Demography, diagnostics, and medication in dementia with Lewy bodies and Parkinson’s disease with dementia: data from the Swedish Dementia Quality Registry (SveDem)

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Introduction: Whether dementia with Lewy bodies (DLB) and Parkinson’s disease with dementia (PDD) should be considered as one entity or two distinct conditions is a matter of controversy. The aim of this study was to compare the characteristics of DLB and PDD patients using data from the Swedish Dementia Quality Registry (SveDem).

Methods: SveDem is a national Web-based quality registry initiated to improve the quality of diagnostic workup, treatment, and care of patients with dementia across Sweden. Patients with newly diagnosed dementia of various types were registered in SveDem during the years 2007–2011. The current cross-sectional report is based on DLB (n = 487) and PDD (n = 297) patients. Demographic characteristics, diagnostic workup, Mini-Mental State Examination (MMSE) score, and medications were compared between DLB and PDD groups.

Results: No gender differences were observed between the two study groups (P = 0.706). PDD patients were significantly younger than DLB patients at the time of diagnosis (74.8 versus 76.8 years, respectively; P < 0.001). A significantly higher prevalence of patients with MMSE score ≤24 were found in the PDD group (75.2% versus 67.6%; P = 0.030). The mean number of performed diagnostic modalities was significantly higher in the DLB group (4.9 ± 1.7) than in the PDD group (4.1 ± 1.6; P < 0.001). DLB patients were more likely than PDD patients to be treated with cholinesterase inhibitors (odds ratio = 2.5, 95% confidence interval = 1.8–3.5), whereas the use of memantine, antidepressants, and antipsychotics did not differ between the groups.

Conclusion: This study demonstrates several differences in the dementia work-up between DLB and PDD. The onset of dementia was significantly earlier in PDD, while treatment with cholinesterase inhibitors was more common in DLB patients. Severe cognitive impairment (MMSE score ≤24) was more frequent in the PDD group, whereas more diagnostic tests were used to confirm a DLB diagnosis. Some similarities also were found, such as gender distribution and use of memantine, antidepressants, and antipsychotics drugs. Further follow-up cost-effectiveness studies are needed to provide more evidence for workup and treatment guidelines of DLB and PDD.

Keywords: dementia with Lewy bodies, Parkinson’s disease with dementia, age, diagnostic approach, medication, Mini-Mental State Examination

Introduction
Dementia with Lewy bodies (DLB) overlaps clinically with Parkinson’s disease (PD) with dementia (PDD). Epidemiological studies show that DLB is a common form of dementia, having an estimated incidence rate of 112 per 100,000 person-years.1
Similarly, the incidence of dementia in PD is approximately 100 per 100,000 person-years, with a cumulative prevalence rate of as high as 80%. This leads to a prevalence rate of 0.2%–0.5% for PDD among the general population aged ≥65 years.

Although there is controversy about whether DLB and PDD are one entity or two distinct conditions, there may be clinically relevant differences, such as differences in sensitivity to neuroleptic drugs and response to anti-Parkinson and antidementia drugs. The importance of a correct diagnosis is highlighted in studies showing that appropriate treatment of symptoms can improve quality of life in both conditions.

Diagnostic criteria for DLB include progressive dementia and fluctuating cognition in association with visual hallucination and Parkinsonism, while diagnosis of PDD requires a period with motor symptoms only, and cognitive impairment that begins more than 1 year after the onset of motor symptoms. These clinical overlaps and uncertainties highlight the need for more research to compare DLB and PDD, in particular because previous studies have been based on small samples from single-center investigations. The Swedish Dementia Quality Registry (SveDem) makes it possible to perform such a comparison, given its enrollment of a large number of dementia cases including patients with DLB and PDD. This study aimed to compare the characteristics of DLB and PDD patients, with a focus on age, gender, level of cognitive impairment, pharmaceutical treatments, and diagnostic approach.

**Methods**

**Swedish dementia quality registry**

Data were obtained from the SveDem registry. SveDem is a national web-based quality registry initiated to improve the quality of diagnostic workup, treatment, and care of patients with dementia across Sweden. Patients with newly diagnosed dementia (according to the *International Classification of Diseases version 10* [ICD-10] Classification of Mental and Behavioural Disorders criteria) who registered in this incident-based survey during the years 2007–2011 were the bases for this report. Most patients were registered at memory clinics, representing almost 90% of all new dementia diagnosis at these specialized clinics during 2007–2011 in Sweden. The current cross-sectional report is based on two subgroups: patients with a diagnosis of DLB and patients with a diagnosis of PDD. Data were collected from patients’ files and registered locally into the web-based database.

