Introduction of a Management Toolkit for Lewy Body Dementia: A Pilot Cluster-Randomized Trial

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Introduction of a management toolkit for Lewy body dementia: A pilot cluster randomised trial

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Abstract

Background: Lewy body dementia, comprising both dementia with Lewy bodies and Parkinson's disease dementia, is challenging to manage because of a complex symptom profile and lack of clear evidence-based management guidelines.

Objectives: We assessed the feasibility of undertaking a cluster randomised study of the introduction of an evidence-based management toolkit for Lewy body dementia, assessing outcomes for patients and carers as secondary measures.

Methods: We randomised 23 memory/dementia, movement disorder or non-specialist secondary care services to the management toolkit or usual care. People with dementia with Lewy bodies or Parkinson's disease dementia underwent assessments of cognition, motor and neuropsychiatric symptoms and global outcome at baseline, 3 and 6 months. Healthcare, personal and social care costs, and carer-related outcomes of carer stress, depression and anxiety were also examined.

Results: 131 participants were recruited (target 120), for whom 6-month data were available on 108 (83%). There was a benefit of being in the intervention arm for carers (reduced Zarit burden scale ($p<0.01$), reduced depressive symptoms ($p<0.05$)), who also reported less marked patient deterioration on the global outcome measure ($p=0<.05$). There were no significant differences in other outcomes or in costs between groups.

Conclusions: The introduction of an evidence-based management toolkit for Lewy body dementia was feasible and associated with some benefits, especially for carers.

Lewy body dementia, comprising both dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), is the second commonest degenerative dementia with limited treatment options and a poor outcome, including increased mortality, compared to other dementias [1, 2, 3, 4]. Recent reviews of pharmacological and non-pharmacological treatment of DLB and PDD have highlighted the relative paucity of the evidence base underpinning current clinical management [5, 6, 7, 8, 9]. However, these reviews have shown that good evidence does exist for cholinesterase inhibitors, some limited evidence for memantine, and there is emerging evidence for strategies aimed at other key aspects of the disease, including the management of autonomic symptoms, Parkinsonism, sleep disturbance, and psychosis, especially visual hallucinations [9, 10].

The management of Lewy body dementia is challenging, as patients present with a complex symptom profile, which can vary over time, and treatments for one symptom (e.g., dopaminergic drugs for Parkinsonism) can exacerbate another (e.g., psychosis)[1, 9]. There are no comprehensive management guidelines in clinical practice, and internationally regarded organisations such as the National Institute for Health and Care Excellence (NICE) have made only limited recommendations about some aspects of DLB and PDD, for example regarding the use of cholinesterase inhibitors [11, 12]. Quality of life is impaired in people with Lewy body dementia and their carers, with studies showing

that both in patients and carers it is even lower than in other dementias [13, 14] and Lewy body dementia is associated with increased carer stress [15, 16]. Costs of care may also be higher in Lewy body dementia than Alzheimer's disease [17, 18].

As part of the NIHR-funded "Improving the diagnosis and management of neurodegenerative dementia of Lewy body type" (DIAMOND-Lewy) Programme we undertook detailed literature reviews [5, 7, 9] and used this information within an expert Delphi consensus process to produce a management toolkit [9]. The expert Delphi panel consisted of 26 people from the fields of psychology, geriatrics, psychiatry, neurology, primary care, nursing and physiotherapy. The toolkit is aimed at healthcare professionals involved in the management of people with DLB and/ or PDD. It was developed in close consultation through a series of meetings with a group of people affected by the disease and carers, and we engaged with intended users, i.e. healthcare professionals, through extensive piloting and review of the toolkit in a service where we had previously developed an assessment toolkit for the diagnosis of DLB and PDD [19]. The management toolkit covers both disorders, includes pharmacological and non-pharmacological recommendations and is structured around the key symptom domains of cognition, motor function, neuropsychiatric features, sleep disturbances and autonomic features. The toolkit, which is available at: https://research.ncl.ac.uk/diamondlewy/, consists of three parts which can be viewed electronically or printed and used as a hard copy: i) a summary sheet; ii) five more detailed sheets covering the above symptom domains; iii) a detailed reference guideline containing full details of the source of the recommendations.

