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RESEARCH ARTICLE

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

John T. O'Brien, DM,[1,2*] Ian G. McKeith, FMedSci,[3] Alan J. Thomas, PhD,[3] Claire Bamford, BA,[4] Luke Vale, PhD,[4] Sarah Hill, PhD,[4] Louise Allan, PhD,[5] Tracy Finch, PhD,[6] Richard McNally, PhD,[4] Louise Hayes, PhD,[4] Ajenthan Surendranathan, PhD,[1] Joseph P.M. Kane, PhD,[7] Sarah Dunn, MSc,[8] Allison Bentley, MSc,[1,2] Sally Barker, BSc,[3] James Mason, PhD,[9] David Burn, MD,[4] and John-Paul Taylor, PhD[3]

[1]*Department of Psychiatry, University of Cambridge, Cambridge, UK*
[2]*Cambridgeshire and Peterborough National Health Service Foundation Trust, Cambridge, UK*
[3]*Translational and Clinical Research Institute, Newcastle University, Newcastle, UK*
[4]*Population Health Sciences Institute, Newcastle University, Newcastle, UK*
[5]*Institute of Health Research, University of Exeter, Exeter, UK*
[6]*Department of Nursing, Midwifery and Health, Faculty of Health & Life Sciences, Northumbria University, Newcastle, UK*
[7]*Centre for Public Health, Queen's University, Belfast, UK*
[8]*Newcastle Clinical Trials Unit, Newcastle University, Newcastle, UK*
[9]*Warwick Medical School, University of Warwick, Coventry, UK*

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 randomized study of the introduction of an evidence-based management toolkit for Lewy body dementia, assessing the outcomes for patients and carers as secondary measures.

Methods: We randomized 23 memory/dementia, movement disorder, or nonspecialist 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 and 3 and 6 months. Healthcare, personal and social care costs, and carer-related outcomes of carer stress, depression, and anxiety were also examined.

Results: A total of 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. © 2020 The Authors. *Movement Disorders* published by Wiley Periodicals LLC. on behalf of International Parkinson and Movement Disorder Society.

Key Words: Lewy body dementia; clinical trial; management; dementia with Lewy bodies; Parkinson's disease dementia

*__Correspondence to:__ Dr. John O'Brien, Department of Psychiatry, University of Cambridge School of Clinical Medicine, Box 189, Level E4 Cambridge Biomedical Campus, Cambridge, CB2 0SP, United Kingdom; E-mail: john.obrien@medschl.cam.ac.uk

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Lewy body dementia, comprising both dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), is the second most common degenerative dementia with limited treatment options and a poor outcome, including increased mortality, compared with other dementias.[1–4] Recent reviews of pharmacological and nonpharmacological treatments of DLB and PDD have highlighted the relative paucity of the evidence base underpinning current clinical management.[5–9] 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 (eg, dopaminergic drugs for parkinsonism) can exacerbate another (eg, psychosis).[1,9] There are no comprehensive management guidelines in clinical practice, and internationally regarded organizations such as the National Institute for Health and Care Excellence 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 National Institute for Health Research–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, that is, healthcare professionals, through extensive piloting and a 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 nonpharmacological 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 the following 3 parts that can be viewed electronically or printed and used as a hard copy: (1) a summary sheet, (2) 5 more detailed sheets covering the aforementioned symptom domains, and (3) a detailed reference guideline containing full details of the source of the recommendations.

We undertook this pilot cluster-randomized controlled trial to see if the introduction of the toolkit to routine clinical services and the 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 randomized controlled trial for 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 National Health Service (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 United Kingdom, 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 randomized to receive it. Memory clinics (n = 5), movement disorder clinics (n = 7), and nonspecialist 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 randomization 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 randomized to the intervention arm, the management toolkit was introduced during an in-

person site initiation visit undertaken by the research team. This comprised standardized 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 during a 21-month period from services randomized to either receive the management toolkit or continue with usual care. Inclusion criteria for participants were (1) aged 60 or older and received a diagnosis of DLB[22] or PDD[23]; (2) considered by the treating clinical team to have at least 1 active clinical problem; and (3) 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 2 patients). As we wanted 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 (1) patients with a severe or terminal illness and reduced life expectancy that compromised their ability to take part and (2) 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 prespecified 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 and 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 (management toolkit or standard care).

