Comorbidity profile in dementia with Lewy bodies versus Alzheimer’s disease: a linkage study between the Swedish Dementia Registry and the Swedish National Patient Registry

Seyed-Mohammad Fereshtehnejad1, Soheil Damangir1, Pavla Cermakova2,3, Dag Aarsland2,4, Maria Eriksdotter1,5 and Dorota Religa2,5*

Abstract

Introduction: Compared to Alzheimer’s disease (AD), dementia with Lewy bodies (DLB) is usually associated with a more complex clinical picture and higher burden of care. Yet, few investigations have been performed on comorbidities and risk factors of DLB. Therefore, we aimed to compare clinical risk factors and comorbidity profile in DLB and AD patients using two nationwide registries.

Methods: This is a linkage study between the Swedish dementia registry (SveDem) and the Swedish National Patient Registry conducted on 634 subjects with DLB and 9161 individuals with AD registered during the years 2007–2012. Comorbidity profile has been coded according to the International Classification of Diseases version 10 (ICD 10) in addition to the date of each event. The main chapters of the ICD-10, the Charlson score of comorbidities and a selected number of neuropsychiatric diseases were compared between the DLB and AD groups. Comorbidity was registered before and after the dementia diagnosis.

Results: “Mental and behavioral disorders”, “diseases of the nervous system”, “diseases of the eye and adnexa”, diseases of the “circulatory”, “respiratory”, and “genitourinary” systems, “diseases of the skin and subcutaneous tissue” and “diseases of the musculoskeletal system and connective tissue” occurred more frequently in the DLB group after multivariate adjustment. Depression [adjusted OR = 2.12 (95%CI 1.49 to 3.03)] and migraine [adjusted OR = 3.65 (95%CI 1.48 to 9.0)] were more commonly recorded before the diagnosis of dementia in the DLB group. Following dementia diagnosis, ischemic stroke [adjusted OR = 1.89 (95%CI 1.21 to 2.96)] was more likely to happen among the DLB patients compared to the AD population.

Conclusions: Our study indicated a worse comorbidity profile in DLB patients with higher occurrence of depression, stroke and migraine compared with the AD group. Deeper knowledge about the underlying mechanisms of these associations is needed to explore possible reasons for the different pattern of comorbidity profile in DLB compared to AD and their prognostic significance.

* Correspondence: dorota.religa@ki.se

1Division of Neurogeriatrics, Department of Neurobiology, Care Sciences, and Society, Center for Alzheimer Research, Karolinska Institutet, Stockholm, Sweden
2Department of Geriatric Medicine, Karolinska University Hospital, Stockholm, Sweden

Full list of author information is available at the end of the article

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Introduction
Dementia with Lewy bodies (DLB) is the second most common type of degenerative dementia after Alzheimer’s disease (AD) [1]. Compared with AD, DLB is associated with poorer prognosis, shorter time to nursing home admission, higher care burden and higher healthcare costs [2-4]. However, cognitive and functional decline do not seem to differ between these two groups [5]. In addition to a more complex clinical picture of DLB that is characterized by visual hallucinations, motoric symptoms, sleep disorders and autonomic dysfunction, comorbidities may be crucial predictors of worse outcomes in DLB patients. Comorbid diseases significantly increase utilization of healthcare resources [2], predict key outcomes of acute hospital care in older people [6] and are associated with a higher risk of death after dementia diagnosis [7].

Little attention has been paid to research on comorbidities and risk factors of DLB. Previous studies showed that occurrence of depression [8,9] and anxiety [10] is higher in DLB patients when compared with AD. Depression has been suggested as a risk factor for DLB [9] and was more likely to persist over time in DLB subjects compared with AD patients [11]. History of stroke and anxiety has been reported to occur more often in DLB patients than in healthy controls, but not in comparison with AD patients [9].

Correct assessment of risk factors and comorbidities is a central part of clinical management of DLB patients. Furthermore, understanding them may provide new insights into the underlying pathophysiology of DLB. In this study, capitalizing on two nationwide registries, we compared clinical risk factors and comorbidity profiles for AD and DLB in 9,795 subjects, including 634 patients with DLB. To the authors’ best knowledge this is one of the largest published DLB cohorts.