We undertook this pilot cluster randomised controlled trial to see if introduction of the toolkit to routine clinical services and recruitment of DLB and PPD subjects from within such services was feasible, and as a secondary outcome to collect data on outcome measures

for patients and carers, including whether costs increased for those allocated to the management toolkit.

Methods

Trial Design

We performed a pragmatic cluster randomised controlled trial over 26 weeks of 23 clinical services that assessed people with DLB or PDD, with 1:1 allocation to either receive the management toolkit or continue with usual care. This was a pilot study and the sample size for subject recruitment was set at 120 (30 DLB and 30 PDD in each arm) on the basis of existing guidance on sample sizes for pilot studies [20] with the aim of including a range of representative NHS services in which patients with LBD are seen and to obtain pilot data on patient outcomes to inform power calculations for a future definitive study. In the UK, people with DLB and PDD can be seen in secondary care services of 3 main types: memory clinics, movement disorder clinics and general secondary care clinics/ services for older people. As we wanted services in this study to be representative of where DLB and PDD is managed in secondary care, we included all 3 service types.

At the time of the study, the toolkit was not available online and was distributed only to those services randomised to receive it. Memory clinics (n=5), movement disorder clinics (n=7) and non-specialist secondary care clinics/services for older people (n=11) from the northeast of England and East Anglia participated in the study. The trial was supported by the Newcastle Clinical Trials Unit, who undertook the randomisation via a statistician blinded to other aspects of the study. One service was subsequently unable to recruit any patients, and withdrew part way through the study.

All services received a previously developed assessment toolkit to help diagnose DLB and PDD [19, 21] and, for services randomised to the intervention arm, the management toolkit was introduced during an in-person site initiation visit undertaken by the research team. This comprised standardised presentations and handouts followed by a question and answer session. All healthcare staff within services allocated to receive the toolkit were provided with the toolkit and support in how to use it. Follow-up support and further information sessions were available, and the study team maintained regular contact with all services during the course of the recruitment and follow up period.

Assessment and management toolkits were provided as paper copies with laminated copies of the overview and symptom summary sheets for the management toolkit. Some sites requested electronic (.pdf) versions and, when requested, they were supplied.

People with Lewy body dementia and their carers were recruited over a 21-month period from services randomised to either receive the management toolkit or continue with usual care. Inclusion criteria for participants were: i) aged 60 or more and having received a diagnosis of DLB [22] or PDD [23]; ii) considered by the treating clinical team to have at least one active clinical problem; iii) that informed consent could be obtained from the patient or, for those lacking capacity, from a consultee. A carer/informant was recruited as an informant wherever possible to complete scales requiring an informant (all but two patients). As we wished for an inclusive and representative sample, we did not set inclusion criteria based on severity of dementia or cut-offs on any assessment scale. Exclusion criteria were: i) patients with a severe or terminal illness and reduced life expectancy which compromised their ability to take part; ii) insufficient English to allow completion of the study measures. As this was a pilot study, assessing feasibility of recruiting services and subjects and the utility of our chosen outcomes, there was no pre-

specified primary outcome. The study was approved by the UK National Health Service Health Research Authority national research ethics committee (16/WM/0025) and was registered (ISRCTN 11083027).

Trial Assessments

Participants and carers were assessed at baseline, 3 and 6 months. The primary time point for outcome assessments was at 6 months. All assessments were undertaken by members of the National Institute for Health Clinical Research Network, who were independent of the study team and unaware of the service allocation (to management toolkit or standard care).

Patient-related assessments were of cognition (Mini-mental state examination (MMSE) [24] and Montreal Cognitive Assessment (MoCA) [25]; motor symptoms ((Unified Parkinson's disease rating scale, Part III) [26]; neuropsychiatric features (Geriatric Depression Scale (GDS-15) [27]; Neuropsychiatric symptoms (NPI) [28]); quality of life (DEMQoL [29]; EQ-5D-5L [30]); activities of daily living (Bristol activities of daily living scale) [31]) and Clinical Global Impression of Change (CGIC) on a 7 point scale (ranging from 1= very much worse to 7 = very much better, with 4 = no change) as rated by an independent rater and, as a separate outcome measure, the carer. Carer-related assessments were of stress (Zarit burden scale [32]) and mood (Hospital Anxiety and Depression Scale (HADS) [33]).

