education and higher	16	42.11	20	52.63	18	47.37	21	55.26
Marital status	Single	6	15.79	6	15.79	7	18.42	6	15.79
	Married/ Partnership	32	84.21	32	84.21	31	81.58	32	84.21
Living status	Alone	5	13.16	1	2.63	2	5.26	0	0.00
	With others	33	86.84	37	97.37	36	94.74	38	100.00
Diagnosis	PD-MCI	8	21.05	7	18.42				
	PDD	18	47.37	22	57.89				
	DLB	12	31.58	9	23.68				
Relationship	Spouse/ partner					28	73.68	31	81.58

	Son/daughter					9	23.68	4	10.53
	Other					1	2.63	3	7.89
Caregiving weekly hours (Up to an average of)	1 hour per day					10	26.32	5	13.16
	8 hours per day					9	23.68	13	34.21
	24 hours a day					19	50.00	20	52.63
Continuous variables		**n**	**Median; IQR [range]**	**n**	**Median; IQR [range]**	**n**	**Median; IQR [range]**	**n**	**Median; IQR [range]**
Age, years		38	75; 72-81 [61-90]	38	74.50; 68-77 [55-84]	38	68.50; 59-72 [43-85]	38	67; 59-71 [21-88]
Dyad known, years						29	50; 43-56 [3-68]	34	46; 30-52 [0.5-70]
Caregiving, years						38	2.50; 1-6 [0-15]	38	3.25; 1.5-8 [0-20]
Montreal Cognitive Assessment (MoCA)		35	19; 15-22 [7-24]	36	17.5; 15-21.5 [8-30]				
Schwab-England score		37	60; 35-80 [10-100]	37	60; 30-70 [10-90]				
UPDRS motor score		38	34; 17.50-40.25 [9-69]	37	24; 18-38 [8-58]				
Duration of clinical symptoms, years		38	5.5; 2-10 [0-33]	38	4; 2-10.50 [0.5 –24]				

Baseline variables		**n**	**Mean (SD)**	**n**	**Mean (SD)**	**n**	**Mean (SD)**	**n**	**Mean (SD)**
Cognition	ACE-III total	36	63.78 (15.15)	35	68.69 (14.73)				
	Attention	36	13.06 (2.78)	35	13.23 (2.52)				
	Memory	36	14.22 (5.17)	35	15.91 (5.87)				
	Verbal Fluency	36	4.69 (2.64)	35	6.23 (3.21)				
	Language	36	20.92 (4.04)	35	22.37 (3.05)				
	Visuospatial	36	10.89 (3.76)	35	10.94 (3.20)				
	Dementia Fluctuation scale	35	10.56 (3.61)	35	12.46 (3.80)				
Function	Pill questionnaire	34	1.74 (1.02)	34	1.76 (1.10)				
Quality of life	PDQ-39	27	28.88 (14.48)	28	39.13 (17.18)				
	EuroQoL-index	36	0.58 (0.33)	35	0.50 (0.34)	36	0.84 (0.19)	35	0.77 (0.27)
	EuroQoL-VAS	36	68.42 (18.57)	35	61.34 (14.97)	35	78.03 (15.11)	35	73.77 (16.99)
Neuropsychiatric symptoms	NPI Total	34	14.50 (14.71)	35	18.37 (15.20)				
	NPI % clinically significant ≥4	36	18% (0.24)	35	22.57% (0.21)				
	NPI % presence/absence	36	36% (0.25)	35	40.29% (0.22)				
	NPI Care partner distress					34	7.03 (7.29)	35	9.06 (8.82)
	HADS anxiety	31	6.65 (4.22)	31	8.07 (4.78)	35	5.11 (4.22)	35	6.20 (4.54)
	HADS depression	34	6.35 (3.03)	34	6.50 (2.91)	35	3.74 (3.82)	35	4.77 (4.19)
	LARS	34	-14.24 (9.02)	33	-15.58 (8.30)				
Health rating	SF-12 physical health					35	51.80 (8.81)	35	47.81 (11.95)
	SF-12 mental health					35	49.14 (10.66)	35	46.36 (13.15)
	RSS	32	34.13 (8.28)	32	32.81 (7.83)	36	31.67 (9.11)	35	26.51 (11.72)