Collected data included age at diagnosis, gender, living conditions, use of different diagnostic tests (yes/no) in the dementia workup, diagnosis of DLB or PDD (ICD-10 codes of G31.8 and F02.3 for DLB and PDD respectively), medication, and support from the community. Of note, the diagnosis of DLB was based on the modified criteria from the DLB Consortium, and PDD was diagnosed using the criteria recommended by Emre et al. Geriatricians, neuropsychologists, or psychiatrists established the diagnoses. The use of the following assessments in the diagnostic workup were registered with a yes or no answer: the Mini-Mental State Examination (MMSE), other simple cognitive tests such as the clock test and/or A Quick Test of Cognitive Speed, blood and cerebrospinal fluid sampling, computed tomography (CT), magnetic resonance imaging, electroencephalography, nuclear imaging (including either single-photon emission computed tomography [SPECT], positron emission tomography [PET], or ioflupane iodine-123 [DaT] scan), assessments by occupational, speech, and physical therapists, as well as assessment by a neuropsychologist. In the registry, there is no information on the outcome of the tests in the dementia workup, except for the MMSE scores. The mean number of drugs included all medications that patients already received at the time of referral to memory clinics. More detailed information on cholinesterase inhibitors (ChEIs), N-methyl-D-aspartate antagonists, antidepressants, antipsychotics, anxioytics, hypnotics, and cardiovascular drugs were recorded when the diagnosis was confirmed.

**Ethical issues**

The study was approved by the regional Ethical Committee of Stockholm (dnr 2009/209-31). The patients and their relatives were informed orally and in writing about SveDem and could decline participation. Data were coded and anonymized before statistical analysis.

**Statistical analysis**

Data were analyzed using the Statistical Package for the Social Sciences software version 20 (SPSS; IBM Corporation, Armonk, NY, USA). To describe quantitative and categorical variables, means, standard deviations (SD), and frequencies (%) were reported. Pearson’s chi-square and Fisher’s exact tests were performed to compare relative frequency of qualitative variables between study groups. To compare the mean value of quantitative variables between DLB and PDD, we used independent-sample t-tests. The relationship between different pairs of numerical
measurements was assessed by means of Spearman rank correlation.

Multivariate analysis was performed using binary logistic regression modeling to calculate the odds ratio (OR) for differences in diagnostic and medication characteristics between PDD patients versus DLB patients after adjusting for age. A general linear model of analysis of covariance was also applied to evaluate whether the mean number of obtained diagnostic tests was different between the two study groups, controlling for the effect of other continuous variables. A two-tailed α of 0.05 was considered to be statistically significant in all analytical procedures.

**Results**

**Baseline characteristics**

A total of 487 patients with DLB and 297 with PDD were included in this study. Demographic data are presented in Table 1. The DLB patients were significantly older than the PDD patients at the time of dementia diagnosis (t = 3.82, P < 0.001); no gender differences were observed (P = 0.706), and in both groups, male gender was more prevalent. The degree of cognitive decline assessed by the MMSE at the time of diagnosis was mild in both groups and the need for support from the community (ie, day care, home care) was low (Table 1). Figures 1 and 2 show the histogram plots for the frequency distribution of age at diagnosis and for MMSE scores in the DLB and PDD groups, respectively.

**Diagnostic modalities**

Diagnostic investigations used in the dementia workup of the two groups are compared in Table 2. In univariate statistics, the mean number of the diagnostic modalities used to reach a diagnosis was significantly higher in the DLB group (4.9 [SD = 1.7]) than in the PDD group (4.1 [SD = 1.6]; t = 5.95, P < 0.001) (Table 2). Results from the analysis of covariance showed that the difference remained significant after age adjustment in both the DLB (mean = 4.9; 95% confidence interval [CI] = 4.77–5.06) and PDD (mean = 4.0; 95% CI = 3.84–4.21) groups (P < 0.001).