Statistical analysis

Baseline characteristics between groups were compared using T or Mann-Whitney U tests or, for categorical variables, chi-square test. Due to the non-normal distribution of

the variables bootstrapped median regression analysis was used to determine differences between groups at six-month follow-up, with adjustment for baseline values and cluster. CGIC was assessed using the Wilcoxon Mann-Whitney test and chi squared test. All of the analyses except the Mann Whitney U test were conducted in Stata 16.1. The Mann Whitney U test was done using SPSS v24.

Health economic analysis

Health economic data on the use of health and social care resources were captured by using a bespoke service utilisation questionnaire that was developed based on questions included in the Client Service Receipt Inventory [34] and administered to carers at baseline, 3 and 6 months. The participants were asked about their use of a broad range of services including: inpatient services, outpatient services, day activity services, and community care services over the preceding three months. Costs were determined for the perspective of the UK NHS and Personal and Social Services (PSS), which include costs of medications [35] and health and social service use [36, 37] Costs falling on other sectors (e.g. other local authority services) were not included. Costs associated with the delivery of the toolkit to intervention-arm participants were included, such as the production of the management toolkits and training staff to use them. All costs are reported in pounds sterling (£) for the financial year 2017/18. As the study follow-up was less than 12 months, no discounting was performed.

Results

One hundred and thirty-one participants consented to take part in the study (See Figure 1 for CONSORT diagram). Of the carers, 87 were spouses/ partners, 20 were children/ children in law, 4 were siblings, 4 were other family members, 6 were friends and 5 were paid carers.

127 participants underwent a baseline assessment, and 6-month data were available for 109 (83% of all participants who consented, 86% of those who completed baseline, respectively). Eighteen participants were lost to follow-up, seven of whom died (four in the intervention arm; three in the control arm). Those lost to follow up were similar in demographic characteristics to those remaining in the study except for age: those lost to follow up were significantly older (median age of 83 compared with median age of 77; U value = 547, p =0.003).

We exceeded the recruitment target, aiming to recruit 120 patients and actually recruiting 131. Patient characteristics at baseline are shown in Table 1. Participants randomised to receive the intervention did not differ significantly from those randomised to the usual care group on any of the baseline measures except for carer-reported DEMQoL and carer anxiety symptoms on the Hospital Anxiety and Depression Scale (HADS). Changes in secondary outcomes at study end (6 months) are shown in Table 2. Controlling for baseline measures and inter class clustering coefficient, there were significant improvements in carer-related outcomes of carer burden (Zarit scale; difference = -6.9, 95% CI -12.4 to -1.4; p=0.011) and depressive symptoms (Hospital Anxiety and Depression Scale; difference = -1.2, 95% CI – 2.8 to -0.1; p=0.043). There were no significant differences in other scales.

Outcomes using the clinical global impression of change are shown in Figure 2. There was a trend for fewer subjects in the toolkit arm to be rated as worse or very much worse. This was not significant for the independent rater CGIC (Mann-Whitney U=1195; p=0.11). However, significantly fewer participants in the toolkit arm were rated as worse or very much worse for the carer-rated CGIC (Mann-Whitney U=1032; p= 0.03). To further illustrate this, the proportion of subjects who showed marked deterioration (much or very

much worse) was lower in the toolkit arm compared to usual care (17% v 33% for independently rated, Chi Square = 3.79, p=0.051; 19% v 42%, Chi Square =6.56, p=0.01 for carer rated).

Using results from this study to inform a power calculation for a future study (80% power, alpha 0.05) gives a required sample size of 328 for clinician rated global outcome (17.2% much/very much worse in the intervention group compared with 33.3% in the control group). Assuming 80% completion rates then a recruitment sample of 410 would be required.