Relationship satisfaction	DRS positive interaction					31	9.74 (3.79)	34	9.56 (3.41)
	DRS negative strain					30	10.80 (3.24)	31	9.94 (3.43)
	FCR satisfaction	36	3.95 (0.60)	35	4.08 (0.56)				
	FCR resentment	36	2.34 (0.99)	35	2.46 (1.09)				
	FCR anger	36	1.72 (0.72)	35	1.96 (0.83)				
Burden	ZBI					35	30.06 (16.21)	30	34.90 (18.01)
	Rel.SS					35	20.80 (11.87)	35	23.37 (11.51)
Resilience	BRS	33	19.73 (4.57)	34	18.91 (4.52)	36	23.53 (5.28)	35	21.69 (4.82)
Empathy	IRI total of 2 sub-scales	33	24.48 (3.99)	33	24.21 (4.96)				

Abbreviations: ACE-III – Addenbrooke's Cognitive Evaluation; BRS – Brief Resilience Scale; DLB – Dementia with Lewy bodies; DRS – Dyadic Relationship Scale, positive interaction or negative strain sub-scale; EQ5D – EuroQoL-5D index or visual analogue scale (VAS); FCR – Family Caregiving Role scale; HADS – Hospital Anxiety and Depression Scale; IQR – interquartile range; IRI – Interpersonal Reactivity Index; LARS – Lille Apathy Rating Scale; MoCA – Montreal Cognitive Assessment; NPI – Neuropsychiatric Inventory; PDD – Parkinson's disease dementia; PD-MCI – Parkinson's disease and mild cognitive impairment; PDQ-39 – Parkinson's Disease Questionnaire; PD-MCI/PDD/DLB – Parkinson's-related dementia; Rel.SS – Relatives' Stress Scale; RSS – Relationship Satisfaction Scale; SD – standard deviation; SF-12 – Short Form 12 Health Survey; ZBI – Zarit Burden Interview.

Table 3 Exploratory results for participant-dyads in the two arms showing the difference between baseline and 12 weeks.

		Control		**Intervention**				
People with PD-MCI/PDD/DLB		**n**	**Mean (SD)**	**n**	**Mean (SD)**	Adjusted mean difference* (Intervention – Control)	80% Confidence interval limit†	P value‡
Cognition	ACE-III total [a]	32	62.84 (18.44)	24	69.39 (14.99)	-1.70	>-3.62	0.227
	Attention	32	12.53 (3.28)	24	13.52 (2.57)	0.48	>-0.01	0.206
	Memory	32	14.22 (6.31)	24	16.70 (5.17)	0.46	>-0.33	0.311
	Verbal Fluency	32	4.97 (3.38)	24	6.17 (3.49)	-0.74	<-0.18	0.134
	Language	32	20.69 (4.91)	24	22.57 (2.33)	-0.25	>-0.97	0.388
	Visuospatial	32	10.44 (3.78)	24	10.43 (3.74)	-0.34	>-0.87	0.298
	Dementia Fluctuation scale [b]	32	10.97 (3.57)	24	11.57 (3.90)	-0.37	>-0.97	0.303
Functional ability	Pill questionnaire [b]	32	2.06 (1.01)	24	1.96 (1.30)	-0.05	>-0.30	0.435
Quality of life	PDQ-39 [b]	23	29.31 (13.74)	17	38.29 (13.39)	0.91	>-1.66	0.382
	EuroQoL-index [a]	32	0.57 (0.32)	24	0.57 (0.32)	0.05	>-0.01	0.241
	EuroQoL (VAS) [a]	31	62.35 (22.22)	24	62.30 (17.94)	1.75	>-2.69	0.370
Neuropsychiatric symptoms	**NPI Total [b]**	**32**	**9.88 (8.88)**	**24**	**15.04 (16.06)**	**4.46**	**>2.21**	**0.049**
	NPI clinically significant	**32**	**0.11 (0.14)**	**24**	**0.17 (0.19)**	**0.05**	**>0.02**	**0.078**