Patient-related assessments were of cognition (Mini-Mental State Examination[24] and Montreal Cognitive Assessment),[25] motor symptoms (Unified Parkinson's Disease Rating Scale, Part III),[26] neuropsychiatric features (Geriatric Depression Scale,[27] Neuropsychiatric Inventory[28]), quality of life (Dementia Quality of Life Measure[29] and EQ-5D-5L[30]), and activities of daily living (Bristol Activities of Daily Living Scale)[31] and the 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).[33]

Statistical Analysis

Baseline characteristics between groups were compared using *t* or Mann-Whitney *U* tests or, for categorical variables, χ^2 tests. Because of the non-normal distribution of the variables, bootstrapped median regression analysis was used to determine differences between groups at 6-month follow-up with adjustments for baseline values and cluster. CGIC was assessed using the Wilcoxon Mann-Whitney test and χ^2 test. All of the analyses except the Mann-Whitney *U* test were conducted in Stata 16.1 (StataCorp, College Station, TX). The Mann-Whitney *U* test was done using SPSS version 24 (IBM Corp., Armonk, NY).

Health Economic Analysis

Health economic data on the use of health and social care resources were captured by using a bespoke service use questionnaire that was developed based on questions included in the Client Service Receipt Inventory[34] and administered to carers at baseline and 3 and 6 months. The participants were asked about their use of a broad range of services including in-patient services, out-patient services, day activity services, and community care services during the preceding 3 months. Costs were determined for the perspective of the UK NHS and Personal and Social Services, which include costs of medications[35] and health and social service use.[36,37] Costs falling on other sectors (eg, 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 2017/2018. As the study follow-up was <12 months, no discounting was performed.

Results

A total of 131 participants consented to take part in the study (see Fig. 1 for Consolidated Standards of Reporting Trials 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.

A total of 127 participants underwent a baseline assessment, and 6-month data were available for 109 (83% of all participants who consented, 86% of

