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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Scientific summary

The DIAMOND-Lewy research prgramme

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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 ≤ 5% of dementia cases and Parkinson's disease dementia in ≤ 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.ephpp.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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