The MMSE was performed in most of the patients in both groups (~97%); other simple cognitive tests such as the clock test and A Quick Test of Cognitive Speed were more likely to be used to diagnose DLB (OR = 3.12; 95% CI = 2.06–4.71). As shown in Table 2, after baseline adjustment, lumbar puncture (LP) and SPECT/PET/DaT were 3.25 (95% CI = 2.29–4.63) and 2.34 (95% CI = 1.60–3.43) times more likely, respectively, to be performed in the DLB than in the PDD group. Figure 1 illustrates that the mean number of diagnostic modalities significantly decreased with increasing age in both the DLB and PDD groups.

### Table 1 Baseline and demographic characteristics of patients suffering from DLB (n = 487) or PDD (n = 297)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DLB (n = 487)</th>
<th>PDD (n = 297)</th>
<th>Effect size</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, %</td>
<td></td>
<td></td>
<td>OR = 1.06</td>
<td>0.706*</td>
</tr>
<tr>
<td>Female</td>
<td>37.4</td>
<td>38.7</td>
<td>(95% CI = 0.79 to 1.42)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>62.6</td>
<td>61.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (years), mean (SD)</td>
<td>76.8 (7.0)</td>
<td>74.8 (6.9)</td>
<td>MD = -1.96</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>MMSE score, mean (SD)</td>
<td>21.4 (5.1)</td>
<td>20.9 (5.2)</td>
<td>MD = -0.53</td>
<td>0.177†</td>
</tr>
<tr>
<td>Living place, %</td>
<td></td>
<td></td>
<td>OR = 1.50</td>
<td>0.079*</td>
</tr>
<tr>
<td>Own house</td>
<td>89.0</td>
<td>83.8</td>
<td>(95% CI = 0.99 to 2.28)</td>
<td></td>
</tr>
<tr>
<td>Nursing home (temporarily)</td>
<td>6.6</td>
<td>7.2</td>
<td>(own house versus nursing home)</td>
<td></td>
</tr>
<tr>
<td>Nursing home (permanently)</td>
<td>4.4</td>
<td>9.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coresident, %</td>
<td></td>
<td></td>
<td>OR = 0.63</td>
<td>0.007*</td>
</tr>
<tr>
<td>Yes</td>
<td>34.6</td>
<td>25.0</td>
<td>(95% CI: 0.45 to 0.88)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>65.4</td>
<td>75.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day care (at referral), %</td>
<td></td>
<td></td>
<td>OR = 0.62</td>
<td>0.371*</td>
</tr>
<tr>
<td>Yes</td>
<td>2.7</td>
<td>1.7</td>
<td>(95% CI = 0.22 to 1.77)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>97.3</td>
<td>98.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home care (at referral), %</td>
<td></td>
<td></td>
<td>OR = 0.98</td>
<td>0.969*</td>
</tr>
<tr>
<td>Yes</td>
<td>3.1</td>
<td>3.0</td>
<td>(95% CI = 0.42 to 2.28)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>96.9</td>
<td>97.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:** *Pearson’s chi-square statistics; †Independent samples t-test.

**Abbreviations:** DLB, dementia with Lewy bodies; n, number; PDD, Parkinson’s disease with dementia; OR, odds ratio; CI, confidence interval; SD, standard deviation; MD, mean difference; MMSE, Mini-Mental State Examination.
Figure 1 Histogram plots for frequency distribution of age at diagnosis in patients with DLB and patients with PDD.
Abbreviations: DLB, dementia with Lewy bodies; PDD, Parkinson’s disease with dementia.

Figure 2 Histogram plots for frequency distribution of MMSE score in patients with DLB and patients with PDD.
Abbreviations: MMSE, Mini-Mental State Examination; DLB, dementia with Lewy bodies; PDD, Parkinson’s disease with dementia.
The mean MMSE scores were 21.4 (SD = 5.1) and 20.9 (SD = 5.2) in the DLB and PDD groups, respectively. No statistically significant difference was observed ($t = 1.35, P = 0.177$). However, when MMSE score was categorized into two groups (≤24 and >24), a significantly higher prevalence of cases with MMSE score of ≤24 were found in the PDD group (75.2% versus 67.6%; $P = 0.030$). As shown in Figure 3, there was a significant direct correlation between the MMSE score and number of obtained tests in both the DLB (Spearman rho = +0.167, $P < 0.001$) and PDD (Spearman rho = +0.131, $P = 0.030$) groups. Moreover, a significant inverse correlation was found between the MMSE score and age at diagnosis in both the DLB (Spearman rho = −0.127, $P = 0.007$) and PDD (Spearman rho = −0.173, $P = 0.004$) groups (Figure 4).

