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# Improving the diagnosis and management of Lewy body dementia: the DIAMOND-Lewy research programme including pilot cluster RCT

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**Disclaimer:** This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.



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# Abstract

## Improving the diagnosis and management of Lewy body dementia: the DIAMOND-Lewy research programme including pilot cluster RCT

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**Background:** Lewy body dementia, comprising both dementia with Lewy bodies and Parkinson's disease dementia, is the second commonest cause of neurodegenerative dementia. Existing evidence suggests that it is underdiagnosed and without a consistent approach to management.

**Objectives:** To improve the diagnosis and management of Lewy body dementia by (1) understanding current diagnostic practice for dementia with Lewy bodies and Parkinson's disease dementia; (2) identifying barriers to and facilitators of diagnosis and management; (3) developing evidence-based assessment toolkits to improve diagnosis of dementia with Lewy bodies and Parkinson's disease dementia; (4) producing a management toolkit to facilitate management; and (5) undertaking a pilot cluster randomised clinical trial.

**Design:** Work package 1 assessed clinical diagnostic rates from case notes for dementia with Lewy bodies and Parkinson's disease dementia before and after (work package 1 repeated) introduction of an assessment toolkit. In work package 2, we developed a management toolkit for Lewy body dementia. In work package 3, we developed assessment toolkits for dementia with Lewy bodies and Parkinson's disease dementia and piloted these and the management toolkit in a clinical service. In work package 4, we undertook a pilot study of 23 services in nine NHS trusts that were cluster randomised to receiving and using the management toolkit or standard care. Work package 5 comprised a series of qualitative studies, examining barriers to and facilitators of diagnosis and management.

**Setting:** Secondary care memory assessment and movement disorder services in England.

**Interventions:** Assessment toolkits for Lewy body dementia consisted of questions for diagnostic symptoms, and management toolkits comprised 161 guidance statements grouped under five symptom domains.

**Review methods:** The systematic reviews of pharmacological and non-pharmacological management were based on published literature, with meta-analysis when possible, following a search of several electronic databases and the grey literature using terms related to Lewy body dementia, without restriction on time or language.

**Participants:** Participants aged  $\geq 50$  years diagnosed with dementia with Lewy bodies or Parkinson's disease dementia and, for work package 1 and work package 1 repeated, non-dementia with Lewy bodies and non-Parkinson's disease dementia controls. The qualitative studies included people with Lewy body dementia, carers and professionals.

**Main outcome measures:** For work packages 1 and 1 repeated, diagnostic rates for dementia with Lewy bodies and Parkinson's disease dementia as a proportion of all dementia or Parkinson's disease. For work packages 2 and 3, the production of diagnostic and management toolkits. For work package 4, feasibility of undertaking a cluster randomised trial of the toolkits, measured by number of participants recruited and use of the toolkits, assessed qualitatively.

**Results:** Work package 1 – 4.6% of dementia cases in secondary care received a dementia with Lewy bodies diagnosis (with significant differences in diagnostic rates between services) and 9.7% of those with Parkinson's disease had a diagnosis of Parkinson's disease dementia. There was evidence of delays in diagnosis for both dementia with Lewy bodies and Parkinson's disease dementia compared with control patients, and the costs of dementia with Lewy bodies and Parkinson's disease dementia were also greater than those for matched controls ( $p < 0.01$  for both). Work package 2 – we produced 252 statements regarding Lewy body dementia management and, following a Delphi process, 161 statements were included in a management toolkit. Work package 3 – piloting indicated that separate assessment toolkits for use in memory clinic and movement disorder services were preferred, but a single toolkit for Lewy body dementia management was suitable. Work package 4 – we were able to recruit Lewy body dementia patients to target and recruited 131 patients within 6 months (target  $n = 120$ ), of whom  $> 80\%$  were retained in the study at 6 months. Work package 5 – barriers to diagnosis and management of Lewy body dementia were complex. Managing Lewy body dementia often requires input from a range of specialties and, therefore, care pathways may be fragmented. Positive attitudes to diagnosing Lewy body dementia, working with a team with expertise in Lewy body dementia and opportunities for cross-specialty discussion of patients with complex needs facilitated diagnosis and management. The toolkits were generally well received, particularly the management toolkit. Implementation, however, varied, reflecting differences in attitudes, skills, time and local leadership. Work package 1 repeated – following introduction of the assessment toolkit, we found that 9.7% of dementia cases had dementia with Lewy bodies (a significant increase from baseline;  $p = 0.0019$ ), but Parkinson's disease dementia rates were similar (8.2%) to baseline.

**Limitations:** We included only two geographical regions and evidence informing the management toolkit was limited. Work package 4 was a pilot study and, therefore, we did not set out to assess the extent to which use of the management toolkit altered outcomes at the individual patient level. We noted implementation of the toolkits was variable. The increase in diagnostic rates in dementia with Lewy bodies following introduction of the assessment toolkits cannot be necessarily causally attributed to them.

**Conclusions:** Dementia with Lewy bodies and Parkinson's disease dementia were diagnosed in secondary care NHS services, with a lower frequency (around half) than that expected from known prevalence rates. The introduction of assessment toolkits for dementia with Lewy bodies and Parkinson's disease dementia was associated with increased diagnostic rates of dementia with Lewy bodies, but not Parkinson's disease dementia. Qualitative studies indicated inherent complexities of the disease itself, with treatment requiring input from different specialties and the potential for fragmented services, a workforce with variable training and confidence in Lewy body dementia, and negative attitudes towards diagnosis. The cluster randomised pilot trial demonstrated that patients could be successfully recruited, and provided preliminary evidence that the toolkits could be implemented in clinical services.

**Future work:** The evidence base informing the management of Lewy body dementia is limited, especially for non-pharmacological interventions. More well-designed randomised controlled trials for both cognitive and non-cognitive symptoms are needed.

**Trial registration:** Current Controlled Trials ISRCTN11083027.

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# List of supplementary material

**Report Supplementary Material 1** Management toolkit

**Report Supplementary Material 2** Assessment toolkits for dementia with Lewy bodies

**Report Supplementary Material 3** Health economics plan

**Report Supplementary Material 4** Work package 5 topic guide for interviews and focus groups

Supplementary material can be found on the NIHR Journals Library report page (<https://doi.org/10.3310/pgfar09070>).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.



## List of abbreviations

AMED	Allied and Complementary Medicine Database	MoCA	Montreal Cognitive Assessment
BNF	<i>British National Formulary</i>	NHS EED	NHS Economic Evaluation Database
CENTRAL	Cochrane Central Register of Controlled Trials	NICE	National Institute for Health and Care Excellence
CI	confidence interval	NPT	normalisation process theory
CINAHL	Cumulative Index to Nursing and Allied Health Literature	OAP	old age psychiatrist
CONSORT	Consolidated Standards of Reporting Trials	ONS	Office for National Statistics
DARE	Database of Abstracts of Reviews of Effects	PD	Parkinson's disease
DEMQOL	Dementia Quality of Life	PDD	Parkinson's disease dementia
DeNDRoN	Dementias and Neurodegenerative Research Network	PMG	Programme Management Group
DIAMOND-Lewy	Improving the Diagnosis and Management of Neurodegenerative Dementia of Lewy body type	PPI	patient and public involvement
DLB	dementia with Lewy bodies	PSC	Programme Steering Committee
EQ-5D-5L	EuroQol-5 Dimensions, five-level version	QALY	quality-adjusted life-year
GP	general practitioner	QATQS	Quality Assessment Tool for Quantitative Studies
LBD	Lewy body dementia	RCT	randomised controlled trial
MCI	mild cognitive impairment	REM	rapid eye movement
MMSE	Mini Mental State Examination	SD	standard deviation
		UPDRS	Unified Parkinson's Disease Rating Scale Part 3
		WP	work package
		WP1R	work package 1 repeated





## Plain English summary

**L**ewy body dementia includes dementia with Lewy bodies and Parkinson's disease dementia. It is the second most common cause of neurodegenerative dementia in older people, but is underdiagnosed. There is no consistent approach to management.

We aimed to improve the diagnosis and management of Lewy body dementia by:

- understanding current practice
- identifying barriers to diagnosis and management
- developing evidence-based assessment toolkits
- producing and piloting a management toolkit.

We focused on hospital-based specialist services. Participants included people aged  $\geq 50$  years diagnosed with Lewy body dementia, carers and health-care professionals. Current diagnostic rates for dementia with Lewy bodies and Parkinson's disease dementia were lower than expected (4.6% and 9.7%, respectively). There was evidence of delays in diagnosis for both dementia with Lewy bodies and Parkinson's disease dementia. The use of services and the overall costs of care for patients with dementia with Lewy bodies and Parkinson's disease dementia were greater than for patients who had other dementias. We found many barriers to the diagnosis and management of Lewy body dementia and these indicated the need to upskill staff, challenge negative attitudes towards diagnosis and improve management pathways.

Using published evidence and clinical opinion, we produced assessment and management toolkits for dementia with Lewy bodies and Parkinson's disease dementia. We used these in a pilot clinical study and showed that we were able to recruit people with dementia with Lewy bodies and Parkinson's disease dementia to the study. The toolkits were well received, but their use by clinical staff was variable. Following introduction of the assessment toolkits, there was an increase in diagnostic rates for dementia with Lewy bodies, but not Parkinson's disease dementia. Our findings indicate that a further larger study of the management toolkit is both feasible and merited.



# Scientific summary

## Background

Lewy body dementia includes two closely related conditions: dementia with Lewy bodies and Parkinson's disease dementia. Lewy body dementia is the second most common cause of neurodegenerative dementia in later life, although there remains a large discrepancy between rates from clinical studies and those based on autopsy (4–7% and 15–20% for dementia with Lewy bodies, respectively). Both dementia with Lewy bodies and Parkinson's disease dementia present with a range of clinical features, including cognitive impairment, motor symptoms, autonomic symptoms, sleep problems and neuropsychiatric features. Both dementia with Lewy bodies and Parkinson's disease dementia are associated with lower quality of life and higher carer stress, and have poorer outcomes, including increased mortality and higher rates of functional dependence. Accurate recognition is key for appropriate management, but currently many cases are not correctly recognised at initial assessment.

Little is known regarding prevalence or diagnostic practice in the UK and there are no systematic approaches to management or recognised care pathways.

DIAMOND-Lewy (Improving the DIAGNOSIS and Management of Neurodegenerative Dementia of Lewy body type) was a comprehensive 5-year programme of work seeking to investigate and implement ways to improve both the diagnosis and management of Lewy body dementia (i.e. both dementia with Lewy bodies and Parkinson's disease dementia) within the NHS.

## Objectives

- To undertake a baseline study of current practice in secondary care NHS services regarding the diagnosis and management of Lewy body dementia.
- To develop evidence-based practical toolkits for the assessment and management of Lewy body dementia.
- To implement the assessment toolkit and undertake a study to determine whether or not introduction of the toolkit resulted in an increase in diagnostic rates of dementia with Lewy bodies and Parkinson's disease dementia.
- To implement and undertake a pilot cluster randomised study of the management toolkit in NHS secondary care services to assess the feasibility of patient recruitment and retention, outcome measures and implementation of the toolkits in routine practice.
- To undertake qualitative studies to explore the barriers to and facilitators of making a diagnosis and improving management of Lewy body dementia.

## Methods

These objectives were met through five closely inter-related work packages, with a patient and public involvement group providing regular input throughout. We used mixed methods, including case note screening, systematic reviews, consensus methods, qualitative studies and a pilot cluster randomised trial.

### Work package 1

This provided a baseline measure of the proportion of cases diagnosed as having Lewy body dementia within NHS services and investigated diagnostic practice. Work package 1A focused on dementia with Lewy bodies and work package 1B focused on Parkinson's disease dementia. Our hypotheses were that

dementia with Lewy bodies would be diagnosed in  $\leq 5\%$  of dementia cases and Parkinson's disease dementia in  $\leq 10\%$  of Parkinson's disease cases.

We included services in two geographical parts of the UK, the north-east of England and East Anglia, and examined case notes of consecutive referrals to nine memory assessment services across four NHS trusts over an 18-month period. We identified all patients with a diagnosis of dementia, and of those patients who had been given a diagnosis of dementia with Lewy bodies.

We examined the notes of consecutive referrals to five movement disorders services, each in a separate NHS trust, comprising two geriatric medicine services and three neurology/geriatric medicine services. We identified all patients diagnosed with Parkinson's disease and Parkinson's disease dementia.

### **Work package 2**

We undertook systematic reviews of pharmacological and non-pharmacological management of Lewy body dementia, taking account of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting standards. For the pharmacological review, studies were identified through bibliographic databases, trials registers and grey literature. Reference lists of relevant studies and previous systematic reviews were also examined and input was sought from experts on Lewy body dementia. We used the keywords 'Lewy or parkinson' and 'dementia' and conducted searches until March 2015, without restrictions on publication date or language, but opinion papers were excluded. Studies were grouped and analysed according to pharmacological strategy. Methodological quality was assessed using the QATQS (Quality Assessment Tool for Quantitative Studies) [URL: [www.ehphp.ca/tools.html](http://www.ehphp.ca/tools.html) (accessed April 2021)].

The strategy for the non-pharmacological review was similar. We used the search terms [(Lewy OR Park\*) and Dementia]. Interventions were any non-pharmacological treatment identified using a wide range of terms that covered individual non-pharmacological therapies. Searches were conducted on 30 October 2016.

### **Work package 3**

Work package 3 identified, from the existing literature, validated questions designed to elicit key diagnostic features for dementia with Lewy bodies and, separately, for Parkinson's disease dementia. Toolkits were then produced for dementia with Lewy bodies and Parkinson's disease dementia and implemented, along with the management toolkit developed in work package 2, in a single NHS trust.

### **Work package 4**

In this work package, the assessment toolkit was introduced to 23 memory or movement disorder services, with half the services randomised to receive and use the management toolkit and the other half continuing with standard care (control arm). From these services, patients with dementia with Lewy bodies and Parkinson's disease dementia were recruited and assessed on a number of clinical and cognitive outcome measures at baseline, 3 months and 6 months. Our aim was to determine the feasibility of undertaking such a study and we aimed to recruit 120 subjects with dementia with Lewy bodies or Parkinson's disease dementia.

### **Work package 5**

This work package had three components: first, an investigation of the barriers to and facilitators of making a diagnosis and managing Lewy body dementia; second, and linked with work packages 3 and 4, exploration of views on the assessment and management toolkits; and third, exploration of implementation of the assessment and management toolkits in clinical practice. Methods included qualitative interviews with clinicians, patients and carers, observation of routine practice and clinician questionnaires.

### **Work package 1 repeated**

Finally, we undertook a repeat assessment over 18 months of dementia with Lewy bodies and Parkinson's disease dementia diagnostic rates following introduction of the assessment toolkits in some of the same services that had participated in work package 1.

## **Results**

### **Work package 1**

We identified 4504 patients with dementia, of whom 207 (4.6%) had a diagnosis of dementia with Lewy bodies. Prevalence in individual services ranged from 2.4% to 5.9% and was significantly higher among services in the north-east of England than in East Anglia (5.6% vs. 3.3%,  $\chi^2 = 13.6$ ;  $p < 0.01$ ). From these patients, we recruited 74 patients with dementia with Lewy bodies and 72 non-dementia with Lewy bodies control patients (defined as the next diagnosed dementia case seen by that service, matched for age, sex and Mini Mental State Examination score), all of whom consented to an in-depth case note examination. Patients with dementia with Lewy bodies had a significantly longer time from referral to diagnosis and more frequently received an incorrect prior diagnosis (in 30% of cases) than patients with non-dementia with Lewy bodies dementia. There were significantly higher health-care costs for patients with dementia with Lewy bodies than for patients with non-dementia with Lewy bodies dementia ( $p < 0.01$ ).

We examined the notes of 2263 referral patients to five movement disorders services, each in a separate NHS trust, comprising two geriatric medicine services and three neurology/geriatric medicine services. Of these patients, 1563 were diagnosed with Parkinson's disease, of whom 151 (9.7%) had a diagnosis of Parkinson's disease dementia. There was no significant variation between regions or services. We recruited 38 patients with Parkinson's disease dementia and 35 Parkinson's disease control patients (defined as the next patient with diagnosed Parkinson's disease seen by that service, matched for age and sex), all of whom consented to an in-depth case note examination to determine pathways to diagnosis and management. Those with Parkinson's disease dementia had evidence of delayed diagnosis, with 46% having impaired activities of daily living and 39% receiving a dementia treatment before a dementia diagnosis. There were significantly higher health-care costs for patients with Parkinson's disease dementia than for Parkinson's disease control patients ( $p < 0.01$ ).

### **Work package 2**

The reviews of pharmacological and non-pharmacological management of Lewy body dementia found a limited number of randomised controlled trials and very few non-pharmacological studies. High-level evidence was rare, with only 17 randomised controlled trials. Methodological quality was rated as weak for 41% of included studies, moderate for 39% and strong for 20%. Meta-analysis indicated beneficial effects of donepezil and rivastigmine for cognitive and psychiatric symptoms. Rivastigmine, but not donepezil, was associated with greater risk of adverse events. Meta-analysis of memantine suggested that it is well tolerated, but with few benefits. Descriptive summaries provided some evidence of benefits for galantamine, modafinil, levodopa, rotigotine, clozapine, duloxetine, clonazepam, ramelteon, gabapentin, zonisamide and yokukansan. Piracetam, amantadine, selegiline, olanzapine, quetiapine, risperidone and citalopram did not appear to be effective. This review concluded that high-level evidence related to pharmacological strategies for managing Lewy body dementia was rare. There were very few non-pharmacological studies and most were of poor quality with potential bias, with only one randomised trial. The review concluded that no definite recommendations could be offered regarding non-pharmacological management.

This existing evidence base, supplemented by two public and patient workshops, was used to produce 252 statements regarding Lewy body management. Following assessment by 26 experts using a Delphi approach, 161 statements were included in a final management toolkit that comprised three components: (1) a single summary page, (2) more detailed pages outlining management approaches to different symptom domains and (3) a detailed reference guideline.

### **Work package 3**

Following piloting, the main feedback on the assessment toolkits was that there should be separate assessment toolkits for use in memory/dementia services and general/movement disorder services, rather than separate assessment toolkits for dementia with Lewy bodies and Parkinson's disease dementia. A single management toolkit covering both dementia with Lewy bodies and Parkinson's disease dementia worked well. The assessment toolkits were redesigned and so the final toolkits comprised (1) an assessment toolkit for the diagnosis of dementia with Lewy bodies for use in memory services, (2) an assessment toolkit for the diagnosis of Lewy body dementia (covering both dementia with Lewy bodies and Parkinson's disease dementia) for use in movement disorder services and (3) a management toolkit for Lewy body dementia (covering both dementia with Lewy bodies and Parkinson's disease dementia).

### **Work package 4**

All but one service was able to take part in the study and recruit subjects. A total of 131 patients were recruited and assessed at baseline, 3 months and 6 months on a number of clinical and cognitive outcome measures. One hundred and twenty-seven participants (control arm,  $n = 52$ ; intervention arm,  $n = 75$ ) underwent baseline assessments and 109 participants completed the 6-month follow-up. For both dementia with Lewy bodies and Parkinson's disease dementia, and taking account of the cost of implementing the management toolkits, total costs increased over the course of the study in the control arms and decreased in the intervention arms, although these differences were not significant.

### **Work package 5**

Key barriers to the diagnosis and management of Lewy body dementia included clinician skills, training and knowledge (particularly in nurse-led memory services), service organisation, complexity of Lewy body dementia, and clinician attitudes and beliefs regarding the value of diagnosing Parkinson's disease dementia. The toolkits were generally acceptable, but implementation varied. In memory services, the assessment toolkit was primarily seen as relevant when a diagnosis of dementia with Lewy bodies was already suspected. In movement disorder services, implementation was hindered by time constraints and, for some, negative attitudes to diagnosis. Clinicians valued the management toolkit and found it easier to integrate into practice. Key benefits for clinicians were ease of access to trustworthy, up-to-date knowledge and increased awareness of the range of symptom areas affected by Lewy body dementia.

### **Work package 1 repeated**

We screened 2058 notes from memory services, identifying 1279 patients with dementia, of whom 6.2% had dementia with Lewy bodies (a significant increase from the baseline of 4.6%;  $p = 0.0019$ ). We screened 3405 case notes from movement disorders services and identified 1968 patients with Parkinson's disease. Of these patients, 8.2% had Parkinson's disease dementia (a non-significant change from the 9.7% identified at baseline).

### **Public and patient involvement**

Public and patient involvement was fundamentally important to the quality and relevance of our research. We established a public and patient involvement group that met regularly throughout the programme. The group reviewed the patient information sheet and consent forms, advised on toolkit structure and administration, advised on consent procedures and data capture for work package 5, contributed to the design and content of study newsletters, the website and public and patient involvement workshops, made recommendations about future public and patient involvement in research and wrote sections of this report, including the *Plain English summary*. In addition, separate public and patient involvement workshops in work package 2 highlighted patient and carer management priorities.

## Conclusions

Dementia with Lewy bodies and Parkinson's disease dementia were diagnosed in secondary care NHS services with a lower frequency (around half) than that expected from known prevalence rates. The introduction of assessment toolkits for dementia with Lewy bodies and Parkinson's disease dementia significantly increased the rates of dementia with Lewy bodies diagnosis (from 4.6% to 6.2%), but not of Parkinson's disease dementia. Qualitative approaches showed that clinician barriers to improving diagnosis and management included uncertainty around making the diagnosis and perceptions that it may not alter management. The systematic reviews indicated a limited evidence base to inform the content of the management toolkit, highlighted the lack of non-pharmacological studies and indicated a clear need for trials to be undertaken in dementia with Lewy bodies and Parkinson's disease dementia. A comprehensive management toolkit was introduced in a pilot cluster randomised trial, indicating that such trials are feasible.

## Implications for practice

The main implications of our findings for clinical practice are as follows:

- In the regions we studied, dementia with Lewy bodies and Parkinson's disease dementia appeared to be underdiagnosed compared with expected rates, with variability in diagnostic rates between services. This suggests that improvements may be needed in the way in which clinicians assess people for symptoms and make diagnoses.
- We found that the reluctance of some clinicians to make a formal diagnosis of dementia could be a significant factor contributing to the underdiagnosis of Lewy body dementia (particularly Parkinson's disease dementia). This implies that negative attitudes to disclosure may need to be challenged, possibly through supervision, appraisal or local audits to examine the diagnostic rate of Parkinson's disease dementia.
- Using a structured method, such as the assessment toolkit for diagnosis, may help increase diagnostic rates.

## Recommendations for research

Findings from the programme have a number of important implications for future research:

- The evidence base informing the management of Lewy body dementia is limited, especially for non-pharmacological interventions. More therapeutic studies are needed, especially well-designed randomised controlled trials for both cognitive and non-cognitive symptoms.
- Further study of effective ways of addressing the barriers to implementation of the assessment and management toolkits is merited, particularly as many barriers were outside the scope of our programme.
- Research into how best to co-ordinate multispecialty input to patients with Lewy body dementia is needed to streamline management and facilitate a holistic approach.
- Further work is needed to better understand how assessment toolkits for Parkinson's disease dementia can be integrated into practice to improve diagnostic rates. Qualitative studies indicate that there remain important barriers and negative attitudes to diagnosis and management, and further work is needed to see how these are best addressed.
- Our successful pilot demonstrates that a larger, more comprehensive trial of introducing the management toolkit could be undertaken, but this would need to include a minimum of 410 (and up to 908) patients, depending on the primary outcome.
- In such a study, it would be important to adopt a clear implementation strategy to ensure that it is appropriately resourced. An alternative approach to a larger trial would be to introduce and evaluate the toolkits through service quality improvement initiatives, working with services using principles from implementation science.

## **Trial registration**

This trial is registered as ISRCTN11083027.

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# SYNOPSIS

## Introduction

Lewy body dementia (LBD) is a term used to describe two closely related conditions: dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD). They form the second most common neurodegenerative dementia (after Alzheimer's disease), but it is recognised that they are underdiagnosed. Diagnosis has important implications for management, as those with LBD present with a range of variable clinical features, including cognitive impairment, motor symptoms, autonomic symptoms, sleep problems and neuropsychiatric features.

We undertook this programme because little is known regarding the prevalence or diagnostic practice of LBD in the UK and, although national management guidelines [e.g. National Institute for Health and Care Excellence (NICE) 2018<sup>1</sup>] do recognise the importance of both DLB and PDD and make some limited management recommendations, there are no systematic approaches to management or recognised care pathways. DIAMOND-Lewy (Improving the DIAGnosis and Management of Neurodegenerative Dementia of Lewy body type) was a comprehensive, multidisciplinary 5-year programme of work seeking to investigate and implement ways to improve both the diagnosis and management of LBD (i.e. both DLB and PDD) within the NHS.

We achieved this through a number of interlinked work packages (WPs), with a very strong patient and public involvement (PPI) core running throughout the programme. In this synopsis, we first describe our approach to PPI and how this influenced the design of the programme. In WP1, we undertook a retrospective case note study to investigate current practice in secondary care NHS services with regard to the diagnosis and management of LBD. In WP2, we undertook systematic reviews of pharmacological and non-pharmacological management of LBD and used this evidence, supplemented by a Delphi study of expert clinicians, to produce an evidence-based management toolkit. In WP3, we developed assessment toolkits for the diagnosis of LBD and, incorporating the management toolkit from WP2, piloted these assessment and management toolkits in routine NHS memory assessment and movement disorder services. In WP4, we introduced the assessment and management toolkits more broadly within a pilot cluster randomised trial. WP5 was a series of qualitative studies with three components: (1) an investigation of the barriers to and facilitators of making a diagnosis and managing LBD, (2) exploration of views on the assessment and management toolkits and (3) exploration of implementation of the assessment and management toolkits in clinical practice. Finally, in WP1 repeated (WP1R), we undertook a repeat assessment of DLB and PDD diagnostic rates following introduction of the assessment toolkits in some of the same services that had participated in WP1.

A research pathway diagram showing how these WPs linked together is provided (*Figure 1*). Each WP will now be discussed in turn after a description of the PPI core running throughout the programme.

SYNOPSIS

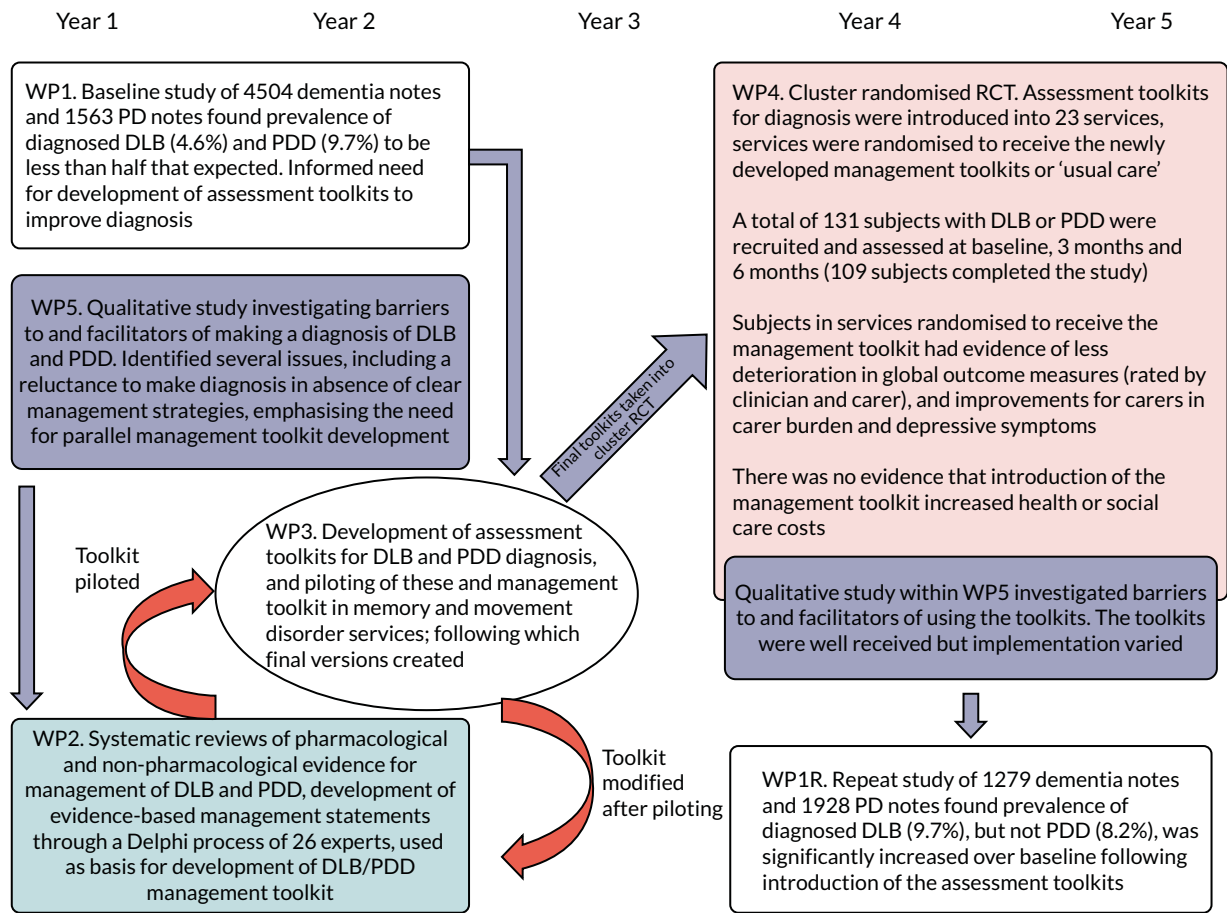


FIGURE 1 Research pathway diagram. PD, Parkinson's disease; RCT, randomised controlled trial.

# Patient and public involvement throughout the DIAMOND-Lewy programme

## Introduction

Patient and public involvement is seen as fundamentally important to the quality and relevance of research. In the light of calls for greater transparency and consistency in reporting PPI, we have followed the GRIPP2-SF (Guidance for Reporting Involvement of Patients and the Public 2-short form) reporting guidelines, highlighting the impacts of PPI and critically reviewing our approach to PPI.<sup>2-4</sup> Much of this section of the report was drafted collaboratively with members of the PPI group.

## Aim

The aim was to use PPI to inform all phases of the study from patient and carer perspectives.

## Methods

Patient and public involvement in this programme started very early, during the development of the proposal, with one PPI member (Derek Forster) being a co-applicant. Once the programme started, we established a PPI group that met regularly throughout the programme. Potential volunteers were sought through a public meeting organised by the North East Dementias and Neurodegenerative Research Network (DeNDRoN) in July 2013 and through the existing networks of Derek Forster and the DeNDRoN PPI co-ordinator. Three PPI representatives agreed to join the group with Derek Forster, and all four members contributed throughout the programme. All members' lives have been touched by neurodegenerative diseases, either as a patient or as a carer. In addition, members were motivated by their desire to 'give something back', interest in medical research and enthusiasm to help progress research into LBD. Experience of PPI varied. One member had been involved in PPI for > 10 years; however, for another this was their first PPI experience. All members received training on research through DeNDRoN. This was supplemented by an introductory session on LBD by Ian McKeith. One of the co-applicants (CB) facilitated the group and meetings were held on university premises. We followed the INVOLVE guidance on reimbursing group members for their time and expenses.<sup>5</sup>

The first PPI meeting focused on how to achieve the desired aim. This led to agreement that the group would:

- share personal knowledge and experience of DLB, Parkinson's disease (PD) and PDD
- comment on the practicalities and pressures that participating in the research could create for patients and carers (safeguarding)
- ensure that information was user-friendly and did not alarm potential participants
- ensure that a patient/carer focus was included in developing the management toolkit
- contribute to study newsletters.

Members agreed that the timing and duration of PPI meetings should reflect the needs of the programme. Although the group thought it was unnecessary to link individual PPI members to specific WPs, they were keen to embed PPI into the programme management structures. To achieve this, Derek Forster attended both the PPI group and the Programme Management Group (PMG) and Valerie Argent joined the Programme Steering Committee (PSC) as a lay member.

In addition to the PPI group, two PPI workshops were convened to inform the development of the management toolkit (see *Work package 2: development of management toolkits for Lewy body dementia*). Potential participants were identified by team members through patient and carer interviews conducted during WP5 and local contacts. One member of the PPI group (Anne Lister) also attended the PPI workshops for WP2. The content of the workshops is described in *Work package 2: development of management toolkits for Lewy body dementia*.

## Outcomes of patient and public involvement

The PPI group met 20 times, with full attendance at nearly all meetings. The number of meetings ranged from one to five per year. Members often prepared for meetings by reading documents, and commented on documents by e-mail between meetings. The initial expectation of group members and the research team was that the group would adopt a consultation approach, with an emphasis on ensuring that documents would make sense to patients and carers, including advising on the feasibility and acceptability of the study procedures. Over time, however, the group grew in confidence and were proactive in developing and expanding their role, adopting collaborative and user-controlled approaches at different times.<sup>6</sup> For example, rather than commenting on the public version of the study newsletter (which was initially drafted by the research team), members took ownership of the newsletter by redesigning the layout, introducing a new structure and writing much of the content themselves.

A user-controlled approach was adopted to obtain feedback on participants' experiences of taking part in the pilot trial. Rather than inviting a single participant to describe their experience at the PPI dissemination event in the North East, members were keen to present a broader range of experiences. This led to the development and inclusion of some open questions about study participation with the letter inviting participants to the PPI event. Overall, 28 detailed responses were received. Two members of the group (VA and AL) reviewed and collated the information and presented their findings at the PPI dissemination event. Key themes were the interpersonal skills of the interviewers and having an opportunity to talk about their situation. Everybody found the home visits convenient and > 70% of respondents said that they would be willing to take part in a similar study. These comments provided useful feedback for the researchers and highlight aspects of study design, which may maximise recruitment and retention in future studies. Furthermore, the comments highlighted the lack of support available after diagnosis, suggesting new avenues for research and intervention.

Key activities undertaken by both the PPI group and the PPI workshops in WP2 are related to the research cycle<sup>7</sup> and are summarised in *Table 1*.

Having highlighted some of the successful contributions made by PPI during the programme, we also acknowledge that its impact in some areas was limited. Owing to uncertainty about which outcome measures would prove sensitive to changes resulting from the introduction of the management toolkit, the team proposed a range of measures. Reconciling the perspectives of PPI members and those of the research team was sometimes challenging, for example in relation to the number of outcome measures and the perceived burden of these on participants, and in relation to the wording of questions in the assessment toolkit, some of which were considered to be inaccessible to patients and carers. However, there was limited scope to make changes because they were validated measures.

TABLE 1 Summary of key PPI outcomes

Stage of the research cycle <sup>7</sup>	Example outcomes
Identifying and prioritising the research agenda	Future research priorities were highlighted by the PPI workshops for WP2 and the feedback collected for the PPI event
Study design	Advised on consent procedures for clinic observation (WP5) and for notes review (WP1)  Reviewed outcome measures to ensure that they were appropriate and relevant (WP4)
Development of the grant proposal	Reviewed draft proposal  Contributed to lay summary  Included as a co-applicant (DF)
Undertaking/managing research	Reviewed PIS and consent forms (WPs 1, 2, 4 and 5)  Advised on most appropriate order of questions in assessment toolkit (WP3) and outcome measures (WP4)  Shared experiences of PD and LBD with a new researcher to raise awareness and understanding prior to data collection (WP5)  Advised on eliciting feedback on the toolkits (WP5)  Identified key principles to underpin the management toolkit (WP2)  Advised on appropriate ways of thanking study participants (WP4)  Wrote a thank-you letter for study participants (WP4)  Member of PMG (DF)  Member of PSC (VA)
Analysing and interpreting	Reviewed qualitative interview data (WP5)  Collected and analysed data on participants' experiences of the pilot trial (WP4)
Dissemination and implementation	Produced biannual programme newsletters  Produced lay summaries of published papers for the programme website  Drafted annual progress reports and this section of the report  Contributed to the organisation of PPI events  Presented at the North East PPI event
Monitoring and evaluation	Reflected on their role  Made recommendations for PPI in future research

PIS, patient information sheet.