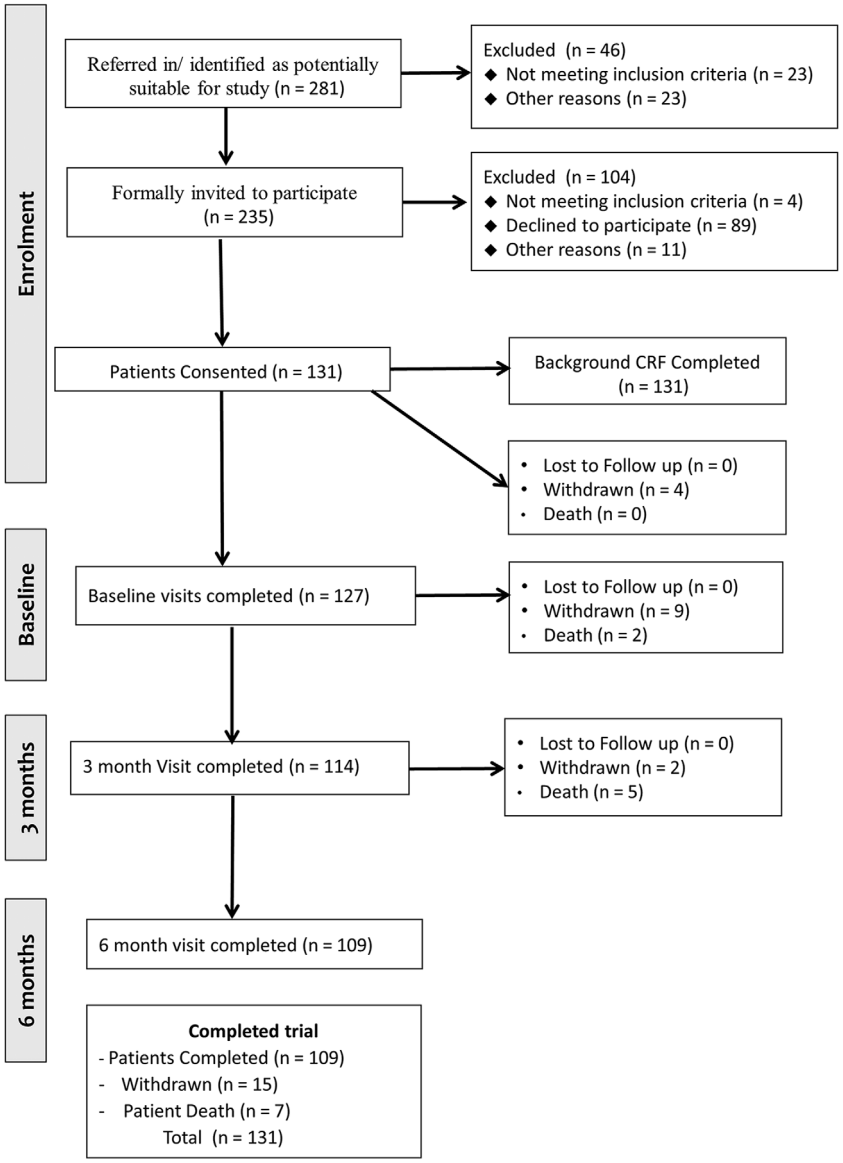

FIG 1. Study Consolidated Standards of Reporting Trials diagram. CRF, case report form.

those who completed baseline, respectively). Of the participants, 18 were lost to follow-up, 7 of whom died (4 in the intervention arm; 3 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 randomized to receive the intervention did not differ significantly from those randomized to the usual care group on any of the baseline measures except for carer-reported Dementia Quality of Life Measure and carer anxiety symptoms on the Hospital Anxiety and Depression Scale. Changes in secondary outcomes at study end (6 months) are shown in Table 2. Controlling for baseline measures and interclass clustering coefficient, there were significant improvements in carer-related outcomes of carer burden (Zarit Burden Scale; difference, −6.9; 95% confidence interval, −12.4 to −1.4; $P = 0.011$) and depressive symptoms (Hospital Anxiety and Depression Scale; difference, −1.2; 95% confidence interval, −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

TABLE 1. Baseline characteristics of the randomized 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, y, 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 Scale			
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

*P-value from t test, Mann-Whitney test, or χ^2 test.
Abbreviations: SD, standard deviation; DLB, dementia with Lewy bodies; PDD, Parkinson's disease dementia; DEMQOL, Dementia Quality of Life Measure; NPI, Neuropsychiatric Inventory; UPDRS, Unified Parkinson's Disease Rating Scale; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; EQ-5D, European Quality of Life 5 Dimensional Scale; HADS, Hospital Anxiety and Depression Scale.

deterioration (much or very much worse) was lower in the toolkit arm compared with usual care (17% vs. 33% for independently rated [χ^2, 3.79; $P = 0.051$]; 19% vs. 42% for carer rated [χ^2, 6.56; $P = 0.01$]).

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

TABLE 2. Change from baseline to 6 months: results of bootstrapped (replications 1000) median regression, adjusting for baseline values and cluster

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

Significance values indicate median and inter-quartile range. Abbreviations: CI, confidence interval; DEMQOL, Dementia Quality of Life Measure; NPI, Neuropsychiatric Inventory; UPDRS, Unified Parkinson's Disease Rating Scale; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; EQ-5D, European Quality of Life 5 Dimensional Scale; HADS, Hospital Anxiety and Depression Scale.

on adoption of the toolkit at the team/service level, although 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 (ie, the control arm). Mean costs associated with healthcare and social service use reduced in the toolkit arm between baseline and 6-month follow-up, whereas 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 ± standard deviation], £223 ± £204, and 6 months, £294 ± £286; usual care baseline, £214 ± 239, and 6 months, £229 ± 206; group difference, $P = 0.098$).