	NPI presence/absence	**32**	**0.33 (0.24)**	**24**	**0.38 (0.22)**	**0.05**	**>0.01**	**0.173**
	HADS anxiety [b]	29	5.66 (3.92)	20	6.75 (3.51)	0.24	>-0.44	0.382
	HADS depression [b]	30	5.33 (3.58)	20	5.25 (2.55)	0.28	>-0.12	0.367
	LARS [b]	28	-13.96 (9.55)	18	-16.56 (7.56)	-1.62	>3.34	0.215
Relationship satisfaction	RSS [a]	30	35.20 (7.02)	24	32.48 (9.69)	-1.25	>-3.13	0.288
Resilience	**BRS [a]**	**29**	**20.97 (5.18)**	**21**	**20.33 (4.89)**	**-1.17**	**>-2.22**	**0.174**
Empathy	IRI Empathic concern [a]	29	25.76 (3.43)	21	25.71 (3.02)	-0.06	>-0.79	0.475
	IRI Perspective taking[a]	**29**	**25.10 (3.84)**	**21**	**24.38 (3.37)**	**-1.32**	**<-0.53**	**0.082**
Care partners								
Quality of life	**EuroQoL-index [a]**	**31**	**0.79 (0.22)**	**24**	**0.82 (0.14)**	**0.08**	**>0.04**	**0.048**
	EuroQoL-VAS [a]	**32**	**75.16 (18.42)**	**24**	**76.52 (19.03)**	**4.76**	**>1.59**	**0.104**
Person with PD-MCI/PDD/DLB NPS	NPI – Care partner distress [b]	32	5.28 (4.64)	24	7.48 (8.27)	2.11	>0.94	0.066
Neuropsychiatric symptoms	**HADS anxiety [b]**	**32**	**5.38 (4.91)**	**24**	**6.78 (4.33)**	**1.03**	**>0.32**	**0.112**
	HADS depression [b]	32	4.34 (3.84)	24	4.91 (4.10)	0.35	>-0.30	0.326
Health rating	SF-12 physical health [a]	32	49.79 (12.08)	24	47.31 (10.26)	1.91	>-0.24	0.228

	SF-12 mental health [a]	32	46.85 (13.09)	24	49.14 (10.66)	1.89	>-0.58	0.260
Relationship satisfaction	**RSS [a]**	**32**	**30.25 (8.08)**	**22**	**30.18 (11.24)**	**3.46**	**>2.07**	**0.020**
	DRS positive interaction [a]	**30**	**8.53 (2.99)**	**24**	**10.30 (3.53)**	**1.76**	**>1.10**	**0.015**
	DRS negative strain [b]	30	10.27 (2.97)	22	9.77 (3.73)	0.23	>-0.41	0.380
	FCR satisfaction [a]	32	3.91 (0.48)	24	3.89 (0.73)	-0.09	>-0.20	0.225
	FCR resentment [b]	32	2.55 (1.10)	22	2.65 (0.94)	0.04	>-0.13	0.417
	FCR anger [b]	32	1.95 (1.14)	24	1.97 (0.83)	-0.08	>-0.27	0.358
Burden	**ZBI [b]**	**30**	**30.47 (15.06)**	**22**	**32.91 (16.07)**	**-2.24**	**<-0.07**	**0.193**
	Rel.SS [b]	**31**	**22.16 (12.29)**	**21**	**22.81 (11.39)**	**-1.75**	**<-0.27**	**0.160**
Resilience	BRS [a]	32	22.63 (5.25)	24	21.31 (5.01)	0.12	>-0.65	0.447

Notes: * Adjusted for baseline outcome value; † One sided confidence interval provides the (upper or lower) limit of range of plausible values of point estimate; ‡ Significance level 0.2; [a] Higher scores better; [b] Higher scores worse