## Discussion and conclusions

Using more than one approach to PPI in the programme proved effective. While the PPI group provided continuity throughout the programme, the workshops enabled the inclusion of a broader range of perspectives, including those of people with dementia. By combining a 'fully intertwined' approach to PPI and the 'one-off' approach for the workshops, we were able to include patients and carers who did not wish to commit to ongoing input.<sup>8</sup> The inclusion of PPI members on the PMG and PSC ensured opportunities for communicating with the full team. The detailed understanding of the programme developed through the PPI group, facilitated the ability of the PPI members to contribute confidently and effectively to meetings.

All members of the PPI group continued to be involved throughout the programme. This continuity helped the group to develop in confidence and expertise. Although we have benefited from stable group membership throughout the programme, members recognise that this may be unusual, as the health or circumstances of PPI members may deteriorate over a 5-year period, particularly if they are directly affected by the condition.

A limitation of the PPI group was the homogeneity of members in terms of ethnicity and class, and the lack of ability to alter some validated questions that members thought contained complex and inaccessible terms. Previous studies have emphasised the challenges of ensuring diversity in PPI, in particular the inclusion of people with dementia.<sup>9</sup> None of the members of the PPI group had dementia (although two had PD). Although caring for a spouse with LBD clearly provides significant insight into living with the condition, this is not the same as first-hand experience.<sup>9</sup> Despite the efforts of the DeNDRoN PPI co-ordinator, no people with dementia were identified for the PPI group. This partly reflects the low diagnostic rates and delays in diagnosing LBD (see *Work package 1: baseline study of the diagnosis and management of Lewy body dementia*). The situation was exacerbated by the high demand for PPI members in Newcastle upon Tyne, a Centre of Excellence in LBD research.

## Reflections

Recent publications on PPI have emphasised the need for increased understanding of effective approaches to PPI.<sup>4,8,10</sup> Unfortunately, we did not obtain formal feedback from workshop participants, although the attendance of several participants at the subsequent PPI dissemination event suggested an ongoing interest in the programme. The perception of the PPI group was that although not everyone in the research team initially recognised the potential value of PPI, their contributions were increasingly valued as the programme progressed. Although no formal evaluation or opportunities for reflection were planned at the outset, the process of drafting newsletters, giving presentations at the PPI event and drafting this section for the final report prompted the group to recognise their wide-ranging contributions and reflect on their experiences of this approach to PPI. Key factors thought to contribute to the success of the PPI group were as follows:

- having a simple two-page overview of the programme to help members understand the different WPs and how they were interlinked
- having regular meetings to maintain interest and understanding of the programme
- working together in a group and sharing ideas
- having a facilitator
- attending to practical issues, for example ease of access, free parking, timely reimbursement of expenses and flexibility over the timing of meetings
- having access to a computer and large screen to enable the group to produce or edit documents collaboratively during meetings
- having stability of group membership
- ensuring that meetings were business-like, but enjoyable.

Several of these factors are consistent with those identified in previous studies.<sup>8</sup> Three suggestions were made for facilitating PPI contributions to future projects. The first concerned the importance of all team members recognising and valuing the different perspectives offered by PPI members, even when these challenged their own views. The second related to greater clarity over the responsibilities and remit of the PPI member within the PSC and finally the group emphasised the need for the chairperson of the PSC to explicitly invite comments from the PPI member.

After 5 years, members of the PPI group are surprised at their continuing levels of enthusiasm and commitment. Reflecting on this, members attribute their loyalty to the relevance of the programme to their lives, compatibility of members and the appreciative facilitation. In terms of personal benefit, members have valued the opportunity to keep up with research, maintain mental agility and develop new skills. Although the programme has now ended, the PPI group is planning to share their experiences to wider audiences through a conference presentation and an article for lay audiences.

In summary, the inclusion of PPI throughout the programme was extremely valuable and added very positively to the design of the DIAMOND-Lewy programme, its conduct and outcome, with PPI members making key contributions that affected the design and administration of the assessment and management toolkits. PPI also played a key role in dissemination and feedback of the study to participants, with members taking ownership of content for regular study newsletters, designing suitable methods for thanking participants and playing key roles in the co-design and delivery of the programme dissemination events.





# Work package 1: baseline study of the diagnosis and management of Lewy body dementia

The aim of this WP was to undertake a baseline study of diagnosis and management of LBD in NHS secondary care services.

## Introduction

The accurate recognition of dementia and the diagnosis of dementia subtype helps ensure appropriate management, and are central to improving patient care. LBD, comprising both DLB and PDD, is the second most common cause of neurodegenerative dementia in older people, accounting for between 15% and 20% of all cases of dementia, according to autopsy studies.<sup>11</sup> However, clinical and epidemiological studies suggest rates of only 5–7%.<sup>12</sup> This suggests that a considerable number of people with LBD go undiagnosed and so are not offered potentially beneficial management strategies. More worryingly, incorrect diagnosis risks inappropriate management with drugs such as antipsychotics, which, even at a low dose, can have serious side effects and cause mortality in those with LBD.<sup>11</sup>

Currently, the proportion of cases of dementia diagnosed with DLB and PDD in NHS secondary care services is not known, nor has there been any systematic study of diagnostic practice or management in secondary care, although a US-based retrospective survey indicated frequent erroneous diagnosis and delays to a final correct diagnosis.<sup>13</sup> This is an essential first step to improving care. Therefore, this WP sought to establish the baseline for current diagnostic rates for DLB and PDD, providing a foundation for the other WPs. The WP was split into two parts: (1) WP1A examined diagnostic and management practice for DLB and took place in old age psychiatry and memory services, and (2) WP1B examined diagnostic and management practice for PDD. This latter element was undertaken in movement disorders services run by neurologists and geriatricians.

Initially, the plan had been to undertake WP1 solely in services in one geographic region of the UK (the north-east of England). However, there arose an opportunity to undertake a much more informative two-region study, whereby diagnostic rates for DLB and PDD could be ascertained in both the North East and East Anglia, two representative but clearly separate UK regions. This change also allowed some comparison of whether or not any variation in diagnostic rates and practice existed between regions.

## Work package 1A: baseline study of the diagnosis and management of dementia with Lewy bodies

### Methods

This WP took place over the first 2 years of the programme, with the aim of comparing rates of current clinical diagnosis of DLB with expected prevalence figures, confirming the accuracy of DLB diagnosis and comparing diagnostic and management pathways of those with DLB with those with non-DLB dementia. The hypothesis was that the actual rate of diagnosis of DLB would be  $\leq 5\%$  and that pathways to diagnosis of DLB would be longer and more complex than for non-DLB dementia.

The study had two phases: (1) a case note-screening phase to obtain information on consecutive referrals to services and (2) a phase involving detailed case note examination by clinical members of the research team (specialty registrars). Ethics approval was obtained for both phases from

National Research Ethics Service Committee North East – Newcastle and North Tyneside 1 (reference 13/NE/0268). In addition, we obtained approval from the Confidentiality and Advisory Group to allow the extraction of some information during phase 1 without the explicit consent of the person with dementia [reference CAG 8.03(PR8)/2013].

We included nine old age psychiatry/memory services across four NHS trusts (two in East Anglia and two in the North East). Approvals were obtained from all trust research and development departments. Referral lists were obtained over an 18-month period and consecutive case notes screened by the research team, with key data extracted, including age, sex, diagnosis and Mini Mental State Examination (MMSE) score. Those with a DLB diagnosis who were alive and felt to be well enough by the clinical team (105/207 cases identified) were approached for their consent to be included in a more detailed study of their notes, with the extraction of information regarding diagnostic and management pathways collected using a standardised case report form. To describe the management pathway for each participant, data were collected on the use of services, spanning several years of clinical records before and after final diagnosis. Data collected included the number of appointments before and after diagnosis, and the number and type of diagnostic investigations undertaken before and after diagnosis.

For each DLB participant who consented, a non-DLB control participant was recruited by selecting the next participant seen in the respective service who was diagnosed with non-DLB dementia, matched for age ( $\pm 5$  years), sex and MMSE score (in three bands: 0–10, 11–20 and 21–30) and who consented to participate. To assess the accuracy of the clinical diagnosis of DLB, a panel of three expert clinicians (not involved in the original diagnoses) independently reviewed clinical documentation and applied the 2005 international DLB consensus criteria to each case,<sup>14</sup> with a primary diagnosis of probable or possible DLB taken as agreement with a clinician diagnosis of DLB. The expert panel agreed with the clinical diagnosis in 99% of cases of DLB (74/75) and 97% of cases with non-DLB dementia (72/74). One DLB case was excluded because the panel felt that there was insufficient evidence to assign any dementia subtype. Two non-DLB cases were excluded: one because the panel felt that the case had a diagnosis of mild cognitive impairment (MCI) and the other because the diagnosis was thought most likely to be PDD.

The data on use of services were combined with unit cost data taken from routine sources, including NHS reference costs<sup>15</sup> and Personal Social Services Research Unit costs.<sup>16</sup> This enabled the cost of service use to be estimated and comparison between the cost of pathways to diagnosis and post-diagnosis care for DLB participants compared with control participants. Full details of the methods for this are included in *Appendix 1*. This study (and WP1B) were approved by the North East – Newcastle & North Tyneside 1 Research Ethics Committee (reference 13/NE/0268) and the Confidentiality and Advisory Group [reference 8.03(PR8)/2013].

### Statistical analysis

Continuous data were assessed using *t*-tests, with chi-squared tests used for categorical data. Differences in costs between DLB and non-DLB participants were explored using independent-samples *t*-tests with unequal variance for normally distributed variables, Wilcoxon rank-sum tests for continuous non-normally distributed variables and chi-squared tests were used to explore differences in proportions. Differences in average cost between those with DLB and controls in the costs of diagnosis and of post-diagnosis treatment were estimated using marginal effects from a generalised linear model of costs. The generalised linear model was specified with a gamma distribution and a log-link function to account for skewness in the distribution of costs.

### Results

We identified 9449 consecutive referrals, of whom 4504 received a diagnosis of dementia. Of those patients receiving a diagnosis of dementia, 207 (4.6%) received a diagnosis of DLB and of these, 74 DLB patients and 72 non-DLB dementia control patients consented for more detailed study of their notes (see *Appendix 1, Table 8*, for details of cohort characteristics).

Dementia with Lewy bodies was diagnosed in 4.6% of all those with dementia and there was evidence of a difference in diagnostic rates between the two regions, with the rate in the North East being higher (5.6%) than in East Anglia (3.3%) ( $\chi^2 = 13.6$ ;  $p < 0.01$ ). There were differences in the number of core diagnostic features for DLB between the North East and East Anglia, with more clinical features being present in DLB cases diagnosed in East Anglia, suggesting a higher 'threshold' for diagnosis, which would be consistent with the lower rates of diagnosis. Use of biomarkers, such as dopaminergic imaging, was also significantly different between the two areas, with the use of biomarkers being much less common in East Anglia. Overall, there was evidence of an impact of age, with younger participants taking longer to receive an accurate DLB diagnosis than older patients. Those with DLB were more likely to have received another diagnosis before DLB (mean alternative diagnoses before final dementia diagnosis 1.1 vs. 0.6;  $p = 0.003$ ). DLB participants also had significantly more clinical assessments and imaging tests prior to their diagnosis than those with non-DLB dementia (Table 2). Data on costs were estimated over a time of 6.4 years for DLB participants compared with 5.1 years for non-DLB participants. Overall, the average cost of care for DLB participants was £6557, compared with £3425 for non-DLB participants [mean difference £2868, 95% confidence interval (CI) -£68 to £4013;  $p = 0.055$ ] (see Appendix 1, Table 9). After controlling for sex, time since diagnosis, total resource use time and other patient characteristics, having a DLB diagnosis resulted in an increase of £3600 in total costs compared with non-DLB participants ( $p < 0.001$ ). For DLB participants, medical history costs represented the largest contribution, with an average across participants of 40% of total costs compared with 27% for non-DLB participants ( $p = 0.042$ ) (see further details in Appendix 1, Tables 10 and 11).

## Work package 1B: baseline study of the diagnosis and management of Parkinson's disease dementia

This study, also undertaken over the first 2 years of the programme, looked at diagnostic and management practice in those with PDD, with the aim of establishing baseline diagnostic rates for PDD and comparing investigations, assessment and management of those with PDD with control participants (i.e. patients with PD without dementia).

### Methods

We included five PD or movement disorder services, each from a separate trust, comprising two geriatric medicine services and three services that combined geriatric medicine and neurology expertise. The research team reviewed notes of all referrals to services over an 18-month period. Those patients identified with PDD who were alive and felt to be well enough by the clinical team (44/151 identified) were approached for consent for a more detailed study of their notes, with the

TABLE 2 A comparison between regions of factors relevant to diagnosis

Results: regional diagnostic variation	North East, n	East Anglia, n	Statistic	p-value
Core features of DLB at time of diagnosis (mean)	1.5	2.1	-2.78 (Student's t-test)	0.007
Suggestive features of DLB at time of diagnosis, including DaT scans (mean)	0.8	0.4	2.63 (Student's t-test)	0.0011
Abnormal DaT scans prior to diagnosis	24	1	12.9 (chi-squared test)	0.001
DaT scans prior to diagnosis (including normal)	31	1	20.6 (chi-squared test)	< 0.001
Total diagnostic features (core and suggestive) of DLB at time of diagnosis	2.4	2.6	0.80 (Student's t-test)	0.42
Time between first secondary care appointment and final diagnosis (years)	1.4	0.9	1.03 (Student's t-test)	0.31
DaT, dopamine transporter.				

extraction of information with regard to diagnostic and management pathways collected using a case report form. For each PDD participant who consented, a person with PD but without dementia (control) was recruited by selecting the next case seen in the respective service who was diagnosed with PD, matched for age ( $\pm 5$  years) and sex, and who consented to participate.

Similar methods of analysis as those described for WP1A (see *Work package 1A: baseline study of the diagnosis and management of dementia with Lewy bodies*) were used to collect and analyse data, and ethics, Confidentiality Advisory Group and research and development approvals were sought and obtained.

### Results

The research team identified 2263 referral patients, of whom 1563 had a diagnosis of PD. Of these patients, 151 (9.7%) had received a diagnosis of PDD and of these, 38 PDD patients and 35 PD control patients were approached and consented for detailed review of their notes (see *Appendix 1, Table 8*, for details of cohort characteristics). For PDD, unlike DLB, there was no evidence of a difference in diagnostic rates between the two regions ( $p = 0.2$ ), although mean MMSE scores at time of diagnosis were lower in East Anglia than in the North East ( $p = 0.008$ ).

Examining the management pathways, there was evidence that dementia was probably present well before the diagnosis of PDD was made. For example, 46% of those with PDD had impaired activities of daily living due to cognitive impairment, with a mean intervening time of 1.5 years prior to diagnosis. Cognitive impairment in multiple domains was present in 57% of patients at a mean period of 2 years before diagnosis and 39% of patients had received an antidementia drug at an average of 1.75 years before a dementia diagnosis.

Data on costs were available for an average of 9.3 and 7.8 years of management for PDD patients and PD control patients, respectively. There was no evidence of a difference in average total costs between PDD and PD controls (average difference £2024, 95% CI  $-\text{£}3598$  to  $\text{£}5548$ ;  $p = 0.462$ ) (see *Appendix 1, Table 9*). After controlling for sex, time since diagnosis, total resource use time and other patient characteristics, PDD participants had an average total cost of care of £7655 more than PD controls (95% CI  $\text{£}3676$  to  $\text{£}11,634$ ;  $p < 0.001$ ). PDD participants had higher average costs of investigations (£250 more, on average, 95% CI  $\text{£}237$  to  $\text{£}306$ ;  $p = 0.001$ ) and higher post-diagnosis management costs (£570 more, 95% CI  $\text{£}281$  to  $\text{£}808$ ;  $p = 0.001$ ) (see *Appendix 1, Tables 10 and 11*).

### Discussion

Our results showed, in keeping with our expectations, that DLB and PDD were diagnosed at around half (or less) the rates that one would expect them to be, based on prior epidemiological and pathological studies.<sup>12</sup> There was clear evidence of differences in diagnostic practice between different services and different regions, with a higher threshold for diagnosing DLB being, unsurprisingly, associated with lower diagnostic rates. For PDD, there was evidence that the diagnosis was delayed, with those diagnosed by services in one region having a significantly lower MMSE score at point of diagnosis than the other, and those diagnosed with PDD had evidence of dementia being present up to 2 years before the actual diagnosis was made. Our study had limitations, including the use of retrospective data and sampling of only some services in two geographical regions. Services were not randomly selected, but selected on the basis of geography. For the detailed case note assessment of subjects, we were able to obtain only a modest number of cases and there may have been selection bias, as we could consent only people who were alive and not deemed too unwell by their clinical teams to approach. The diagnostic rate findings have been fully published<sup>17</sup> and the differences in pathways to diagnosis and management are currently in preparation. In terms of costs for both DLB and PDD groups, there was evidence that after controlling for sex, time since diagnosis, total resource use time and other patient characteristics that the costs of care were higher for both DLB and PDD groups than their respective controls.

# Work package 2: development of management toolkits for Lewy body dementia

## Objectives

The objectives of WP2 were to (1) complete a systematic review of evidence about the management of LBD and (2) use this to develop a clinical guideline, using a Delphi process incorporating the views of a multidisciplinary panel of independent experts combined with two facilitated PPI workshops.

## Systematic reviews

At the time that these reviews were undertaken and to the best of our knowledge, no evidence-based reviews of the comprehensive management of LBD existed. As a consequence, little formal management guidance for LBD was offered in the NICE dementia guideline used at that time,<sup>18</sup> despite the fact that this group of patients has multiple symptoms requiring treatment. Clinical guidance at the time appeared solely in the form of pharmacological reviews and expert consensus opinion statements.<sup>14,19,20</sup> This was an unsatisfactory situation for prescribers, health-care providers and recipients of care. We therefore conducted systematic reviews on pharmacological and non-pharmacological management of DLB.

## Methods

The first of our two systematic reviews<sup>21</sup> examined research on treatment effects and costs, and patient and carer views of pharmacological management strategies for LBD. Studies were identified through bibliographic databases, trials registers, grey literature, reference lists and experts. The review protocol is provided in *Appendix 2*.<sup>22</sup> In brief, we used the keywords 'Lewy or parkinson' and 'dementia', conducting searches until March 2015, without restrictions on publication date or language. Titles and abstracts were screened, with non-English-language papers screened by native speakers, and criteria used were (1) participants who had a diagnosis of DLB, PDD or LBD, (2) studies examined pharmacological strategies and (3) outcome measures and scores were specified. No restrictions were placed on study design, but opinion papers were excluded. Data were extracted in relation to participant demographic characteristics, selection criteria, study design, management strategies, outcome measures and scores, adverse events and withdrawals. Studies were grouped and analysed according to pharmacological strategy. Methodological quality was assessed using the Quality Assessment Tool for Quantitative Studies (QATQS) [URL: [www.ehpc.ca/tools.html](http://www.ehpc.ca/tools.html) (accessed April 2021)]. The QATQS examines selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs. Domains are rated as being of weak, moderate or strong quality, which feeds into an overall rating of study quality.

Meta-analyses were conducted and, when studies could not be combined, summaries were provided. The level of evidence and grade of recommendations for each management strategy were assessed using the Oxford Centre for Evidence-Based Medicine criteria.<sup>23</sup>

Forty-four studies examining 22 strategies were included in the review. Meta-analysis indicated beneficial effects of donepezil and rivastigmine for cognitive and psychiatric symptoms. Rivastigmine, but not donepezil, was associated with greater risk of adverse events. Meta-analysis of memantine suggested that it is well tolerated, but with few benefits. Descriptive summaries provided some evidence of benefits for galantamine, modafinil, levodopa, rotigotine, clozapine, duloxetine, clonazepam, ramelteon, gabapentin, zonisamide and yokukansan. Piracetam, amantadine, selegiline, olanzapine, quetiapine, risperidone and

citalopram did not appear to be effective. Methodological quality was rated as weak for 41% of included studies, moderate for 39% and strong for 20%. This review concluded that high-level evidence related to pharmacological strategies for managing LBD is rare and that strategies for important areas of need in LBD, such as autonomic symptoms and carer burden, had not been investigated, nor had the views of patients and carers about pharmacological strategies.

This review<sup>21</sup> of pharmacological management was published in the *American Journal of Psychiatry* (impact factor = 13.6) and by the end of 2018 had been cited 92 times, with an Altmetric Attention Score of 26 placing it in the top 5% of all research outputs scored. It formed the basis for the subsequent development of the management guideline and the first round of statements for Delphi panel evaluation.

Our second systematic review in WP2 regarded the non-pharmacological management of LBD.<sup>24</sup> Details of the search strategy are described in *Appendix 3*. As with pharmacological management, the literature and guidance available about LBD management available to clinicians and families at that time was virtually non-existent and mainly accessed through not-for-profit support organisations. Bibliographic databases were searched using a wide range of search terms and no restrictions were placed on study design, language or clinical setting. We used the search terms [(Lewy OR Park\*) and Dementia]. Interventions were any non-pharmacological treatment and identified using a wide range of terms covering individual non-pharmacological therapies: activit\*, acupuncture, alternative, animal, aromatherapy, art therapy, assisted, balance, behav\*, bicycle, calisthenics, carer intervention, caregiver intervention, CBT, Chi gong, cognit\*, cognitive behavioral therapy, cognitive behavioural therapy, counsel\*, creative arts, dance, dancing, diet, direct current stimulation, drama, ECT, educat\*, electroconvulsive therapy, enhanc\*, environmental intervention, environmental modification, exercise, flexibility, humor therapy, humour therapy, hydrotherapy, intervention\*, leisure, light therapy, management, martial arts, massage, meditation, Montessori, multisensory, music, non-pharm\*, nonpharm\*, nutrition, occupational therapy, pet therapy, physical activity, physical therapy, physiotherapy, pilates, psychoeducation, psychol\*, psychosocial, psychotherapy, Qi gong, reality orientation, recreation\*, reminiscence, resistance training, run\*, sensory, simulated presence, stimulation, Snoezelen, support\*, support group\*, swim\*, tai chi, therap\*, therapeutic activity, TMS, training, training carers, training caregivers, transcranial magnetic stimulation, treatment\*, validation, weight training, yoga. Searches were conducted on 30 October 2016.

The search identified 21 studies [including two randomised controlled trials (RCTs) with available subgroup data], seven case series and 12 case studies. Most studies reported beneficial effects of the interventions used, although the only sizeable study was on dysphagia, showing a benefit of honey-thickened liquids. Given the heterogeneity of interventions and poor quality of the studies overall, no quantitative synthesis (meta-analysis) was possible. Overall, identified studies suggested possible benefits of non-pharmacological interventions in LBD, but the small sample sizes and low quality of studies meant that no definite recommendations could be offered. This work underscored the clear and urgent need for future research on this topic.

The review of non-pharmacological management was published in *Psychological Medicine*<sup>24</sup> (impact factor = 5.4) and was also subsequently incorporated into the development of the management toolkit.

### **Public-patient workshops**

Two public-patient workshops were held, with the participation of 38 people with LBD and their family/carers. The first event focused on identifying best practice in LBD clinical management, based on their own experiences. The content of the workshops is shown in *Figure 2*. The emergent themes were developed further in the second event and refined into a set of guiding principles.

Some of the key themes that were held to be important are listed in *Table 3*. The themes were structured in such a way as to help the clinical team deliver the guideline recommendations in a user-friendly format.



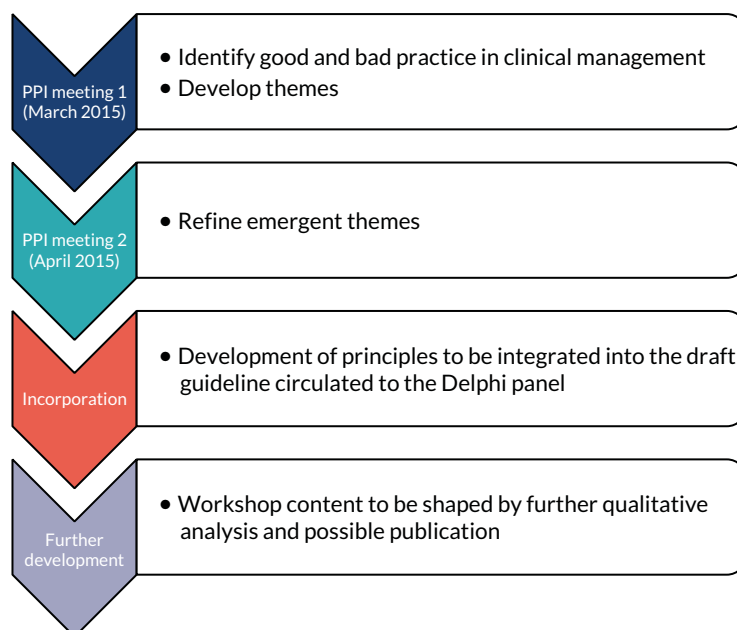


FIGURE 2 Workshops and content.

TABLE 3 Management principles arising from public–patient workshops

Management principle	Summary of discussion point
1	<ul style="list-style-type: none"> <li>• Provide practical information at an early stage (e.g. power of attorney, attendance allowance, council tax)</li> </ul>
2	<ul style="list-style-type: none"> <li>• Advantages and disadvantages to a problem list were identified:               <ul style="list-style-type: none"> <li>○ Risks that problem lists generate unwarranted concerns</li> <li>○ A long list of problems could be demoralising</li> <li>○ Reassuring as realise that these are expected symptoms not part of a new illness</li> </ul> </li> </ul>
3	<ul style="list-style-type: none"> <li>• Recognise that the carer is often the expert on the patient</li> <li>• Recognise the danger of doctors treating what they know best</li> </ul>
4	<ul style="list-style-type: none"> <li>• Main reliance on decision-making is guidance from the doctor; people want to be told what the doctor feels would be best for them</li> </ul>
5	<ul style="list-style-type: none"> <li>• Carer diary can be useful to see the pattern of response to medication on good and bad days (but may not be completed when things are OK or improving)</li> </ul>
6	<ul style="list-style-type: none"> <li>• Increased carer stress in DLB – need to explicitly discuss with carer on their own</li> </ul>
7	<ul style="list-style-type: none"> <li>• Peer support groups may be helpful (providing people have the same condition)</li> <li>• Where geographical distance is a problem, telephone or e-mail contact may still be helpful</li> <li>• Carer groups are very valuable for support and practical help</li> </ul>

From our work, a core element was the recognition that the carer is often the expert on the person with dementia and they need to feel that this is recognised. Although people want to be told what the clinician feels would be best for them, they also expressed concern about doctors treating what they know best, rather than following patient and carer preferences, or seeking help from other types of expert. Carer diaries were often mentioned as a useful way of dealing with these issues. Opinions were divided as to whether or not the patient and carer should be seen together by the clinical team, separately or offered both. Some issues, such as increased carer stress, which is high in LBD, probably need to be explicitly discussed with the carer on their own.

Although the advantages of developing and working through a problem list were recognised, it was also said that a long list of problems could be demoralising, something that is particularly relevant for LBD where there are often many symptoms, not all of which may need to be formulated as problems. It was noted as helpful that an expert experienced in LBD is often able to offer reassurance that these symptoms can be expected as part of the disorder and not part of another illness.

Carer and peer support groups are very valuable for support and practical help, providing people have similar conditions. Support groups are one source of practical information at an early stage on important general matters, including power of attorney, attendance allowance and council tax. Where geographical distance is a problem, telephone or e-mail contact may still be helpful.

A clear message throughout the PPI consultations was that although they appreciated the levels of care and concern that clinical teams offered, they often had difficulty in obtaining and understanding information about LBD. A lack of post-diagnostic support, advice and counselling was frequently mentioned, as was a shortage of easily accessible materials. As a result, the guideline that we produced contained links to what were judged to be the best-quality information sources at the time of writing, and it is hoped that these will be made freely available to those attending our NHS services and that they will, in turn, be replaced by improved versions and adapted for local use.

### **Guideline development**

Using the systematic reviews and public-patient feedback, an initial draft of the guidelines was developed by two authors (J-PT and IMcK). Statements relating to symptom domains were created and, using an anonymised online platform, reviewed by the Delphi panel. The panel comprised experts in the field ( $n = 26$ ), including psychology, geriatrics, psychiatry, neurology, primary care, physiotherapy, nursing and academic experts and some key international opinion leaders (see *Appendix 4* for list of contributors), who were identified through consultation with relevant stakeholder groups and supported by an extensive publication search and/or their role as keynote speakers on management of LBD at conferences. The Delphi process was undertaken over three rounds. A high level of agreement was sought across the three rounds (85% for rounds 1 and 2, and 75% for round 3). Controversial statements were modified on the basis of feedback and rerun in the subsequent round or removed. Of 252 original statements, 161 were kept, with 78 of these (48.4%) gaining full consensus panel agreement for inclusion, 52 (32.3%) with 90–99% consensus agreement and 31 (19.3%) agreed by 75–89% of the panel. After this process, the guideline statements were re-collated and formulated into one document. More controversial statements (but still meeting majority consensus opinion of > 50%) were included as clarifying footnotes, where appropriate, in the guideline document.

The guideline statements were then supplemented by summary management sheets (one overall summary figure and separate summary figures for each key symptom domain, produced by J-PT and IMcK, with input from the DIAMOND-Lewy team) that accompanied the written guideline, with the whole package being called the management toolkit. This toolkit was then subjected to further evaluation and feedback in WP3 and typographical corrections or clarification of guideline statements (although no change to content or meaning) were made based on the feedback from clinicians.

The management toolkit was finalised at this point and put forward for evaluation in WP4 (see *Report Supplementary Material 1*). The toolkit comprised an overview (see *Appendix 5*), brief summaries for each symptom area and the management guideline.

### **Dissemination of the toolkit**

Our major output has been the acceptance of an authoritative management review,<sup>25</sup> which contains reference to the Delphi statements and the evidence base used to produce the management toolkit, in *Lancet Neurology* (impact factor = 27.14). This has made the findings from our guidelines accessible for adaption and implementation in clinical services internationally.



Specific to the UK and NHS context, we have a dissemination plan, including:

- making the management toolkit freely available via our website
- embedding the use of the management toolkit in significant national educational fora (e.g. the British Association of Psychopharmacology)
- developing an online learning resource with video discussing management approaches in LBD.



# Work package 3: development of assessment toolkits for the diagnosis of Lewy body dementia

## Introduction

Work package 3 was developed because the accurate recognition of LBD is crucial to ensuring appropriate management and, therefore, central to improving patient care in dementia.<sup>26-28</sup>

Prior to this programme, there was no single simple-to-administer toolkit that incorporated assessment of all the symptoms needed to make a diagnosis of DLB and PDD. Therefore, WP3 aimed to develop such assessment toolkits to improve the recognition and diagnosis of both DLB and PDD.

## Methods

We developed the final LBD assessment toolkits in three stages: (1) identifying validated assessments for different symptoms and signs needed for a LBD diagnosis to make a pilot instrument, (2) obtaining feedback on the acceptability and feasibility of the toolkit through interviews with clinicians and the programme PPI group, and (3) piloting the toolkits in memory and movement disorder services prior to producing a final version to be used in WP4.

### *Stage 1: development of pilot assessment toolkits*

Following funding, the DIAMOND-Lewy PMG first discussed the basic approach to the problem and, in particular, whether one overall assessment and assessment toolkit should be developed or two separate ones, one for DLB (aimed at memory services) and one for PDD (aimed at movement disorder services or neurology and geriatric medicine services that also see people with movement disorders). It was concluded that two different instruments would be needed that matched the international diagnostic criteria for DLB<sup>14</sup> and PDD.<sup>29</sup> The clinical experts in the DIAMOND-Lewy programme (AT, J-PT, IMcK, LA, DB and JOB) then reviewed the published literature and supplemented this with their expert knowledge to identify available validated assessment instruments<sup>26-28,30</sup> that would form the contents of the toolkits. The PMG identified appropriate components for each toolkit from the identified assessment instruments.

For the DLB toolkit, the aim was to improve identification of the core and suggestive diagnostic symptoms, as diagnosis of cognitive impairment and dementia in specialist memory services is not a concern. At the time of toolkit development, there were six core and suggestive symptoms for diagnosing DLB. One was dopaminergic imaging, which would not form part of a clinical assessment tool, and another was neuroleptic sensitivity, which can only be identified following exposure to antipsychotic drugs, which is now a rare event.<sup>31,32</sup> Therefore, the focus was on assessment of the four remaining symptoms: (1) persistent complex visual hallucinations, (2) spontaneous cognitive fluctuations, (3) spontaneous parkinsonism and (4) rapid eye movement (REM) sleep behaviour disorder. The following components of the instrument were identified:

- cognitive fluctuation – four questions to carers from the Dementia Cognitive Fluctuation Scale<sup>28</sup>
- REM sleep behaviour disorder – a single screening question to carers from the Mayo Sleep Questionnaire<sup>27</sup>
- visual hallucinations – two core questions for patients and two for carers from the North East Visual Hallucinations Inventory<sup>30</sup>
- motor features of parkinsonism – five items from the Unified Parkinson's Disease Rating Scale.<sup>26</sup>

For the PDD toolkit, the aim was to improve identification of cognitive impairment and to facilitate matching of symptoms to the PDD diagnostic criteria.<sup>29</sup> The Montreal Cognitive Assessment (MoCA) was identified as most appropriate for brief cognitive assessment in this context.<sup>33</sup>

### **Stage 2: feedback and modification of toolkits**

During 2014, as WP3 lead, Alan Thomas put together the two instruments and there followed a period of iteration with the rest of the PMG. This led to the formulation of draft versions of the toolkits, which were then sent to the PPI panel for feedback in early 2015. PPI panel feedback was incorporated into a revised version, which was again commented on by the PMG and PPI members until final agreed versions of the toolkits and text were agreed for the pilot study. These iterative rounds led to changes in the wording of questions to try to improve clarity. In addition, a major change suggested was to separate the PDD toolkit into one version for use with carers and one for use with patients, based on how patients present to PD services where they may or may not have a carer present. After final iterations between PMG and PPI groups, three final assessment toolkits were produced for the pilot and feasibility study.

### **Stage 3: pilot and feasibility of assessment toolkits**

During early 2015, as the final versions of the toolkits were developed and by mid-2015, the necessary research ethics approval was obtained from Yorkshire and The Humber – Bradford Leeds Research Ethics Committee (reference 15/NE/0028). Trust research and development approval was also obtained prior to the start of the study.

In the autumn of 2015, we conducted the pilot study of the feasibility of the assessment toolkits in memory and PD services at Gateshead Health NHS Foundation Trust. Details are published in Thomas *et al.*<sup>34</sup> Briefly, we obtained engagement from medical and nursing staff in these services who administered the toolkits to > 20 patients, with individual clinicians using the toolkits between zero and seven times in patients with and without LBD. Feedback on acceptability and thoughts on improvement were obtained by direct comments to the WP lead (AT) and the research nurse by comments written on the toolkits and from qualitative interviews with patients, carers and clinicians.

Clinicians found the toolkits straightforward to use, although in the PD service they found attempting the cognitive assessment to be a problem because of time constraints. These clinicians were also keen to have the questions about core symptoms of DLB included in the toolkit for PD services. Patients and carers had no concerns about their use or how the questions were phrased. Therefore, following the pilot, a revision of the toolkits was produced that took these comments into account. Specifically, we produced a single assessment toolkit (the LBD toolkit) for PD services, which included the questions from the DLB toolkit for identifying core DLB features. Finally, by this time, the revised DLB consensus diagnostic criteria were being published,<sup>11</sup> which led to a few final minor changes to these toolkits to ensure that they were aligned with the revised criteria. Details of these changes were published.<sup>35</sup>

### **Use of the toolkits in work package 4**

These final published versions of the DIAMOND-Lewy toolkits (see *Report Supplementary Material 2*) were utilised in WP4 of the programme, with all services, whether randomised to intervention or usual care, being supported in using the toolkits. The toolkits were published online in 2016 and in print in 2017,<sup>34</sup> and this contributed to making these toolkits publicly available through open access. In parallel, the toolkits have also been made available through the DIAMOND-Lewy study website [URL: <https://research.ncl.ac.uk/diamondlewy/> (accessed April 2021)].