Discussion

Our pilot cluster-randomized trial investigated the introduction of an evidence-based management toolkit for Lewy body dementia compared with 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 nonspecialist services for older people to participate and to recruit participants in all but 1 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

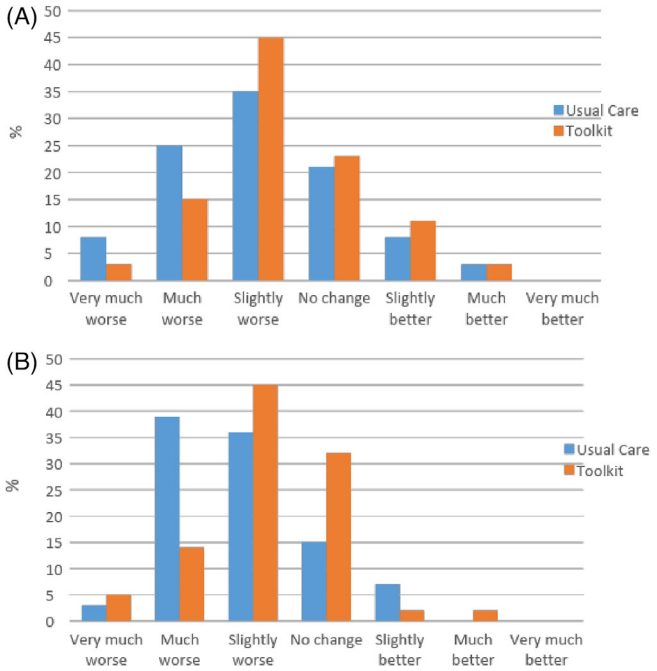

FIG 2. Outcome in terms of rating on the clinical global impression of change at 6 months on the Clinical Global Impression of Change as rated by (**a**) an independent rater (group difference $P = 0.11$) and (**b**) the carer (group difference $P = 0.03$).

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 1 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-recognized marked fluctuations in Lewy body dementia that may make more specific scales less reliable in detecting change compared with other dementias such as Alzheimer's disease or that the global outcome detects a number of small benefits that sum to make a global difference. This is particularly likely for our management toolkit, which was applied in a bespoke individualized way, according to the symptoms each patient had, which may be better detected by a global measure. In addition, carers may be particularly sensitive to the particular symptoms being managed in their case and also see patients during 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 that 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 recognized in carers of people with dementia. This is especially so for carers of those with Lewy body dementia, likely attributed 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 that are most associated with alleviating carer stress. Lewy body dementia is associated with a particularly poor outcome in terms of cognitive and functional declines and increased mortality.[3] There

TABLE 3. Total care costs by intervention arm

	Intervention			Usual care			Difference (intervention - control)	*p*-value*
	N**	Mean	SD	N	Mean	SD		
NHS&PSS resources								
Baseline	75	£2,153	£4,283	52	£1,373	£1,816	£779	>0.1
6MFU	64	£1,333	£1,393	45	£1,873	£3,825	−£540	>0.1
NHS resources only								
Baseline	75	£1,784	£4,057	52	£1,032	£1,293	£752	>0.05
6MFU	64	£831	£584	45	£1,386	£3,658	−£555	>0.05
PSS resources only								
Baseline	75	£589	£1,244	52	£555	£1,158	£34	>0.1
6MFU	64	£872	£1,280	45	£716	£1,309	£156	>0.1

* *p*-value from *t*-test with equal variances.
Abbreviations: NHS = National Health Service costs; PSS = Personal social care costs.

was no difference in mortality between those in services with or without the management toolkit, although this is unsurprising given most participants 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 because of the 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 although these differences were not statistically significant, they may have an economic impact. Interestingly, although costs decreased in the toolkit arm, medication costs showed a trend to rise that 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 because of our modest sample size. Because the costs of Lewy body dementia are higher than other dementias,[17,18] the demonstration of cost savings would be important to health services.

The strengths of this study include the systematic introduction of an evidence-based toolkit in a cluster-randomized 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-rated and carer-rated outcomes 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 recognize several limitations to the study. This was a pilot study and therefore underpowered, with efficacy as a secondary outcome, and although 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 the 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 the participants themselves or carers were fully blinded as to which arm they were allocated. 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 (eg, cholinesterase inhibitors are National Institute for Health and Care Excellence–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, although our survey indicated that the majority (50%) were experienced (consultant) medical staff and that around 30% of healthcare professionals who used the toolkit were nonmedical (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 article, the qualitative findings provided additional insights into how the toolkit was implemented and used within sites.