Staff who used the toolkit

We did not collect detailed demographic information on which staff members used the toolkit, given the focus on adoption of the toolkit at the team/service level, though we did undertake a survey during the study asking those who used to toolkit to reply with feedback. Replies were obtained from 34 people, 17 (50%) consultant medical staff, 7 (21%) medical staff below consultant grade, 8 (24%) nursing staff and 2 (6%) allied health professionals.

Healthcare and social service resource use

As this was a pilot study, the focus of the economic component was to provide a descriptive analysis of the costs for participants in each arm (toolkit or usual care) and these are shown in Table 3. The total delivery cost of the management toolkit was divided by the number of participants in the intervention arm (n=75) to estimate a mean delivery cost per participant (£76.32) receiving the intervention. This was added for each participant in the toolkit arm, with no costs added for those receiving usual care (i.e. the control arm). Mean costs associated with healthcare and social service use reduced in the toolkit arm between baseline and six-month follow-up, whilst in the usual care group,

costs increased. There is a substantial amount of imprecision around the service use cost data and there was no evidence of a difference. Mean medication costs increased slightly in both arms. There was slight evidence that on average the toolkit arm cost increased more from baseline than the usual care arm (toolkit baseline (mean±SD) £223±£204; 6 months £294±£286: usual care baseline £214±239; 6 months £229±206; group difference p=0.098).

Discussion

Our pilot cluster-randomised trial investigated the introduction of an evidence-based management toolkit for Lewy body dementia compared to usual care in representative clinical services in England. We showed that such a study was feasible. We were able to recruit a sufficient number of memory/dementia, movement disorder and non-specialist services for older people to participate, and to recruit participants in all but one of these. Furthermore, participant recruitment exceeded our original intended goal (final number recruited 137; target of 120). We obtained 24-week data on 83% of consented participants. Although there was no evidence of any difference in many of the assessment scales this is unsurprising in view of the pilot nature of the study, which was not powered to detect such differences. Nonetheless there was a trend (p=0.051) for differences on the CGIC with less severe or very severe deterioration in the patient group managed within services allocated to the management toolkit, with this outcome becoming significant (p=0.01) when rated by carers. Global outcome has been shown in previous pharmacological studies of Lewy body dementia to be one of the most consistent of all outcome measures to show a treatment effect [5, 38]. The reasons for this are not clear but

may include the well-recognised marked fluctuations in Lewy body dementia which may make more specific scales less reliable in detecting change compared to other dementias like Alzheimer's disease or that the global outcome detects a number of small benefits which sum to make a global difference. This is particularly likely for our management toolkit, which was applied in a bespoke individualised way, according to the symptoms each patient had, which may be better detected by a global measure. Additionally, carers may be particularly sensitive to the particular symptoms being managed in their case and also see patients over a longer time period, which may be why they detected change better than an independent rater. Our findings support those from some previous pharmacological studies suggesting that global outcome is a sensitive measure which could be used as a primary outcome in future studies.

We also found important benefits for carers, with reduced stress assessed using the Zarit Burden Scale and reduced depressive symptoms. High levels of burden and stress are well-recognised in carers of people with dementia. This is especially so for carers of those with Lewy body dementia, likely due to the complexity of caring for those with a complex and fluctuating disorder with cognitive, motor and neuropsychiatric symptoms [15, 16]. There have been no studies investigating ways of reducing stress or burden in those with Lewy body dementia, and so our findings that the introduction of the management toolkit may improve these symptoms is striking. Although the magnitude of the changes was modest, it could conceivably have been the case that use of the management toolkit might even have increased burden and stress. We showed this was not the case, and further work should seek to investigate whether there are particular components of the management toolkit which are most associated with alleviating carer stress. Lewy body dementia is associated with a particularly poor outcome in terms of cognitive and

functional decline and increased mortality [3]. There was no difference in mortality between those in services with or without the management toolkit, though this is unsurprising given that most subjects had mild or moderate disease and the short duration of the study, leading to low mortality rates. There was no evidence of a differential effect of the toolkit for those with DLB or PDD.