## Work package 4: a pilot cluster randomised trial of the management toolkit

This WP involved the introduction of the assessment toolkits (developed in WP3) to memory/old age psychiatry and PD/movement disorder services, with the aim of facilitating diagnosis of DLB and PDD, and the introduction through a cluster randomised trial (randomised at the individual service level) of the management toolkit (developed in WP2) into half of the services taking part, with the other half continuing with standard care. The objectives of the pilot RCT were to (1) see if such a study was feasible [i.e. that we could recruit subjects with DLB and PDD (target  $n = 120$ ) and retain them for 6 months] and (2) obtain data to inform power calculations for future studies.

### Methods

We included 11 services in four NHS trusts in the North East and 12 services in four NHS trusts in East Anglia. The trial was supported by the Newcastle Clinical Trials Unit, which undertook the randomisation via a statistician blinded to other aspects of the study. One service in the North East was subsequently unable to recruit any patients and withdrew part-way through the study. This study was approved by the West Midlands – Coventry and Warwickshire Research Ethics Committee (reference 16/WM/0025).

Assessment toolkits and, for services randomised to the intervention arm, the management toolkit were introduced during an in-person site initiation visit undertaken by the research team. The site initiation visits comprised standardised presentations and handouts followed by a question and answer session. The site initiation visits included as many clinical team members as were able to attend and all those involved in the diagnosis and management of those with DLB and PDD were encouraged to use the diagnostic and management toolkits. Follow-up support and further sessions were provided as required, 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 [Portable Document Format (PDF)] versions and, where these were requested, they were supplied. If services had questions regarding the assessment or management toolkits, they were free to ask members of the research team. Regular trial newsletters that contained a 'frequently asked questions' section were sent to services to facilitate engagement with the study. Questionnaires regarding the value and use of the management toolkit were sent to services in the intervention arm halfway through the study and at the study end. Qualitative interviews (see *Work package 5: qualitative studies throughout the DIAMOND-Lewy programme*) were conducted to ascertain barriers to and facilitators of the implementation of both the diagnostic and management toolkits.

In all services, patients with DLB and PDD were recruited for data collection at baseline, 3 months and 6 months. A carer/informant was recruited for all but two patients. The full study protocol, which includes all the assessments undertaken, is available on the DIAMOND-Lewy website.<sup>36</sup> In brief, assessments included those of cognition (MMSE and MoCA), neuropsychiatric symptoms (Neuropsychiatric Inventory and Geriatric Depression Scale), fluctuations (Cognitive Fluctuation Scale), activities of daily living (Bristol Activities of Daily Living Scale), motor symptoms [Unified Parkinson's Disease Rating Scale Part 3 (UPDRS)] and quality of life [DEMQOL (Dementia Quality of Life) and EuroQol-5 Dimensions, five-level version (EQ-5D-5L)]. Current management and use of health care and personal/social care services were

collected on a bespoke questionnaire. Global outcome scales were completed by the visiting researcher and the carer/informant. Informant assessments included quality of life of the carer (EQ-5D-5L), carer burden (Zarit Burden Interview) and the Hospital Anxiety and Depression Scale.

All baseline and 3- and 6-month assessments were undertaken by members of the Clinical Research Network DeNDRoN teams in the North East and East Anglia, who were unaware of the service allocation (to management toolkit or standard care).

Data entry was completed by those undertaking the assessments, and central checking and quality assurance followed double-entry at local sites with an error rate of < 0.1% (all errors noticed were, of course, corrected). Database integrity was therefore felt to be very good. Identical shell databases were completed in the North East and East Anglia and then merged and sent to the study statistical team.

## Results

One hundred and thirty-one participants consented to take part in the study. A CONSORT (Consolidated Standards of Reporting Trials) flow diagram, indicating patient progression through the study, is shown in *Figure 3*. One hundred and twenty-seven participants underwent a baseline assessment, and 6-month data were available for 109 participants (86% of those who completed baseline, 83% of all participants who consented). 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, with those lost to follow-up being significantly older (median age of 83 vs. 77 years).

The recruitment target was more than achieved. We aimed to recruit 120 patients and actually recruited 131. Patient characteristics at baseline are shown in *Table 4*. Participants randomised to receive the intervention did not differ significantly from those randomised to the control group on any of the baseline measures except for carer-reported DEMQOL and carer anxiety symptoms as assessed on the Hospital Anxiety and Depression Scale.

## Health economics

The main objective of the economic component of the pilot RCT was to rehearse the methods for a future definitive economic evaluation of the new management toolkit compared with the usual care provided for dementia. As is typical for pilot trials, the modest sample size meant that a full economic evaluation was not appropriate because estimates would be both imprecise and unreliable. Therefore, the focus of the economic component was restricted to provide a descriptive analysis of the costs and outcomes. Data on costs and outcomes for each patient sample (DLB and PDD) were examined separately, as it was expected that the different diagnoses would lead to a differential use of services and outcomes.

### *Deviations from protocol*

The protocol, and the analysis plan (see *Report Supplementary Material 3*), which was based on the protocol, stated that a cost-effectiveness analysis would be conducted, reporting an incremental cost-effectiveness ratio. A stochastic analysis, reporting results in the form of cost-effectiveness acceptability curves and cost-quality-adjusted life-year (QALY) plots, was also planned. However, because of the smaller number of data collected than expected, this analysis was not conducted to avoid reporting imprecise and unreliable results.

A full report of the economic component can be found in *Appendix 6*. A summary of the key results is presented below.

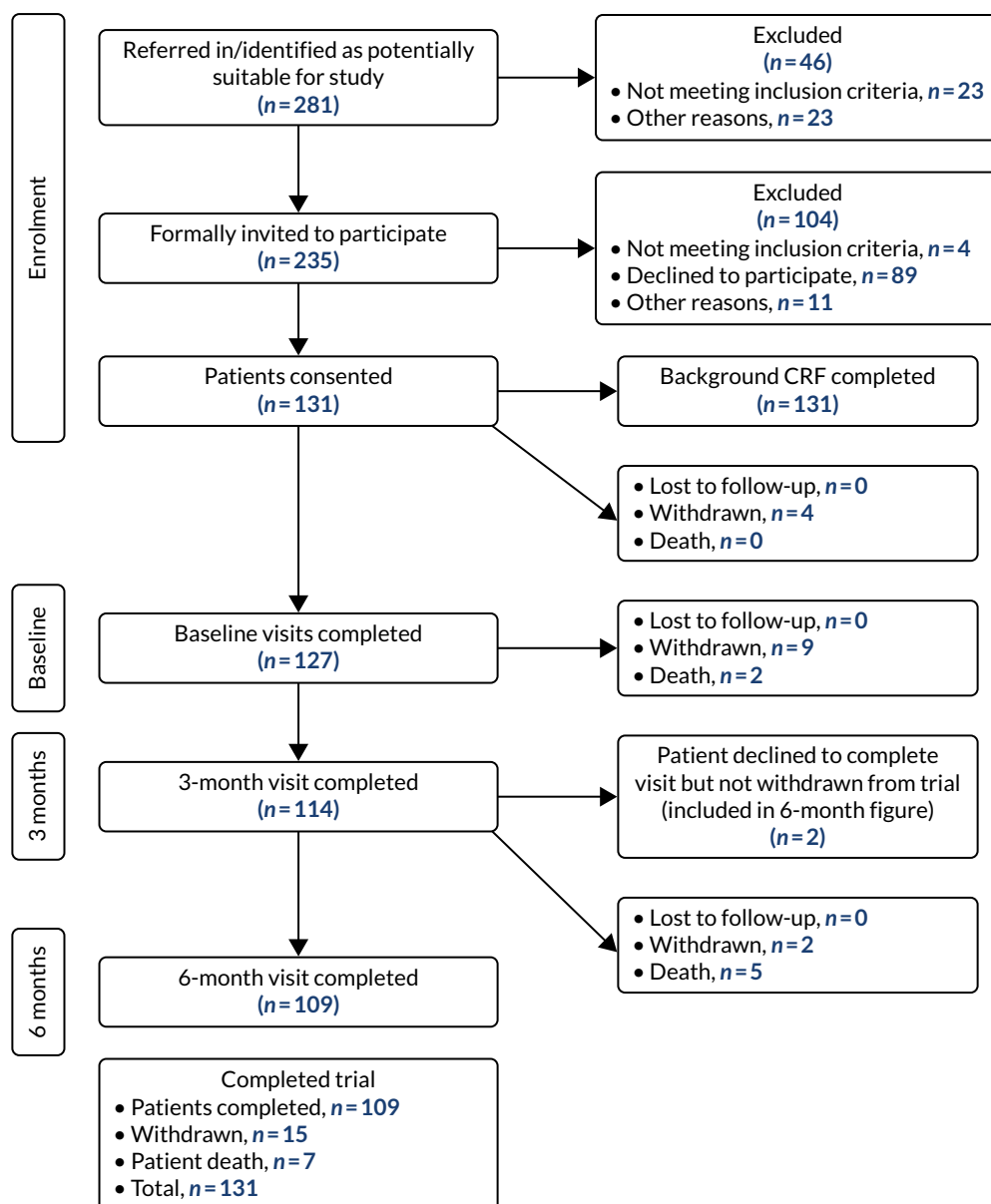


FIGURE 3 DIAMOND-Lewy WP4 CONSORT flow diagram of participants' completion rate (27 March 2019). CRF, case report form.

### Costs

Costs were examined from the perspectives of the UK NHS and Personal Social Services, which includes costs of medications and health and social service use. Costs incurred by other sectors (e.g. local authorities) were not included; however, private costs incurred by patients and carers for attending health-care services were included. Data on costs using a service use questionnaire administered to the carer were collected at baseline and at the 3- and 6-month follow-ups. Data on private costs to patients were collected using a time and travel questionnaire at the 6-month follow-up.

### Health care and social service resource use

In both patient samples, mean costs associated with health and social service use decreased in the intervention arms between baseline and the 6-month follow-up. However, in the control groups, costs increased. There is a substantial amount of imprecision around the service use cost data, however, and median values are considerably smaller than the mean values, which suggests that there is a substantial right skew to the data, with some participants incurring much higher costs than the remainder of the sample (see *Appendix 6, Table 12*).

TABLE 4 Baseline characteristics of the randomised participants

Characteristic	Control (N = 52)	Intervention (N = 75)	p-value <sup>a</sup>
Number of sites	11	12	
Age (years)			
Mean (SD)	77.0 (7.59)	79.3 (6.97)	0.086
Median	77.0	79.0	0.094
Interquartile range	72.0–83.0	75.0–84.0	
Diagnosis, n (%)			0.846
DLB	31 (59.6)	46 (61.3)	
PDD	21 (40.4)	29 (38.7)	
Sex, n (%)			0.642
Female	10 (19.2)	17 (22.7)	
Male	42 (80.8)	58 (77.3)	
DEMQOL			
Mean (SD)	0.76 (0.13)	0.78 (0.12)	0.229
Median	0.78	0.80	0.215
Interquartile range	0.70–0.82	0.70–0.88	
Carer DEMQOL-proxy			
Mean (SD)	0.70 (0.14)	0.76 (0.12)	0.021
Median	0.67	0.79	0.026
Interquartile range	0.55–0.82	0.67–0.85	
Neuropsychiatric Inventory			
Mean (SD)	25.0 (17.5)	20.0 (18.0)	0.125
Median	22.0	15.0	0.038
Interquartile range	12.0–31.0	9.0–24.0	
UPDRS			
Mean (SD)	43.7 (19.1)	38.2 (18.6)	0.112
Median	41.0	35.5	0.137
Interquartile range	28.0–55.0	26.0–51.0	
Cornell Scale for Depression in Dementia			
Mean (SD)	9.31 (6.10)	7.41 (4.85)	0.056
Median	9.0	7.0	0.104
Interquartile range	4.0–13.0	4.0–11.0	
Geriatric Depression Scale			
Mean (SD)	5.7 (3.5)	5.6 (3.3)	0.899
Median	5.0	5.0	0.952
Interquartile range	3.0–7.0	3.0–7.0	
MMSE			
Mean (SD)	20.8 (6.1)	21.4 (6.1)	0.581
Median	22.0	22.0	0.503
Interquartile range	17.0–25.0	19.0–26.0	



TABLE 4 Baseline characteristics of the randomised participants (continued)

Characteristic	Control (N = 52)	Intervention (N = 75)	p-value <sup>a</sup>
MoCA			
Mean (SD)	15.1 (4.9)	15.6 (6.0)	0.644
Median	15.5	16.0	0.690
Interquartile range	12.0–19.0	12.0–19.0	
EQ-5D-5L			
Mean (SD)	0.67 (0.27)	0.67 (0.21)	0.998
Median	0.74	0.73	0.516
Interquartile range	0.55–0.85	0.57–0.80	
EQ-5D-5L (proxy)			
Mean (SD)	0.55 (0.27)	0.56 (0.27)	0.769
Median	0.62	0.62	0.929
Interquartile range	0.37–0.73	0.40–0.77	
Hospital Anxiety and Depression Scale: anxiety			
Mean (SD)	6.7 (4.2)	5.2 (4.1)	0.052
Median	6.0	4.0	0.037
Interquartile range	3.0–9.0	2.0–8.0	
Hospital Anxiety and Depression Scale: depression			
Mean (SD)	4.6 (3.8)	4.2 (3.5)	0.553
Median	3.0	3.5	0.610
Interquartile range	1.0–7.0	1.0–7.0	
Zarit Burden Interview			
Mean (SD)	27.5 (15.6)	22.6 (15.3)	0.082
Median	26.0	18.0	0.070
Interquartile range	14.5–38.5	10.0–33.0	
Carer EQ-5D-5L			
Mean (SD)	0.80 (0.20)	0.81 (0.19)	0.822
Median	0.84	0.82	0.902
Interquartile range	0.72–1.0	0.69–1.0	

SD, standard deviation.

<sup>a</sup> p-value from a t-test, Mann-Whitney U-test or chi-squared test.

## Medication costs

There was little variation in mean medication costs between baseline and the 6-month follow-up in both patient samples. There was a trend towards increasing costs for both arms over the follow-up period. A greater increase in mean medication costs can be observed in the intervention arms of both patient samples than in the control arms. However, the increase is larger for the PDD patients (see *Appendix 6, Table 13*).

## Intervention delivery costs

The cost of the intervention included the production of the management toolkits and training staff to use them. The total delivery cost was divided by the number of participants in the intervention arm in both patient groups combined ( $n = 75$ ) to estimate a mean delivery cost per participant receiving the intervention. The mean intervention delivery cost was estimated at £76.32 per participant in the intervention arms and £0 for those not receiving the intervention (i.e. control arms) (see *Appendix 6, Table 14*).

### Total costs

Total costs included health and social service use, medication costs and intervention delivery costs (to illustrate cumulative costs at that time point they were added to the cumulative costs, estimated at the 3- and 6-month follow-ups only). The health and social care use costs made up the largest proportion of the total cost. In both patient samples, there was an overall increase in total costs between baseline and the 6-month follow-up in the control arms, whereas total costs at the 6-month follow-up were lower than baseline in both sample intervention arms (see *Appendix 6, Table 15*). There remains substantial imprecision in the total cost values because of the small sample size and, therefore, the total costs are, at best, illustrative.

### Private costs

Private costs included the cost of travelling to inpatient services, outpatient appointments, general practitioner (GP) visits and community dementia service visits for both patients and carers who may have accompanied patients. The cost of time spent travelling to each appointment and the cost of time spent at each appointment were also estimated. Costs were attributed to time based on activity rates for various activities, using estimates published by the Office for National Statistics (ONS)<sup>37</sup> (see *Appendix 6* for further details). For both patients and carers, mean travel costs decreased between baseline and the 6-month follow-up in both trial arms and patient samples. An exception to this was the control group of the PDD sample, which incurred higher mean costs at the 6-month follow-up than at baseline.

With reference to the cost of patients' time spent attending health-care services, the intervention groups of both patient samples incurred lower mean costs over the 3-month period between the 3- and 6-month follow-ups than during the 3-month period prior to baseline data collection, whereas the control groups had a higher mean cost for the same 3-month period prior to the 6-month follow-up than at baseline (see *Appendix 6, Table 16*). A similar pattern was observed for costs to carers, with the exception that carers in the control group of the DLB sample incurred lower mean costs at the 6-month follow-up than at baseline (see *Appendix 6, Table 17*).

### Quality of life

Patients' generic quality of life was derived from the responses to the EQ-5D-5L questionnaire,<sup>38</sup> completed at baseline and at the 3- and 6-month follow-ups (missing EQ-5D-5L data at each time point are recorded in *Appendix 6, Table 18*). Responses to the EQ-5D-5L questionnaire were transformed into health state utilities, using tariffs derived from the UK population.<sup>39</sup> Using the change from baseline approach, the health state utilities were used to estimate generic QALYs for each participant so that the change in QALYs between baseline and the 6-month follow-up was estimated.

Overall, changes in QALYs in each trial arm for each sample were small to modest, but with consistent decreases in mean and median scores for those with DLB, indicating a benefit for those in the intervention arm. An extremely small decrease in QALYs was observed in the intervention arm of the PDD sample, compared with a small increase in mean QALYs for the control arm (see *Appendix 6, Table 19*).

## Discussion

This study demonstrated the feasibility of successfully recruiting a large number of participants with DLB and PDD over an 18-month period from 23 sites, and we more than achieved the recruitment target (target,  $n = 120$ ; recruited,  $n = 131$ ). Follow-up rates were good (85%), given the condition under study, as LBD is known to be associated with more rapid functional decline and increased mortality than other dementias.<sup>11,40</sup> Completion rates of assessments for both patients and carers were high.

Using results from this study to inform a power calculation (80% power, alpha 0.05) gives a required sample size of 726 for outcome based on the Neuropsychiatric Inventory {18.8 [standard deviation (SD) 19.3] in the intervention and 22.6 [SD 16.3] in the control group}. Assuming 80% completion rates,

the recruitment sample would need to be 908 for the Neuropsychiatric Inventory. However, given that the toolkits are already evidence based and associated with some positive outcomes, even in this pilot study, it is not clear that a larger trial based around demonstrating efficacy of the toolkits is needed. Instead, an approach focused more on their routine implementation, through service improvement or other approaches, may be preferable.

Taking account of the cost of implementing the management toolkits, the health economic analysis indicated that the total costs for both DLB and PDD increased over the course of the study in the control arms and decreased in the intervention arms, despite a slight increase in medication costs in intervention groups. With such a modest sample size, data were insufficient to draw conclusions, although there is no indication that the intervention increased costs. Data indicated that further study on health economic consequences in a larger sample is needed.

The qualitative studies (see *Work package 5: qualitative studies throughout the DIAMOND-Lewy programme*) indicate that implementation and use of the management toolkit varied considerably between individual clinicians and between services. Limitations of the study are that we were not able to standardise or measure this, nor – because this was randomised at a cluster level – could we directly associate the impact of the management toolkit on patient outcomes at the individual patient level. Further study should investigate these issues, but our results strongly support the need for a large, definitive trial of the management toolkit and indicate that its introduction is not associated with increased costs.



## Work package 5: qualitative studies throughout the DIAMOND-Lewy programme

The reasons for underdiagnosis and suboptimal management of LBD have not previously been empirically investigated using qualitative methods. Research has focused on clarifying diagnostic criteria, identifying biomarkers or screening tools to facilitate diagnosis, with little attention to potential barriers to diagnosis. The emphasis has therefore been on identifying technical solutions, rather than considering the full range of factors that might contribute to the underdiagnosis of LBD. There is growing recognition of the contribution qualitative research can make to feasibility studies, pilot trials and RCTs,<sup>41,42</sup> for example by understanding the context into which interventions are to be introduced, optimising interventions, understanding factors influencing the implementation of the intervention and facilitating the interpretation of findings.<sup>41,43,44</sup> In the DIAMOND-Lewy programme, the objectives of the qualitative work were to:

- understand current practice in diagnosing and managing LBD (WP5.1)
- explore stakeholder views on the acceptability of the toolkits (WP5.2)
- explore the implementation of the assessment and management toolkits in routine NHS practice (WP5.3).

A range of theories are available to assess the likelihood of a new intervention being successfully embedded into routine practice.<sup>45</sup> Normalisation process theory (NPT) is a well-established theory of implementation, which has been used extensively in studies of health-care interventions.<sup>46</sup> NPT considers factors that affect implementation in relation to four key areas: (1) how people make sense of a new practice (coherence), (2) the willingness of people to sign-up and commit to the new practice (cognitive participation), (3) their ability to take on the work required of the practice (collective action) and (4) activity undertaken to monitor and review the practice (reflexive monitoring) [URL: [www.normalizationprocess.org](http://www.normalizationprocess.org) (accessed April 2021)].<sup>47</sup>

The qualitative work aimed to generate practical knowledge to inform subsequent stages of the programme (e.g. by providing feedback that could be used in revising toolkits, proposing an implementation strategy to address key barriers and proposing change mechanisms for the study findings). Ethics and research governance approvals were sought in two phases. Favourable ethics opinion for phase 1 was obtained from the Newcastle and North Tyneside 1 Research Ethics Committee (reference 13/NE/0322). Subsequent research and development and Caldicott approvals were granted from each participating site. Favourable ethics opinion for phase 2 was obtained from Wales Research Ethics Committee 5 (reference 16/WA/0098). Health Research Authority approval for phase 2 was obtained on 29 June 2016.

### Methods

We used ethnographic methods, including semistructured interviews, focus groups and observations of clinical practice, throughout WP5. Structured questionnaires were used to collect information on current practice, confidence in diagnosing and managing LBD, and (in WP5.3) views on the assessment and management toolkits (Table 5).

### Participants

Participants included clinicians working in memory and movement disorder services (including geriatricians and/or neurologists) and patients attending participating services together with any companions (hereafter 'carers'). We aimed to recruit maximum variation samples throughout (with the exception of WP5.2 where we recruited all available participants). Relevant clinician characteristics

TABLE 5 Overview of aims, methods and recruitment to qualitative studies

WP	Methods	Participants
WP5.1: understanding current practice	Clinician questionnaire (T0)	146/336 completed questionnaires
	Clinician interviews	20
	Clinician focus groups	Two (16 participants)
	Observation of routine practice	17 clinical sessions (44 patients and 36 carers)
		Three clinical discussions (eight patients and eight carers)
WP5.2: acceptability of assessment and management toolkits	Clinician interviews	60 (across whole study)
	Observation of acceptability of toolkits in feasibility study	0
	Interviews with patients and carers with whom the toolkits had been used	Six patients Four carers
WP5.3: implementation of assessment and management toolkits	Clinician questionnaires (T1 towards the start of WP5 and T2 after the pilot trial)	60/124 completed T1 questionnaires 52/140 completed T2 questionnaires
	Clinician interviews	40 (including nine from the feasibility study)
	Clinician focus groups	Five (32 participants)
	Observation of routine practice	25 clinical sessions
	Interviews with patients and carers were only planned in the event of any indication of the toolkits having had an impact on consultations	None

T0, initial data collection; T1, follow-up 1 (towards the start of WP5); T2, follow-up 2 (after the pilot trial).

were professional background (doctors, nurses, allied health professionals), specialty (e.g. geriatrics, neurology, old age psychiatry), geographical location (East Anglia, North East) and, in WP5.3, study arm (control, intervention). Only 22 services took part in WP5.3. The remaining service involved in WP4 dropped out prior to the start of WP5.3.

All clinicians in participating services were eligible for all components of WP5, although WP5.3 questionnaires were targeted primarily at those who had been exposed to the toolkits. All patients and carers seen by participating clinicians on the dates of observation were eligible. Patients and carers for interview in WP5.2 were identified by participating clinicians and the local research nurse. Recruitment continued until no new themes or issues emerged from further interviews or observation. In WP5.3 interviews with patients and carers were only planned in the event of any indication of the toolkits having had an impact on consultations.

### Data collection and analysis

Data collection and analysis were iterative to ensure that insights from observation informed the interviews and vice versa. Clinician interviews and focus groups explored current practice, the perceived relevance of the assessment and management toolkits, and facilitators of and barriers to

their implementation (see *Report Supplementary Material 4* for topic guides). The guides were informed by NPT, but allowed additional issues to be raised. Interviews and focus groups were audio-recorded, transcribed, checked and anonymised prior to analysis. Interviews with patients and carers explored their perceptions of the assessment toolkit and also used cognitive interviewing techniques to obtain feedback on question wording.<sup>48</sup> Observation provided insight into clinic organisation, content of consultations, team roles and the use of standardised tests. In the pilot trial, observation focused primarily on if and how the toolkits were used. Anonymised field notes were written as soon as possible after observation.

Questionnaires explored the views of clinicians on diagnosis and management of LBD and on implementation in the pilot trial. Postal (WP5.1) and electronic questionnaires (WP5.3) were used, with one reminder to non-responders. For full details of analysis, response rates and respondent characteristics see *Appendix 7, Tables 20–24*.

Qualitative data were analysed thematically,<sup>49</sup> with themes from WP5.3 subsequently mapped to the core constructs of NPT. Questionnaire data were analysed using simple descriptive statistics using SPSSX version 22 (IBM SPSS Statistics, Armonk, NY, USA).

The final data set for the qualitative work comprised 60 interviews with clinicians, seven focus groups (with 48 clinicians), observation of 42 clinical sessions, four clinical discussions, two multidisciplinary team meetings and interviews with six patients and four carers (see *Table 5*).

## Results

### *Understanding current practice in the diagnosis and management of Lewy body dementia (work package 5.1)*

Factors influencing the diagnosis and management of LBD were grouped into four overarching themes: (1) complexity of LBD, (2) service organisation, (3) skills, training and knowledge, and (4) clinician attitudes and values (*Table 6*). Each comprised a number of subthemes (those identified as particularly relevant to LBD are listed first and those relevant to dementia in general are shown in italics in *Table 6*). The complexity of LBD and service organisation were relevant to both diagnosis and management, whereas training and attitudes primarily related to diagnosis. The relative importance of each theme and subtheme in movement disorder and memory services is explored below. For further illustrative quotations and details of ID numbers see *Appendix 8, Tables 25 and 26*.

### **Complexity of Lewy body dementia**

Variability in presentation within and between patients with LBD, together with a trend towards earlier presentation to memory services, meant that diagnosing LBD was not straightforward. Several old age psychiatrists (OAPs) commented on the subtleties of presentation, which were easy to miss unless explicitly explored during assessments:

*... this is a very special kind of dementia, which is very difficult to diagnose in the first stages of the illness. Because the cognitive function is not that prominent, it's mostly a sleep problem and falls, unsteadiness. Sometimes, they are almost the same as the Alzheimer's type [...]. In the early stages, it's not easy to diagnose.*  
0501, trainee OAP

Fluctuating cognition, a characteristic of LBD, meant that key symptoms were not necessarily present during a single assessment or short follow-up appointment. Several clinicians in movement disorder services commented on the difficulties in distinguishing dementia and delirium and identifying dementia subtypes, as symptoms were not exclusively associated with a particular diagnosis. Although scans could assist with diagnosis, access to some types of scans varied. The lack of a specific, definitive test for LBD made it difficult for clinicians to develop confidence in their diagnostic skills.

TABLE 6 Factors influencing the diagnosis and management of LBD

Theme	Subtheme
Complexity of LBD	Variability in presentation
	Lack of a definitive test
	Balancing treatments
	<i>Shift to earlier presentation</i>
	<i>Availability of an informant</i>
Service organisation	Shift to nurse-led memory services
	Follow-up arrangements
	Fragmented care
Training, knowledge and experience	Awareness of LBD and cognitive biases
	If and how core symptoms were covered in consultations
	Interpreting cognitive tests
	Knowledge of dementia subtypes
Attitudes and values	Perceived prevalence and status of LBD
	Perceived value of diagnosing LBD
	Perceived responsibility for LBD
	<i>Perceived value of diagnosing dementia subtypes</i>

**Note**

Those identified as particularly relevant to LBD are listed first and those relevant to dementia in general are shown in italics.

Complexity also influenced the management of LBD. Sensitivity to medication required a cautious approach to introducing new treatments to minimise side effects. Eliciting patient priorities for treatment was crucial to ensure that symptoms of most relevance to the patient (or carer) were addressed. Understanding how patients had responded to new treatments in the context of fluctuation posed a further challenge and made the availability of an informant particularly important.

### Service organisation

The increasing demand on services, in a context of stable or diminishing resources, had a significant impact on the diagnosis and management of LBD. In some memory services, new referrals were triaged, with 'straightforward' patients being allocated for assessment by a nurse or memory assessor. This could lead to DLB being missed, particularly when such staff had not received adequate training.

The limited time for follow-up appointments in movement disorder services influenced the extent to which clinicians proactively explored memory problems. Although cognitive function was routinely assessed (usually annually) in some services, this was not feasible in less well-resourced services: a further difficulty related to disclosing a diagnosis of PDD in a short follow-up appointment.

Strategies adopted to support the diagnosis of PDD included using nursing staff to conduct annual cognitive tests and developing a separate cognitive clinic with longer appointment times for patients with suspected PDD. Some clinicians approached the possible diagnosis of dementia over a number of visits to prepare patients and their families for disclosure gradually. Others emphasised the need to educate patients at an early stage about the potential cognitive impairment associated with PD.



Current service organisation emerged as a key barrier to the effective management of LBD, with considerable inequity of provision. Where patients developed cognitive symptoms first and were diagnosed with DLB by memory services, most were discharged back to GP care following diagnosis and treatment initiation. Referrals were then made as and when needed, resulting in episodic care with limited proactive management. PD patients who developed cognitive problems were typically managed in line with the NICE PD guideline, with reviews every 6–12 months.<sup>50</sup> Many PDD patients had access to a specialist nurse and few were discharged. Clinicians in movement disorder services nevertheless identified time as a barrier to holistic management of PDD patients:

*The most frustrating thing is seeing a patient you may have known for a long time or who has been under follow-up for a long time and then you have a 10-minute slot to deal with them when they have got advanced Parkinson's with dementia. It is ridiculous really but that is what happens [...] And so the most needy patients actually get the least attention and time which is very frustrating.*

*2101, consultant neurologist*

Although some experienced geriatricians preferred to manage all symptoms to ensure continuity of care or expedite treatment, the complexity of LBD meant that most patients were referred between old age psychiatry, older people's medicine and neurology departments. In the UK NHS, joint working or shared care by different specialties was difficult to achieve in practice because of funding arrangements, lack of shared geographical boundaries, incompatible information technology systems and limited direct consultant–consultant communication (with communication typically routed via the GP).

Although clinicians described a number of strategies to improve shared care of people with LBD, few had proved sustainable. These included joint meetings between services about complex patients, and adapting the care pathway to provide rapid access to interventions offered by memory services for patients already diagnosed with PDD by a movement disorder specialist without further diagnostic assessment. Although informal approaches, where clinicians in different specialties were co-located and had worked together for a number of years, appeared most successful, such arrangements were rare.

### Training, knowledge and experience

Training, knowledge and experience were identified as key barriers to the diagnosis of LBD, but were less often discussed in relation to management. The questionnaires indicated that clinicians in memory assessment services were less confident in diagnosing DLB and PDD than other types of dementia (with the exception of frontotemporal dementia, see *Appendix 7, Figure 7*). Similarly, few clinicians were confident in managing both cognitive and physical symptoms (see *Appendix 7, Figures 8 and 9*), reflecting the need for shared care by different specialists.

Cognitive biases (where clinicians anticipated a default diagnosis of Alzheimer's disease and framed questions in ways that would confirm their expectation) were thought to contribute to underdiagnosis of DLB:

*I suppose I used to get told in medical school, that **what the mind does not know, the eye will not see**. So, unless you actually have this as a probable differential in the back of your mind, you're not going to consider it, or then check to make sure that you aren't missing something.*

*0601, consultant OAP, author's emphasis in bold*

In addition to awareness of LBD, clinicians needed to ask the right questions to elicit relevant symptoms. Observation of memory services indicated that although symptoms such as hallucinations, sleep and fluctuation were often explored, questions tended to be non-specific and/or leading. The lack of formal neurological examination was also confirmed, although participants often described assessing

parkinsonism informally, for example by observing or asking about gait, blink rate and facial expression, and looking for tremor. Even when clinicians were aware of the need to explore core symptoms, such as fluctuation, they were sometimes unsure how to do so. In movement disorder services, observation confirmed the variable assessment of cognitive function. In addition, interviews suggested that, even when cognitive tests were completed, declining scores were sometimes simply documented without formally making a diagnosis of PDD.

The main facilitator to developing skills and confidence in diagnosing DLB was working alongside experienced clinicians and exposure to DLB patients:

*I think experience is the biggest thing and working with somebody who is experienced who can point things out. [...] I think it's quite nuanced. I think it is pattern recognition. The more you see, the more comfortable you are with 'this is ...' or 'this isn't ...' You just have a bit of a hunch with things.*

*2307, trainee, older people's medicine*

### **Staff attitudes and values**

There was little evidence that staff attitudes or values influenced management beyond personal preferences for managing certain symptoms themselves or referring patients to other specialties. Staff attitudes, however, had an impact on the diagnosis of LBD, particularly in movement disorder services. Where clinical experience of the number of patients with DLB contradicted published prevalence rates, some clinicians acknowledged that they might be missing cases or wondered whether or not DLB patients were being referred to other services. Others questioned the prevalence figures, for example referring to DLB as 'the Newcastle disease'.

Although clinicians in movement disorder services did not dispute the prevalence of PDD, some expressed reservations over the value of making a formal diagnosis. Clinicians' own views and attitudes clearly influenced if and how they explored cognition in PD patients, and how they labelled and explained any problems to patients. A range of benefits and disadvantages of formal diagnosis of PDD were identified. Potential benefits were increased patient and carer understanding of symptoms, opportunities for planning for the future and ensuring that potentially dangerous treatments were avoided. Formal diagnosis was sometimes avoided because of the difficulties of disclosing dementia in the context of an ongoing relationship, concerns over the potential negative impacts for patients and the stigma associated with dementia. Clinicians in movement disorder services also expressed varied views concerning the responsibility for diagnosis and management of LBD. Although some staff were confident to make the diagnosis themselves, others thought confirmation of a diagnosis of dementia in PD by a specialist memory service was essential. Views over responsibility for management similarly varied.

Although some clinicians questioned the value of diagnosing dementia subtypes, others argued that a clear diagnosis was important in terms of understanding and access to support:

*I think it [diagnosis] matters to carers if they are going to get a diagnosis because they can put the symptoms into a context. They can obviously get frustrated and stressed seeing all these different symptoms and not understanding, and if you can say 'that's because of their diagnosis of Lewy bodies, that's completely normal and you can expect this kind of prognosis' then that is helpful for them to know what to expect in the future. So we can support the carers better if they've got a proper diagnosis.*

*0904, community nurse, memory service*

### **Stakeholder perspectives on the acceptability of the toolkits (work package 5.2)**

#### **Clinician views**

Clinicians generally held positive views towards the concept of the toolkits. Potential benefits of the assessment toolkits included increased awareness of core and suggestive features of LBD and a more

consistent and systematic approach to assessment. The management toolkit successfully translated academic papers to a format and style suitable for practice:

*I think the good thing about it is it's all in one place, and it's really clear. The instructions and the advice are really clear, which certainly, when I was training, Parkinson's and Lewy body dementia always seemed quite complicated illnesses to look after. You felt like you might not know quite what the current guidance was. Whereas, at least with that, it's a one-stop shop, which tells you everything that you need to know.*

*0701, consultant OAP*

Feedback on the assessment and management toolkits covered a range of areas (for illustrative quotations see *Appendix 9, Tables 27 and 28*). The majority of the feedback on the management toolkit related to the version used in the pilot trial, as the format changed substantially after the feasibility study. Issues relating to the assessment toolkits (already covered in *Work package 3: development of assessment toolkits for the diagnosis of Lewy body dementia*) are not reiterated here, with the exception of question wording where additional comments were made during the pilot trial.