Abbreviations: ACE-III – Addenbrooke's Cognitive Evaluation; BRS – Brief Resilience Scale; DRS – Dyadic Relationship Scale, positive interaction or negative strain sub-scale; EQ5D – EuroQoL-5D index or visual analogue scale (VAS); FCR – Family Caregiving Role scale; HADS – Hospital Anxiety and Depression Scale; IRI – Interpersonal Reactivity Index; LARS – Lille Apathy Rating Scale; MoCA – Montreal Cognitive Assessment; NPI – Neuropsychiatric Inventory; PDQ-39 – Parkinson's Disease Questionnaire; PD-MCI/PDD/DLB – Parkinson's-related dementia; Rel.SS – Relatives' Stress Scale; RSS – Relationship Satisfaction Scale; SD – standard deviation; SF-12 – Short Form 12 Health Survey; ZBI – Zarit Burden Interview.

Qualitative evaluation

Synthesis of qualitative data elicited six themes presented in Table 4 together with the corresponding outcome domain related to each theme, and example extracts supporting each theme. Overall findings suggest "in the moment" enjoyment of CST-PD (Enjoyment/Fun). In addition, consistent with quantitative data regarding efficacy outcomes, the qualitative data suggest participants experienced improvements in cognition, with subsequent impact on communication and conversation with care partners (Communication/Cognition). The findings regarding physical and mental abilities suggested that while for some participants CST-PD afforded the opportunity to demonstrate retained abilities, for others the intervention highlighted changes and loss. The care partner outcomes indicated that CST-PD provided opportunities for conversation and reminiscence that would not have otherwise have occurred (Interpersonal relationships), although some degree of challenge and burden regarding the delivery of the CST sessions was reported by three care partners (Care partner aspects).

Table 4 Key themes emerging from the semi-structured interview with participant-dyads.

Theme	**Outcome Domain**	**Quote**
Enjoyment/ fun	Quality of Life/ Health	C: Everything you try gives you a different insight into things, doesn't it, and we've so enjoyed talking, haven't we? P: Yeah, it produces a feeling of, uh, wellbeing, doesn't it? C: It does, yeah, gets the endorphins. [Patient and Care partner, CS12, interview]
		You know, it's just enjoyable and it just gives you that chance to come outside of all your problems…just sit down and have a laugh. [Care partner, CS12, interview]
		It was almost like when he was back in work, brainstorming and getting involved and feeling valued where I think a lot in life now where you just plodding through every day, you don't feel the value, you don't feel that your opinions are valued and I think for the first time in a long time I think he felt valued or that his experiences were meaningful. [Care partner, CS9, interview]
Communication / Cognition	Cognition	[Liked] seeing [name] exercising his analytical skills, making intelligent observations. [Care partner, CS18, interview]
		We'd got quite uncommunicative not intentionally but it had just happened and it's been lovely sometimes even the picture has, [husband's name] has started talking about it before I've suggest anything. [...] It's like getting him back again, which is good. [Care partner, CS11, interview]
		When we open a new, a new chapter, a new scene, I'm, I'm starting to think more structured and I'm thinking, you know, well this is going to be what it is, why is it, what's, I'm starting to prepare thought processes before we, we actually read the information and because, and it's going to be questions on every