The introduction of any evidence-based guideline or toolkit comes with a risk that costs may increase, either due to use of more expensive medication, greater investigations or more referrals to other agencies or increased levels of care as needs become more apparent. We found no evidence of increased costs associated with the use of the management toolkit. However, the level of imprecision was such that economically important differences could exist. There was a tendency for costs to increase slightly over 6 months in those allocated to the usual care arm, and decrease in those in the management toolkit arm and though these differences were not statistically significant, they may be of economic impact. Interestingly, although costs decreased in the toolkit arm medication costs showed a trend to rise which would be consistent with the many pharmacological recommendations in the toolkit. Any further evaluation should include cost-effectiveness as a core component and seek to undertake a rigorous cost-effectiveness analysis, which was not possible due to our modest sample size. Since costs of Lewy body dementia are higher than other dementias [17, 18] the demonstration of cost saving would be very important to health services.

Strengths of this study include the systematic introduction of an evidence-based toolkit in a cluster-randomised design to representative services. We also aimed to include representative patients with Lewy body dementia, so inclusion criteria were broad with no

limit set for dementia severity. The severity in terms of cognitive and other features, however, is broadly representative of those described in other naturalistic cohorts. Importantly, outcome assessments including the clinician and carer rated outcome, were undertaken without knowledge of whether the person with Lewy body dementia was being managed within a service allocated to the management toolkit or usual care.

We recognise several limitations to the study. This was a pilot study and so underpowered, with efficacy as a secondary outcome, and though it generated evidence of differences for carer-related measures, none would have survived correction for multiple comparisons and only for global outcome was there evidence of a difference for patient related measures. Sample size, although relatively large for a study of Lewy body dementia, was still modest to make definitive conclusions about the benefits of the toolkit. Given that even usual-care sites knew they were participating in a study of Lewy body dementia this may have prompted them to focus more on management of this condition than may be usual at times when studies are not being undertaken. This would tend to reduce our ability to detect a difference. Although raters of the outcome measures were blind to subject group allocation, we cannot be sure that particiants themselves or carers were fully blinded as to which arm they were. The management toolkit is evidence-based but most of the recommendations are available already from published literature. Therefore, many participants in the usual care arm would be receiving treatment recommended in the toolkit (for example, cholinesterase inhibitors are NICE-recommended treatments for all people with Lewy body dementia, unless otherwise contraindicated). As we introduced the toolkit to whole services, we could not assess the extent to which the toolkit was used with individual patients. We did not collect detailed information about the users of the management toolkit, though our survey indicated the majority (50%) were experienced (consultant) medical staff, and that around 30% of healthcare professionals who used the toolkit were non-medical (largely nursing staff). A qualitative process evaluation was conducted alongside the pilot trial, that included participant interviews and site observations. Although outside scope for this paper, the qualitative findings provided additional insights into how the toolkit was implemented and used within sites.

The toolkit was a broad intervention consisting on a number of recommendations, so we cannot directly determine the “mechanism of action” or “dose” of the toolkit, and further studies should

include measures which could directly assess this. However, every recommendation was based either on published evidence or from a Delphi consensus and has been published, and the recommendations should be useful to those involved in the management and care of people with DLB and PDD (9). Finally, as this study was performed in secondary care services within a single country, we cannot necessarily generalise our findings to other countries or healthcare settings.

In conclusion, we undertook a pilot cluster-randomised study of an evidence-based toolkit in Lewy body dementia. Our results show that such studies are feasible, with benefits suggested for measures of global outcome for patients and carer measures of reduced burden and depressive symptoms. Importantly, there was no evidence that the introduction of the management toolkit may potentially increase costs. Further work should investigate the impact of wider implementation of the toolkits, either through a much larger trial (which would need to include over 400 subjects) or through other methods including clinical audit or realist evaluation. Future research should also investigate other outcomes, including those that may be more relevant and salient to people with Lewy body dementia and their carers, and positive outcome measures (for both people with dementia and carers) such as resilience, coping and efficacy [39, 40].