**Medication characteristics**

Dementia-related medication characteristics of the two study groups are compared in Table 2. The mean number of drugs the patients were treated with at the time of diagnosis was significantly higher among PDD patients (6.4 [SD = 3.2]) than in the DLB group (4.6 [SD = 3.0]; $t = 7.66, P < 0.001$) (Table 2). An average of 35.6% and 16.7% of the patients in both groups were treated with antidepressants and antipsychotic drugs, respectively, with no significant differences between the groups. Multivariate logistic regression analysis after adjustment showed that a significantly higher proportion of DLB patients than PDD patients were treated with ChEIs (OR = 2.55; 95% CI = 1.83–3.55; $P < 0.001$).
than in DLB patients (75 years versus 77 years of age). In one European cohort with a 15-year follow-up in France (Personnes Agées Quid [PAQUID] cohort), the mean age for the incidence of suspected DLB was also higher than for PDD (83 years versus 78 years of age).\(^1\) Similarly, one small series of PDD and DLB patients showed that the mean age at disease onset (71 years versus 55 years of age) and the mean age when dementia appeared (73 years versus 71 years of age) were higher for patients with DLB compared with patients with PDD, respectively.\(^{14}\) Similar conclusions were also drawn by Horimoto et al.\(^15\) who reported that PDD tends to affect younger patients than does DLB. Our findings are thus in line with studies showing earlier, and to some extent more severe dementia in PDD patients.\(^{16,17}\) Although some studies have found similar histopathological and biochemical features between these two conditions,\(^18\) an earlier
onset of PDD may be attributed to the specific topographic pathological course of PDD itself, which might accelerate cognitive impairment. Another reason for the lower mean age of registered PDD compared to DLB patients could be that when regularly monitoring the Parkinsonian symptoms, controlling for signs of dementia also takes place. According to the key role of dementia in prognosis and survival of PD, many PD patients referred to movement disorder clinics may be routinely checked for cognition status and therefore, it is plausible that such patients may be referred to memory clinics in the early phase of dementia.

Our findings show that the number of performed diagnostic tests to reach a diagnosis is significantly higher in the DLB group. Even after the age adjustment, approximately one additional modality was used to diagnose DLB in Sweden. This might reflect more difficulty in establishing a DLB diagnosis compared with a PDD diagnosis. Until now, no previous study has compared this aspect of diagnostic features between DLB and PDD patients. Our results reveal that blood tests and LP, simple cognitive and neurophysiological tests, and imaging modalities such as CT and SPECT/PET/DaT scan were more common in DLB patients. The highest variation belongs to LP with a frequency difference of 20% between the patient groups. However, the rate of performing LP in both groups was quite high compared with some other settings. This finding is consistent with a previous report from diagnostic workup in memory clinics of Sweden where the rate of LP was 62% in patients with dementia aged 65–75 years and 34% in those older than 75 years. This may be a reflection of Swedish guideline recommendations stating that an extended diagnostic workup that includes LP is recommended when the dementia diagnosis is uncertain. With regard to nuclear imaging, the rate of SPECT/PET/DaT scans was almost 2.5 times higher in DLB patients, which could be explained by the important role of DaT scanning in differential diagnosis of DLB from other types of dementia. CT scanning was the most frequent imaging modality, obtained from more than 80% of both DLB and PDD patients. This is in line with the recommendations for basal dementia workup published by the Swedish national Board of Health and Welfare. However, as highlighted by the recent guidelines, no established structural magnetic resonance imaging pattern is characteristic for DLB or PDD. One explanation for the higher number of diagnostic tests in DLB may be the uncertainty that exists in the DLB diagnosis compared with that of PDD. PDD is usually considered as one probable add-on condition that is often taken into account within routine visits; conversely, DLB is a new condition for the patient, and other diagnostic possibilities need to be ruled out. One common finding in both DLB and PDD patients was the significant decrease in the number of obtained diagnostic tests parallel to increasing age, which was also shown in the previous report from SveDem on all dementia patients registered during 2007–2009.