### **Views on layout and presentation**

The assessment toolkit for movement disorder services began with questions about relevant symptoms and ended with diagnostic criteria. In contrast, the toolkit for memory services began with the diagnostic criteria, followed by specific questions. Although few comments were made about the order of the PDD toolkit, some participants thought that the order of the DLB toolkit was counterintuitive. Furthermore, non-medical staff who did not make the diagnosis could find the first page off-putting.

Although few participants explicitly commented on signposting in the assessment toolkits, several did not realise that the diagnostic criteria in the DLB toolkit were followed by specific questions to explore core and suggestive features, or that instructions on how to perform and score the five-item UPDRS were provided. The structure of the PDD assessment toolkit was widely misunderstood, with many participants thinking that they were required to perform a formal cognitive test with all patients, whereas this was relevant only if responses to the initial questions indicated potential problems.

The management toolkit was organised in three levels (*Figure 4*). A one-page overview provided a brief, accessible summary of the symptom areas covered and the general principles for managing LBD. The colour coding of the overview then carried through to the next level, which comprised one-page summaries of recommendations for each of the five symptom areas. The final level comprised the full reference guidelines.

Clinicians valued the colour coding, which facilitated navigation to different levels of detail. The majority of clinicians found the symptom summaries most useful, although some relied primarily on the overview.

### **Format**

Participants suggested a number of alternative formats to facilitate use of the toolkits, most commonly integration with existing information technology systems or paperwork. Using the local intranet to display the toolkits automatically for patients with relevant diagnostic codes was also suggested. Applications were identified as an alternative way to ensure that the toolkits were easily accessible. For the assessment toolkit, participants suggested portable summary 'prompts' for each section (similar to the symptom summaries).

Several clinicians requested an A5 version of the overview and/or symptom summaries from the management toolkit to make it more portable. Others recommended displaying a poster of the overview to maintain awareness of the management toolkit. Another suggestion was to embed the management toolkit within an e-learning module for trainee doctors.

Management Guideline for Lewy body dementia



Identify key problems under domain headings such as cognition, gait, balance and movement, hallucinations, fluctuations, behaviour and mood; sleep, and autonomic system dysfunction. Establish which problems have high priority for treatment. Discuss benefits and risks of treatment. Be aware that symptom response is variable and that benefits in one might be at the cost of worsening of others. Individual treatments may have global benefits e.g. cholinesterase inhibitors.

**COGNITIVE**  
**Non-pharmacological**  
 • cognitive stimulation, use of memory aids, increased social interaction and stimulation, and exercise.  
**Pharmacological**  
 • Cholinesterase inhibitors first-line.  
 • Memantine second-line.

**NEUROPSYCHIATRIC**  
**Psychosis**  
 • May respond to cholinesterase inhibitors especially visual hallucinations.  
 ⚠ Be cautious in the use of antipsychotics.  
**Mood**  
 • Use of social interventions may enhance mood.  
 ⚠ No evidence for antidepressants in LBD to treat mood therefore use pragmatically and avoid agents with significant anti-cholinergic side effects.

**SLEEP**  
**Insomnia**  
 • Give advice on sleep hygiene.  
 • Review all medications that could be affecting sleep.  
 • Melatonin may help some.  
 ⚠ Z-drugs may have a role but use cautiously.  
**REM-sleep behaviour disorder**  
 • Consider non-pharmacological as first-line and only treat if troublesome.  
 ⚠ Clonazepam may help although significant side effects.  
 • Melatonin may be alternative.  
**Motor related sleep disturbances**  
 • May be improved with long-acting levodopa.

Remember that LBD patients may exhibit exaggerated responses to medications. Reverse antipsychotic sensitivity can occur in up to 50% of patients therefore use antipsychotic agents with a high degree of caution. Review the need for common drugs which can affect brain function and/or cause sedation and falls. Minimize cholinergic burden as this may worsen cognition and behaviour, and counteract cholinesterase inhibitors.

**AUTONOMIC**  
**Orthostatic hypotension**  
 • non-pharmacological management e.g. compression stockings, fluid salt intake, stand slowly etc.  
 • pharmacological e.g. fludrocortisone, midodrine  
 ✗ Reduce/remove exacerbating drugs e.g. antihypertensives.  
**Constipation**  
 • Stool softeners.  
 • mild laxatives/suppositories.  
 ✗ Avoid centrally acting anticholinergics.  
**Urinary dysfunction**  
 • Non-pharmacological first-line e.g. pads, sheath catheter etc.  
 ✗ Avoid centrally acting anticholinergics.  
**Gastroparesis**  
 ✗ Avoid using metoclopramide.  
 ⚠ Domperidone can be used but is cardiotoxic.  
**Sexual dysfunction**  
 ⚠ Phosphodiesterase-5 inhibitors may be considered with caution in men.  
**Sialorrhoea**  
 ✗ Anticholinergics should not generally be used  
 • Botulinum toxin injections to salivary glands is an effective treatment.  
**MOTOR**  
 • Preferred pharmacological treatment of parkinsonism in LBD is levodopa monotherapy.  
 • Use minimal dose needed for benefit.  
 ✗ Withdraw in order, one at a time: anticholinergic drugs, amantadine, selegiline, dopamine agonists and catechol-O-methyltransferase inhibitors.

**Neuropsychiatric symptoms**

**General Principles**

- Establish the presence, severity and impact of significant neuropsychiatric symptoms requiring treatment. These may include visual hallucinations, fluctuations in other realities, delusions and apathy.
- Obtain collateral history for symptoms from reports of the patient and an informed carer. Systematic interviewing may help.
- Other factors causing or aggravating mood and behaviour disturbances should be excluded e.g. depression, pain, ill-fitting environmental provisions, system & equipment, depression & anxiety.

**Cholinesterase inhibitor use**

- Consider as a first line treatment.
- Dose will be influenced by previous experience, ease of administration, dose titration regime and side effect profile.
- Donepezil and rivastigmine are usually effective in LBD.
- There is less evidence for the benefit/effectiveness of galantamine in LBD.
- Before starting Cholinesterase Inhibitors (ChEI)
  - Check for clinically significant cardiovascular disease, particularly arrhythmias.
  - Review current drug therapy for drugs which may interact with ChEIs.
  - Consider starting at an LBD severity ChEI, particularly if there is a history of cardiac issues and/or autonomic dysfunction.
  - Cautioning advice should be made in cases of uncertainty including decisions regarding:
    - Cholinesterase inhibitors in:
      - Depression
      - Alcohol
      - Respiratory
      - Anti-cholinergics
      - Anti-epileptics

**Antipsychotic use**

- There should be a full discussion with the patient with dementia and/or carers about the possible benefits and risks of antipsychotic treatment. This should be recorded in medical notes.
- Reason for severe antipsychotic sensitivity reactions.
- The degree of the significant severity and morbidity associated with the use of antipsychotics in dementia.
- Identify target symptoms and monitor these regularly.
- Watch for worsening of cognition and more subtle deteriorations in motor function.
- Full antipsychotic titration.
- The choice of antipsychotic should be made after an individual risk-benefit analysis.
  - Clonidine, alone or with an L10 antagonist, may also help in LBD, although the evidence is lacking.
  - There is no evidence to favour any individual antipsychotic drug in LBD although atypical and the primary agents have an advantage in terms of the least adverse effects.
  - The lower potential dose should be initiated and then titrated upwards.
  - Treatment should be time limited and regularly reviewed.

**Motor symptoms**

**Dementia with Lewy bodies**

**General Principles**

- Establish the presence of significant motor difficulties which are impacting function and quality of life.
- Exclude other factors which may be a cause of a worsening of motor function e.g. cholinesterase inhibitor or antipsychotic use, constipation.
- Be aware that extramotor symptoms may be less treatable than in PD.

**Parkinson's disease dementia**

**General Principles**

- The general principles are similar to those for LBD. PD patients will usually already have been on one or more anti-parkinsonian agents.
- Management decisions are therefore typically around dose reduction/cessation or optimization.

**Cognitive symptoms**

**General Principles**

- Establish the presence of significant cognitive difficulties affecting treatment. Treatments in cooperation with family may be more effective.
- Exclude other factors which may be a cause of a worsening of cognitive function e.g. constipation, depression, malnutrition, malnutrition, malnutrition, malnutrition.
- Establish the presence of significant cognitive difficulties affecting treatment. Treatments in cooperation with family may be more effective.
- Exclude other factors which may be a cause of a worsening of cognitive function e.g. constipation, depression, malnutrition, malnutrition, malnutrition, malnutrition.

**Cholinesterase Inhibitors**

- Dose will be influenced by previous experience, ease of administration, dose titration regime and side effect profile.
- Donepezil and rivastigmine are usually effective in LBD.
- There is less evidence for the benefit/effectiveness of galantamine in LBD.
- Before starting Cholinesterase Inhibitors (ChEI)
  - Check for clinically significant cardiovascular disease, particularly arrhythmias, hypertension, or pre-tension.
  - Consider starting at an LBD severity ChEI, particularly if there is a history of cardiac issues and/or autonomic dysfunction.
  - Cautioning advice should be made in cases of uncertainty including decisions regarding drug interactions.
  - Cholinesterase inhibitors are best started at the maximum tolerated dose and maintained at this level. For example:
    - Donepezil 10mg once daily for 4 weeks, increased to 15mg daily if significant side effects occur.
    - Rivastigmine patch, if 1mg two daily for 4 weeks, increased to 1mg twice daily steady state can be increased to 1.5mg two daily if no significant side effects.
    - Rivastigmine patch, if 1mg twice daily for 4 weeks, increased to 1.5mg twice daily if no significant side effects. May have advantages in patients with visually hallucinations.
    - galantamine 12mg once daily for 4 weeks, increased to 18mg once daily if no significant side effects.
    - Cholinesterase inhibitors are best started at the maximum tolerated dose and maintained at this level. For example:
      - Donepezil 10mg once daily for 4 weeks, increased to 15mg daily if significant side effects occur.
      - Rivastigmine patch, if 1mg two daily for 4 weeks, increased to 1mg twice daily steady state can be increased to 1.5mg two daily if no significant side effects.
      - Rivastigmine patch, if 1mg twice daily for 4 weeks, increased to 1.5mg twice daily if no significant side effects. May have advantages in patients with visually hallucinations.
      - galantamine 12mg once daily for 4 weeks, increased to 18mg once daily if no significant side effects.

Overview Symptom Summaries Reference Guidelines

FIGURE 4 Formats of the management toolkit.

Some clinicians in movement disorder services suggested that the initial questions on memory and executive function from the assessment toolkit could form a separate document to be completed by patients and carers before their consultation. Other clinicians, however, thought that this would be too burdensome for patients and carers.

The common perception that the toolkits were more relevant to doctors led to suggestions that separate versions be produced for non-medical staff. This would enable non-medical staff to focus on those aspects of the toolkits most relevant to their work and skills (e.g. questions on core and suggestive criteria in the DLB toolkit and non-pharmacological interventions in the management toolkit). Although some consultants saw the assessment toolkits as more valuable to nurses or trainees than themselves, others thought that it was a useful reminder even for experienced staff. Some participants thought that the management toolkit would be useful in other settings, notably primary care or inpatient wards.

### **Content**

Feedback on the content of the toolkits related to five themes, some of which were more relevant to specific toolkits.

**Perceived relevance of content** The inclusion of the diagnostic criteria was typically seen as a useful reminder and prompt by medical staff. A number of clinicians, however, asked why key features they associated with LBD (e.g. falls) were not included in the assessment toolkits. Some clinicians in movement disorder services queried the absence of questions on hallucinations and fluctuations, as they saw these as essential for differentiating between LBD and other dementias in PD. Although the toolkit for movement disorder services was modified after the feasibility study, questions on hallucinations, REM sleep behaviour disorder and fluctuations were not integrated into the toolkit for patients with established PD.

Some clinicians queried the omission of key areas, such as carer support, psychosocial interventions and information for patients and carers, from the management toolkit. These comments suggest that the rationale for focusing on selected areas should be included in the toolkits.

**Terminology and question wording** Comments on terminology and question wording related mainly to the assessment toolkits, particularly the DLB version. Unfamiliar terminology (such as 'kinetic tremor', 'spontaneous parkinsonism' and specific types of scans) was alienating, particularly for non-medical staff.

Although some clinicians emphasised the need for standardised questions, some questions were thought to be inappropriate for patients and carers, or to lack sensitivity. Less experienced clinicians valued the questions on REM sleep behaviour disorder, as they were sometimes unsure how to explore this symptom. Few comments were made about wording in the management toolkit, although greater clarity about incontinence (i.e. whether faecal or urinary) was suggested.

**Details of drug dosages** Several clinicians valued being able to use the symptom summaries to check drug dosages. For drug treatments used infrequently, some clinicians suggested providing more detailed protocols:

*Clozapine is such a complicated drug. People like psychiatrists are afraid to touch it. You put it in one line saying clozapine. There is some evidence for clozapine and I think clozapine should be written out in like almost a protocol how to use it [...] Nobody really knows how often you are supposed to do the blood test. When do you start and what is the best maximum dose. So, unless you de-mystify it and put it in there [...] I think people will be worried to [use it].*

*1901, consultant geriatrician*

The recommendations regarding melatonin were inconsistent with the clinical experience of some participants, and several reported that GPs were reluctant to prescribe melatonin. To address this issue, one clinician suggested including an information leaflet to support prescribing in primary care.

**Feasibility of the five-item UPDRS in memory services** Although few comments were made about the five-item UPDRS during the feasibility study, this was the most contentious aspect of the DLB assessment toolkit in the pilot trial. Three main issues with the five-item UPDRS were highlighted: (1) the rationale for focusing on these five items, (2) uncertainty over the value of scoring each item and (3) the challenges of introducing the scale in services where non-medical staff were responsible for assessments.

The toolkits used in the feasibility study and pilot trial gave no explanation for using the five-item UPDRS. Understanding that the items in the scale had been demonstrated to be useful in distinguishing between DLB and AD<sup>26</sup> could have increased staff buy-in to the scale. Although the current version of the toolkits (v3) includes a brief statement, it is unclear whether or not this is enough to counterbalance the negative attitudes to this scale.

Clinicians frequently questioned the need to score each item on the UPDRS on a five-point scale, preferring to record simply the presence or absence of symptoms. Common arguments against scoring related to the difficulties in scoring accurately without extensive training, the additional time needed and the perception that scoring was more relevant to research than to clinical practice.

Although non-medical staff in memory services were often confident in informally assessing for parkinsonism, most saw physical examination as outside their area of expertise and role:

*Because you haven't got a full caseload of clients with Lewy body dementia you're doing it occasionally. So, for me, I need to be doing something all the time for it to click. I'm fine with asking the questions, speaking to the carers and speaking to the patients, but when it comes to the actual of doing some of the assessment here I lack confidence.*

*0904, community nurse, memory service*

Consultants had varied views on whether or not it was feasible and/or appropriate to train non-medical staff to perform the five-item UPDRS. Some were keen to train their colleagues, whereas others felt that physical examination was a medical responsibility.

**Feasibility of formal cognitive assessment in movement disorder services** Some clinicians thought that their ongoing contact with patients facilitated identification of emerging cognitive problems, but others argued that symptoms could easily be missed without a formal assessment. Several clinicians in movement disorder services described (or were observed) using selected items from formal cognitive tests to explore cognitive impairment. Most clinicians in movement disorder services showed little interest in changing their existing approach often because of time constraints:

*I just think as a concept it is really frightening to try and commit to doing it [the assessment toolkit] in a standard clinic. I think if you are going to do it, you would have to set up a stand-alone clinic [...] but that's the problem isn't it? The sort of balancing the desirable against the practical.*

*2402, consultant geriatrician*

### **Patient and carer views of the assessment toolkits**

A number of patients and carers invited to take part in an interview declined because they felt unable to comment on the assessment toolkit because they had been unable to distinguish it from the rest of the consultation.

Interviews with six patients and four carers confirmed that the assessment toolkit was 'invisible' to them. None of the questions from the assessment toolkit stood out as being inappropriate, unclear or in any way different from the rest of the consultation. In view of the consistency of these findings, data collection ceased before achieving the target sample size. Cognitive interviews with patients and



carers highlighted some issues with question wording, typically with the same questions identified as problematic by clinicians.

### **Implementation of the toolkits (work package 5.3)**

The implementation of the toolkits is summarised in *Table 7*, using the framework of NPT (for illustrative quotations see *Appendix 10, Tables 29 and 30*). Comments relating to all of the main NPT constructs were made about both the assessment and management toolkits and by staff working in memory and movement disorder services. Lack of investment in the assessment toolkits in many movement disorder services meant that few of these clinicians had experience relating to collective action or reflexive monitoring. They were able to comment, however, on both of these areas when discussing the management toolkit.

### **Making sense of the toolkits (coherence)**

The concept of the toolkits was relatively straightforward to grasp and clinicians valued the translation of technical knowledge into practical tools. Key potential benefits of the assessment toolkits were improving the consistency of assessment (both within and between clinicians) and increasing diagnostic accuracy.

Although many clinicians reported that their current practice was similar to the assessment and management toolkits, this did not necessarily detract from their value. Most consultant and trainee doctors were confident in the recommendations in the management toolkit because of the expertise of the study team. Non-medics, however, were not necessarily familiar with the authors and some

**TABLE 7** Implementation of the assessment and management toolkits

Making sense of the toolkits (coherence)	All toolkits	Translation of technical information into more practical formats
		Similarity to existing practice
	Assessment toolkit	Improve consistency
	Management toolkit	Confidence in robustness of toolkit
Investing in the toolkits (cognitive participation)	All toolkits	Perceived as more appropriate for 'others':
		<ul style="list-style-type: none"> <li>• Medical staff</li> <li>• Less experienced/trained staff</li> <li>• Other services</li> </ul>
		Lack of investment as a team
Adopting the toolkits (collective action)	All toolkits	Lack of integration with existing paperwork or information technology system
	Assessment toolkits	Selective use when LBD suspected (memory services)
	Management toolkit	Lack of resource for implementation
Assessing impacts of the toolkits (reflexive monitoring)	All toolkits	Insufficient alone to change practice
	Assessment toolkits	Increased awareness of LBD
	Management toolkit	Increased confidence in diagnosing LBD
		Increased exploration and documentation of core and suggestive features (memory services)
		More holistic practice (memory services)
		Increased confidence
		Use to offer suggestions to GP for drug treatment or referrals

would have valued more detail on the background and references to source papers. The need to update the toolkits was emphasised by several participants, in part prompted by changes to the diagnostic criteria for DLB<sup>11</sup> and to the NICE guidelines for management of PD<sup>50</sup> during the pilot trial.

### **Investing in the toolkits (cognitive participation)**

The generally positive views towards the toolkits did not, however, necessarily translate into a commitment to implementation. Consistent with earlier findings on the acceptability of the toolkits, they were often seen as more relevant to 'other' clinicians, typically junior doctors and non-medical staff. In addition, some clinicians queried whether or not the toolkits were relevant to their specialty, service or geographical location. Some movement disorder clinicians viewed diagnosis and management of LBD (particularly DLB) as more appropriate for memory services. Participants in some memory services argued that the management toolkit was of limited relevance, as their focus was primarily on diagnosis.

In three memory services, the lead clinician successfully made concerted and ongoing efforts to engage staff with the toolkits. In movement disorder services, such efforts were less evident, with only two services making efforts to engage some of the staff team. The majority of services, therefore, were characterised by a striking lack of collaborative work regarding the implementation of both toolkits. In these services, it was largely up to individual members of staff to decide if and how to use the toolkits:

*For me, it was because we weren't all invested as a team together. If you are trying to work with a team it is really important to know, 'This is what we are all going to sign up to. This is what we are all going to do. This is how we are going to work together. This is how it will or won't work'. You just feel as a team we never had those conversations about, 'How can this be used in practice? How are we going to implement it?'*

*2602, specialist PD nurse*

For some non-medical staff, the lack of perceived relevance of the toolkits limited their willingness to engage with the pilot trial.

### **Putting the toolkits into practice (collective action)**

Implementation of both toolkits varied within and between services. Although the lack of integration with existing electronic or paper documentation was identified as a significant barrier to implementation, several clinicians reported incorporating some questions from the assessment toolkits into their routine practice:

*What I've done is, actually, I've taken some of those criteria that are easy and then I have prepared my own clinic pro forma. So that when I see someone I have a piece of paper and the kind of things I need to ask. And part of my standard assessment question is to cover those criteria. That's how I use them.*

*0102, trainee OAP*

Although views varied on the additional time required to use the assessment toolkits, most participants in memory services used the toolkits only when LBD was suspected, and often did so after a consultation or during supervision, rather than embedding the questions into routine practice. The training on the five-item UPDRS provided by the clinical research associates to staff in some services in the pilot trial was well received, but insufficient to change practice on its own. The questionnaire explored the extent to which respondents explored core and suggestive features of DLB in consultations with new patients. Although over three-quarters of respondents from memory services reported that they always conducted a cognitive test and explored fluctuation and hallucinations, fewer than half explored REM sleep behaviour disorder, parkinsonism or used diagnostic criteria (see *Appendix 7, Figure 10*). Use of the assessment toolkits was limited in movement disorder services, with most services continuing with their usual approach to exploring cognition, although several individuals reported incorporating the initial questions on executive function into their consultations.

The management toolkit was similarly typically used after consultations, partly because of the logistics of accessing the documents but also because of concerns over patient reactions. Some clinicians



appeared reluctant to change their practice purely on the basis of the management toolkit, preferring to continue with tried and tested prescriptions (even if the evidence for these was less robust):

*We had that discussion this morning about clozapine being the most helpful but we don't tend to use that, we tend to go for quetiapine.*

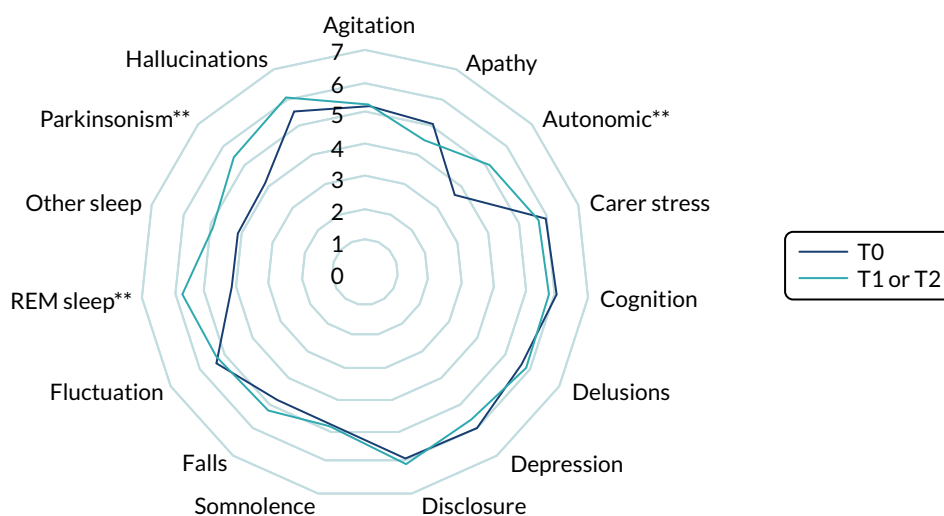
*Unidentified female participant, memory service 07*

The questionnaires also explored views on the likelihood of embedding the toolkits into routine practice. Similar views were expressed about integration and sustainability of the assessment and management toolkits, although respondents had slightly more positive views about the management toolkit becoming part of their normal practice (see *Appendix 7, Figure 11*). Data also indicated that more positive views towards integration of the assessment toolkit were associated with having access to the management toolkit (see *Appendix 7, Figure 12*) and working in memory services (see *Appendix 7, Figure 13*).

### Assessing impacts of the toolkits (reflexive monitoring)

For many clinicians, a key outcome of both toolkits was increased awareness of LBD. Where lead consultants in memory services had encouraged implementation of the DLB assessment toolkit, they reported improved documentation of core and suggestive features by non-medical staff. Other changes resulting from use of the assessment toolkit identified by staff in memory services included more consistent documentation of negative findings and a more holistic approach to assessment. Even when non-medical staff did not perform the five-item UPDRS, the assessment toolkit was thought to have increased awareness of the range of possible signs of parkinsonism.

We tried to identify possible mechanisms through which the management toolkit could lead to improved outcomes. Qualitative data from clinicians suggested that only a small number had adopted new treatments and there was little evidence of increased management of new symptom areas. We included questions on confidence in managing common LBD symptoms in all three WP5 questionnaires administered during the programme (see *Appendix 7*). Comparison over time indicated that confidence in managing three symptom areas (autonomic symptoms, parkinsonism and REM sleep behaviour disorder) increased significantly in control practices during the programme (*Figure 5*). Clinicians who received the management toolkit showed small, but (statistically) significant, changes in confidence in managing all but two symptom areas (*Figure 6*). This suggests that a possible mechanism of change may be the accumulation of marginal gains in confidence over a wide range of areas. However, the results should be interpreted with caution, as the respondents at each time point are overlapping, but not identical.



**FIGURE 5** Mean confidence ratings for symptom management for respondents in control services. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . T0, initial data; T1, follow-up data 1; T2, follow-up data 2.

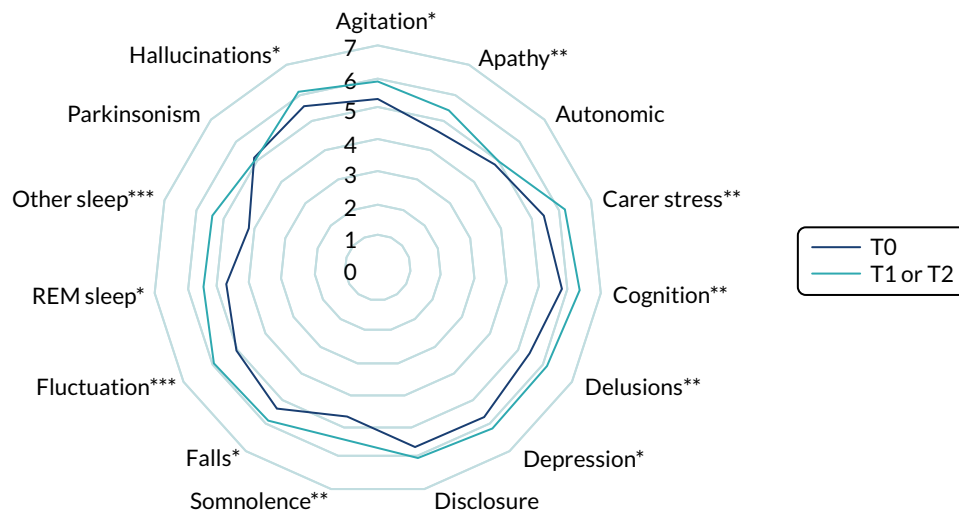


FIGURE 6 Mean confidence ratings for symptom management for respondents in intervention services. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . T0, initial data; T1, follow-up data 1; T2, follow-up 2.

An alternative mechanism may be that change is achieved via indirect routes. For example, some clinicians reported that they were now more willing to suggest possible changes of medication or referral to other specialties to the patient’s GP. This more holistic approach to management is potentially a mechanism through which change could be achieved:

*It gives guidelines for things that I wouldn’t consider treating in a memory service [...] So, I’m not really starting medications for constipation and even things like hypotension, but they might trigger me to ask the falls clinic or somebody else to see people.*

1601, consultant OAP

### Views on implementation

The insights from the qualitative work in WP5.1 and WP5.2 were used to develop an implementation strategy for the pilot trial (see Appendix 11, Tables 31–34). The extent to which this was implemented during the pilot trial was limited because of the restricted time and resources available, concerns over the risk of challenging and potentially alienating professionals, availability of credible professionals to address some issues (particularly for movement disorder services) and lack of skills within the research team to develop local implementation strategies.

During interviews and focus groups, we explored participant views on implementation in the pilot trial and alternative ways to support toolkit use. The interviews and focus groups were often the first opportunity for clinicians to reflect on if and how they were using the toolkits. Participants thought that implementation had been influenced by local leadership and tailored education sessions. In a small number of sites, a lead professional adopted the role of a local champion, typically acting as a focal point for the intervention, engaging the wider team and maintaining momentum (e.g. by adding the toolkits to the agenda of regular meetings). Some participants suggested that the lack of a lead clinician had been a factor contributing to poor implementation:

*What I would say in retrospect, is I’m not sure that we’ve maximised the value of this within the service. But to do that, we would have actually needed a more sustained input, I think, from the team. And somebody, one or two of us, actually, really taking a role in terms of getting hold of this and running with it. You, actually, need somebody in the team who is going to take a real lead to try and sort of keep it on people’s minds. Find out what people’s experience was, address any issues, advocate for its value, which, to be fair, I don’t think there was somebody who took on that role.*

1209, consultant OAP

The above quotation also mentions the need for sustained input from the research team. Tailored educational sessions were delivered by the study team to some sites (usually at their request). Feedback on the sessions indicated that they were valued by practitioners and often provided new insights into the assessment or management of LBD:

*We had your colleague who came along and did the training on a Wednesday morning – which was excellent, I learned loads from that [. . .] [He] was much better at assessing for increased tone and did a far greater range of movement than I would have been routinely doing.*

1101, consultant OAP

Although the site initiation visit provided an overview of the study and toolkits, several participants would have preferred a more interactive approach in which they could have reviewed the toolkits in detail with a knowledgeable clinician from the study team. This would have allowed queries to be raised and discussed and could explicitly have addressed the misperception among many movement disorder clinicians that the assessment toolkit required them to perform a cognitive assessment on all patients. A final strategy suggested by several participants was to use team meetings or peer learning groups to identify divergences between their current practice and the assessment or management toolkits as a way of highlighting scope for change.

## Discussion

The detailed qualitative work provided new insights into the complex and inter-related factors influencing the diagnosis and management of LBD. The inherent complexities of the disease itself required input from different specialties, leading to potential fragmentation of services. Other important factors identified were a workforce with variable levels of training and confidence in LBD, and persisting negative attitudes among some clinicians towards diagnosis and disclosure of dementia in patients with pre-existing PD.

Observation confirmed the lack of routine assessment of core and suggestive features of LBD in memory services. In movement disorder services, resources were a key factor in determining whether or not cognitive function was formally assessed. The assessment toolkits potentially address these issues by including standardised questions for memory services and brief screening questions for movement disorder services to determine whether or not formal cognitive assessment is required. The management toolkit could potentially facilitate management of the complex and multiple symptoms in LBD. Other barriers to diagnosis and management were not amenable to change through the toolkits and some acted as barriers to their implementation.

Most clinicians welcomed the concept of the toolkits to facilitate the diagnosis and management of LBD. Key potential benefits were increased awareness of LBD, more consistent and comprehensive assessment and evidence-based management. The assessment toolkits were thought to be particularly beneficial to junior doctors and non-medical staff.

Qualitative data highlighted aspects of the assessment toolkits requiring further revision. It is now clear that training non-medical staff to administer the five-item UPDRS<sup>26</sup> is neither feasible nor acceptable. However, with nurse-led models of memory assessment services becoming more common, alternative ways to conduct a simple neurological screen for non-medical staff are needed. Other issues related to question wording, signposting and the rationale underpinning the diagnostic criteria and choice of symptoms.

The positive feedback on the presentation of the management toolkit suggests that applying the same design principles to the assessment toolkits may make them more appealing and easier to use in practice. Ideally, the toolkits would be available in a variety of formats to suit personal preferences.

Implementation of the assessment toolkits in the pilot trial varied within and between sites. In many movement disorder services, key barriers related to cognitive participation or willingness to invest in the assessment toolkits. This resulted in limited use of the assessment toolkits (which is likely to explain the unchanged diagnostic rates of PDD observed in WP1R, see *Work package 1 repeated: re-assessment of diagnostic rates for Lewy body dementia after introduction of the assessment toolkits for diagnosis*). In three memory services in the North East, the lead clinician successfully encouraged widespread adoption throughout the team. Although this was attempted in two further memory services (both in East Anglia), uptake in these teams remained patchy. In other memory services, there was little collective work to support implementation and it seemed largely up to individual members of staff to decide if and how to implement the toolkits.

Uptake of the management toolkit varied, with some participants reporting that their practice was already consistent with the toolkit. Barriers to implementation were that few LBD patients were seen and that (memory) services focused on diagnosis with little involvement in management. Identifying possible mechanisms through which the management toolkit could lead to improved outcomes was challenging. Few participants reported changing their prescribing habits or managing additional symptom areas. However, the use of the toolkit appeared to raise awareness of the range of symptom areas affected in LBD and to increase confidence in managing common symptoms, and this may have facilitated a more holistic approach to care. In any future implementation study, we recommend the collection of data on prescriptions and referrals, and content analysis of letters to GPs, as it is possible that some benefits accrue from changes made by GPs, rather than directly by the specialist clinicians using the management toolkit.

### **Limitations**

The increase in the number of services in WP4 (from 8 to 22), and the inclusion of East Anglia as a second geographical region, meant that resources for the qualitative component were stretched. One consequence was that a follow-up interview was conducted with only a single clinician in WP4 and, therefore, we have limited data on how the implementation and views of the toolkits changed over time. It proved impossible to engage four services in the qualitative work in WP4. The response rates to the questionnaires were acceptable, although disappointing. The views of less engaged clinicians are likely to be under-represented in our data set and consequently we may not have identified all barriers to implementing the toolkits.

Although only a small number of patients and carers provided feedback on the toolkits, the consistency of their comments means that we do not consider this a significant limitation. We achieved data saturation with a small number of interviews and there was no indication in the pilot trial that further data collection from patients and carers was merited.

We developed an implementation strategy for the pilot trial based on the initial qualitative data; however, because of limited resources, many suggestions were not adopted. Participants in the pilot trial identified additional strategies to inform future implementation.

Some services reported limited opportunities to use the management toolkit, as they focused on diagnosis and discharged patients shortly afterwards. This suggests that additional criteria may be required to identify potential services for a future trial.

There were occasionally some tensions between research paradigms, in particular in relation to managing qualitative feedback on question wording in the assessment toolkits, with the value given to 'validated' questions derived from clinical research.

# Work package 1 repeated: re-assessment of diagnostic rates for Lewy body dementia after introduction of the assessment toolkits for diagnosis

One of the aims of the programme was to seek to improve the diagnosis of DLB and PDD by facilitating diagnosis so that more cases receive a correct diagnosis. To this end, approximately 2.5 years after WP1 was undertaken, and following the development and piloting of the assessment toolkits in WP3 (see *Work package 3: development of assessment toolkits for the diagnosis of Lewy body dementia*), they were introduced to 23 services as part of the pilot cluster randomised trial of the management toolkit undertaken in WP4.

Some of the same services that took part in WP4, where the assessment toolkits were introduced, also participated in WP1, which established the baseline diagnostic rates for DLB and PDD (see *Work package 1: baseline study of the diagnosis and management of Lewy body dementia*). The aim of WP1R was therefore to undertake, using exactly the same methodology as baseline, a revised study over an 18-month period, following the introduction of the assessment toolkits to examine diagnostic rates for DLB and PDD. Our hypothesis was that the introduction of the assessment and diagnostic toolkits would result in significantly increased diagnostic rates for DLB and PDD. This study was approved by the North East – Newcastle & North Tyneside 1 Research Ethics Committee (reference 17/NE/0362) and the Confidentiality and Advisory Group (reference 17/CAG/0188).

## Methods

We used exactly the same methods as in WP1 (see *Work package 1: baseline study of the diagnosis and management of Lewy body dementia*) to ensure comparability of findings. For DLB, case notes of patients in four of the same memory services in three different NHS trusts from the two regions were examined. For PDD, case notes were reviewed from three movement disorder services in three NHS trusts in the two regions.

## Results

Of 2058 referrals to the memory services over an 18-month period, 1279 received a diagnosis of dementia, of whom 6.2% received a diagnosis of DLB.

This rate, found after introduction of the assessment toolkits, was significantly higher than the 4.6% found at baseline before the introduction of the toolkits ( $\chi^2 = 5.3$ ;  $p = 0.021$ ). On further examination, diagnostic practice in East Anglia was unchanged, whereas rates had significantly increased in the North East (9.7% vs. 5.6% at baseline,  $\chi^2 = 14$ ;  $p = 0.000019$ ).