The toolkit was a broad intervention consisting of a number of recommendations, so we cannot directly determine the "mechanism of action" or "dose" of the toolkit, and further studies should include measures that 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 generalize our findings to other countries or healthcare settings.

In conclusion, we undertook a pilot cluster-randomized 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 >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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References

1. Walker Z, Possin K, Boeve B, Aarsland D. Lewy body dementias. Lancet 2015;386(10004):1683-1697.
2. McKeith I, Boeve B, Dickson D, et al. Diagnosis and management of dementia with ALewy bodies: fourth consensus report of the DLB consortium. Neurology 2017;89(1):88-100.
3. Price A, Farooq R, Yuan JM, Menon V, Cardinal R, O'Brien J. Mortality in dementia with Lewy bodies compared with Alzheimer's dementia: a retrospective naturalistic cohort study. BMJ Open 2017; 7(11):e017504.
4. Mueller C, Soysal P, Rongve A, et al. Survival time and differences between dementia with Lewy bodies and Alzheimer's disease following diagnosis: a meta-analysis of longitudinal studies. Ageing Res Rev 2019;50:72-80.
5. Stinton C, McKeith I, Taylor JP, et al. Pharmacological management of Lewy body dementia: a systematic review and meta-analysis. Am J of Psychiatry 2015;172(8):731-742.
6. Wang HF, Yu JT, Tang SW, et al. Efficacy and safety of cholinesterase inhibitors and memantine in cognitive impairment in Parkinson's disease, Parkinson's disease dementia, and dementia with Lewy bodies: systematic review with meta-analysis and trial sequential analysis. J Neurol Neurosurg Psychiatry 2015;86(2):135-143.
7. Connors M, Quinto L, McKeith I, et al. Non-pharmacological interventions for Lewy body dementia: a systematic review. Psychol Med 2018;48(11):1749-1758.
8. Morrin H, Fang T, Servant D, Aarsland D, Rajkumar A. Systematic review of the efficacy of non-pharmacological interventions in people with Lewy body dementia. Int Psychogeriatr 2018;30(3):395-407.
9. Taylor JP, McKeith I, Burn D, et al. New evidence on the management of Lewy body dementia. Lancet Neurol 2020;19(2):157-169.
10. O'Brien J, Taylor JP, Ballard C, et al. Visual hallucinations in neurological and ophthalmological disease: pathophysiology and management. J Neurol Neurosurg Psychiatry 2020;91:512-519.
11. National Institute for Health and Care Excellence (UK). Parkinson's disease in adults: diagnosis and management: full guideline. https://www.nice.org.uk/guidance/ng71/evidence/full-guideline-pdf-4538466253. Published 2017. Accessed March 6, 2019.
12. National Institute for Health and Care Excellence (UK). Dementia: assessment, management and support for people living with dementia and their carers. https://www.nice.org.uk/guidance/ng97. Published 2018. Accessed March 6, 2019.
13. Boström F, Jdnsson L, Minthon L, Londos E. Patients with dementia with lewy bodies have more impaired quality of life than patients with Alzheimer disease. Alzheimer Dis Assoc Disord 2007;21(2):150-154.
14. Van de Beek M, Van Steenoven I, Ramakers I, et al. Trajectories and determinants of quality of life in dementia with Lewy bodies and Alzheimer's disease. J Alzheimer's Dis 2019;70(2):389-397.
15. Galvin J, Duda J, Kaufer D, Lippa C, Taylor A, Zarit S. Lewy body dementia: the caregiver experience of clinical care. Parkinsonism Relat Dis 2010;16(6):388-392.
16. Lee D, McKeith I, Mosimann U, Ghosh-Nodyal A, Thomas A. Examining carer stress in dementia: the role of subtype diagnosis and neuropsychiatric symptoms. Int J Geriatr Psychiatry 2013;28(2): 135-141.
17. Mueller C, Perera G, Rajkumar A, et al. Hospitalization in people with dementia with Lewy bodies: frequency, duration, and cost implications. Alzheimer's Dement 2017;10:143-152.