With respect to the degree of cognitive decline, a significantly higher prevalence of patients with MMSE scores ≤24 was found in the PDD group, demonstrating increasingly impaired cognition at the time of the dementia diagnosis. The DLB group was significantly older at the time of dementia diagnosis, and due to the previously well-known relationship between age and severity of dementia, a lower MMSE score would have been expected even though the opposite was observed. Although the overall difference in MMSE score between the two groups was only 0.5 points, more severe cases were reported in the PDD group in patients older than 75 years of age after statistical adjustment. In general, the interquartile range of the MMSE score was between 18–24 and 19–25 in the PDD and the DLB groups, respectively. Only less than 10% of recruited patients had MMSE scores below 14, which shows that most patients in both study groups had mild to moderate cognitive impairment. A few studies have shown no differences in the severity of cognitive impairment between DLB and PDD, although other researchers have found more executive cognitive impairment in DLB.

In the SveDem registry, treatment with ChEIs was shown to be almost 2.5 times more common in DLB compared with PDD. A recent study from the SveDem registry indicated that treatment with ChEIs in DLB was even more common than in Alzheimer’s disease. Based on the cholinergic deficit in PD, treatment with ChEIs such as rivastigmine has been shown to be beneficial in PDD with an acceptable tolerance and safety profile. Also, the ease of donepezil administration has been presented in two small randomized controlled trials. Moreover, rivastigmine has been shown to be beneficial in DLB patients. In a recent paper, it was suggested that ChEIs may be more effective in PDD than in DLB. In a recent Cochrane review, ChEIs are shown to be an efficient treatment with positive impact on global assessment, cognitive and behavioral functions, and activities of daily living in PDD, and recommendations for their use should be more stressed in guidelines for management of PDD. However, in memory clinics in Sweden, ChEIs were less frequently prescribed in PDD patients (56% versus 76%).

Antidepressant, antipsychotic, anxiolytic, and hypnotic treatments did not differ between the groups. More than a third of the patients used antidepressants (33.6% in DLB and...
impairment might need further family and social support. Patients living alone, and this group of frail patients with cognitive impairment are common even in the mild phase of DLB and PDD. However, psychotic symptoms in PDD patients could be due to side effects of levodopa therapy. Still, despite the fact that DLB patients are sensitive to antipsychotics, a high percentage (almost 18%) of DLB patients are being prescribed with this medication, and ways to reduce this use could be considered. Regarding the total number of drugs, the observed difference includes the treatments that patients already received at the time of referral to memory clinics. This includes dopaminergic medications such as levodopa that are undoubtedly more frequently prescribed in the PDD group.

One potential limitation of this study is a selection bias. The SveDem registry is based on memory clinics in Sweden and covers more than 90% of these centers, which are estimated to recruit nearly 30% of all dementia patients across the country, according to incidence data. Selection bias may occur if only selected cases of PDD and DLB are referred to memory clinics in SveDem, while most of the patients are examined and treated at neurology and/or movement disorder clinics not affiliated with SveDem. Compared with DLB patients, PDD patients might be referred less often to memory clinics. Apart from these limitations, this study contains a large sample size of DLB and PDD cases from a considerable number of memory clinics across the entire country.

This report demonstrated some significant differences in the dementia workup and drug treatment in patients with DLB versus those with PDD. These relationships and differences must be further investigated using follow-up data on cognition, treatment, and care protocols, and should take into account the latest diagnostic guidelines. Having data on different diagnostic approaches, including the frequency of different imaging techniques or paraclinical tests from clinics, will provide evidence for the better management of health care services, policymaking, and the development of more efficient guidelines, together with cost-effectiveness analyses and longitudinal outcome assessments.

Conclusion
Our study has clinical and practical implications for health care staff, patients, and families. As shown in the demographic data, 65%–75% of PDD and DLB patients in Sweden are living alone, and this group of frail patients with cognitive impairment might need further family and social support. Antidepressant medications were being taken by 34%–39% of DLB and PDD patients, showing the relatively high prevalence of depression among these patients, which warrants more attention to depressive disorders. On the other hand, more than 56% of DLB and PDD patients were also under treatment with cardiovascular medication, which necessitates careful consideration of potential drug interactions. It would be worth assessing and comparing movement disorder-related therapies, such as levodopa and dopamine agonists, between the DLB and PDD patients. Moreover, difference in the longitudinal progress of cognitive decline should be another source of comparison between these two groups of patients in future investigations. Follow-up cost-effectiveness studies are needed to provide more evidence for the improvement of workup and treatment guidelines of DLB and PDD.

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Disclosure
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