A total of 3405 referrals to movement disorder services were identified, of whom 1968 received a diagnosis of PD. Of these, 8.2% received a diagnosis of PDD. This diagnostic rate, after introduction of the assessment and diagnostic toolkits, was not significantly different from the 9.7% found at baseline ( $\chi^2 = 2.8$ ;  $p = 0.09$ ). For PDD, there was a difference between regions, with the North East showing a significant decrease in PDD rates (7.8% vs. 10.5%;  $p = 0.006$ ); however, East Anglia showed a significant increase (13.3% vs. 8.3% at baseline;  $p = 0.046$ ).

## Discussion

The introduction of assessment and diagnostic toolkits for DLB and PDD was associated with a significant increase in diagnostic rates for DLB, but not PDD. However, there were significant differences between services and regions, with some services increasing their diagnostic rates and others not. Differences between regions were also noted for WP1 in terms of baseline rates for DLB diagnosis, although it is not entirely clear what factors drive these differences. There was diversity both within and between North East and East Anglia in terms of service organisation. Both sites included memory services where initial assessments of 'straightforward' patients were conducted by non-medical staff. Access to scans in the North East appeared to be better. In East Anglia, issues with scans reflected both the significant travelling required by some patients in rural areas and the informal limits described by some participants on the 'appropriate' number of scans. The North East has a long track record of research in DLB and many clinicians working in the North East have been exposed to DLB, either during training and/or through their involvement in research studies. This was reflected in a number of comments made by participants in the qualitative work on the North East being particularly sensitised to DLB. There were, however, clinicians in East Anglia with a long-standing interest in DLB who had similarly been involved in training medical staff over a period of years. Interest in DLB was therefore by no means limited to the North East.

The strengths of this study include the inclusion of the same services for which we ascertained baseline diagnostic rates in WP1, and use of exactly the same methodology for determining cases and diagnosis. Limitations include that, as this was not a controlled study, we cannot definitely conclude that the introduction of the assessment toolkits was causally related to the change in diagnostic rates. Other factors may have been involved, including generally heightened awareness of DLB over time and/or service or other changes. Finally, unlike WP1, in WP1R we did not undertake a repeat of the more detailed case note study and so we could not determine whether or not the factors associated with the diagnosis of DLB and PDD found at baseline had been moderated in any way. We did not collect data on the additional time taken to administer the toolkits and so cost-effectiveness of the toolkits for increasing diagnostic rates cannot be determined.

The qualitative studies (WP5) provide some insights as to why diagnostic rates for PDD (and DLB in East Anglia) were unchanged, but further research is required to better understand whether the unchanged diagnostic rates were linked to variation in implementation or whether additional factors were involved. Further exploration of ways to tackle the barriers to diagnosis identified in WP5 and to improve implementation of the assessment toolkit, especially in sites with low diagnostic rates at baseline, is required.



## Overall programme discussion

The DIAMOND-Lewy programme achieved all its core aims. We demonstrated in WP1 that diagnostic rates for DLB and PDD were below, less than half, of those expected. For DLB, we found significant variation between regions and services. There appeared to be several contributing factors to this, including variations in availability of diagnostic tests, differences in service organisation and a great awareness of some clinical staff to DLB and PDD as a diagnostic possibility. We could not examine all these factors in detail within this programme. WP1 was retrospective in nature and used case records. Although this was a strength in terms of examining an unselected group of referrals to secondary care, there was some selection bias, as we could include people in the more detailed case note study only if they were alive.

In WP2, we developed evidence-based management toolkits. One major limitation was that the evidence base was thin, with most pharmacological studies focusing on a few agents, largely cholinesterase inhibitors and memantine, and there were very few non-pharmacological studies. To address these gaps, we used a Delphi approach with an expert clinical panel to develop a final management toolkit. Assessment toolkits were assembled within WP3 and, together with the management toolkit, trialled in a busy NHS trust that provided both memory assessment and movement disorder services. The toolkits were well received, but the extra time needed to undertake cognitive assessments in movement disorder services (where they are not standard) was a limitation. The toolkits had been designed to be as brief as possible, while also being consistent with the evidence base informing their development. This will always be a tension, and a limitation of WP3, as well as the pilot cluster randomised trial, is that we did not formally gather information on the time taken to administer the toolkits. In WP4, we successfully undertook a pilot cluster randomised trial of their implementation, demonstrating that such a study was possible, and we achieved the recruitment target of 120 participants ( $n = 131$  recruited) within 23 services. Our qualitative studies (WP5) showed that implementation was variable, and one key lesson learned was that a clear implementation plan is needed for future studies or introduction of the toolkits.

Power calculations showed that a main trial would need to be of around 900 people, allowing for attrition and using an outcome measure such as the Neuropsychiatric Inventory. This would require a substantial investment and would be a complex trial to undertake. There are alternative models to implementing the assessment and management toolkits, including through service quality improvement initiatives and working with services using principles from implementation science to tailor implementation to the local context. In WP1R we used the same methodology as in WP1 to reassess diagnostic rates for DLB and PDD after introduction of the assessment toolkits in services where we had baseline data from WP1. We found a significant increase in diagnostic rates for DLB but not PDD; however, rates did not increase in every service. One limitation is that we were not able to examine, in detail, factors associated with a change in diagnostic rates. It appeared, contrary to expectation, that services that already had higher baseline rates of DLB diagnosis showed the greatest increase in diagnostic rates. This may be because the toolkits were introduced on the background of a high level of knowledge and interest in DLB diagnosis. It also suggests that in areas of low diagnostic activity for DLB, the introduction of the assessment toolkits themselves will not be sufficient to increase rates. Diagnostic rates for PDD did not change following introduction of the assessment toolkits. Qualitative work indicated that this may be because of a combination of insufficient time to always use these, as well as continued negative attitudes to making the diagnosis of dementia in PDD. Further work needs to examine how to improve diagnostic rates for PDD.





# Conclusions and recommendations for research

The DIAMOND-Lewy programme has provided considerable new knowledge about diagnostic and management practice of DLB and PDD in the NHS, has produced evidence-based assessment and management toolkits, and has shown, through a pilot cluster randomised trial, the feasibility of undertaking a study following their introduction into NHS services. In addition, introduction of the assessment toolkits was associated with an increase in diagnostic rates for DLB, although we cannot definitely conclude a causal link.

## Implications for practice and any lessons learned

The findings of the programme have a number of important implications for clinical practice:

- In the regions we studied, DLB and PDD appeared to be underdiagnosed compared with expected rates, with variability in diagnostic rates between services. This suggests that improvements may be needed in the way in which clinicians assess people for symptoms and make diagnoses.
- We found that the reluctance of some clinicians to make a formal diagnosis of dementia could be a significant factor contributing to the underdiagnosis of LBD (particularly PDD). This implies that negative attitudes to disclosure may need to be challenged, possibly through supervision, appraisal or local audits to examine the diagnostic rate of PDD.
- In eliciting symptoms, observation suggested that leading questions were not uncommon and that some symptom areas (e.g. sleep) were often explored only superficially during memory assessments. Existing clinical practices, such as supervision, may provide an opportunity to address both of these areas. An iterative process of discussing and sharing ways of asking questions may enable staff to critically evaluate their existing approach and develop more consistent ways of approaching certain symptoms or issues. The concerns expressed over whether or not non-medical staff had received adequate training for their role in assessment imply that additional on-the-job training on dementia subtypes may improve diagnostic accuracy.
- There may be benefits for more training to enhance awareness in secondary care clinical teams of how to make a diagnosis, and of why, including raising awareness of the opportunities for evidence-based management.
- Using a structured method, like the assessment toolkit, for diagnosis may help increase diagnostic rates.
- The complexities of managing LBD may require input from a range of specialties, which has the potential to lead to fragmentation of care pathways. Successful strategies for joint working included telephone multidisciplinary team meetings for complex patients, informal consultation arrangements across specialties where clinicians were co-located and adapting a memory service pathway to enable patients diagnosed with LBD by a geriatrician or neurologist to access support without further assessment. These initiatives highlight the potential value of developing tailored, local strategies to address barriers to cross-specialty working.

## Recommendations for research

Findings from the programme highlight a number of areas for future research:

- Further study to ascertain whether or not unchanged diagnostic rates, despite access to the toolkits, reflect poor implementation of the assessment toolkits or additional factors.
- Research into how best to co-ordinate multispecialty input to patients with LBD is needed to streamline management and facilitate a holistic approach.

## CONCLUSIONS AND RECOMMENDATIONS FOR RESEARCH

- Further work is needed to better understand how assessment toolkits for PDD can be integrated into practice to improve diagnostic rates. Qualitative studies indicate that there remain important barriers and negative attitudes to diagnosis and management, and further work is needed to see how these are best addressed.
- The evidence base informing the management of LBD is limited, especially for non-pharmacological interventions. More therapeutic studies are needed, especially well-designed RCTs for both cognitive and non-cognitive symptoms.
- Future research should investigate the specific domains contained within the management toolkit and the extent to which global improvements are due to specific symptom improvement, as opposed to a number of marginal gains in several areas.
- Our successful pilot demonstrates that a larger, more comprehensive trial of introducing the management toolkit could be undertaken, but it would need to include a minimum of 410 (and up to 908) people, depending on the primary outcome.

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## Publications

Stinton C, Bamford C, Cambridge V, Lafortune L, Mak E, Mason J, *et al.* A Systematic Review of Management Strategies for Lewy Body Dementia (*Dementia with Lewy Bodies and Parkinson's Disease Dementia*). PROSPERO 2014:CRD42014007180. URL: [www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=7180](http://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=7180) (accessed April 2021).

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## Data-sharing statement

We shall make data available to the scientific community with few restrictions as feasible, while retaining exclusive use until the publication of major outputs. Anonymised data can be obtained by contacting the corresponding author.

## Patient data

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that it is stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: <https://understandingpatientdata.org.uk/data-citation>.



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# Appendix 1 Health economic analysis for work package 1

## Comparison of health-care service utilisation and costs between Lewy body and non-Lewy body dementia patients: the DIAMOND-Lewy study

### Introduction

This appendix describes the methods and results of the economics component of WP1. The aim of this component was to compare the cost of the pathway to final diagnosis and costs of care for those with DLB with non-DLB dementia (WP1A), and those with PDD with those with PD without dementia (WP1B). For both comparisons, the main objective of the study was to explore differences in the cost of assessments, appointments and diagnostic investigations undertaken, as well as hospital inpatient/day hospital resources and treatment.

### Methods

#### Study sample and recruitment

Patients for the study were recruited into a DLB cohort and a PDD cohort. All participants were recruited from four UK NHS trusts in two different geographical regions of England (North East and East Anglia). DLB patients were recruited from nine psychiatry of old age/memory services from January 2013 to December 2014. PDD patients were recruited between August 2015 and February 2016 across eight movement disorder clinics (four neurology services and four geriatric medicine services). For each of the DLB and the PDD patient groups, control groups were also recruited (non-DLB dementia and PD without dementia, respectively), identified as the next control patient seen that could be matched. These controls were matched for sex, age ( $\pm 5$  years) and MMSE score (in three bands 0–10, 11–20 and 21–30) to match for dementia severity.<sup>51</sup>

At the point of recruitment, all participants had had their cognitive function assessed and had been diagnosed with dementia and/or PD 12 months prior to the start date of the study. This reflects the fact that the determination of diagnosis can take several months, especially for DLB. Diagnoses were confirmed by an independent expert panel of three clinicians (a method previously validated as an acceptable approach to discriminating incorrect diagnoses, compared with autopsy and imaging measures).<sup>52</sup>

#### Data

For the DLB cohort, the research team screened the clinical notes of 9449 consecutive people seen within old age psychiatry/memory assessment services. Of these 9449 people, 4504 (47.7%) had a dementia diagnosis. Of these, 207 (4.6%) received a clinical diagnosis of DLB during this period and 105 were approached to participate in the study. Seventy-four people consented and granted researchers further access to their clinical records. Seventy-two non-DLB dementia control participants were also recruited into the study.

For the PDD cohort, consecutive clinical notes of 2263 patients in movement disorder neurology and geriatric medicine services were screened. Of these 2263 patients, 151 (6.7%) received a clinical diagnosis of PDD. Out of these 151 cases, 53 patients were approached for consent and 38 were recruited into the study. A total of 1474 people received a diagnosis of PD. Forty-four people were approached to take part in the study, with 35 providing consent.

#### Measures

The records of consenting participants in both the DLB and PDD cohorts were reviewed and extracted into case report forms tailored to each patient cohort. For each participant, data were collected on the

use of services spanning several years of clinical records before and after final diagnosis. Data collected included the number of appointments before and after diagnosis and the number and type of diagnostic investigations undertaken before and after diagnosis.

To estimate the cost of service use and to compare differences between the pathway to diagnosis and the post-diagnosis cost of care for LBD (DLB and PDD) participants compared with control participants, the data on use of services were combined with unit cost data taken from routine sources, such as NHS reference costs<sup>15</sup> and Personal Social Services Research Unit costs.<sup>16</sup> These data were then used to estimate the total cost of diagnosis and management for each participant. All costs were reported in Great British pounds (£) for the year 2017. Costs were categorised into components of total cost of diagnosis and care as 'medical history costs', 'medication costs', 'investigation costs', 'pathway to diagnosis costs' and 'post-diagnosis costs'. 'Investigation costs' excluded neuropsychology and tests of cognition and function (e.g. MMSE, Addenbrooke's Cognitive Examination Revised and Bristol Activities of Daily Living Scale) because the costs of these were thought to be negligible. Investigation costs did include blood tests, brain imaging and other imaging examinations (such as ultrasounds and computerised tomography, radiographs, electrocardiograms, echocardiograms, etc.). 'Pathway to diagnosis costs' covered the cost of home visits by specialists (e.g. OAP, physiotherapist, social worker), clinic appointments (e.g. specialist PD nurse, physiotherapist, geriatric physician) and appointments with secondary care specialists (e.g. Community Mental Health Team, clinical psychologist, memory support service). 'Medical history costs' included operations, hospitalisations and attendances at accidents and emergency departments after the date of final diagnosis. 'Medication change costs' were based on the only available complete list of medications recorded for each patient in the case report form and refers to post-diagnosis medication changes. Finally, 'post-diagnosis costs' included home visits by specialists and clinic appointments, but excluded services associated with dementia management strategies, as these would have already been captured in other cost categories.

### Statistical analyses

Demographic and clinical characteristics of the sample were summarised using proportions and measures of central tendency. Differences between DLB and non-DLB participants and PDD and PD without dementia participants were explored using independent-samples *t*-tests with unequal variance for normally distributed variables, Wilcoxon rank-sum tests for continuous non-normally distributed variables and chi-squared tests to explore differences in proportions. Differences between cases and controls in average costs of the different components of diagnosis and care costs and differences in the proportion to the total of each cost category were also estimated. A third set of analyses explored the contribution of patient characteristics to total costs.

The dispersion around the average was estimated using 95% CIs, with bias correction from 1000 bootstrap replications clustered by study site. The difference between patient groups was explored using Wilcoxon rank-sum tests. Finally, the marginal effects from a generalised linear model, using a gamma distribution with log-link function, adjusting by time of resource use and clustered standard errors by study site, were used to explore the effect of participant demographic and clinical characteristics on the total cost of diagnosis and care.

## Results

### Cohort characteristics

For the DLB comparison, the proportion of men in the sample was comparable between the DLB and non-DLB dementia groups at around 60% of participants (*Table 8*). The average age of participants across the two groups was 77 years and almost all participants reported a white British background. DLB participants had received a larger number of previous diagnoses before achieving a final diagnosis, and presented with more clinical features of LBD (e.g. fluctuating cognition, recurrent visual hallucinations, features of parkinsonism) than non-DLB participants.

TABLE 8 Characteristics of the participant cohort. Percentages across different characteristics unless otherwise stated

Characteristic	DLB (n = 74)	Non-DLB dementia (n = 72)	Difference between DLB groups, p-value (test statistic)	PDD (n = 38)	Non-PDD (n = 35)	Difference between PDD groups, p-value (test statistic)
Sex						
Male	59	58		73	74	
Female	41	42	0.890 ( $\chi^2 = 0.019$ )	27	26	0.899 ( $\chi^2 = 0.016$ )
Ethnicity						
White British	95	98		96	95	
Other	5	2	0.370 ( $\chi^2 = 0.802$ )	4	5	0.947 ( $\chi^2 = 0.004$ )
Age (years), <sup>a</sup> mean (SD)	77.6 (8.4)	77.2 (8.0)	0.757 (t = 0.311)	66.3 (19.7)	68.1 (15.2)	0.661 (t = -0.441)
Number of previous diagnoses <sup>b</sup>						
Mean (SD)	1.1 (1.0)	0.6 (0.8)	0.004 (z = 2.911)	1.4 (1.1)	0.5 (0.6)	< 0.001 (z = 3.837)
None	31	51		24	51	
One	39	36		24	43	
Two to four	30	13	0.012 ( $\chi^2 = 8.856$ )			
Two to five				53	6	< 0.001 ( $\chi^2 = 19.136$ )
Living arrangements <sup>c</sup>						
Home or family	56	68		49	100	
Institution	44	32	0.145 ( $\chi^2 = 2.121$ )	51	0	< 0.001 ( $\chi^2 = 23.839$ )
Use of care support <sup>c</sup>						
No	0	3		75	45	
Yes	82	75		6	52	
Not applicable (%)	18	22	0.282 ( $\chi^2 = 2.534$ )	19	3	< 0.001 ( $\chi^2 = 18.805$ )

continued

TABLE 8 Characteristics of the participant cohort. Percentages across different characteristics unless otherwise stated (continued)

Characteristic	DLB (n = 74)	Non-DLB dementia (n = 72)	Difference between DLB groups, p-value (test statistic)	PDD (n = 38)	Non-PDD (n = 35)	Difference between PDD groups, p-value (test statistic)
Time of resource use (years), mean (SD)	6.4 (4.7)	5.1 (4.6)	0.052 (t = 1.637)	9.2 (3.5)	7.8 (4.4)	0.129 (t = 1.537)
Time since diagnosis (years), mean (SD)	1.8 (1.4)	1.7 (1.9)	0.290 (t = 0.554)	3.2 (4.3)	5.9 (3.9)	0.007 (t = -2.797)
Number of clinical features of DLB or PDD <sup>d</sup>						
Mean (SD)	3.5 (2.1)	0.9 (1.3)	< 0.001 (z = 7.848)	7.2 (3.4)	1.8 (2.0)	< 0.001 (z = 5.732)
None	4 <sup>e</sup>	46 <sup>e</sup>		8 <sup>f</sup>	20 <sup>f</sup>	
One or two	36	44				
Three or more	59	10	< 0.001 ( $\chi^2 = 52.249$ )			< 0.001 ( $\chi^2 = 41.043$ )
One to five				16	77	
Six or more				16	77	< 0.001 ( $\chi^2 = 41.043$ )

a Age at referral.

b Number of previous diagnoses before final diagnosis. Previous diagnoses refers to other diagnoses the patient received before the final diagnosis of DLB or PDD dementia. Previous diagnoses before final diagnoses included Lewy bodies dementia, PDD, vascular dementia, Alzheimer's disease, frontotemporal dementia, mixed vascular dementia and Alzheimer's disease, MCI and 'other'.

c Captured at the end of the study recruitment period. Carer involvement refers to both formal and informal carers. One visit per week was the minimum required for a 'yes' condition of carer involvement.

d Clinical features recorded before the date of final diagnosis. Institutions where patients resided included nursing homes, elderly mentally infirm care homes, NHS long stay and sheltered accommodation.

e Three DLB cases with no recorded clinical features before final diagnosis and 33 non-DLB cases with no recorded clinical features before final diagnosis. Clinical features for DLB includes fluctuating cognition, recurrent visual hallucinations, features of parkinsonism, REM sleep behaviour, severe neuroleptic sensitivity, repeated falls and syncope, transient unexplained loss of consciousness, constipation, incontinence, orthostatic hypotension, depression, hallucinations in other modalities, delusions, abnormal sense of smell and swallowing difficulties.

f Three PDD participants with no recorded clinical features before final diagnosis and seven non-PDD participants with no recorded clinical features before final diagnosis. Clinical features for PDD includes parkinsonism, cognitive impairment, dementia impact on activities of daily living, cognitive deficits in two or more domains, anxiety, apathy, depression, delusions, visual hallucinations, excessive daytime sleepiness, changes in personality, REM sleep behaviour disorder, fluctuation, swallowing difficulties, repeated falls, abnormal sense of smell, orthostatic hypotension, constipation and bladder instability.

#### Notes

z-scores from Wilcoxon rank-sum test.

t-score from an independent-samples t-test with unequal variance.

Chi-squared tests of differences in proportions.



For the PDD cohort (across the 38 PDD and 35 non-PDD participants) the proportion of men in the sample was comparable between the two groups, with mean age across the two PDD cohort groups of 67 years. Those with PDD had received a larger number of previous diagnoses before reaching a final diagnosis than those with non-PDD dementia, and presented with more clinical features (e.g. cognitive impairment, dementia impact on activities of daily living, cognitive deficits). The proportion of participants who were receiving support from a formal or informal carer was higher for those in the non-PDD group than for those with PDD.

### Cost of diagnosis and care

Dementia with Lewy bodies participants had higher costs arising from medication changes, investigations and the use of primary and secondary care services associated with the pathway to diagnosis (*Table 9*). Overall, the average cost of care for DLB participants was £6557, compared with £3425 for non-DLB participants (mean difference £2868, 95% CI -£68 to £4013;  $p = 0.055$ ).

Parkinson's disease dementia participants also had higher average costs of investigations, at around £250 per patient (95% CI £237 to £306;  $p = 0.001$ ) and higher post-diagnosis management costs (average difference of £570 per patient, 95% CI £281 to £808;  $p = 0.001$ ). However, there was no evidence of a difference in overall costs between those in the non-PDD group (£2024, 95% CI -£3598 to £5548;  $p = 0.462$ ) and those with PDD.

*Table 10* shows the contribution to total cost of the different cost subcategories associated with pathway to diagnosis, medical history post diagnosis and post-diagnosis treatment. For DLB participants, medical history costs represented the largest contribution, with an average across patients of 40% of total costs (27% for non-DLB participants) ( $p = 0.042$ ). The share of investigation costs was lower for DLB participants (20%) than for non-DLB participants (26%) ( $p = 0.042$ ), although, on average, investigation costs were higher for DLB patients (see *Table 9*), probably reflecting the effect of the higher medical history costs on the share of total DLB costs.

No evidence of differences was observed between PDD and non-PDD participants, except for the share of cost of pathway to diagnosis and the post-diagnosis costs. For pathway to diagnosis, these represented 19% of total costs for PDD participants [a lower share than for those in the non-PDD group (36%;  $p = 0.004$ )]. For the post-diagnosis management costs, these were higher in the PDD group (see *Table 9*), which is also reflected in the much higher proportion of total cost of post-diagnosis management in PDD participants than in control participants (15% vs. 1%;  $p < 0.001$ ).

### Factors influencing costs of diagnosis and care

*Table 11* shows the estimated difference in total costs of diagnosis and care between participants with DLB and participants with non-DLB dementia (see *Table 11*, top rows, panels A and B), and between participants with PDD and participants with PD but without dementia, after taking into account the influence on costs of differences in sex, time since diagnosis, total resource use time and other patient characteristics (see *Table 11*, bottom rows, panels A and B).

Results show that for DLB participants, having a DLB diagnosis represented higher total costs of approximately £3683 (95% CI £1478 to £5507;  $p < 0.001$ ) than for non-DLB participants (see *Table 11*, top panel A). When disaggregating the DLB group according to the number of clinical features associated with DLB (recorded before final diagnosis), participants with two or fewer clinical features before diagnosis ( $n = 30$ ) had costs at an average of £5763 higher than those of non-DLB participants (95% CI £2432 to £9093;  $p = 0.001$ ), and DLB participants with three or more clinical features had, on average, higher costs than non-DLB participants (of around £2482, 95% CI £1664 to £2833;  $p < 0.001$ ) (see *Table 11*, top panel B).

Average costs across all patient types in the DLB cohort (i.e. participants with DLB and non-DLB dementia) were influenced by the number of previous diagnoses and type of delivery of care.

TABLE 9 Summary statistics for the costs (£) of DLB and non-DLB and of PDD and non-PDD dementia

Cost	Mean	DLB (£)				PDD (£)				
		SD	Median	Maximum	Minimum	Mean	SD	Median	Maximum	Minimum
Medical history costs										
Case	4715	6901	1547	29,081	0	5303	8828	537	32,667	0
Control	2398	5327	1408	32,860	0	5054	9010	0	35,114	0
Difference (95% CI)	2202 (-2035 to 3164)					285 (-6876 to 4344)				
Difference <i>p</i> -value	0.170					0.957				
Medication changes costs										
Case	208	348	97	2433	0	2244	3695	473	16,325	23
Control	86	170	52	1245	0	1439	3235	221	13,282	0
Difference (95% CI)	104 (28 to 137)					828 (-1235 to 1777)				
Difference <i>p</i> -value	<b>0.002</b>					0.580				
Investigation costs										
Case	462	333	22	2313	28	473	448	311	2287	43
Control	278	174	0	997	18	212	229	186	994	0
Difference (95% CI)	153 (5 to 216)					257 (237 to 306)				
Difference <i>p</i> -value	<b>0.042</b>					<b>&lt; 0.001</b>				
Pathway to diagnosis costs										
Case	480	633	305	4351	0	889	778	674	2949	0
Control	206	248	126	1515	42	869	494	863	1988	0
Difference (95% CI)	250 (160 to 311)					33 (-323 to 350)				
Difference <i>p</i> -value	<b>&lt; 0.001</b>					0.886				

Cost	Mean	DLB (£)				PDD (£)				
		SD	Median	Maximum	Minimum	Mean	SD	Median	Maximum	Minimum
Post-diagnosis costs										
Case	693	750	517	3449	0	656	734	594	3555	0
Control	458	598	309	4027	0	39	174	0	995	0
Difference (95% CI)	176 (-2 to 281)					574 (281 to 808)				
Difference <i>p</i> -value	0.062					<b>&lt; 0.001</b>				
Total of all costs										
Case	6557	7303	3745	30,954	274	9567	9738	6556	43,437	744
Control	3425	5514	1186	33,977	60	7614	9769	2886	38,646	330
Difference (95% CI)	2868 (-62 to 4013)					2024 (-3598 to 5548)				
Difference <i>p</i> -value	0.055					0.462				

#### Notes

For DLB a case equals a dementia with Lewy bodies (DLB) participant, and a control equals a non-DLB participant. For PDD a case is someone with Parkinson's Disease Dementia (PDD) and control is a participant with Parkinson's disease but without PDD. *p*-values of the difference in mean costs between A and B from generalised linear model with gamma distribution and log-link function, with an indicator variable for patient type and adjusting for differences in total resource use time. *p*-values reported in bold are statistically significant at the 5% level. Standard errors clustered by study site. CIs of the difference from 1000 bootstrap replications, with resampling by patient type (stratum) and study area (cluster).

TABLE 10 Average share (%) of total costs by cost subcategories: DLB and non-DLB dementia participants (WP1A) and PDD and non-PDD participants (WP1B)

Cost subcategory	Mean DLB	95% CI	Mean non-DLB	95% CI	Difference	
					z-value	p-value
Total cost of care	100.0		100.0			
Medical history	40.0	38.1 to 41.9	26.7	11.8 to 41.5	2.034	0.042
Medications	6.0	5.6 to 6.4	4.6	4.3 to 4.9	0.861	0.389
Investigations	19.5	16.9 to 22	25.9	17.1 to 34.7	-2.035	0.042
Pathway to diagnosis	15.5	15 to 16.1	17.6	14.9 to 20.3	-0.799	0.425
Post diagnosis	19.0	18.6 to 19.5	25.2	22.1 to 28.2	-1.675	0.094
	Mean PDD		Mean non-PDD			
Total cost of care	100.0		100.0			
Medical history	33.3	15.5 to 51.2	33.1	4.4 to 61.9	0.667	0.505
Medications	22.8	17.4 to 28.3	19.0	11.4 to 26.6	1.204	0.229
Investigations	10.3	9.9 to 10.7	11.0	5.7 to 16.3	1.027	0.304
Pathway to diagnosis	18.8	15.1 to 22.5	35.9	22.3 to 49.5	-2.866	0.004
Post diagnosis	14.8	6.7 to 22.9	0.9	0.0 to 2.03	6.826	<0.001

**Notes**  
CIs are based on 1000 replications, with clustering over project site.  
p-value from a Wilcoxon rank-sum test of the difference across the two groups.

TABLE 11 Regression estimates of factors influencing total cost of care for participants

Factor	A				B			
	Coefficient (£)	SE	p-value	95% CI	Coefficient (£)	SE	p-value	95% CI
<b>DLB</b>								
Non-DLB dementia	(Reference)							
DLB dementia	3638	1028	<0.001*	1478 to 5507				
DLB with two or less clinical features					5763	1699	0.001*	2432 to 9093
DLB with three or more clinical features					2248	298	<0.001*	1664 to 2833
Number of previous diagnoses	2247	421	<0.001*	1421 to 3072	2315	382	<0.001*	1566 to 3064
Institution care	3373	1067	0.002*	1281 to 5465	3312	1079	0.002*	1198 to 5426
Sex	-562	601	0.350	-1740 to 616	-456	700	0.515	-1827 to 916
Total resource use time	-299	166	0.072	-623 to 27	-324	106	0.002*	-532 to -116
Time since diagnosis	5565	546	<0.001*	4495 to 6636	5278	451	<0.001*	4395 to 6161
n	136 <sup>a</sup>				136 <sup>a</sup>			
AIC	2507				2503			

TABLE 11 Regression estimates of factors influencing total cost of care for participants (continued)

Factor	A				B			
	Coefficient (£)	SE	p-value	95% CI	Coefficient (£)	SE	p-value	95% CI
<b>PDD</b>								
PD without dementia	(Reference)							
PDD	7655	2030	< 0.001*	3676 to 11,634				
PDD with five or fewer clinical features					6856	1600	< 0.001*	3721 to 9991
PDD with six or more clinical features					8691	2612	0.001*	3571 to 13,810
Number of previous diagnoses	-625	3411	0.855	-7311 to 6061	-706	3461	0.838	-7489 to 6076
Institution care	-3394	3753	0.366	-10,749 to 3961	-3809	3446	0.269	-10,563 to 2946
Sex	-5235	1365	< 0.001*	-7909 to -2561	-4391	2576	0.088	-9441 to 658
Total resource use time	618	270	0.022*	90 to 1146	610	265	0.021*	90 to 1130
Time since diagnosis	3177	3895	0.415	-4458 to 10,811	3319	3893	0.394	-4310 to 10,948
n	69 <sup>b</sup>				69 <sup>b</sup>			
AIC	1367				1367			

\*Significant at  $p < 0.05$ .

AIC, Akaike information criterion; n, total sample size; SE, standard error.

a Sample size decreases from 146 to 136 because of one missing value in age at referral and nine missing values for living arrangements.

b Sample size decreases from 73 to 69 because of one missing value in the sex variable, one missing value in time since diagnosis and two missing values for living arrangements.

#### Notes

Values expressed in GBP (£).

Clinical features recorded before the date of final diagnosis.

Clinical features in DLB includes fluctuating cognition, recurrent visual hallucinations, features of parkinsonism, REM sleep behaviour, severe neuroleptic sensitivity, repeated falls and syncope, transient unexplained loss of consciousness, constipation, incontinence, orthostatic hypotension, depression, hallucinations in other modalities, delusions, abnormal sense of smell and swallowing difficulties.

Clinical features for PDD includes parkinsonism, cognitive impairment, dementia impact on activities of daily living, cognitive deficits in two or more domains, anxiety, apathy, depression, delusions, visual hallucinations, excessive daytime sleepiness, changes in personality, REM sleep behaviour disorder, fluctuation, swallowing difficulties, repeated falls, abnormal sense of smell, orthostatic hypotension, constipation and bladder instability.

Previous diagnoses before final diagnoses included LBD, PDD, vascular dementia, Alzheimer's disease, frontotemporal dementia, mixed vascular dementia and Alzheimer's disease, MCI and 'other'.

Institutions where patients resided included nursing homes, elderly mentally infirm care homes, NHS long stay and sheltered accommodation.

Time of resource use (in years) included in the DLB model with a quadratic trend, and time since diagnosis included in the model with a square root transformation. Time of resource use (in years) included in the PDD model with a quadratic trend, and time since diagnosis included in the model with a linear function.

Average marginal effects from a generalised linear model with a gamma family and a log-link function.

Total costs of diagnosis and care increased, on average, around £2250 for each time a participant was diagnosed with a dementia-related condition before receiving a final diagnosis ( $p < 0.001$ ). Those participants who were residing in a care institution at the time of the study had, on average, £3300 higher total costs of care than those residing at home or with a family member ( $p = 0.002$ ). As time over which resource use data increased, total cost declined, although this effect was small and not always significant. In contrast, there was strong evidence of a positive relationship between time since diagnosis and total costs.

Participants with PDD had, on average, higher total costs of diagnosis and care of approximately £7650 than non-PDD participants (95% CI £3676 to £11,634;  $p < 0.001$ ) (see *Table 11*, bottom panel A). When disaggregating the PDD group according to the number of clinical features recorded before final diagnosis (five or fewer, or six or more), those participants with five or fewer clinical features before diagnosis ( $n = 24$ ) had, on average, £6800 higher costs than non-PDD patients (95% CI £3721 to £9919;  $p < 0.001$ ), and PDD participants with six or more clinical features had, on average, higher costs than non-PDD cases (of around £8700, 95% CI £3571 to £13,810;  $p = 0.001$ ) (see *Table 11*, bottom panel B).

In the PDD cohort, across all participant types, there was no evidence of an impact of the number of previous diagnoses on total costs, on residing in a care institution at the time of recruitment to the study or on time since diagnosis. Each additional year of recorded service use increased total costs by an average of £610 ( $p = 0.021$ – $0.022$ ). Finally, there was some evidence of a difference in cost between men and women, with women having lower costs (between £4400 and £5200) than men ( $p < 0.10$ ).

## Appendix 2 Review protocol for systematic reviews

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### PROSPERO: international prospective register of systematic reviews

#### *A systematic review of management strategies for Lewy body dementia (dementia with Lewy bodies and Parkinson's disease dementia)*

Chris Stinton, Claire Bamford, Victoria Cambridge, Louise Lafortune, Elijah Mak, James Mason, Ian McKeith, John-Paul Taylor, Alan Thomas, John O'Brien.

#### Citation

Stinton C, Bamford C, Cambridge V, Lafortune L, Mak E, Mason J, *et al.* A Systematic Review of Management Strategies for Lewy Body Dementia (Dementia with Lewy Bodies and Parkinson's Disease Dementia). PROSPERO 2014:CRD42014007180. URL: [www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=7180](http://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=7180).

#### Review question(s)

What are the benefits, harms and costs of management strategies for Lewy body dementia delivered to (1) patients and (2) carers?

How, when and where should management strategies for Lewy body dementia be implemented?

What views do patients and carers have of management strategies for Lewy body dementia?

#### Searches

We will search the following electronic bibliographic databases: AgeInfo, Allied and Complementary Medicine, Applied Social Sciences Index and Abstracts (ASSIA), BiblioMap, British Nursing Index (BNI), Campbell Collaboration, CenterWatch, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Abstracts of Reviews of Effects (DARE), Database of Systematic Reviews, Cochrane Dementia and Cognitive Improvement Group Specialised Register, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Database of Promoting Health Effectiveness Reviews (DoPHER), EMBASE, Educational Resources Information Centre (ERIC), Health Services Research Projects in Progress, Health Technology Assessment database, IFPMA Clinical Trials Portal, Lilacs: Latin American and Caribbean Health Sciences database, MEDLINE, *meta*Register of Controlled Trials, NHS Economic Evaluation Database (NHS EED), NHS Evidence, PROSPERO, PsycInfo, Scopus, Social Care Online, Trials Register of Promoting Health Interventions, UK Clinical Research Network Portfolio database, UMIN Clinical Trials Registry, WHO International Clinical Trials Registry Platform.