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Author Roles

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DB: 1A, 1B, 1C, 2C, 3B

JPT: 1A, 1B, 1C, 2C, 3B

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Ethical Compliance Statement

This study was approved by the UK West Midlands – Coventry and Warwickshire Research Ethics Committee (reference: 16/WM/0025). The study was registered as ISRCTN number 11083027. Written informed consent was obtained for all participants with capacity, for those without capacity consultee written assent was obtained. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Figure 1. Study CONSORT diagram

Figure 2. Outcome in terms of rating on the clinical global impression of change at 6 months on the CGIC as rated by **(a)** an independent rater (group difference p=0.11) and **(b)** the carer (group difference p=0.03).

574 **Table 1: Baseline characteristics of the randomised participants.**

		Control (n=52)	Intervention (n=75)	p-value *
Number of sites		11	12	
Service type (Memory Clinic/ General/ PD Clinic)		2/6/3	3/5/4	
Age (years, mean (SD))		77.0 (7.59)	79.3 (6.97)	0.086
Diagnosis DLB: PDD n (%)		31:21 (60:40)	46:29 (61:39)	0.846
Sex Female: Male n (%)		10:42 (19:81)	17:58 (23:77)	0.642
DEMQOL	Mean (SD)	0.76 (0.13)	0.78 (0.12)	
	Median (interquartile range)	0.78 (0.70, 0.82)	0.80 (0.70, 0.88)	0.215
Carer DEMQOL-proxy	Mean (SD)	0.70 (0.14)	0.76 (0.12)	
	Median (interquartile range)	0.67 (0.55, 0.82)	0.79 (0.67, 0.85)	0.026
NPI	Mean (SD)	25.0 (17.5)	20.0 (18.0)	
	Median (interquartile range)	22.0 (12.0, 31.0)	15.0 (9.0, 24.0)	0.038
UPDRS	Mean (SD)	43.7 (19.1)	38.2 (18.6)	
	Median (interquartile range)	41.0 (28.0, 55.0)	35.5 (26.0, 51.0)	0.137
Cornell depression scale	Mean (SD)	9.31 (6.10)	7.41 (4.85)	
	Median (interquartile range)	9.0 (4.0, 13.0)	7.0 (4.0, 11.0)	0.104
Geriatric depression scale	Mean (SD)	5.7 (3.5)	5.6 (3.3)	
	Median (interquartile range)	5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	0.952
MMSE	Mean (SD)	20.8 (6.1)	21.4 (6.1)	
	Median (interquartile range)	22.0 (17.0, 25.0)	22.0 (19.0, 26.0)	0.503
MoCA	Mean (SD)	15.1 (4.9)	15.6 (6.0)	
	Median (interquartile range)	15.5 (12.0, 19.0)	16.0 (12.0, 19.0)	0.690
EQ-5D-5L	Mean (SD)	0.67 (0.27)	0.67 (0.21)	
	Median (interquartile range)	0.74 (0.55, 0.85)	0.73 (0.57, 0.80)	0.516
EQ-5D-5L (proxy)	Mean (SD)	0.55 (0.27)	0.56 (0.27)	
	Median (interquartile range)	0.62 (0.37, 0.73)	0.62 (0.40, 0.77)	0.929
HADS anxiety	Mean (SD)	6.7 (4.2)	5.2 (4.1)	
	Median (interquartile range)	6.0 (3.0, 9.0)	4.0 (2.0, 8.0)	0.037
HADS depression	Mean (SD)	4.6 (3.8)	4.2 (3.5)	
	Median (interquartile range)	3.0 (1.0, 7.0)	3.5 (1.0, 7.0)	0.610
Zarit burden	Mean (SD)	27.5 (15.6)	22.6 (15.3)	
	Median (interquartile range)	26.0 (14.5, 38.5)	18.0 (10.0, 33.0)	0.070
Carer EQ-5D-5L	Mean (SD)	0.80 (0.20)	0.81 (0.19)	
	Median (interquartile range)	0.84 (0.72, 1.0)	0.82 (0.69, 1.0)	0.902

575 ** p-value from T-test, Mann-Whitney test or chi-square test*

576 **Table 2: Change from baseline to six months - results of bootstrapped (replications 1000)**