18. Chen Y, Wilson L, Kornak J, et al. The costs of dementia subtypes to California Medicare fee-for-service, 2015. Alzheimers Dement 2019;15(7):899-906.
19. Thomas A, Taylor J, McKeith I, et al. Development of assessment toolkits for improving the diagnosis of the Lewy body dementias: feasibility study within the DIAMOND Lewy study. Int J Geriatr Psychiatry 2017;32(12):1280-1304.
20. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. J Eval Clin Pract. 2004; 10(2):307-312.
21. Thomas A, Taylor J, McKeith I, et al. Revision of assessment toolkits for improving the diagnosis of Lewy body dementia: the DIAMOND Lewy study. Int J of Geriatr Psychiatry 2018;33(10): 1293-1304.
22. McKeith I, Dickson D, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB consortium. Neurology 2005;65(12):1863-1872.
23. Emre M, Aarsland D, Brown R, et al. Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord 2007;22 (12):1689-1707.
24. Folstein M, Folstein S, McHugh P. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12(3):189-198.
25. Nasreddine Z, Phillips N, Bédirian V, et al. The Montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53(4):695-699.
26. Goetz C, Tilley B, Shaftman S, et al. Movement Disorder Society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov Dis 2008;23(15):2129-2170.
27. Sheikh JI, Yesavage JA. Geriatric depression scale (GDS): recent evidence and development of a shorter version. Clin Gerontol 1986;5 (1–2):165-173.
28. Cummings J, Mega M, Gray K, Rosenberg-Thompson S, Carusi D, Gornbein J. The neuropsychiatric inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44(12): 2308-2314.
29. Smith S, Lamping D, Banerjee S, et al. Development of a new measure of health-related quality of life for people with dementia: DEMQOL. Psychol Med 2007;37(5):737-746.
30. EuroQol Group. EQ-5D-5L instrument. EuroQol EQ-5D. https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/2009. Accessed February 26, 2019.
31. Bucks R, Ashworth D, Wilcock G, Siegfried K. Assessment of activities of daily living in dementia: development of the Bristol activities of daily living scale. Age Ageing 1996;25(2):113-120.
32. Zarit S, Reever K, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20(6):649-655.
33. Zigmond A, Snaith R. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67(6):361-370.
34. Beecham J, Knapp M. Costing psychiatric interventions. In: Thornicroft, G, editor. *Measuring Mental Health Needs (Second Edition)*. London, UK: Royal College of Psychiatrists; 2001:200–224.
35. British National Formulary. British Medical Association and the Royal Pharmaceutical Society. Pharmaceutical Press, London, UK; 2019.
36. National Health Service. 2017/18 reference costs and guidance: national schedule of reference costs. National Health Service improvement. https://improvement.nhs.uk/resources/reference-costs/ 2018. Accessed November 22, 2018.
37. Curtis LA, Burns A. Unit costs of health and social care 2018. Kent, UK: University of Kent; 2018. https://doi.org/10.22024/UniKent/01.02.70995.
38. Aarsland D, Ballard C, Walker Z, et al. Memantine in patients with Parkinson's disease dementia or dementia with Lewy bodies: a double-blind, placebo-controlled, multicentre trial. Lancet Neurol 2009;8(7):613-618.

39. Harding AJE, Morbey H, Ahmed F, et al. Developing a core outcome set for people living with dementia at home in their neighbourhoods and communities: study protocol for use in the evaluation of non-pharmacological community-based health and social care interventions. Trials 2018;19(1):247.

40. Horton MC, Oyebode J, Clare L, et al. Measuring quality of life in carers of people with dementia: development and psychometric evaluation of scales measuring the impact of DEmentia on CARers (SIDECAR). Gerontologist 2019;gnz136. https://academic.oup.com/gerontologist/advance-article/doi/10.1093/geront/gnz136/5613258?searchresult=1.