The search strategy will include terms relating to Lewy body dementia.

We will also search the grey literature (i.e. data reported outside peer-reviewed publications), reference lists of studies included in the review and seek expert input from within the extended review team.

There will be no restrictions on language or publication period.

Where the function is available, we will set up auto-alerts in databases to capture any new data arising after we have conducted our searches.

## **Types of study to be included**

There are no restrictions on the types of study designs for this review, but opinion papers will be excluded.

## **Condition or domain being studied**

Lewy body dementia (LBD) is the second most common cause of neurodegenerative dementia after Alzheimer's, accounting for around 15% of cases. It is characterised by psychiatric symptoms (e.g. hallucinations), impairments and fluctuations in cognition, and parkinsonism. LBD comprises two related disorders: dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD). DLB and PDD are distinguished on the basis of the temporal sequence of the onset of motor symptoms; a diagnosis of PDD is applied when motor symptoms occur at least one year before dementia and a diagnosis of DLB when dementia precedes motor symptoms or they arise within one year of one another.

## **Participants/population**

**Patients:** We will include study participants who have received a formal diagnosis of LBD on the basis of operationalised criteria or clinical judgement.

**Carers:** We will include participants who provide care (formal or informal) to people who have received a diagnosis of LBD.

## **Intervention(s), exposure(s)**

Any management strategy, or combination of strategies, that are intended to address the needs (medical, social, economic, etc.) of people who have LBD or their carers. These will include, but not be limited to, pharmacotherapy, psychotherapy, physiotherapy, education, speech and language therapy, support services.

## **Comparator(s)/control**

We will include studies with and without comparison/control groups.

## **Context**

We will place no restriction on the settings in which managements strategies are delivered.

## **Outcome(s)**

### ***Primary outcomes***

The primary outcome variables of interest are cognition and psychiatric and motor symptoms.



### **Secondary outcomes**

The secondary outcome variables of interest will include carer burden, costs, sleep disorder, autonomic symptoms, falls, activities of daily living, quality of life, hospitalisation, institutionalisation, mortality, acceptability of management strategies, and harms/side-effects (e.g. physical, psychological, financial).

## **Data extraction, (selection and coding)**

### **Selection of studies**

Titles and abstracts will be screened independently by two reviewers. Studies that are considered by either reviewer to be relevant (or potentially relevant) will be obtained in full. Full-text articles will be assessed by each of the reviewers for inclusion in the review. Any discrepancies between the studies selected for inclusion by the reviewers will be resolved through discussion, with the involvement of a third reviewer if necessary.

### **Data extraction**

Data from studies will be extracted into forms designed by the reviewers. We will collect information relating to eligibility, quality, participant details, study methods, management strategies employed, outcomes, results and author conclusions.

## **Risk of bias (quality) assessment**

The assessment of quality of studies will be conducted independently by two reviewers using the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project, 1998), the NICE Methodology Checklist: Qualitative Studies (NICE, 2009), and the Drummond Checklist for Economic Evaluations (Drummond & Jefferson, 1996). Any disagreement between the reviewers will be resolved through discussion and, if necessary, by consulting a third reviewer. Where reviewers identify significant lack of quality, these studies will be excluded.

## **Strategy for data synthesis**

Quantitative and qualitative data will be treated as separate streams in the initial phase of the review. Qualitative evidence will subsequently be used to aid in the interpretation of quantitative evidence.

We will distinguish between published and unpublished literature and assess the impact that publication status has on the results of the review using sensitivity analysis and/or descriptively.

### **Quantitative data**

Where studies of management strategies employ quantitative methods we will select appropriate data against a hierarchy of evidence (i.e. giving preference to RCTs over studies with cohort designs) and synthesise the results using meta-analysis. Where we identify significant heterogeneity, we will employ random-effect models. If there is no significant heterogeneity we will use fixed-effect models. Where we are not able to combine data from different studies, we will provide a descriptive summary of the results.

### **Qualitative data**

We anticipate that qualitative data will be synthesised thematically. Descriptive analysis will be conducted if this is not possible.

### **Ongoing studies**

Data from ongoing studies will not be available for quantitative or thematic analyses but we will provide a list of ongoing research to inform on the gaps in the evidence.

## **Analysis of subgroups or subsets**

If sufficient data are available, we will consider data for participants who have DLB and those who have PDD separately.

If sufficient data are available, we will conduct subgroup analyses based on dementia severity.

## **Dissemination plans**

The findings will be disseminated to NHS professionals, NHS commissioners, Social Care, and patient/public organisations. Scientific findings will be published in academic journals and presented at conferences.

## **Contact details for further information**

Chris Stinton

## **Organisational affiliation of the review**

University of Cambridge, University of Newcastle, University of Durham.

## **Review team**

Dr Chris Stinton, University of Cambridge.

Ms Claire Bamford, University of Newcastle.

Dr Victoria Cambridge, University of Cambridge.

Dr Louise Lafortune, University of Cambridge.

Mr Elijah Mak, University of Cambridge.

Professor James Mason, University of Durham.

Professor Ian McKeith, University of Newcastle.

Dr John-Paul Taylor, University of Newcastle.

Professor Alan Thomas, University of Newcastle.

Professor John O'Brien, University of Cambridge.

## **Anticipated or actual start date**

16 September 2013.

## Anticipated completion date

30 April 2014.

## Funding sources/sponsors

NIHR Programme Grants for Applied Research (Project ref. DTC-RP-PG0311-12001) – Improving the diagnosis and management of neurodegenerative dementia of Lewy body type in the NHS (DIAMOND-Lewy).

## Conflicts of interest

None known.

## Language

English.

## Country

England.

## Subject index terms status

Subject indexing assigned by CRD.

## Subject index terms

Humans; Lewy Body Disease.

## Any other information

This review is being conducted as part of a programme of research to improve the care of people who have LBD within routine NHS secondary care.

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Date of registration in PROSPERO: 16 January 2014

Date of publication of this revision: 16 January 2014

Stage of review at time of this submission	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No



## Appendix 3 Search strategies for systematic reviews

Work package 2 was underpinned by two major systematic reviews conducted by the Diamond-Lewy study group. The reviews focused on pharmacological<sup>21</sup> and non-pharmacological<sup>24</sup> management strategies in LBD. Details of the search strategy, study selection and data synthesis are described below.

### Pharmacological management strategies<sup>21</sup>

#### Search strategy

We searched the following electronic bibliographic databases: AgeInfo, Allied and Complementary Medicine Database (AMED), Applied Social Sciences Index and Abstracts (ASSIA), BiblioMap, British Nursing Index (BNI), The Campbell Collaboration Social, Psychological, Educational, and Criminological Trials Register, CenterWatch, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), Database of Systematic Reviews, Cochrane Dementia and Cognitive Improvement Group Specialised Register, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Database of Promoting Health Effectiveness Reviews (DoPHER), EMBASE™ (Elsevier, Amsterdam, the Netherlands) Educational Resources Information Center (ERIC), Health Services Research Projects in Progress, Health Technology Assessment database, International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Clinical Trials Portal, Latin American and Caribbean Health Sciences Literature (LILACS), MEDLINE, *meta*Register of Current Controlled Trials, NHS Economic Evaluation Database (NHS EED), NHS Evidence, PROSPERO, PsycInfo® (American Psychological Association, Washington, DC, USA), Scopus® (Elsevier), Social Care Online, Trials Register of Promoting Health Interventions, UK Clinical Research Network Portfolio database, University hospital Medical Information Network (UMIN) Clinical Trials Registry and the World Health Organization's International Clinical Trials Registry Platform. The search strategy included terms relating to LBD. We also searched grey literature (i.e. data reported outside peer-reviewed publications), reference lists of studies included in the review, and sought expert input from within the extended review team. There were no restrictions on language or publication period. Where the function was available, we set up auto-alerts in databases to capture any new data arising after we conducted our searches.

#### Study selection

Titles and abstracts were screened independently by four of the authors, with non-English-language papers screened by native speakers. Discrepancies were resolved through discussion between screeners. Potentially relevant studies were obtained in full and examined in detail by the first author against the following criteria: (1) participants had a diagnosis of DLB, PDD or LBD (or were the carers of patients with these diagnoses), (2) studies examined pharmacological strategies and (3) outcome measures and scores were specified. No restrictions were placed on study design, but opinion papers were excluded.

#### Data extraction

Data were extracted by two reviewers and recorded in an a Microsoft Excel® spreadsheet (Microsoft Corporation, Redmond, WA, USA). We collected information relating to participant demographic characteristics, selection criteria, study design, management strategies, outcome measures and scores, adverse events and withdrawals.

#### Data synthesis

Studies were grouped and analysed according to pharmacological strategy. For each strategy, studies of the highest level of evidence were included in the review. Classification of level of evidence was determined using guidelines from the Oxford Centre for Evidence-Based Medicine.<sup>23</sup>

### Methodological quality

Methodological quality was assessed by three of the authors using the QATQS,<sup>54</sup> which was developed to assess quality across study designs, aiding consistency and clarity of reporting. The QATQS examines selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs. Domains are rated as being of weak, moderate or strong quality, which feed into an overall rating of study quality. The reliability and validity of the QATQS have been demonstrated.<sup>6</sup>

### Statistical analysis

Meta-analysis was conducted using RevMan version 5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark), employing the inverse variance method. Heterogeneity was assessed using the chi-squared and  $I^2$ -statistics and considered significant with  $p$ -values  $< 0.10$  for chi-squared and  $> 40\%$  for  $I^2$ . We employed random-effects models when there was significant study heterogeneity and fixed-effect models when heterogeneity was not significant. Missing data were sought from study authors. For data that were not obtainable, values were estimated using methods outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*.<sup>55</sup> We estimated risk ratio with 95% CIs for dichotomous outcomes and weighted mean difference or standardised mean difference with 95% CIs for continuous outcomes. Descriptive summaries were provided when studies could not be combined.

## Non-pharmacological management strategies<sup>24</sup>

### Search strategy

The search identified studies through bibliographic databases, trial registers and the grey literature. Bibliographic databases and trial registers included the following: MEDLINE (1946–present), PreMEDLINE, PubMed, EMBASE (1974–present), Scopus, the Web of Science™ (Clarivate Analytics, Philadelphia, PA, USA) (1900–current), PsycInfo (1806–present), CINAHL (1981–present), Cochrane libraries [Cochrane Database of Systematic Reviews (2005–October 2016), CENTRAL (August 2016) and the Cochrane Methodology Register (third quarter of 2012), other evidence-based medicine databases [American College of Physicians® (ACP)] Journal Club (1991–September 2016), DARE (first quarter of 2015), Health Technology Assessment database (third quarter of 2016) and NHS EED (first quarter of 2015)]; AgeLine (1978–present); ALOIS (ALzheimer’s and cOgnitive Improvement Studies register); AMED (1985–present); Physiotherapy Evidence Database (PEDro) (1929–present); Social Work Abstracts (1968–present) and the National Association of Social Workers (NASW) clinical register (14th edition). The grey literature was searched using such resources as the System for Information on Grey Literature in Europe (SIGLE), National Technical Information Service (NTIS) database and PsycExtra® (American Psychological Association) (1908–present).

The search strategy used only population and intervention terms to maximise the likelihood of identifying relevant studies. Comparator and outcome terms were not used. The population was people with LBD or their carers and this was identified using the search terms: [(Lewy OR Park\*) and Dementia].

Interventions were any non-pharmacological treatment and identified using a wide range of terms: (activit\*, acupuncture, alternative, animal, aromatherapy, art therapy, assisted, balance, behav\*, bicycle, calisthenics, carer intervention, caregiver intervention, CBT, Chi gong, cognit\*, cognitive behavioral therapy, cognitive behavioural therapy, counsel\*, creative arts, dance, dancing, diet, direct current stimulation, drama, ECT, educat\*, electroconvulsive therapy, enhanc\*, environmental intervention, environmental modification, exercise, flexibility, humor therapy, humour therapy, hydrotherapy, intervention\*, leisure, light therapy, management, martial arts, massage, meditation, Montessori, multisensory, music, non-pharm\*, nonpharm\*, nutrition, occupational therapy, pet therapy, physical activity, physical therapy, physiotherapy, pilates, psychoeducation, psychol\*, psychosocial, psychotherapy, Qi gong, reality orientation, recreation\*, reminiscence, resistance training, run\*, sensory, simulated presence, stimulation, Snoezelen, support\*, support group\*, swim\*, tai chi, therap\*, therapeutic activity, TMS, training, training carers, training caregivers, transcranial magnetic stimulation, treatment\*, validation, weight training, yoga). Searches were conducted on 30 October 2016.

In addition to bibliographic database searches, the reference lists of papers included in the review and previous systematic reviews on both LBD and non-pharmacological interventions were checked for relevant papers. Advice was also sought from experts in the field.

### **Study selection**

Two reviewers independently assessed search results for inclusion by title and abstract. All articles deemed relevant by either reviewer were obtained in full. Both reviewers then independently evaluated full-text articles for inclusion. Any disagreements were resolved through discussion or, if necessary, with a third reviewer.

### **Data extraction**

Two reviewers independently extracted relevant data from publications using a standardised form. This included participant details (e.g. demographics, number, recruitment, clinical context, dementia severity), intervention type, study design, measures and results. Qualitative data were also collated.

The primary outcomes were measures of cognition, function, neuropsychiatric symptoms and motor symptoms. The secondary outcomes were measures of any other clinically relevant outcomes, such as quality of life, carer burden, financial costs, other symptoms (e.g. sleep or autonomic disturbances) and objective end points (e.g. falls, hospitalisation, institutionalisation, mortality). Secondary outcomes also included the perceived acceptability of treatments, reported side effects and drop-out rates (a measure of treatment acceptability).

### **Quality assessment**

Two reviewers independently assessed study quality and risk of bias using standardised tools. These included the Effective Public Health Practice Project QATQS<sup>54</sup> and the NICE methodology checklist for qualitative studies.<sup>56</sup> Any disagreements were resolved through discussion.





## Appendix 4 List of Delphi panel contributors

Contributor	Location
Dag Aarsland	King's College London, London, UK
Neil Archibald	South Tees Hospitals NHS Foundation Trust, Middlesbrough, UK
Louise Allan	University of Exeter Medical School, Exeter, UK
Clive Ballard	University of Exeter Medical School, Exeter, UK
Bob Barber	Newcastle University, Newcastle upon Tyne, UK
Roger Barker	University of Cambridge, Cambridge, UK
Brad Boeve	Mayo Clinic, Rochester, MN, USA
Daniel Collerton	Newcastle University, Newcastle upon Tyne, UK
Tom Dening	University of Nottingham, Nottingham, UK
Murat Emre	Istanbul University, Istanbul, Turkey
Duncan Forsyth	Cambridge University Hospitals Foundation Trust, Cambridge, UK
John Hindle	Bangor University, Bangor, UK
Clive Holmes	University of Southampton, Southampton, UK
Clare Lawton	Cambridgeshire and Peterborough NHS Foundation Trust (retired), Cambridge, UK
Ian Maidment	Aston University, Birmingham, UK
Eneida Mioshi	University of Cambridge, Cambridge, UK
Sean Page	Bangor University, Bangor, UK
Jill Rasmussen	The Lewy Body Society, London, UK
Sharon Reading	Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
Louise Robinson	Newcastle University, Newcastle upon Tyne, UK
Lynn Rochester	Newcastle University, Newcastle upon Tyne, UK
Ben Underwood	Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK



# Appendix 5 Overview of management guideline

## Management of LBD

- Identify key problems under domain headings such as cognition; gait, balance and movement; hallucinations; fluctuations; behaviour and mood; sleep, and autonomic system dysfunction.
- Establish which problems have high priority for treatment.
- Discuss benefits and risks of treatment.
- Be aware that symptom response is variable and that benefits in one might be at the cost of worsening of others
- Individual treatments may have global benefits e.g. cholinesterase inhibitors.

### COGNITIVE

**Non-pharmacological**

- cognitive stimulation, use of memory aids, increased social interaction and stimulation, and exercise.

**Pharmacological**

- Cholinesterase inhibitors** first-line.
- Memantine** second line.

### AUTONOMIC

**Orthostatic hypotension**

- non-pharmacological** management e.g. compression stockings, fluid/salt intake, stand slowly etc.
- pharmacological e.g. fludrocortisone, midodrine
- ✗ Reduce/remove exacerbating drugs** e.g. antihypertensives.

**Constipation**

- Stool softeners.
- mild laxatives/suppositories.

**Urinary dysfunction**

- Non-pharmacological** first-line e.g. pads, sheath catheter etc.
- ✗** Avoid centrally acting anticholinergics.

**Gastroparesis**

- ✗** Avoid using metoclopramide.
- ⚠ Domperidone can be used but is **cardiotoxic**.

**Sexual dysfunction**

- ⚠ **Phosphodiesterase-5 inhibitors** may be considered with caution in men

**Sialorrhoea**

- ✗** Anticholinergics should not generally be used
- Botulinum toxin** injections to salivary glands is an effective treatment

### NEUROPSYCHIATRIC

**Psychosis**

- May respond to **cholinesterase inhibitors** especially visual hallucinations.
- ⚠ Be cautious in the use of antipsychotics.

**Mood**

- Use of **social interventions** may enhance mood.
- ⚠ No evidence for antidepressants in LBD to treat mood therefore use pragmatically and avoid agents with significant anti-cholinergic side effects.

### SLEEP

**Insomnia**

- Give advice on **sleep hygiene**.
- Review all medications** that could be affecting sleep.
- Melatonin** may help some.
- ⚠ **Z-drugs** may have a role but use cautiously.

**REM-sleep behaviour disorder**

- Consider **non-pharmacological** as first-line and only treat if troublesome.
- ⚠ **Clonazepam** may help although significant side effects
- Melatonin** may be alternative.

**Motor related sleep disturbances**

- May be improved with long-acting **levodopa**.

### MOTOR

- Preferred pharmacological treatment of parkinsonism in LBD is **levodopa monotherapy**.
- Use **minimal dose** needed for benefit.
- ✗ Withdraw in order, one at a time:** anticholinergic drugs, amantadine, selegiline, dopamine agonists and catechol-O-methyltransferase inhibitors.

- Remember that LBD patients may exhibit exaggerated responses to medications.
- Severe antipsychotic sensitivity can occur in up to 50% of patients therefore use antipsychotic agents with a high degree of caution.
- Review the need for common drugs which can affect brain function and/or cause sedation and falls.
- Minimise anticholinergic burden as this may worsen cognition and behaviour, and counteract cholinesterase inhibitors.



# Appendix 6 Health economic analysis for work package 4

## Introduction

The main objective of the economic component of the pilot cluster RCT was to rehearse the methods for a definitive economic evaluation of the new management toolkit for DLB and PDD compared with usual care. For a definitive study, a within-trial economic evaluation is anticipated. Such a study would seek to estimate costs and outcomes for each trial participant over the duration of the trial follow-up. These data would then be used to estimate cost-effectiveness. As is typical for pilot trials, because of the modest sample size available for each randomised patient group, a full economic evaluation was not conducted. The small sample size would not provide reliable conclusions on the cost-effectiveness of the management toolkit. Therefore, the focus of the economic component deviated slightly from protocol and the analysis aimed rather to provide a descriptive analysis of the costs and outcomes. Data on costs and outcomes for each patient sample (DLB and PDD) were examined separately, as it was expected that different diagnoses would lead to a differential use of services and outcomes. Suggestions for reducing the number of missing data will be made and methods that would be employed in a full evaluation of a definitive trial will also be discussed.

## Methods

### Costs

Costs were examined from the perspectives of the NHS and Personal Social Services, which includes costs of medications and health and social care use. Costs incurred by other sectors (e.g. local authorities) were not included. Data on use of health and social care were captured by using a bespoke service utilisation questionnaire that was developed based on questions included in the Client Service Receipt Inventory (CSRI).<sup>57</sup> Data were collected at baseline and at the 3- and 6-month follow-ups. 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 3 months. All costs are reported in GBP (£) for the financial year 2017/18. As the study follow-up was < 12 months, no discounting was performed.

### Health care and social service resource use

Unit costs were estimated using the *National Schedule of Reference Costs 2017/18*<sup>15</sup> and *Unit Costs of Health and Social Care 2018*.<sup>58</sup> Resources from the voluntary sector (e.g. dementia cafes) and local authority-run services (e.g. local authority day activity services) were not included in the NHS and Personal Social Services perspective; however, these services would be included in a broader societal perspective.

Resource use costs per patient at each time point (baseline and at the 3- and 6-month follow-ups) were estimated by multiplying total reported use of each service by each relevant unit cost. A total resource use cost for each participant was calculated by summing all individual service use costs for the individual. Mean and median resource use costs were then estimated by trial arm for each patient group.

### Medication costs

Data were collected at each visit (baseline and at the 3- and 6-month follow-ups) on all medications taken by participants for the previous 3 months. Data on dose, frequency and duration taken were collected for each medication. Unit costs for medications were obtained from the *British National Formulary (BNF)*.<sup>59</sup>

Over-the-counter supplements (e.g. cod liver oil) were excluded from the analysis, as these were not assumed to be provided as part of NHS care and the costs would be considered 'out-of-pocket' costs for the participant. Medications that were insufficiently specific to obtain costs for (e.g. general antibiotics or steroids) were also excluded, as costs vary depending on the precise medication prescribed. Where data were missing on either dosage or frequency, recommended dosage was taken from the BNF where possible. Where this was not possible, the use of that medication was excluded, as no assumptions could be made on the average use of those medications. Therefore, where data were missing on dose, frequency or duration, and data could not be estimated using the BNF, costs could not be calculated.

### Intervention delivery costs

The delivery of the intervention incurred costs from the production of the management toolkit and training staff to use it. The cost of producing the toolkit included materials and staff time. Unit costs for each element of production were obtained from invoices provided by the trial support team and service costs listed on the Newcastle University print services website.<sup>60</sup> The service costs stated by print services were assumed to include labour time.

The cost of training staff to use the toolkit was estimated from data collected on staff attending training sessions and approximate duration of the sessions, in addition to staff time required to develop training sessions. Unit costs for staff were obtained from publicly available pay scales for university staff and the *Unit Costs of Health and Social Care 2018*.<sup>58</sup>

### Total costs

Costs from each area of resource use (medications and health and social care) were combined at each time point. For the cumulative totals at the 3- and 6-month follow-ups, intervention delivery costs are also added to reflect the additional cost of receiving the intervention. In a definitive trial, cost differences between trial arms would be estimated using regression analysis, which would estimate total follow-up costs at 6 months, adjusting for baseline costs (which may differ between trial arms despite randomisation). To avoid double counting in the regression analysis, delivery costs would be included only once in the total follow-up costs, which would combine cost data collected at both the 3- and 6-month time points.

### Patient and carer private costs

Costs incurred by patients and by carers who accompanied patients to appointments were also measured using data collected from a time and travel questionnaire combined with data on use of resources. The time and travel questionnaire was administered at the 6-month follow-up and elicited information on patients' and carers' most recent inpatient attendance, outpatient appointment, GP appointment and community dementia specialist appointment (i.e. community neurologist, OAP or geriatrician). Information on the mode of transport used to travel to the appointment, the time taken to travel and the time spent at the appointment (or days spent in inpatient care) was elicited. Where public transport or taxis were used to travel to an appointment, the cost of travel one-way was recorded. Where a private car was used, the cost of travel was estimated from the distance travelled using a cost of £0.45 per mile taken from the *2018 TAG Data Book*<sup>61</sup> and any additional parking charges. If both patient and carer travelled by taxi or private car, it was assumed that this journey was taken together and, therefore, the cost of travel was calculated for only the patient to avoid double counting.

The cost of time spent attending an appointment for both the patient and carer was calculated based on activity rates for various activities published by the ONS, according to the activity that either the patient or carer reported they would have been doing at the time of attending the appointment. Paid work, child care, caring for a relative or friend and voluntary work was valued as £13.88, which is the average hourly wage, according to the ONS.<sup>37</sup> Housework and leisure activities were valued at £10.10 an hour. Time spent in unemployment, retirement or in education was valued as £6.04 an hour.

The mean unit costs of time and travel for both patients and carers were calculated and multiplied by the number of attendances or appointments reported at each time period.

### Quality of life

Patients' generic quality of life was derived from the responses to the EQ-5D-5L questionnaire, completed at baseline and at the 3- and 6-month follow-ups. The EQ-5D-5L asks about a patient's general quality of life over five dimensions (i.e. mobility, pain, usual activities, anxiety and depression, and self-care) and five levels. Responses to the EQ-5D-5L questionnaire were transformed into health state utilities using tariffs derived from the UK population. Values for the EQ-5D-5L were recently derived by Devlin *et al.*;<sup>62</sup> however, there is some debate over the accuracy of values in this new value set. Therefore, NICE<sup>63</sup> recommends applying index values from a 'crosswalk' between the original EuroQol-5 Dimensions, the three-level version and the new five-level version, until the concerns over the new value set have been addressed. Therefore, the 'crosswalk' value set was used in this study to derive utility values for each participant. The crosswalk index value calculator, developed by EuroQoL Foundation<sup>39</sup> and based on the index values estimated by van Hout *et al.*,<sup>64</sup> was used to estimate the health state utilities for each participant.

The health state utilities were then used to estimate generic QALYs for each participant using the change from baseline approach.<sup>65</sup> This approach was chosen because the difference in baseline utilities was very small between trial arms.<sup>66</sup> In a full evaluation, QALYs would be calculated using the area under the curve approach<sup>67</sup> and QALYs at the 6-month follow-up would be adjusted using regression analysis, including baseline utilities as a covariate. As unadjusted values are being reported here, the change from baseline approach was used because it accounts for differences at baseline, which the area under the curve approach does not, in the absence of regression analysis.

## Results

### Costs

#### Missing cost data

For the data from the service utilisation questionnaire, substantially more participants for the PDD sample were missing all service use data in the intervention arm than in the control arm at the 6-month follow-up (*Table 12*). It is possible that participants were missing because they were unable to complete follow-up visits because of deterioration in their health, which would imply that the intervention arm costs are lower than they should be. Conversely, there are more participants missing all service use data in the control arm in the DLB patient sample. Therefore, higher costs would be expected in the control arm than are observed.

A similar pattern of missing data was observed when examining data collected for each individual component of service utilisation across all visits. In the PDD patient sample, 11% of data across all areas of service use was missing in the intervention arm compared with 6% in the control arm. For the DLB patient sample, 7% of data across all areas of service use was missing in the intervention arm compared with 16% in the control arm. The majority of these missing data can be attributed to participants missing at each visit.

The pattern of missing data on all medication use is almost identical to that identified for health and social care resource use (*Table 13*). Data missing on dose, frequency or duration (therefore preventing the calculation of a cost for the medication reported) were also examined. For participants with a diagnosis of DLB, 7% of data were missing in the intervention group and 9% of data in the control group. For the PDD sample, the corresponding proportions were 3% and 4%, respectively.

TABLE 12 Mean and median total health and social care resource use costs at each time point by trial arm

Time point	DLB				PDD			
	N	Missing, n <sup>a</sup> (%)	Mean (SD) (£)	Median (IQR) (£)	N	Missing, n <sup>a</sup> (%)	Mean (SD) (£)	Median (IQR) (£)
Baseline								
Control	33	0 (0)	1454 (2118)	561 (790)	18	1 (5)	685 (812)	410 (385)
Intervention	44	0 (0)	2369 (5007)	648 (1055)	31	0 (0)	1312 (2697)	359 (631)
3 months								
Control	25	8 (24)	2852 (5759)	535 (1134)	18	1 (5)	905 (1378)	345 (1026)
Intervention	40	4 (9)	1393 (2745)	411 (845)	28	3 (10)	2148 (3917)	502 (1080)
6 months								
Control	26	7 (21)	2091 (4738)	520 (1585)	18	1 (5)	1089 (1637)	322 (499)
Intervention	40	4 (9)	1070 (1472)	519 (951)	24	7 (23)	783 (1119)	369 (603)

IQR, interquartile range.

a Participants with data related to all services missing at visit.

TABLE 13 Mean and median medication costs by trial arm at each time point

Time point	DLB				PDD			
	N	Missing, n <sup>a</sup> (%)	Mean (SD) (£)	Median (IQR) (£)	N	Missing, n <sup>a</sup> (%)	Mean (SD) (£)	Median (IQR) (£)
Baseline								
Control	33	0 (0)	225 (268)	141 (230)	19	0 (0)	195 (182)	126 (190)
Intervention	43	1 (2)	218 (220)	156 (197)	31	0 (0)	231 (182)	180 (269)
3 months								
Control	26	7 (21)	222 (200)	161 (239)	18	1 (5)	210 (193)	153 (167)
Intervention	39	5 (11)	264 (247)	225 (276)	28	3 (10)	269 (195)	248 (282)
6 months								
Control	27	6 (18)	245 (216)	166 (253)	18	1 (5)	206 (192)	156 (171)
Intervention	40	4 (9)	272 (258)	223 (263)	24	7 (23)	331 (331)	264 (329)

IQR, interquartile range.

a Participants with all medication data missing at visit.

### Health and social care resource use

Table 12 suggests a difference in mean health and social care resource use costs between the trial arms at baseline in both patient groups, although the small sample size cautions against any conclusions being drawn. The mean costs in the intervention arm for the DLB sample decreased at each follow-up visit, compared with costs calculated at baseline, whereas costs increased for the control arm. For the PDD sample, intervention arm costs also decreased at the 6-month follow-up compared with costs incurred between baseline and 3 months, whereas control group costs increased at each follow-up visit. The SDs for both randomised arms, both groups and at all time periods are larger than the mean values, suggesting substantial imprecision. The median values are considerably smaller than the mean values, which suggests that there is a substantial right skew to the data, with some participants incurring very much higher costs.



### Medication costs

Table 13 shows little variation in both mean and median medication costs between baseline and the 6-month follow-up for both patient samples. There is a trend towards increasing medication costs for both arms over the 6-month follow-up period. Given the degenerative nature of both dementia and PD, this is unsurprising.

A greater increase in mean medication costs is observed for the intervention arms of both patient samples than in the control arms. However, the increase is greater for the PDD sample than for the DLB sample (see Table 13). Alternative rationales for this could be advanced. For example, the data may indicate that the management toolkit encouraged increased medication prescribing. An alternative explanation is that the larger proportion of missing observations in the intervention arm of PDD patients was a result of these participants being less well and, therefore, less able to complete follow-up visits. However, the small sample size prevents any robust conclusions being drawn.

### Intervention delivery costs

Table 14 shows the breakdown of the resource costs associated with the intervention delivery. The total delivery cost was divided by the number of participants in the intervention arm in both patient groups combined ( $n = 75$ ) to estimate a mean delivery cost per participant receiving the intervention. Mean intervention delivery cost was estimated at £76.32 per participant in the intervention arms. Participants in the control arms did not receive the intervention and, therefore, delivery costs are £0 for the control groups.

### Total costs

Table 15 shows the total costs for each trial arm at all time points. Total costs include health and social service use, medication costs and intervention delivery costs (for the intervention arms at the 3- and 6-month follow-ups). The health and social care use costs make up the largest proportion of the total cost. In both patient samples, there is an overall increase in total costs between baseline and the 6-month follow-up in the control arms, whereas there is an overall decrease in total costs in the DLB sample intervention arm. In the PDD sample, an increase in costs occurs between baseline and 3 months; however, a decrease in costs occurs between the 3- and 6-month follow-ups, and the mean 6-month cost is lower than the baseline cost for the control arm.

The median costs imply a right skew to the total cost data, indicating that a small number of participants incurred much higher costs than the remainder of the sample. The SDs are larger than the mean values for each reported cost, which demonstrates imprecision. The imprecision is probably caused by the small sample size. For this reason, these total costs should be considered only illustrative.

TABLE 14 Breakdown of intervention delivery costs

Resource	Cost (£)
Total staff preparation time	133
Total staff training time	2338
Total materials	3252
Total	5724
Total per person with dementia	76.32

**TABLE 15** Mean and median total costs, including health service use, medications and delivery cost (intervention arm only) by trial arm at each time point

Time point	DLB			PDD				
	N	Missing, n <sup>a</sup> (%)	Mean (SD) (£)	Median (IQR) (£)	N	Missing, n <sup>a</sup> (%)	Mean (SD) (£)	Median (IQR) (£)
Baseline								
Control	33	0 (0)	1679 (2154)	797 (1237)	19	0 (0)	844 (793)	593 (677)
Intervention	44	0 (0)	2582 (5076)	806 (1214)	31	0 (0)	1543 (2769)	572 (913)
3 months								
Control	26	7 (21)	2964 (5681)	797 (1203)	18	1 (5)	1114 (1385)	591 (928)
Intervention	40	4 (9)	1726 (2807)	783 (1040)	28	3 (10)	2493 (3961)	770 (1314)
6 months								
Control	27	6 (18)	2259 (4763)	574 (1645)	18	1 (5)	1295 (1607)	600 (653)
Intervention	40	4 (9)	1419 (1506)	947 (1207)	24	7 (23)	1191 (1196)	730 (917)

IQR, interquartile range.

a Participants with all cost data missing at visit.

#### Notes

Participants assumed missing at follow-up if cost data missing. Intervention delivery costs not included for participants who are considered missing in intervention arm.

## Private costs

Table 16 shows the mean combined travel costs incurred by patients from travelling to all inpatient, outpatient, GP and community dementia specialist appointments for each time point. Table 16 also shows the mean combined time costs for the time spent in attendance at each of the four aforementioned areas of health-care services. There is an overall decrease in mean travel costs between baseline and the 6-month follow-up for both intervention and control groups, with the exception of the control group of the PDD sample whose mean travel costs increased at the 6-month follow-up. For both patient samples, there is an observed increase in mean time costs between baseline and the 6-month follow-up for the control group, yet a decrease in mean time costs for the intervention group. However, the median time costs imply a strong right-skew, which indicates that a small number of patients incurred much higher costs than the remainder of the sample.

Table 17 shows the mean and median travel and time costs incurred by carers for attending appointments with patients, including the time cost of visiting patients who were hospital inpatients. The mean travel costs are lower for carers (see Table 17) than for patients (see Table 16), largely because of the assumption that patients incur the cost of travel if a carer has accompanied a patient in a taxi or private car.

There is a slight decrease in mean travel costs for the carers of both patient samples in both trial arms between baseline and the 6-month follow-up, with the exception of carers of PDD patients in the control arm whose mean travel costs increased between baseline and the 6-month follow-up. The same pattern is observed for the mean time costs, which decrease between baseline and the 6-month follow-up for carers of patients in both trial arms and patient samples, except for the control group of PDD patients.

The mean travel and time costs for carers of DLB patients are typically slightly higher for carers of patients in the intervention group than for carers of patients in control group. The opposite is observed for carers of PDD patients, as both mean time and travel costs are typically higher for carers of patients in the control group than for carers of patients in the intervention group.

**TABLE 16** Mean and median total travel and time costs for patients attending inpatient services, outpatient appointments, GP appointments and dementia specialist appointments, combined, based on data from a time and travel questionnaire combined with data on resource use

Time point	DLB				PDD			
	Travel cost <sup>a</sup>		Time cost <sup>b</sup>		Travel cost <sup>a</sup>		Time cost <sup>b</sup>	
	Mean (SD) (£)	Median (IQR) (£)	Mean (SD) (£)	Median (IQR) (£)	Mean (SD) (£)	Median (IQR) (£)	Mean (SD) (£)	Median (IQR) (£)
Baseline								
Control	33 (42)	27 (43)	255 (671)	22 (30)	36 (58)	25 (29)	26 (40)	18 (20)
Intervention	44 (40)	33 (40)	378 (729)	33 (73)	32 (39)	17 (38)	121 (383)	16 (30)
3 months								
Control	21 (16)	20 (20)	260 (573)	16 (24)	18 (21)	12 (16)	13 (17)	8 (11)
Intervention	29 (35)	17 (39)	174 (468)	12 (38)	19 (19)	16 (25)	342 (764)	14 (35)
6 months								
Control	27 (36)	17 (16)	314 (757)	14 (25)	53 (138)	19 (28)	121 (370)	14 (19)
Intervention	30 (33)	19 (33)	213 (516)	15 (38)	21 (25)	16 (23)	79 (313)	12 (17)

IQR, interquartile range.

a Travel cost includes the cost of travel from either the fare of travel (if public transport or taxi) or cost of mileage and parking if in a private car, in addition to the time cost from the length of time spent travelling.

b Time cost refers to the cost of the length of time spent attending each appointment based on the ONS activity rates for the activity patients reported that they would have been engaged in at the time of each appointment.