		one, it's keeping my brain ticking over a bit further. [Patient, CS12, interview]
Behavioural features	Neuropsychiatric Symptoms	I didn't expect the reaction from dad, so the fact that he was so interested and so wanting to take part and be helpful. [Care partner, CS9, interview]
		He didn't sort of show joy or you know anxiety or none of them. [Care partner, CS13, interview]
Interpersonal relationships	Relationship Quality/ Empathy	[Our granddaughter] done a session with him, and that was quite interesting to see the banter between them, between the young and the old and interacting and she was very good at it, very good, and he responded well, that was a really fun one really. [Care partner, CS13, interview]
		Togetherness, reminiscing, good conversation, good topic. [Care partner, CS7, diary]
		P: It's doing the best we can to keep our brains active. I think that, that's the key and… C: Yeah, and also to take from me the caring side, because it was a joint thing, wasn't it? It was a joint enjoyable thing, rather than, you know, um, uh, a task or something, you know, that had to be done. [Patient and Care partner, CS12, interview]
Physical and mental abilities	Functional Ability	Well he can't write and he struggled with drawing. [...] He struggled with initiating to answer. [Care partner, CS19, interview]
		[He] was very good at being systematic and getting a list of things and getting the book opened, you know, and maybe a lot of people will not be able to do that, you know maybe he was very proactive. [Care partner, CS3, interview]
		He really wanted to do it because he really wanted to show what he could do. [Care partner, CS9, interview]
		Reminded him of his disability and not being mobile enough to visit these places on his own. [Care partner, CS5, interview]
Care partner aspects	**Resilience/ Burden**	I didn't feel it was fun, it was something else for me to get [my husband] to participate. [...] I felt I had to do it. [Care partner, CS4, interview]
		We did enjoy when my sister and her husband came around, and that session, you know…I find that the effort, the weight was taken off my shoulders [my husband] engaging with the other person more than he was engaging with me. [...] I just thought that he had such a great time [with other people], it was so enjoyable for him, whereas it was much of a chore when you were doing it with me. [Care partner, CS4, interview]

Abbreviations: C- care partner; P – person with Parkinson's-related dementia.

DISCUSSION

This is the first randomised controlled feasibility trial of a CST-based intervention specifically adapted for people with Parkinson's-related MCI or dementia (PDD/DLB), and is the largest study of its kind to date. It thus makes a valuable contribution to the emerging field of non-pharmacological interventions for cognition and other dementia-related outcomes in this population. The CST-PD programme retains the core principles of the already well-established CST, but is specifically tailored to the needs of people with a complex form of dementia characterised by motor and other physical problems. The preserved CST features include positive discussion, enjoyable activities, affection, supportive feedback and a focus on opinions rather than facts. Critical modifications included removing motor-dependent activities, potentially hallucinogenic or unclear images and updating manual content by increasing the usability of the format.[12] The ability to tailor the intervention to specific needs and preferences of the participants enabled us to offer successfully the intervention to people with a wide range of cognitive abilities and interest, without the risk of the intervention not being challenging enough. Furthermore, we designed CST-PD to be a home–based, individualised, care partner-delivered intervention, which strengthened the dyadic relationship of the person and their care partner, which is key in predicting positive outcomes of home-based care.[40,41]

We have already demonstrated the feasibility of conducting such a study in this population, as well as it being an acceptable and well tolerated intervention in people with PD-MCI/PDD/DLB and their care partners.[13] Here, our exploratory analysis of potential efficacy outcomes in the intervention recipients indicated improvements for cognition overall, but did this did not reach statistical significance. This is consistent with a previous study of individualised CST (iCST) in people with other forms of dementia,[8] but not group CST studies in non-PD groups demonstrating significant improvement in cognition.[7,42,43] It is possible that the imbalance in the education level of the two experimental arms may have impacted on this, as the participants in the CST-PD arm had a lower education level compared to those in the TAU group. A potential mechanism for improvement in cognition with this type of intervention could be the activation of compensatory mechanisms of synaptic plasticity.[44] As suggested by the original study of iCST in non-PD dementia,[8] it is possible that a higher dose of therapy is needed to impact cognition. In our study, the average dose was 1.76 (SD = 0.72) per week,[13] and this may not have been high enough. Higher intervention doses of cognitive rehabilitation have been shown to beneficial in very early stage cognitive impairment in PD.[45] This is despite previous suggestions that in non-PD dementia cognitive benefits can be seen with twice weekly

sessions of CST.[46] The added burden of physical disability and PD-associated fatigue and apathy may further hinder any potential benefit and necessitate an even higher dose.