577 **median regression, adjusting for baseline values and cluster.**

		Standard care	Intervention	Difference (95% CI)	p-value
Number of sites		11	12		
DEMQOL	Baseline	0.78 (0.70, 0.83)	0.80 (0.70, 0.88)		
(n= 86)	6 months	0.79 (0.7, 0.86)	0.84 (0.77, 0.88)	0.03 (-0.02, 0.07)	0.268
Carer DEMQOL-proxy *(n=103)*	Baseline	0.70 (0.62, 0.82)	0.79 (0.67, 0.85)		
	6 months	0.78 (0.56, 0.82)	0.82 (0.70, 0.87)	0.03 (-0.02, 0.09)	0.185
NPI	Baseline	22.5 (12.0, 30.0)	14.0 (9.0, 26.0)		
(n=105)	6 months	20.0 (11.0, 33.0)	11.0 (5.0, 24.0)	-1.8 (-6.2, 2.6)	0.408
UPDRS	Baseline	40.0 (30.0, 55.0)	35.0 (25.0, 51.0)		
(n=94)	6 months	43.0 (34.0, 60.0)	37.0 (25.0, 52.5)	-2.3 (-7.9, 3.4)	0.428
Cornell depression	Baseline	9.0 (4.0, 12.5)	7.0 (4.0, 11.0)		
score *(n=105)*	6 months	9.0 (4.0, 14.0)	6.0 (3.0, 10.0)	-1.5 (-3.9, 0.81)	0.198
Geriatric depression	Baseline	5.0 (3.0, 7.0)	6.0 (3.0, 7.0)		
scale *(n=92)*	6 months	6.0 (3.0, 8.0)	5.0 (4.0, 8.0)	-0.5 (-1.9, 0.9)	0.469
MMSE	Baseline	22.0 (12.5, 25.5)	22.5 (19.0, 27.0)		
(n=98)	6 months	22.0 (17.0, 26.0)	22.0 (17.0, 25.0)	0.5 (-1.4, 2.5)	0.607
MoCA	Baseline	15.5 (12.0, 19.0)	16.0 (13.0, 20.0)		
(n=93)	6 months	16.0 (12.0, 18.5)	16.0 (12.0, 19.0)	0.5 (-2.1, 3.0)	0.722
EQ-5D-5L	Baseline	0.78 (0.55, 0.88)	0.71 (0.55, 0.78)		
(n=89)	6 months	0.67 (0.56, 0.84)	0.68 (0.57, 0.78)	0.05 (-0.04, 0.15)	0.242
Proxy EQ-5D-5L	Baseline	0.65 (0.45, 0.73)	0.63 (0.43, 0.79)		
(n=101)	6 months	0.57 (0.43, 0.71)	0.67 (0.39, 0.80)	0.06 (-0.05, 0.17)	0.246
HADS anxiety	Baseline	6.5 (3.0, 9.0)	4.0 (2.0, 8.0)		
(n=101)	6 months	6.0 (4.0, 9.0)	5.0 (2.0, 9.0)	0.04 (-2.1, 2.2)	0.973
HADS depression	Baseline	3.0 (2.0, 7.0)	4.0 (1.0, 7.0)		
(n=101)	6 months	4.0 (2.0, 6.0)	3.0 (1.0, 6.0)	-1.2 (-2.8, -0.1)	0.043
Zarit Burden Scale	Baseline	26.0 (14.0, 36.0)	22.0 (13.0, 34.0)		
(n=99)	6 months	29.5 (16.0, 42.0)	23.5 (10.0, 32.0)	-6.9 (-12.4, -1.4)	0.011
Carer EQ-5D-5L	Baseline	0.84 (0.71, 1.0)	0.84 (0.70, 1.0)		
(n=102)	6 months	0.80 (0.74, 0.91)	0.84 (0.77, 1.0)	0.04 (-0.06, 0.15)	0.419

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579 DEMQOL = Dementia quality of life measure; NPI = Neuropsychiatric inventory; UPDRS
580 = Unified Parkinson's disease rating scale; MMSE= Mini-mental state examination;
581 MoCA =Montreal cognitive assessment; EQ5D= European quality of life 5 dimensional
582 scale; HADS = Hospital anxiety and depression scale