**TABLE 17** Mean and median total travel and time costs for carers accompanying patients to inpatient services, outpatient appointments, GP appointments and dementia specialist appointments, combined, based on data from a time and travel questionnaire combined with data on resource use

Time point	Carers of DLB patients				Carers of PDD patients			
	Travel cost <sup>a</sup>		Time cost <sup>b</sup>		Travel cost <sup>a</sup>		Time cost <sup>b</sup>	
	Mean (SD) (£)	Median (IQR) (£)	Mean (SD) (£)	Median (IQR) (£)	Mean (SD) (£)	Median (IQR) (£)	Mean (SD) (£)	Median (IQR) (£)
Baseline								
Control	9 (13)	6 (13)	21 (24)	15 (26)	10 (18)	5 (8)	17 (31)	8 (15)
Intervention	13 (12)	9 (12)	28 (26)	23 (37)	9 (11)	4 (11)	16 (22)	9 (19)
3 months								
Control	6 (5)	5 (7)	15 (15)	9 (16)	5 (8)	2 (5)	9 (13)	3 (9)
Intervention	9 (11)	4 (11)	18 (21)	7 (27)	5 (6)	3 (7)	16 (20)	5 (25)
6 months								
Control	8 (11)	4 (7)	20 (28)	9 (18)	15 (40)	6 (6)	28 (71)	9 (11)
Intervention	9 (11)	5 (9)	20 (22)	9 (26)	6 (8)	4 (6)	11 (15)	7 (12)

IQR, interquartile range.

a Travel cost includes the cost of travel from the fare of public transport in addition to the time cost from the length of time spent travelling.

b Time cost refers to the cost of the length of time spent accompanying a patient at each appointment (including time spent visiting patients during inpatient stays) based on the ONS activity rates for the activity carers reported that they would have been engaged in at the time of each appointment.

## Quality of life

### Missing EQ-5D-5L data

The DLB group had a larger proportion of missing observations for the EQ-5D-5L utilities at the 6-month follow-up than the PDD group, although the difference was not large (4 percentage points). Both groups had between 30% and 35% data missing at the final follow-up (Table 18).

### Health state utilities and quality-adjusted life-years

Using the change from baseline method, the difference in QALYs between baseline and the 6-month follow-up was calculated for each arm. Table 19 shows the mean and median utility score at each time point and the QALY change from baseline at the 6-month follow-up for each patient group. As the sample size was small, these values should be considered only illustrative. Overall, changes in QALYs in each trial arm for each sample were small to modest, but with consistent decreases in mean and median scores for those in the DLB sample. A similar pattern was not evident for the PDD sample. However, with such small samples, data are insufficient to draw conclusions.

TABLE 18 Proportion of sample missing self-reported EQ-5D-5L utility at each time point

Sample	Baseline				3-month follow-up				6-month follow-up			
	DLB		PDD		DLB		PDD		DLB		PDD	
	n	%	n	%	n	%	n	%	n	%	n	%
Control	3	9	2	11	11	33	4	21	12	36	4	21
Intervention	3	7	4	13	8	18	5	16	11	25	9	29
Total	6	8	6	12	19	25	9	18	23	30	13	26

TABLE 19 Mean and median QALY change from baseline at the 6-month follow-up

Utility score	DLB			PDD		
	n	Mean (SD)	Median (IQR)	n	Mean (SD)	Median (IQR)
Health state utilities						
Control: baseline	30	0.681 (0.267)	0.763 (0.295)	17	0.640 (0.283)	0.739 (0.298)
Intervention: baseline	41	0.658 (0.214)	0.707 (0.211)	27	0.678 (0.219)	0.746 (0.217)
Control: 3 months	22	0.658 (0.190)	0.699 (0.195)	15	0.743 (0.184)	0.742 (0.19)
Intervention: 3 months	36	0.612 (0.278)	0.657 (0.295)	26	0.694 (0.159)	0.735 (0.223)
Control: 6 months	21	0.592 (0.291)	0.619 (0.391)	15	0.696 (0.180)	0.720 (0.227)
Intervention: 6 months	33	0.683 (0.206)	0.714 (0.246)	22	0.613 (0.228)	0.663 (0.185)
QALYs						
Control	18	-0.029 (0.068)	-0.015 (0.065)	15	0.007 (0.060)	0.000 (0.037)
Intervention	30	-0.009 (0.039)	-0.001 (0.040)	22	-0.001 (0.057)	-0.001 (0.023)

IQR, interquartile range.

## Discussion

Robust conclusions cannot be drawn on the impact of the intervention on costs and quality of life, given the small sample size of the trial. In a definitive trial, the impact on cost would be more reliably assessed in conjunction with the impact on quality of life. The impact of the intervention on quality of life, indicated by this pilot study, is small and appears to differ between patient samples. As with costs, the impact of the intervention on QALYs cannot be reliably assessed from this sample.

Given the disease area being studied in this trial, a substantial number of missing data might be expected because of difficulties in collecting data from people with dementia. Within a definitive trial, precision of results could be improved through the use of statistical methods to replace missing data with appropriate values where some data collection was unsuccessful. Numerous methods exist for handling missing data. The choice between these methods depends on the nature and pattern of missing data.

A substantial number of quality-of-life data were missing from responses to the EQ-5D-5L. If participants are unable to complete the questionnaire themselves, as a sensitivity analysis, proxy utilities from EQ-5D-5L responses completed by a carer on behalf of the patient participant could be used. Statistical tests for correlation between proxy and self-reported EQ-5D-5L can be conducted to assess whether or not the proxy values are sufficiently similar to the self-reported values (where both are available). If the tests indicate that proxy and self-report EQ-5D-5L utilities are not strongly correlated, using proxy values would introduce bias to the outcome. In a base-case analysis, imputation may be more reliable if there is sufficient data for this to be a reliable option.

### Lessons learned

During the analysis of this pilot study data, lessons have been learned on how to approach a full economic evaluation of a definitive trial. These are briefly discussed below.

In a definitive trial, it would be important to include all costs associated with the health and social service use, including voluntary and local authority sectors, as they have an opportunity cost that could be relevant to NHS costs. For instance, if voluntary care services were discontinued, it would be likely that NHS resource use may increase, as NHS-provided services absorb the voluntary service users, or the burden would be placed on informal carers. This would have an impact on informal carers' time available for work or leisure and may affect their own health, resulting in further NHS resource use. However, costs associated with voluntary sector and some community resources (e.g. educational classes) are not readily available. Therefore, these would have to be estimated via direct contact with services for a definitive trial.

In addition, informal care from relatives and friends is common for people with dementia and, therefore, it would be beneficial to assess the impact of the intervention on carers if a broader societal perspective is to be considered for the definitive analysis. If the intervention reduces or increases the need for informal care then this has a societal impact in terms of productivity (i.e. if the carer is still an active member of the workforce) and an opportunity cost in terms of care being provided informally, as opposed to via the formal care sector. Therefore, the costs (both time and financial) associated with care responsibilities and carer quality of life would be analysed in a definitive analysis.

The difficulty in conducting reliable analysis imposed by a small initial sample and compounded by missing data indicates that a much larger sample would be needed in a definitive trial. The number of total missing data identified in this pilot analysis could be used to estimate a sample size that would allow for a sufficiently large sample, given the expected numbers of participant drop-off across follow-up visits.



## Appendix 7 Analysis of clinician questionnaires from work package 5

During the programme, three questionnaires were sent to professionals working in participating services to supplement the qualitative work. The aim of the first questionnaire (T0, distributed during WP5.1) was to explore self-reported confidence in diagnosing and managing conditions typically seen in memory and/or movement disorder services. The second questionnaire (T1, distributed towards the start of the pilot trial) aimed to collect baseline data on assessment practices and views of the assessment toolkits (and management toolkit in intervention services). The final questionnaire (T2, distributed after the end of the pilot trial) aimed to explore views on the toolkits, assessment practices, implementation and sustainability of the toolkits. A set of questions on confidence in managing common LBD symptoms was repeated in all three questionnaires. Details of potential explanatory variables (e.g. role, region and experience/training) were also collected. We hoped that using questionnaires would enable us to achieve greater coverage of respondents than was possible through interviews and observation.

### Data collection

In January 2015, the first questionnaire was sent by post to staff working in most participating services, along with a prepaid envelope. One reminder was sent, including a copy of the questionnaire and a prepaid envelope, after approximately 3 weeks. As one NHS trust was unwilling to release staff details, we had to rely on local contacts to distribute the questionnaires. Although some attempts were made to send reminders within this trust, the process was hampered by a lack of information on individual participants and limited local resources to support distribution of the questionnaires.

The intention was to distribute the second questionnaire (T1) shortly after completion of all site initiation visits for the pilot trial. As there was insufficient capacity within the team to send out questionnaires to each site as approvals were obtained, distribution was delayed until all approvals were in place. Unfortunately, approvals for the qualitative work were not necessarily processed in parallel with approval for the pilot trial and obtaining approval from one trust was a protracted process. As a result, by the time T1 questionnaires were sent out (in January 2017), some sites had been using the toolkits for some time. The final questionnaire (T2) was sent out after the end of the pilot trial, as planned (in October 2018). The T1 and T2 questionnaires were administered using SurveyMonkey® (Palo Alto, CA, USA), with one electronic and one paper reminder.

Questionnaires completed on paper were entered into SPSS version 16 (IBM, New York, NY, USA). Questionnaires completed electronically were transferred to SPSS for analysis. All questionnaires were identified by a unique identifier.

### Analysis

The questionnaires were analysed using simple descriptive statistics. Analysis of variance was used to explore the impact of potential explanatory variables. The reasons for selecting potential plausible explanatory variables are summarised in *Table 20*. It is evident that these potential explanatory variables are not independent, with region and role, in particular, being confounded.

There were difficulties in examining changes over time, as, although the respondents to the three questionnaires overlapped, they were not identical and only seven individuals completed questionnaires at all three time points. For the analysis of confidence in symptom management

TABLE 20 Rationale for identifying potential explanatory variables

Explanatory variable	Rationale
Specialty	The marked differences in organisation of movement disorder and memory services suggested that staff views might systematically differ. Furthermore, the introduction of the assessment toolkits had different implications for the services, which might influence views of their acceptability and feasibility
Region	Newcastle upon Tyne is a leading centre in LBD research and doctors who have trained in the region are likely to have experienced greater exposure to LBD. There are also marked regional differences in the organisation of memory services, with nurse-led models predominating in East Anglia and a higher proportion of consultant-led services in the North East
Role	Knowledge of and training in LBD are likely to differ systematically between doctors and other allied health professionals
Study arm (relevant to T1 and T2 only)	Access to the management toolkit may influence perceptions of the value and purpose of the assessment toolkits, as respondents may feel that there are greater benefits in identifying and diagnosing people with LBD if they have resources to support better management
Time	Impacts on practice and perceptions of the toolkits may change over time, either as a result of successful embedding into practice or because of growing realisation of the difficulties of integrating the toolkits into routine practice

(for which information was available at all time points), we maximised the number of observations for analysis by constructing a file containing people who responded to the T0 questionnaire and either the T1 and/or T2 questionnaires (where respondents completed both questionnaires, the T2 response took precedence).

## Response rates

Response rates to each questionnaire are summarised in *Table 21*. Undelivered questionnaires are excluded from calculation of the response rate. Overall response rates were similar for each of the questionnaires (ranging from 37% to 48%). Data from SurveyMonkey indicated that, overall, nearly two-thirds of questionnaires delivered electronically (62%) were unopened, highlighting the need to provide copies of the questionnaire by post as well as e-mail.

Data were available to compare response rates to each questionnaire by region and specialty. There was no evidence of differential response rates by region. Response rates were significantly higher for movement disorder than for memory services at T0 ( $p < 0.01$ ) and T2 ( $p < 0.001$ ), but not at T1 (*Table 22*). Response rates were examined by study arm for T1 and T2 questionnaires. There was no difference at baseline, but a trend for a better response rate from the control arm at T2 (54.5% vs. 31.8%;  $p < 0.05$ ). This is likely to reflect the unequal distribution of larger teams between study arms.

TABLE 21 Response rates to questionnaires

Response	T0, n (%)	T1, n (%)	T2, n (%)
Distributed	346	127	145
Not delivered	0	3	5
No response/incomplete	193 (56)	64 (51.6)	88 (62.9)
Completed	153 (44)	60 (48.4)	52 (37.1)



TABLE 22 Response rates by specialty

Questionnaire returned	T0, n (%)	T1, n (%)	T2, n (%)
Memory services			
Yes	109 (40.5)	48 (45.7)	31 (28.7)
No	160 (59.5)	57 (54.3)	77 (71.3)
Total	269	105	108
Movement disorder services			
Yes	44 (57.1)	12 (63.2)	21 (65.6)
No	33 (42.9)	7 (36.8)	11 (34.4)
Total	27	19	32

## Characteristics of respondents

Respondent characteristics at each time point are shown in *Table 23*. Respondents had a range of roles, although the majority were either consultants or nurses. To facilitate subsequent analyses, role was recoded into doctors (including trainees) and allied health professionals (including nurses).

At T0, information was collected on experience of working with patients with dementia and/or PD. This varied from < 1 to 40 years, with an average of 13 years' experience with dementia (median 12 years) and just under 10 years' experience of working with PD patients (median 9 years). The T1 and T2 questionnaires asked more specifically about the training in LBD received by respondents. The response categories were chosen on the basis of comments made by interview participants that

TABLE 23 Characteristics of questionnaire respondents

Characteristic	T0 (N = 153), n (%)	T1 (N = 60), n (%)	T2 (N = 52), n (%)
Sex			
Male	53 (34.6)	20 (33.3)	22 (42.3)
Female	100 (65.4)	40 (66.7)	30 (57.7)
Specialty			
Memory service	110 (71.9)	48 (80)	31 (59.6)
Movement disorder service	43 (28.1)	12 (20)	21 (40.4)
Role			
Consultants and trainees	72 (47.1)	29 (48.3)	31 (59.6)
Nurses	56 (36.6)	28 (46.7)	18 (34.6)
Others	25 (16.3)	3 (5.0)	3 (5.8)
Region			
East Anglia	104 (68.0)	34 (56.7)	24 (46.2)
North East	49 (32.0)	26 (43.3)	28 (53.8)
Study arm			
Intervention	NA	44 (73.3)	34 (65.4)
Control		16 (26.7)	18 (34.6)

NA, not applicable.

emphasised the value of exposure to LBD through working with experts in the field. Data were combined to explore training received by each unique participant to T1 and/or T2 questionnaires ( $n = 80$ ). A series of binary variables was constructed and we explored whether or not training varied systematically by professional background (doctors vs. others), specialty (movement disorder vs. memory services), region (East Anglia vs. North East) or study arm (intervention vs. control). Overall, around one-third of respondents (33.8%) had received only basic training, a similar proportion (32.5%) reported self-directed study (through reading or attendance at conferences) and nearly half (45.0%) had worked with a team with expertise in LBD (the totals do not sum to 100, as some respondents reported both self-directed study and working with an expert team).

No differences in training were found by specialty or study arm. Respondents in East Anglia were more likely to report only basic training than those in the North East (43.2% vs. 22.2%;  $p < 0.05$ ). Although working with an expert team was not associated with professional background, doctors were more likely to report self-directed study and less likely to have received only basic training (Table 24). The findings suggest that those completing and returning the questionnaires may have considerable knowledge of and expertise in LBD, and highlight the need to provide additional training on LBD for non-medical staff.

### Confidence in diagnosing selected conditions (T0 only)

A seven-point scale was used to assess confidence in diagnosing and managing a range of conditions commonly seen in memory and/or movement disorder services. A not applicable column was included, as some staff were not responsible for making diagnoses or for managing certain conditions (the number of respondents therefore varies for different conditions). Figure 7 presents the mean level of confidence (where 1 = low and 7 = high confidence).

TABLE 24 Training in LBD by professional background (T1 and T2 respondents)

Training in LBD	Doctors, n (%)	Non-medics, n (%)
Basic training only	7 (17.5)	20 (50)
Self-directed study, conferences and/or LBD research	23 (57.5)	3 (7.5)
Worked in a team with LBD expertise	16 (40.0)	20 (50.0)
Total	40	40

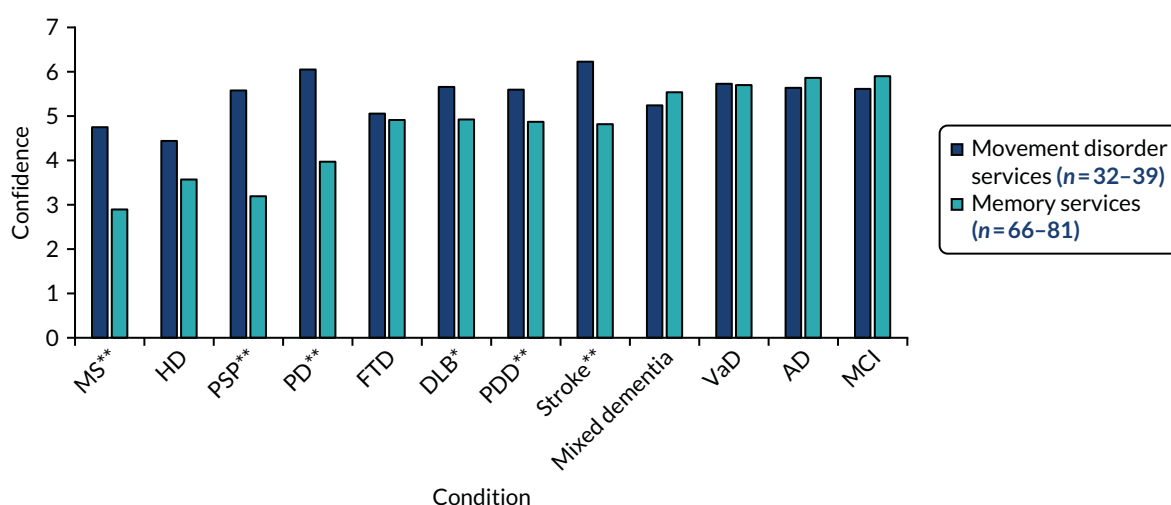


FIGURE 7 Confidence in diagnosing selected conditions by specialty at T0 ( $n = 98-120$ ). \* $p < 0.01$ , \*\* $p < 0.001$ . AD, Alzheimer's disease; FTD, frontotemporal dementia; HD, Huntington's disease; MS, multiple sclerosis; PSP, progressive supranuclear palsy; VaD, vascular dementia.

With the exception of FTD, clinicians were, generally, less confident in diagnosing DLB and PDD than other types of dementia. There were significant differences between specialties in confidence in diagnosing six conditions (see *Figure 7*). Greater confidence in diagnosing predominantly physical conditions would be anticipated for staff in movement disorder services (i.e. multiple sclerosis, progressive supranuclear palsy, PD and stroke, all  $p < 0.001$ ). Staff in these services also rated their confidence higher in diagnosing both PDD and DLB than those in memory services ( $p < 0.001$  and  $p < 0.01$ , respectively).

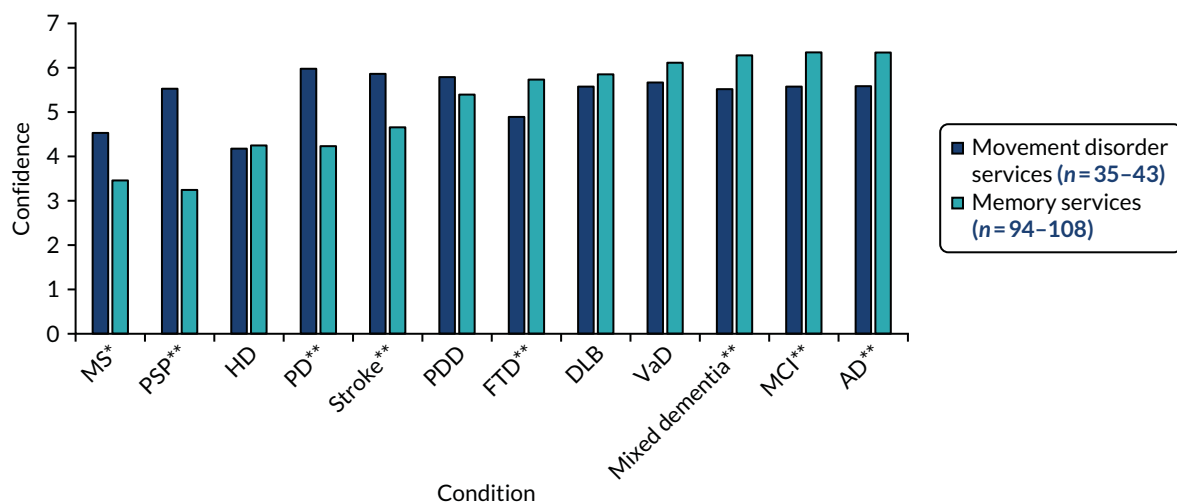
### Confidence in managing selected conditions (T0 only)

Parallel analyses were conducted for confidence in managing the same set of conditions (*Figure 8*). Significant differences between specialties were generally as would be anticipated. Professionals in movement disorder services were more confident in managing more physical conditions (multiple sclerosis,  $p < 0.01$ ; progressive supranuclear palsy, PD and stroke, all  $p < 0.001$ ), whereas those in memory services were more confident in managing some dementias, including frontotemporal dementia, mixed dementia, Alzheimer's disease and MCI (all  $p < 0.001$ ). Staff in both specialties reported similar levels of confidence in managing DLB and PDD. Examination of confidence in managing symptoms common in these conditions suggests a possible explanation for this.

### Confidence in managing symptoms common in Lewy body dementia (all time points)

The questionnaire also included a section on confidence in managing common symptoms in LBD (again rated on a seven-point scale). *Figure 9* shows that both specialties have areas of expertise, but neither are confident in managing the full range of symptoms associated with LBD. The pattern of responses underpins the dual pathway experienced by many people with LBD.

As this set of questions was included in all three questionnaires, responses at T0 were compared with those at either T1 or T2. Radar plots were used to illustrate changes in confidence in managing common LBD symptoms between the beginning and end of the programme for respondents in the control and intervention arms (see *Figures 5* and *6*). The plots indicated that confidence in symptom management reported by staff in intervention services later in the programme was significantly higher for all but three symptom areas than at the beginning of the programme. For these figures, we have



**FIGURE 8** Confidence in managing selected conditions by specialty at T0 ( $n = 130-150$ ). \* $p < 0.01$ , \*\* $p < 0.001$ . AD, Alzheimer's disease; FTD, frontotemporal dementia; HD, Huntington's disease; MS, multiple sclerosis; PSP, progressive supranuclear palsy; VaD, vascular dementia.

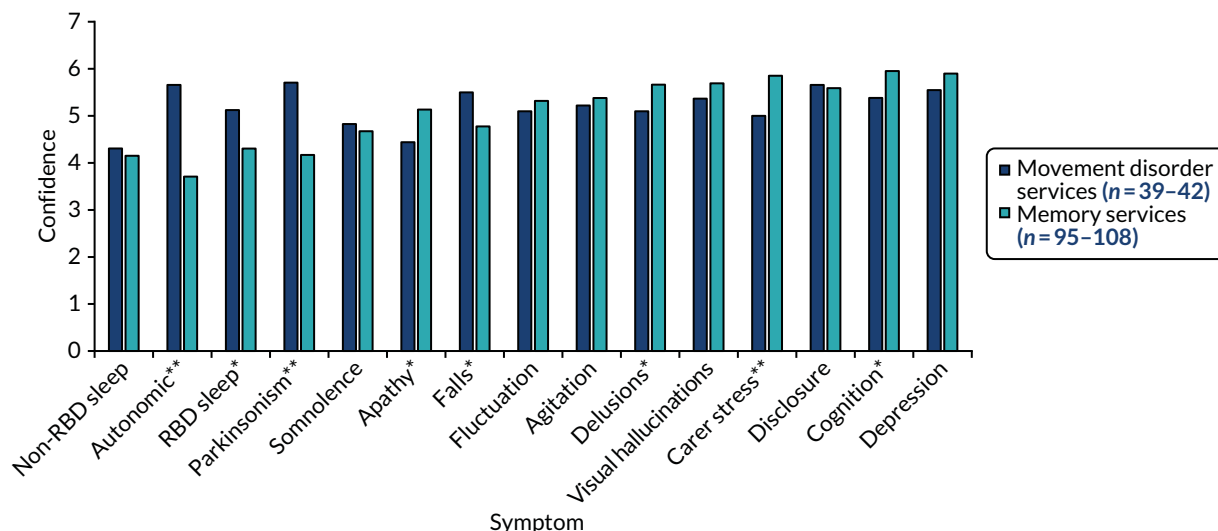


FIGURE 9 Confidence in managing common LBD symptoms by specialty at T0 (n = 136–150). \*p < 0.01, \*\*p < 0.001. RBD, rapid eye movement sleep behaviour disorder.

included changes significant at a p-value < 0.05, as these suggest a trend towards greater confidence in some areas. Although, as previously emphasised, interpretation is hindered by the lack of matched samples, these findings suggest that including questionnaire data may help in understanding the mechanisms through which changes occur, particularly if larger samples are available with more consistent respondents at both time points. The findings lend some support to the hypothesis that the positive outcomes achieved in the pilot trial may result from the accumulation of marginal gains.

### Approach to new assessments (T1 and T2 only)

The questionnaires administered during the pilot trial asked respondents how frequently they explored key LBD symptoms, completed formal cognitive assessments and used formal diagnostic criteria. These items related to the content of the assessment toolkits. As the focus of the toolkits varied for clinicians in movement disorder and memory services, the findings are presented by specialty. Analysis of variance indicated no significant changes between responses to T1 and T2 questionnaires relating to new assessments. Figure 10 therefore presents data from only T1, which indicated that staff working in movement disorder services more consistently reported exploring parkinsonism and REM sleep

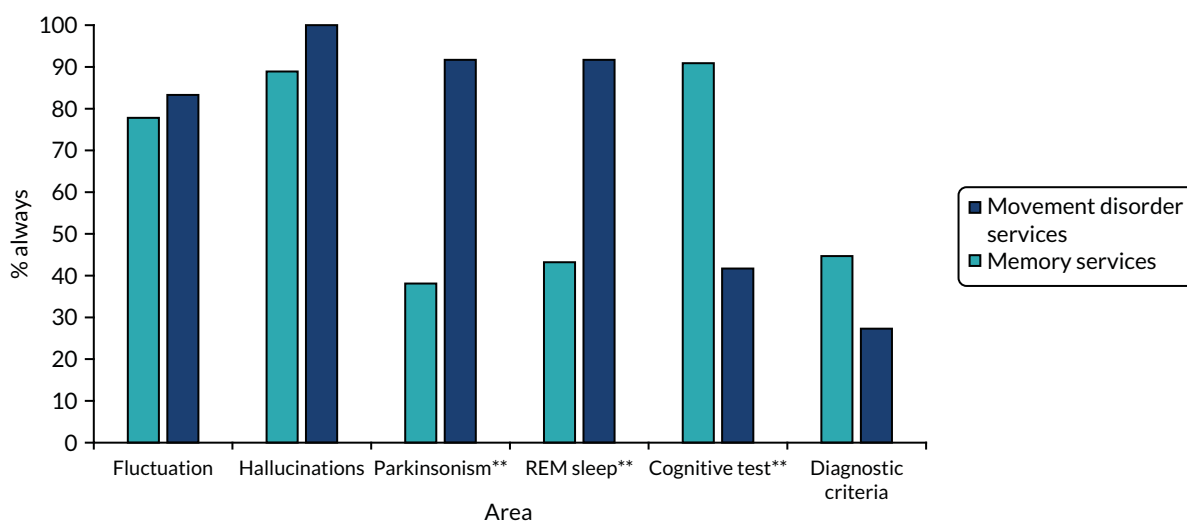


FIGURE 10 Percentage of T1 respondents reporting always covering specific areas in new consultations by specialty. \*\*p < 0.001.

behaviour disorder, whereas those in memory services were more likely to report using formal cognitive tests and applying diagnostic criteria.

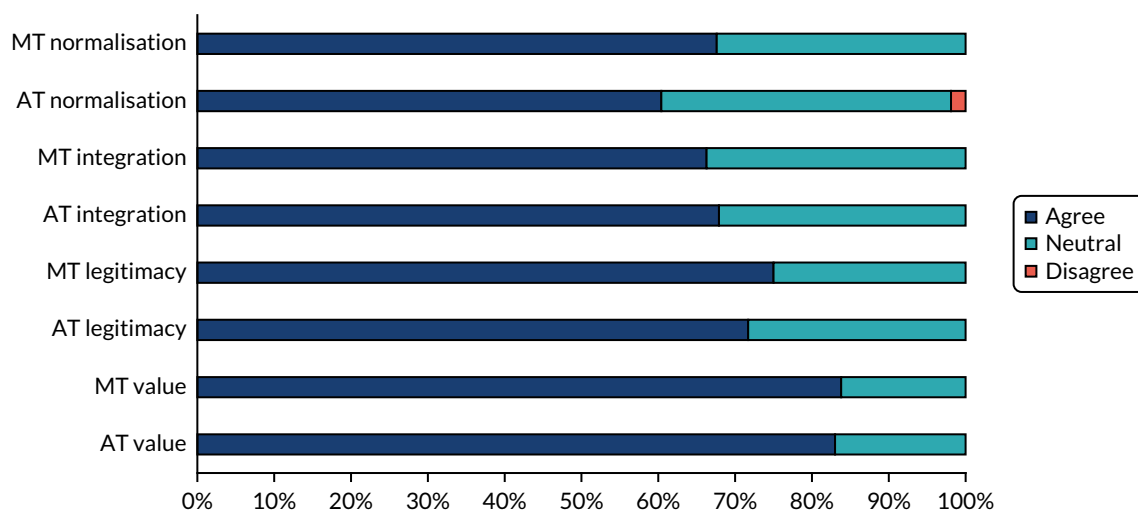
These results suggest that, despite the availability of the assessment toolkits, staff working in memory services were not routinely exploring all key features of DLB in new patient assessments. With respect to diagnosing PDD, it would not be anticipated that formal cognitive testing would be conducted at every new consultation, as clinicians often emphasised that there was insufficient time and that it was not always appropriate to look at cognition in the first appointment. In the absence of data on practice prior to the introduction of the assessment toolkits, it is difficult to interpret these results.

## Integration of the toolkits into routine practice (T1 and T2 only)

Questions related to NPT explored the perceived value of the toolkits, whether or not participants believed that the toolkits were a legitimate part of their role, ease of integrating the toolkits into their work and whether or not they thought that the toolkits would become part of their normal practice. Parallel questions were asked about the assessment and management toolkits, with responses on a seven-point scale (where higher scores indicate greater agreement with each statement). Responses from T1 have been coded into three groups (agree, neutral and disagree) in *Figure 11*. Views on the assessment and management toolkits were generally similar, although respondents had slightly more positive views about the management toolkit becoming part of their normal practice. Only one person disagreed with any of the items, and this was on the item relating to whether or not the assessment toolkit was likely to become part of their normal practice.

Further analyses explored whether or not views on integration of the assessment toolkits were related to role, specialty and study arm or changed between T1 and T2. There were trends for views on implementation to become less positive over time and for allied health professionals to express less positive views on whether or not the assessment toolkit was a legitimate part of their role (both  $p < 0.05$ ). The mean values on the seven-point scale for each NPT item by study arm and specialty are shown in *Figures 12* and *13*.

Respondents in the intervention arm generally held more positive views towards implementation of the assessment toolkits than those in the control arm. Although rarely explicitly mentioned during interviews, the availability of the management toolkit may have created more positive views towards accurate diagnosis of LBD and, therefore, towards the assessment toolkit. Respondents in memory services had



**FIGURE 11** Views on integration of the management and assessment toolkits into routine practice at T1. AT, assessment; MT, management.

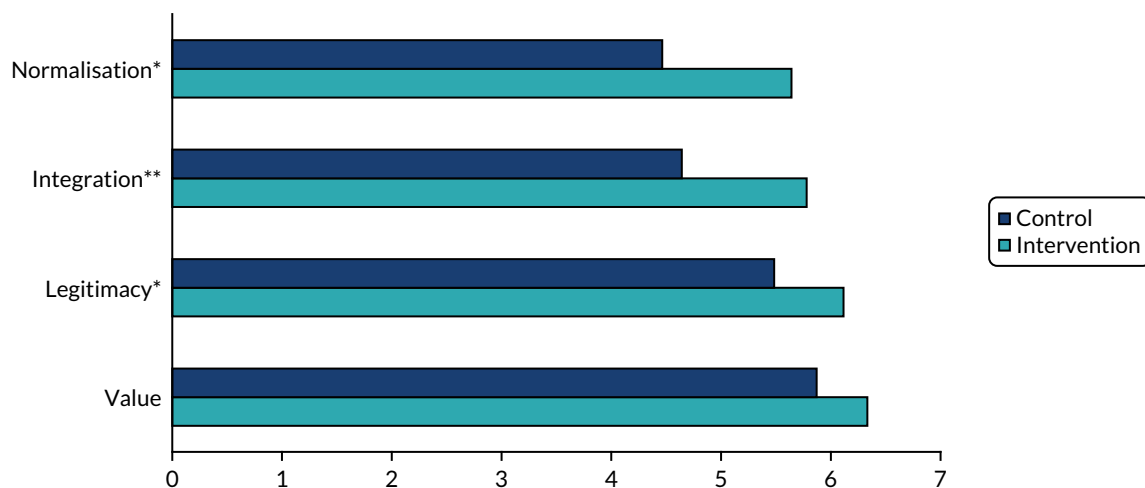


FIGURE 12 Mean scores on NPT questions relating to the assessment toolkit by study arm (T1). \* $p < 0.01$ , \*\* $p < 0.001$ .

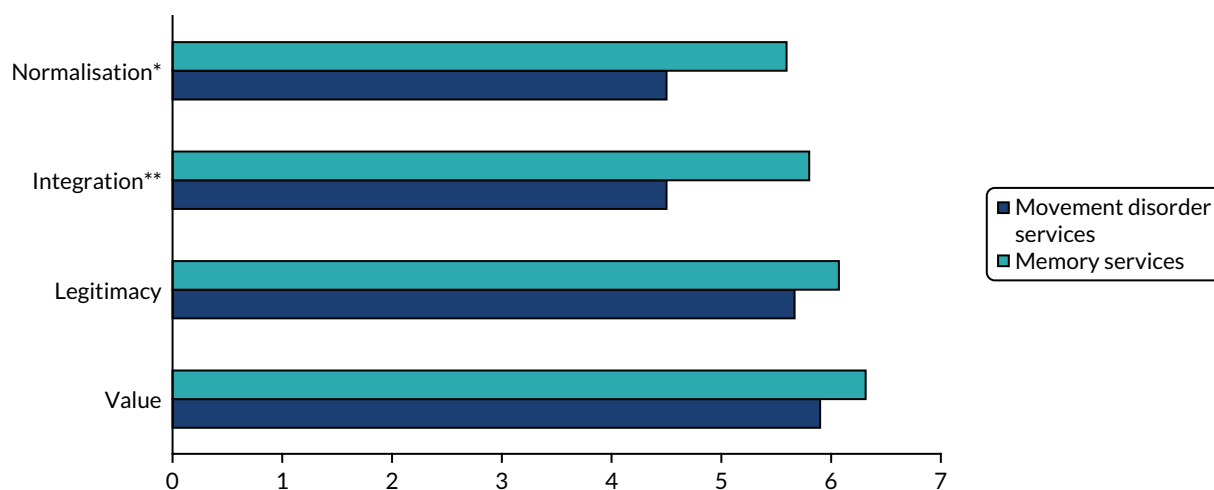


FIGURE 13 Mean scores on NPT questions relating to assessment toolkit by specialty. \* $p < 0.01$ , \*\* $p < 0.001$ .

more positive views towards implementation of the assessment toolkits than their colleagues in movement disorder services (see *Figure 13*). These findings are consistent with the views expressed in qualitative interviews when professionals in movement disorder services often expressed concerns over the feasibility of implementation of the assessment toolkits.