Contrary to expectation, informant-rated behavioural outcomes assessed with the NPI appeared to worsen in the CST-PD group. This included the apathy domain, which has been shown to improve with intensive cognitive rehabilitation in early stage cognitive impairment in PD.[45] It is likely that the additional time spent with the therapy recipient through undertaking the therapy may have highlighted previously unrecognised behavioural and psychiatric symptoms (BPSD), resulting in higher informant ratings across a range of symptoms, or that the slight imbalance in diagnostic sub-types across the two treatment arms may have played a role. However, it is important to note that no participants were withdrawn due to worsening of BPSD and BPSD were not reported as adverse events in the qualitative data.[13] Although the direction of these results suggests a potentially harmful intervention, they should be interpreted with caution since we purposely chose a high significance level to capture any potential effects increasing probability of Type I errors. Combined with the exploratory multiple comparisons, we may be observing false positives. Furthermore, the behavioural outcomes were not mirrored in the qualitative reports, which revealed positive, 'in the moment' experiences in cognition, behaviour and function immediately following therapy sessions.

In contrast to the clinical outcomes in the participants with PD-MCI/PDD/DLB, care partners experienced improvements in several outcomes. This is crucial considering that caregiving in this population is complex, and care burden is best described as a multidimensional construct[47] that has a significant negative effect on a care partners' quality of life, health and relationships,[48-50] in effect creating 'hidden or invisible patients.[51] Specially, care partners in the CST-PD group reported reduced care burden and stress, improved quality of life, and enhanced relationships with the individual with PD-MCI/PDD/DLB. This finding is particularly striking since in previous work, care partners rated relationship quality lower than people with dementia.[52] It also supports and extends the results of the original iCST study, which found that quality of life in care partners improved and that individuals with dementia regarded the care relationship more positively.[8] Maintaining a positive caring relationship and ensuring care partner health and wellbeing is essential to delay or prevent long-term care for people with PD-MCI/PDD/DLB,[39,53] slow progression of cognitive and functional decline,[54]

and lower care partner burden.[55] It may also lower costs of providing care, and reduce length of hospitalisation and rate of crisis interventions.[56,57]

The intervention had no observable effects on either 'resilience' or 'empathy'; however, this was not surprising considering the relatively small sample size of this pilot study and that it was not powered to detect differences on these variables. Resilience, measured with the Brief Resilience Scale (BRS), assesses the ability to bounce back or recover from stress and consists of six items scored using a 5-point Likert scale. Empathy, measured with the Interpersonal Reactivity Index (IRI), encompasses two aspects: empathic concern and perspective taking, each measured on a Likert scale. These are important as they may reflect aspects of the apathy syndrome, which is closely linked with cognitive impairment/dementia in PD. We also saw no significant changes in apathy scores.

A potential limitation of our study is the heterogeneity of the diagnoses of the participant group. We purposefully included the three groups, as this feasibility study was an initial exploration of the appropriateness of the intervention across the range of cognitive impairment within the Lewy body spectrum. However, the heterogeneity renders the findings difficult to interpret and future trials should aim to limit inclusion to a single group or those with PDD/DLB only.

In conclusion, this study, although a pilot exploratory trial, has provided invaluable data to progress the emerging field of psychosocial interventions for PD-MCI/PDD/DLB as well as contributed to the literature on dyadic psychosocial interventions. It strongly supports a role for care partner-delivered interventions through the mechanism of supporting care partner health and wellbeing, as well as strengthening relationship quality. A full scale trial is now warranted to establish clinical effectiveness.

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Authors' roles

1) Research project: A. Conception, B. Organization, C. Execution, D. Clinical oversight, E. Research oversight;
2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3) Qualitative Analysis: A. Design, B. Execution, C. Review and Critique;
4) Manuscript: A. Writing of the first draft, B. Review and Critique.

IL: 1. A, B, C, D, E; 2. C; 3. A,B,C; 4. A, B
SV: 1. B, C; 2. C; 3. B, C; 4. B
LAC: 2. A, B, C; 4. B
SJS: 1. E; 3. A, B, C; 4. B
VO: 1. E; 4. B
EP: 1. E; 4. B
MAS: 1. D; 4. B
JaR: 1. D; 4. B
DJA: 1. D; 4. B
CT: 1. D; 4. B
JoR: 1. D; 4. B
TAG: 1. D; 4. B
SAM: 1. B,C; 2. C; 3. B,C; 4. B

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