Parallel analyses were conducted for the NPT questions about the integration of the management toolkit. There were no significant differences in views expressed according to region, role or specialty (study arm was not relevant, as only those in the intervention arm received the management toolkit).

### Overall views on toolkits (T2 only)

On the final questionnaire, we asked if and how the toolkits had an impact on the respondents' work. These questions were included in only the intervention questionnaire ( $n = 34$ ). Six respondents had not used the assessment toolkits (17.6%), half reported that it had changed their approach to new or follow-up assessments (50.0%), five were unsure (14.7%) and the remaining six felt that it had not changed their approach (17.6%).

Three respondents did not answer the question relating to the impact of the management toolkit and nine reported that they had not used it. The remaining respondents had most commonly used the management toolkit for reference (19/22, 86.4%), with smaller numbers using it to explore new treatment options (9/22, 40.9%) or with trainees (8/22, 36.4%). (As respondents could use the toolkit in more than one way, the percentages do not sum to 100.)

### Comments on open questions (T1 and T2 only)

Overall, just under half (45.5%) of respondents made at least one comment on either the T1 or the T2 questionnaire. Analysis of the comments indicated that they were consistent with the analysis of qualitative interviews and focus groups. As some questionnaire respondents were based in services where it had not been possible to conduct any observation or interviews, this provided useful triangulation of the qualitative analysis from new perspectives.

### Summary

Response rates to the questionnaires were acceptable and staff with a variety of roles took part. The large number of questionnaire invitations left unopened when delivered electronically suggests that both electronic and paper copies of questionnaires should be sent to maximise response rates. The findings from the T0 questionnaire confirm that confidence in diagnosing and managing DLB and PDD is lower than for most other subtypes of dementia. This supports the need for assessment and management toolkits. Confidence in managing common LBD symptoms varied according to specialty and underpinned the dual pathway, with referrals to both movement disorder and memory services, experienced by many people with LBD. Consistent, small but (statistically) significant changes in confidence in managing these common symptoms were found between the first questionnaire and those administered during or after the pilot trial for respondents based in services that received the management toolkit, lending support to the hypothesis that the potential mechanism for change is through the accumulation of marginal gains. Caution is, however, needed in interpreting differences over time, as the respondents at each time point are overlapping, but not identical.





## Appendix 8 Factors influencing the diagnosis and management of Lewy body dementia: illustrative quotations from work package 5

Quotations from interviews and focus groups shown in italics and identified by a unique speaker identifier. The first two digits indicate the service (memory services are represented by 01–16 and movement disorder services by 17–26). Services 01–08 and 17–21 are in East Anglia, and services 09–16 and 22–26 are in the North East. The third and fourth digits indicate the individual within the service.

TABLE 25 Factors influencing the diagnosis of LBD with illustrative quotations

Theme	Subtheme	Illustrative quotation
Complexity of LBD	Variability in presentation	<i>The fluctuating nature of Lewy Body, I think, meant that when he [consultant] saw her – his ward rounds were in the morning – [...] he found that she was pretty good and quite plausible. Then, you'd see her later in the afternoon or evening and she'd be struggling</i> 2307, trainee geriatrician
	Lack of a definitive test and restricted access to scans	<i>The only thing we can't do DaTscans. I mean for DaTscans we probably have to send it to [hospital 1]. I mean to be honest, I don't use DaTscan a lot. I've probably one done one DaT for the last 3 years</i> 2001, consultant geriatrician
	Shift to earlier presentation	<i>... this is a very special kind of dementia, which is very difficult to diagnose in the first stages of the illness. Because the cognitive function is not that prominent, it's mostly a sleep problem and falls, unsteadiness. Sometimes, they are almost the same as the Alzheimer's type [...] In the early stages, it's not easy to diagnose</i> 0501, trainee OAP
	Availability of an informant	<i>Some people will say 'yes, I can do everything' and you're pretty sure they probably can't but, again, it's difficult to know what they're doing for themselves [...] it's quite tricky with that generation as well, with older people. The way their relationships were set up, often women did do everything around the house. Often, retired older men don't do masses of activities of daily living that you can easily assess</i> 2307, trainee geriatrician
Service organisation	Shift to nurse-led memory services	<i>For a start, who are we asking to make the diagnosis of our patients? Is it people who are properly trained and who have good clinical expertise, who've seen a range of different dementias? Or is it people who are trained, who have had exposure to, maybe, lots of Alzheimer's disease? And their clinical repertoire is very narrow</i> 0901, consultant OAP
	Follow-up arrangements	<i>Let's say you have a follow-up review, you have 15 minutes, roughly. All the other things you have to address and then how do you in that time say 'oh, by the way, I think you have got dementia?' It is a huge thing to be diagnosed with dementia, a massive thing. So I think you don't do people justice just throwing it in on the way out 'you have got dementia'. So very rarely do people do that in that setting</i> 2306, trainee neurologist

continued

TABLE 25 Factors influencing the diagnosis of LBD with illustrative quotations (continued)

Theme	Subtheme	Illustrative quotation
Training, knowledge and experience	Awareness of LBD and cognitive biases	<i>I think also one of the problems is that when we think about dementia we would – you're never surprised of a symptom, we put everything down to dementia. So a lot of the things that you see there you just say, 'Well it's their dementia'. And you may not pick out some of those little nuances of Lewy body</i> 0208, community worker, memory service
	If and how LBD symptoms were covered in consultations	<i>I've never really clearly understood what the nature of the fluctuation is despite talking to various people and trying to read up about it, because everybody's cognitive fluctuation, you know, everybody's cognitive function fluctuates a bit, [...] is it a kind of regular fluctuation pattern, but how quickly as well? Are you talking days, or weeks, or hours?</i> 1402, consultant OAP
		<i>I always ask 'Have you noticed any shakiness or tremor?' So that's a question I always ask and I'm always observing for that as well</i> 0403, memory assessment nurse
	Interpreting cognitive tests	<i>I also think that differentiating between MCI and dementia is something that people find more difficult to do, so what we may find in the notes is that a lot of people on their problem list have Parkinson's disease, cognitive impairment. But those people who have cognitive impairment listed could have an MMSE anywhere from 24 to 12</i> 2201, consultant geriatrician
	Knowledge of dementia subtypes	<i>Unfortunately is quite difficult to characterise, whether it's PD dementia or Lewy body dementia or it's Alzheimer's dementia with Parkinson's</i> 1701, consultant geriatrician
Attitudes and values	Perceived prevalence and status of LBD	<i>I don't think we see that many people with Lewy body dementia, which might suggest that it's underdiagnosed or else they're just not coming through to our service. And I wonder whether some of them might be going to neurology instead</i> 0209, community worker, memory service
	Perceived value of diagnosing LBD	<i>I'm sure a psychiatrist will say 'we must know what every sort of dementia is'. You know, and perhaps we should. They're probably right, but I've never felt it makes a great deal of difference to the patient really. [The patient] doesn't care whether she's got Lewy body or Alzheimer's or whatever else really</i> 2401, consultant geriatrician
		<i>I guess it [disclosing dementia] gives them a rough idea how the disease might progress of how their mental function might progress in the next few months so that they're aware of how things might go, as well as the carers and their family, explain that there are possible drugs, if they meet the criteria, to go on temporarily, may to halt progression of the cognitive impairment for some time. It may not improve things, but it might hold the decline of it. Also, I guess once you label people with dementia they're more entitled to some of the support services and benefits and allowances and things like that</i> 1701, consultant geriatrician

TABLE 25 Factors influencing the diagnosis of LBD with illustrative quotations (continued)

Theme	Subtheme	Illustrative quotation
	Perceived responsibility for diagnosing LBD	<i>But you still want the most authoritative person [...] Being in the medical paradigm everything goes to the diagnosis. So what you want is the person who is going to give you a diagnosis and then suggest what to do</i> 2402, consultant geriatrician
		<i>... you have fantastic movement disorder people and then just a few rooms further down are fantastic dementia people, but the overlap is still not good there. There are not many, if any at all, movement disorder people with an interest in dementia and vice versa</i> 2306, trainee neurologist
	Perceived value of diagnosing dementia subtypes	<i>I suppose the other practical thing as well, what difference does it make? And actually it doesn't make that much difference, if it's either Lewy body disease or Alzheimer's, because you'll be treating them pretty much the same way anyway</i> 1402, consultant OAP
		<i>There's not that many common dementias, we should at least be able to diagnose the most common three or four, shouldn't we?</i> 1601, consultant OAP
DaT, dopamine transporter.		

TABLE 26 Factors influencing the management of LBD with illustrative quotations

Theme	Subtheme	Illustrative quotation
Complexity of LBD	Balancing treatments	<i>I think it's getting the balance between the cognitive and motor issues. So cutting back on the motor treatments and the balance between that, hallucinations and the cholinesterase inhibitors</i> 2305, consultant geriatrician
Service organisation	Follow-up arrangements	<i>The way things are at the moment, with the changes to monitoring as well, people are being discharged much more early to GPs than they used to be. We used to have 6-monthly monitoring to go on indefinitely and now it's that people are discharged back to GP</i> 0501, trainee OAP
	Fragmented care pathways	<i>From a technical, diagnostic and pharmacological, perspective, I am happy to diagnose and manage both DLB and PDD. The difficulty that I have, or where I come unstuck, is if I do that I then, quite often, can't get patients into community mental health services because they've been furnished with a diagnosis and therefore, the piece of work is done. It takes longer to get them into services if there are crises, which clearly there quite often are, from a psychological perspective. So I can't, then, get access to Community Mental Health Team, CPN [community psychiatric nurse] support, medical support for those individuals. If I make that diagnosis, and manage that diagnosis initially, they don't get the other softer stuff around the dementia diagnosis that community mental health teams are commissioned to provide</i> 2703, consultant geriatrician
continued		

TABLE 26 Factors influencing the management of LBD with illustrative quotations (continued)

Theme	Subtheme	Illustrative quotation
		<p>... it becomes a lot harder to coordinate care for really complex people who need their care coordinated. What happens then is a little bit of indecision, because nobody wants to take the wrong step if they don't know what either side is doing</p> <p>2301, trainee geriatrician</p>
Skills, training and knowledge		<p>I haven't got enough knowledge about sleep hygiene. I mean, I can offer basic things about people trying to avoid sleeping through the day and taking a regular pattern, but I don't think I have enough knowledge to advise people on a sleep hygiene</p> <p>0503, specialist PD nurse</p>
Attitudes and values	Perceived responsibility for managing LBD	<p>But obviously DLB - the thing is, a lot of people are on things like anticholinergics for urinary dysfunction. It's not up to us to avoid centrally acting anticholinergics because they're always started by other people, by urologists. It's not us, we never start them, but we come across people on them</p> <p>0404, consultant OAP</p>

## Appendix 9 The acceptability of the assessment and management toolkits: illustrative quotations from work package 5

TABLE 27 Feedback on the acceptability of the assessment toolkits with illustrative quotations

Theme	Comment	Illustrative quotation
Layout and presentation	General appearance	<i>I think it's [assessment toolkit] quite nicely formatted and visually it doesn't look too crowded or too dense. So I think that's always important [...] it's not one of those annoying pieces of paper that you feel 'oh, I can't even read what is written here'. It's very clear and easy to go through. It sort of flows naturally</i> O601, consultant OAP
	Signposting and rationale	<i>I could be doing things that aren't necessary, potentially [...] I could literally trim it down to these [five-item UPDRS] and these are the ones that are the most evidence based as being the most discriminatory [...] That's a helpful thing to know</i> 1213, GPSI, memory service
Format	Integration with existing pro formas	<i>Then there's a question of, for any toolkits, remembering where they are because they're not incorporated into our computer system. If I complete a toolkit, I've got to have a pen with me because I would have to do it as a paper version. What do I then do about getting it into our computer system? I'm completing the questions I want to ask, which I want to be in the computer system</i> 1801, consultant geriatrician
	Local intranet	<i>... if the assessment toolkit was made available on, say, the shared drive where people could access [it]</i> O601, consultant OAP
	A self-completion version for patients and carers (PDD toolkit only)	<i>I guess that would be one option, just screen everyone, hand them out while they wait. Give them those things so you have got something when they walk in, you can check already, 'OK, you don't have to worry about it'. Or I do have to worry about it and dig in a bit further</i> 2306, trainee neurologist
	Brief laminated summaries of sections for reference	<i>We thought about making a smaller thing that we could cover in our assessments and then that was always something you could pull out</i> 1104, community psychiatric nurse
Content	Separate versions for medical and non-medical staff	<i>I'm just thinking that the therapists ask a lot of the questions, and if we pull the nursing assessment to pieces and put that in place</i> 1708, specialist nurse, movement disorder service
	Perceived relevance of content	<i>And I guess the other reason is that we might not always recognise them. So, we might be seeing someone with a different type of dementia but we wouldn't know. So, I thought it would be a really good tool for us to remind us of the diagnostic criteria, what questions to ask</i> O101, consultant OAP

continued

TABLE 27 Feedback on the acceptability of the assessment toolkits with illustrative quotations (continued)

Theme	Comment	Illustrative quotation
		<p>... there is nothing in here [toolkit for movement disorder services] that mentions hallucinations, or the fluctuating nature. And actually, I think we might, if we'd used this we might have missed that</p> <p>2403, specialist PD nurse</p>
	Terminology and question wording	<p>With the hallucinations at the moment, all you have to those two questions to the information is 'yes' or 'no' answers. There's a thing about the frequency, the duration, the distress. There's just something else which might give you a feel for how significant this area is. Because my understanding of Lewy Body disease is that [...] it's not just the presence or absence of hallucinations; it's the duration of them, it's the frequency, it's the intensity of those</p> <p>1301, consultant OAP</p>
	Inclusion of five-item UPDRS (memory services)	<p>We probably wouldn't ask 'Does the patient show moderate changes in their level of functioning during the day?' Not with that sentence. People wouldn't know what it was on about</p> <p>0901, consultant OAP</p> <p>I think that is useful in terms of awareness. Because a lot of people, certainly in my team I think, could spot parkinsonism from a tremor point of view, but might not have necessarily from the bradykinesia and the facial expression. As being as important as tremor. I think that's the message, isn't it? Parkinson's disease isn't just about tremor. So I think that there is an awful lot of value in this</p> <p>0901, consultant OAP</p> <p>If you think there's Parkinsonism, it doesn't matter whether it's mild or severe, does it, for DLB? Do you see what I mean? Does it matter? Do you need to go into that amount of detail? It's just whether it's there or not [...] Because we're not Parkinson specialists, we just need to know whether there is enough to meet the diagnostic criteria for DLB not Parkinson's</p> <p>1503, consultant OAP</p>
	Inclusion of formal cognitive assessment (movement disorder services)	<p>I have yet to be convinced that a nurse with good instinct won't pick it up, as part of her general assessment. It's difficult to know what would be gained by routinely doing it because most patients, although I dare say the Carlslake study and everything after it showed you get very high cumulative instance of dementia in Parkinson's, it's not everybody. I think they could pick it up instinctively first, rather than screening</p> <p>2501, consultant neurologist</p> <p>So, briefly, I'll probably do an AMTS [Abbreviated Mental Test] and I do a clock drawing and an intersecting pentagon, just to cover, get a bit of visuospatial things. So, that's why I do the clock drawing, clocks and a pentagon thing. And with the AMTS, I know the AMTS is rubbish in Parkinson's. It's not going to give us anything, but I don't have time to do a detailed thing</p> <p>2001, consultant geriatrician</p>

TABLE 28 Feedback on the acceptability of the management toolkits with illustrative quotations

Theme	Comment	Illustrative quotation
Layout and presentation	Use of colour and ability to access information at different levels was valued	<i>I think the fact that it's broken down into three levels in itself is a help, because if we'd gone straight to the tome [reference guidelines] it would absolutely go over my head, but this breaks it down quite well</i> 1106, community psychiatric nurse, focus group
		<i>The colouring is terrible. People have problems with eyesight. Sorry but the contrast is not so good</i> 0501, trainee OAP
		<i>We need to look at everything. When you go out to see someone in the community, they're going to describe to you something that they've noticed or they're concerned about and it could be anything. So we don't necessarily have the answers, but if you can look at this [one page summary] and say 'Oh actually, with Lewy body dementia, that's quite a common sort of symptom'. To me, then I'd find that really useful</i> 0710, social worker, memory service
Format	Integration with existing electronic records	<i>In an ideal world, you'd be seeing somebody with Lewy body in clinic, and there would be a link from their patient records to say, 'Your toolkit', so that you can just click on it</i> 0701, consultant OAP
	Access via computer or application	<i>I guess if you put it on the computer, you can sort of look at things while you are talking to someone without it being so in your face, if it is easy to access</i> 2302, trainee neurologist
		<i>Having availability of guidance on the management tool I see would fit potentially quite nicely into the sort of guidance that we have on our intranet and put into bite-sized chunks</i> 1801, consultant geriatrician
	Small A5 versions for portability	<i>The only thing is perhaps the size of it. Maybe if you could make it kind of pocket size, so we can carry it around</i> 0702, consultant OAP
	Tailored versions for medical and non-medical staff	<i>I think maybe splitting it and having one that was more about the management role of CPNs [community psychiatric nurses] and one that was more tailored to the medics</i> 1104, community psychiatric nurse
	Version for patients would be useful	<i>I think it would be helpful to have something that you could give to the patient as well, not just something we can use for our own things to ask, but actually something you could physically give to the person as well to go through and explain it a bit more. So rather than it just being something that we can be aware of, ask and talk about, but something that we can actually give out as well</i> 1103, community psychiatric nurse
	Relevance to other settings	<i>Where I most commonly find mismanagement of Lewy body disease is in primary care [...] I think the people for whom computerisation would be especially important, would be in GP surgeries, where, when they are seeing someone with Parkinson's disease, flagging up the things and the different pages that they need to be mindful of</i> 1101, consultant OAP

continued



TABLE 28 Feedback on the acceptability of the management toolkits with illustrative quotations (continued)

Theme	Comment	Illustrative quotation	
Content	Perceived relevance of content	<p><i>But then they probably go out of date quite quickly, so you'd need an online version to keep up to date with it. That would be my only concern, because treatments change</i> 1501, consultant OAP</p> <p><i>There's no point saying there's no evidence for it because if somebody's got low mood, you're going to give them something. You can't ignore it. I'm not going to say to the patient, 'There's no evidence for use of antidepressants', because if it's really impeding their function and causing distress, I will treat [...] It's about alleviating their distress and their symptoms. I don't know that it's that helpful. You might want to say, 'If using antidepressants, just avoid significant anticholinergic things'</i> 1503, consultant OAP</p> <p><i>They seem to push melatonin for poor sleep. Firstly, GPs are not familiar with melatonin [...] A lot of people will start feeling sick, elderly people feel sick on it and can't tolerate it. So you have to warn them that might happen. Because it says, given the relatively benign side effect profile, but in this high dose, it does make them nauseous [...] I can't get to grips with melatonin. I have tried it several times and everybody seems to come back sick [...] But maybe because we are working with people who are frail</i> 1901, consultant geriatrician</p>	
		Appropriate for other professionals	<p><i>I think they are something for a GP, for somebody that is more involved in the long-term management, would be helpful [...] I think that's quite educational for GPs as a whole, that it affects sleep, it affects hypotension, constipation, urinary dysfunction, all these sorts of things that you expect sometimes to happen in the elderly, but you wouldn't necessarily put together as being part of the dementia syndrome</i> 1213, GPSI, memory service</p>
		Dosage information	<p><i>I think it's excellent and I think it's really useful, especially the more detailed ones actually. I like the fact that they actually tell you doses to use as well, which I think most guidelines don't. Most guidelines shy away from actually saying, 'Use this specific dose', or, 'Between these doses'. [...] Actually, people who use things want to be told what they can use and have some support. The doses are very similar to what I'd use. It gives you that additional confidence that you're using the right doses</i> 1601, consultant OAP</p> <p><i>I know we've got the BNF and everything but that's really just quite dry. I think you'd need something a little bit more practical, for example, maybe an information sheet that you could give to patients about melatonin so that both you and they know what to expect from it. Also, just some specific advice on dosage and when to review somebody, how long do you wait for the therapeutic effect to kick in, etc., etc. Yes, I think a well-designed information sheet for using melatonin in DLB would help</i> 1213, GPSI, memory service</p>



# Appendix 10 Implementation of the assessment and management toolkits: illustrative quotations from work package 5

TABLE 29 Implementation of the assessment toolkits with illustrative quotations

NPT construct	Illustrative quotation
Coherence	<p><i>For me, the toolkit is a really good idea that we've got some commonality that we all should be asking the same questions. We should all be working towards the same guidelines [ . . . ]</i> 2602, specialist PD nurse</p> <p><i>I thought it was very useful because as part of our training we have a lot of exams, a lot of basic knowledge and then a lot of practical knowledge, which we gain by experience or seeing other people. But to gain this practical knowledge, there is no specific way of doing it because it is different reading in books and its different doing the things. I think those sorts of toolkits are in the middle. They bring the criteria to day-to-day practice, so I find them very useful</i> 0102, trainee OAP</p> <p><i>Before I actually saw the paperwork of the toolkit, I thought it was a good idea, because I think it's something that people often make errors in diagnosis with. Either they can be too keen and any patient who presents with confusion and hallucinations, people sort of start thinking 'oh, could this be Lewy body dementia?' Or, sometimes, equally it gets completely missed because people haven't asked all the questions. So I did think it would be quite useful, but then, I suppose when I actually looked at the toolkit for assessment, I felt that it didn't add anything to what I already knew. But it was useful in the sense of there being a checklist and that you're forced to go through all of the items and you're then sure that you don't miss anything</i> 0601, consultant OAP</p>
Cognitive participation	<p><i>I think that the toolkits are potentially useful for people who don't feel so confident [ . . . ] as a guide for them as to sorts of questions they might need to be asking. As somebody who feels confident, my view on the toolkits has been I can see how they can be useful for others. They don't necessarily help me that much because I think they cover all of the questions that I think I'm asking but I don't necessarily ask them in the way that they're written in the toolkit</i> 1801, consultant geriatrician</p> <p><i>I run the clinic with my registrar, it was easy to train him quite quickly [ . . . ] it was easy to get my specialist nurse up to speed [ . . . ] We are kind of all united on this assessment tool, so we don't have to discuss and everybody has different opinions [ . . . ] it is ultimately uniting the approach in making assessment more straightforward</i> 1901, consultant geriatrician</p> <p><i>I think it's difficult when we're not getting referrals for Lewy body dementia every week, I think that makes it more difficult to keep your interest and momentum going</i> 1106, community psychiatric nurse</p> <p><i>What I would say in retrospect, is I'm not sure that we've maximised the value of this within the service. But to do that, we would have actually needed a more sustained input, I think, from the team. And somebody, one or two of us, actually, really taking a role in terms of getting hold of this and running with it. You, actually, need somebody in the team who is going to take a real lead to try and sort of keep it on people's minds. Find out what people's experience was, address any issues, advocate for its value, which, to be fair, I don't think there was somebody who took on that role</i> 1209, consultant OAP</p>

continued

TABLE 29 Implementation of the assessment toolkits with illustrative quotations (continued)

NPT construct	Illustrative quotation
Collective action	<p data-bbox="568 309 1369 360"><i>Unless it's incorporated into our computer system it adds another level of complexity, which is just another barrier for me</i></p> <p data-bbox="1150 360 1426 387">1801, consultant geriatrician</p> <p data-bbox="568 416 1358 468"><i>It is just a bit of extra work. I mean just asking a couple more questions and maybe getting into the habit of doing a physical examination for all patients</i></p> <p data-bbox="1246 468 1426 495">1505, trainee OAP</p> <p data-bbox="568 524 1426 680"><i>I honestly wouldn't have the time to go through all the questions. And to be honest with you, most of them, we do ask anyway, like, 'Do you have hallucinations? Do you have that? Do you have a problem with planning? Do you forget familiar names?' We kind of ask that anyway, but as a quick screening thing, we just generally go, 'Oh, yes, any problems with memory?' and I usually turn to the [patient's] wife: 'Have you noticed anything with the memory?' rather than go, formulaic, through the individual</i></p> <p data-bbox="1182 680 1426 707">2301, trainee geriatrician</p>
Reflexive monitoring	<p data-bbox="568 734 1426 891"><i>What I've been particularly impressed with ... Because really this is about team work, I very rarely would see the patients independently. Information is presented to me much earlier in the pathway than it would have been before. I'm not having to ask these symptoms, they're already there. The team are already asking the relatives, 'What is this patient like when they're asleep at night? Are they all over?' They are following and picking up, particularly, those kinds of symptoms</i></p> <p data-bbox="1209 891 1426 918">0901, consultant OAP</p> <p data-bbox="568 947 1426 1104"><i>Personally, I think having had this, it's probably made me document that there's, like no REM sleep behaviour disorder or no visual. Do you see what I mean? [...] And that's maybe me assuring myself that I'm asking, you know, at a later date, if somebody, you know if they come across this person and wondered, I wonder whether – say they develop DLB later on or something like that and you just think, well 'How long have they had it?', then it's a good account for the future</i></p> <p data-bbox="1209 1104 1426 1131">1503, consultant OAP</p> <p data-bbox="568 1160 1426 1261"><i>It improved my understanding of DLB, and maybe I'm thinking more about DLB now. Because I think as a movement disorder service you always tend to focus on Parkinson's dementia, but now with DLB we're doing more of DLB now, I would think, or diagnosing more, definitely</i></p> <p data-bbox="1150 1238 1426 1265">1701, consultant geriatrician</p> <p data-bbox="568 1290 1426 1447"><i>And maybe the heuristic that I use should be different. Because like, I said, I do this if I have a suspicion they might have fluctuation, Parkinsonian symptoms, or visual hallucinations. So, if they have none of these, I'm not going to do this form. So maybe – well, I don't know – I was thinking maybe I should do the form anyway, on everyone, but we don't. [Later in the interview]. But it's just a niggling thought in my mind now. Maybe we're missing some</i></p> <p data-bbox="1209 1447 1426 1473">0101, consultant OAP</p>
GPSI, general practitioner with a special interest.	

TABLE 30 Implementation of the management toolkit with illustrative quotations

NPT construct	Illustrative quotation
Coherence	<p><i>I think it is, at a glance, by all means it is a very complicated condition with a lot of little branches. Again, none of the textbooks will tell you exactly what medication to use on which condition. Although we were doing very much what it says here, before this toolkit came forward [...] this comes in a very supportive way, explaining that you are doing the right thing, this is exactly what we use, so it was very, very helpful</i></p> <p style="text-align: right;">1901, consultant geriatrician</p>
	<p><i>Obviously, coming from a consensus from the best experts available, we trust the material. So it's definitely very useful [...] you regard this as the expert opinion, evidence-based expert opinion. So, you consult it because you are even expecting to find things in it that you wouldn't find in the BNF, or you wouldn't find in some of the other sources that you look to usually</i></p> <p style="text-align: right;">0101, consultant OAP</p>
Cognitive participation	<p><i>We haven't got round on our monthly mentoring sessions to specifically doing one where I would have thought about bringing these in. Some of the mentoring sessions have been about some aspects of the management of dementia, but the questions they've had have been more about which drugs and why. There have been some questions within that about behaviour, so I probably could have used some of it, now I think back</i></p> <p style="text-align: right;">1801, consultant geriatrician</p>
	<p><i>I think the first problem is, would we manage them at all? [...] because to me conceptually it falls into the province of old age psychiatry</i></p> <p style="text-align: right;">2402, consultant geriatrician</p>
	<p><i>I think this would be quite useful for juniors. I think our SHOs [senior house officers] would really find this very informative and practically very useful. I think that would be the case, not just at SPR [specialist registrar] level but also the SHOs, VTS [vocational training scheme] trainees that we have, they'd find it very useful. I think nursing staff, community mental health nurses, memory clinics, they'd find it useful just to give a broad awareness of the various symptoms and management. I think they'd find it useful as well</i></p> <p style="text-align: right;">1504, consultant OAP</p>
Collective action	<p><i>I think one thing is you know if you're sort of flicking through sheets and things it looks a bit rubbish and it also kind of looks like you don't know what you are doing. So, and if they don't know what the diagnosis is and you've got like 'neuropsychiatric' symptoms and stuff, then that's a bit stressful</i></p> <p style="text-align: right;">2302, trainee neurologist</p>
	<p><i>Very occasionally, when I've had somebody, where they've had a problem and you've tried one or two things, I might just refer to it and say 'have I done what the toolkit would say?'</i></p> <p style="text-align: right;">0701, consultant OAP</p>
	<p><i>So when I'm supervising the trainees, I'm supervising memory clinic nurses and they come to me with a specific problem, then we get this out of the cupboard and have a read and make a decision. Sometimes, but very rarely, when the patient is in the room as well</i></p> <p style="text-align: right;">0101, consultant OAP</p>
Reflexive monitoring	<p><i>I suppose I feel like most people did when I first looked at it. You think, 'Is that what I do? Is that what I not do? Should I do be doing it differently?'</i></p> <p style="text-align: right;">1101, consultant OAP</p>
	<p><i>It adds more awareness of other things which might be worrying people, not just cognition and neuropsychiatric and sleep. There are also other things. It sort of gives me an indication of some of the other medical issues which can affect quality of life. I think it also allows me to set the signposts better. [...] I could ask the GP to do things a bit more, like constipation and sexual dysfunction, that sort of thing [...] I guess it's raising awareness of it and raising the profile of it</i></p> <p style="text-align: right;">1502, consultant OAP</p>
	<p><i>Like the melatonin thing, I certainly wouldn't feel confident about that [...] I wouldn't feel that it is appropriate for me to prescribe it. It might prompt 'I have heard melatonin might be used sometimes in this situation'</i></p> <p style="text-align: right;">2402, consultant geriatrician</p>



## Appendix 11 Proposed implementation strategy for work package 4

TABLE 31 Orientation and training on assessment toolkit (intervention and control groups)

Content	Who	Duration	How
Introduction to the programme, study team and WP4	WP1 team	5–10 minutes	Presentation supported by documentation (e.g. PIS)
Study background and summary	WP1 team/CTU		
Objectives – cRCT and process evaluation	WP1 team/ CTU/Claire Bamford		
What study participation involves: for patients and for clinicians	WS1 team/CTU	5 minutes	Presentation supported by flow chart(s)
Discussion of evidence base for the assessment toolkits and potential benefits of improved diagnosis of LBD	Credible professional	10 minutes	Brief presentation on process of developing assessment tool and provision of supplementary materials (e.g. references for validated questions included in the assessment toolkits; rationale for recommending MoCA). Case studies to highlight benefits of improved diagnosis
Explore potential benefits of assessment toolkits (consistency, validated questions, documenting negatives)	CB (feedback from WS2 interviews)	5 minutes	Presentation
Clarify when assessment toolkits could be used and how clinicians can ensure that the assessment toolkit is readily available (e.g. how copies will get into patients' notes)	Facilitator	10 minutes	Group discussion
Highlight variances from usual practice and focus on planning how to integrate new aspects into assessments	Facilitator	10 minutes	Reflection, group discussion to first identify barriers and then strategies to overcome these. Identify additional training needs to be met through web-based materials and/or local training sessions
Training on UPDRS and MoCA	Appropriate (local) professional	Separate session if required	Video/demonstration, practice sessions with feedback, supplementary resources (e.g. web-based materials, document with FAQs)

cRCT, cluster randomised controlled trial; CTU, clinical trials unit; FAQ, frequently asked question; PIS, patient information sheet.

### Notes

Dark purple shading indicates activities supported by WP5 data that would ideally be included, but could be excluded if insufficient time is available.

Light purple shading indicates additional sessions to be locally organised.

Facilitator indicates either team member or external person with appropriate skills to facilitate group discussion and group work.

TABLE 32 Additional training on management guidelines (intervention group only)

Content	Who	Duration	How
Discussion of evidence base for the management toolkit	Credible professional	5 minutes	Brief presentation on process of developing management guidelines; provision of supplementary materials (e.g. systematic review)
Highlight specific issues regarding management of LBD (include feedback from patients/carers regarding unmet needs and worse outcomes)	Credible professional/ Claire Bamford	5 minutes	Summary of literature and case studies
Explore how the management guidelines could be used in practice and consider ways of ensuring that the guidelines are readily available (e.g. is it feasible to include copy of the overview diagram in paper notes of patients with LBD?)	Facilitator	10 minutes	Group discussion: sharing ideas (e.g. use as reference document when writing letters, have a copy of overview diagram in notes of LBD patients to check key aspects covered in consultation)
Identify variances from usual practice and problem-solve to overcome potential barriers to use of management guidelines	Facilitator	15 minutes	Case studies, group discussion (requires time to review the guidelines, identify barriers and strategies to overcome these)
<b>Note</b> Light purple shading indicates additional sessions to be locally organised.			

TABLE 33 Reminders and troubleshooting (all in relation to assessment toolkits and intervention only in relation to management guidelines)

Content	Who	How
Physical prompts: laminated management overview diagram for office wall; DIAMOND-Lewy coasters, pencils, Post-its® (3M, Cynthiana, KY, USA); inserts for diaries with management overview diagram	Project team	Send out at regular intervals
Agenda item at regular team meetings to review use and identify problems	Local services	Local team member to liaise with lead clinician to obtain feedback and to attend occasional meetings to problem-solve, address queries, etc.
Audit and feedback of use of assessment toolkits, either through small-scale notes review or through case discussions	Local services	Local team member to liaise with lead clinician to check progress, etc.
Case-based discussions to discuss use of management guidelines and identify any impacts on management and any queries	Local services	Local team member to liaise with lead clinician to check progress, etc.
<b>Notes</b> Dark purple shading indicates activities supported by WP5 data that would ideally be included, but could be excluded if insufficient time is available. Light purple shading indicates additional sessions to be locally organised.		

TABLE 34 Proposed web-based resources to support implementation

Resource	Aim	Availability	For
Copy of assessment toolkit	Ensure clinicians are able to access copies as required	✓	C/I
Copy of management guidelines	Ensure clinicians are able to access guidelines	✓	I
	To incorporate user-friendly navigation system to facilitate use		
Clinician PIS for cRCT	Easy access to a reminder about the design of the study and what participation involves	✓	C/I
Clinician PIS for qualitative study	Easy access to a reminder about the components of the qualitative study	✓	C/I
Summary of key points from SIV	This may cover the previous two points to identify which resource would be most useful to clinicians		C/I
Videos of UPDRS	To facilitate skill development and provide a reminder if needed	✓	C/I
Videos of MoCA	To facilitate skill development and provide a reminder if needed	✓	C/I
FAQs for assessment toolkits	To provide easily accessible information on common questions about how to use the assessment toolkits		C/I
FAQs for management guidelines <sup>a</sup>	To provide easily accessible information on common questions about how to use the assessment toolkits		I
Published literature review	To enable keen clinicians to review source material for guidelines	✓	I
	To demonstrate credibility of management guidelines		
Copies of training materials on assessment toolkits (e.g. case studies)	To facilitate further discussion within teams if required		C/I
	To enable clinicians who were unable to attend the briefing/training session(s) to work through the materials		
Copies of training materials on management guidelines (e.g. case studies)			I

C, control group; cRCT, cluster randomised controlled trial; FAQ, frequently asked question; I, intervention group; PIS, patient information sheet; SIV, site initiation visit.

<sup>a</sup> These documents will be 'live' on the website and updated regularly with clinicians being able to submit new FAQs as needed.







EME  
HS&DR  
HTA  
**PGfAR**  
PHR

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