Methods
This study was performed by linking the Swedish Dementia Registry (SveDem) and the Swedish National Patient Registry. The personal identity number was used as the unique identifier for merging the two databases. Patients were followed-up until 31 December 2012.

Swedish Dementia Registry
SveDem is a nationwide registry that includes newly diagnosed dementia patients from Sweden [12]. SveDem is a web-based quality registry, initiated in 2007, to collect a comprehensive list of neuropsychiatric diseases were also extracted.

At the end of 2012, 58 specialist units (93% of all in Sweden) and 659 primary care centers (60% of all in Sweden) were affiliated with SveDem. Using an estimated incidence rate of 20,000 patients that develop dementia in Sweden each year [14], the approximate coverage of incident dementia cases in SveDem in 2012 was 36%. However, the study population represents a census of all newly diagnosed dementia patients because all of those who referred to the registered centers were recruited.

This study population comprised only two subgroups, 634 individuals with DLB (DLB group) and 9,161 cases with AD (AD group), recruited during the years 2007 to 2012. Dementia was diagnosed according to the International Classification of Diseases (ICD) version 10 criteria [15]. In addition, McKeith criteria were used to diagnose DLB [16].

Information about age, sex, living conditions, medication profile, diagnosis of DLB and AD (ICD version 10 codes of G31.8 for DLB and G30.0 and G30.1 for AD), baseline Mini-Mental State Examination (MMSE) score [17] and date of referral for dementia work-up were obtained from the SveDem records.

Swedish National Patient Registry
The Swedish National Patient Registry is administered by the Swedish National Board of Health and Welfare, which covers inpatient care in Sweden to 1987 [18]. The doctor responsible for the patient determines the diagnoses in the registry based on clinical evaluations and laboratory assessments on that particular occasion of in-hospital care. Diagnoses were coded using the latest version of the ICD according to the year of registration.

At the time of discharge, the physician registers a main diagnosis and one or more secondary diagnoses if applicable for each patient. A similar procedure is also performed through all outpatient clinics and afterwards. The diagnostic codes are sent by the hospitals and outpatient clinics to the National Board of Health and Welfare. Later, one main diagnosis and up to seven secondary diagnoses are registered together with demographics and administrative information such as hospital, clinic, dates of admission and discharge, surgical procedures and patient characteristics including age, sex and place of residence. Data obtained from 2000 to 2012 were used for this study.

Comorbidity profile
In addition to the main chapters of the ICD version 10, another comparison was performed based on the comorbidity scoring of the ICD version 10 codes recommended by the Royal College of Surgeons called the Charlson Score [19]. The total Charlson score of comorbidities was calculated by counting the number of comorbidity categories without any preassigned weights [20]. Data on a selected list of neuropsychiatric diseases were also extracted.
from the Swedish National Patient Registry using the ICD version 10 codes as follows: depression (F32, F33), anxiety (F40, F41), behavioral disorders (F07, F10, F11, F12, F13, F14, F15, F16, F17, F18, F19, F53, F54, F59, F66, F68, F69, F98, R46), bipolar affective disorder (F31), sleep disorder (F51, G47), syncope (R55), ischemic stroke (I63, I64, I67, I69), cerebral hemorrhage (I60, I61, I62), epilepsy (G40), migraine (G43) and other types of headache (G44, R51). The time of registration was used to check whether the disease occurred before or after dementia diagnosis as well as to calculate the time intervals between the dates.

Since no information is available on the exact time when the symptoms started, we used the date of registration as the initial time point for dementia and the comorbidities. Therefore, if the date of registration for any of the comorbidities has been recorded prior to the date of registration in SveDem, we considered that comorbidity has occurred before dementia, and vice versa.

Statistical analysis
The mean (standard deviation (SD)) and frequency percentage (%) were reported to describe quantitative and categorical variables. For univariate comparisons, the chi-square statistic and Fisher’s exact test were used to compare the relative frequency of nominal variables (that is, sex, comorbidities) between the two study groups where appropriate. To compare the mean value of quantitative variables between the DLB and AD groups, either an independent-sample t test or a Mann–Whitney U test were used for normally or skewed distributions, respectively.

Further multivariate analysis was performed to adjust for the confounding effect of the baseline differences in age and sex between the DLB and AD groups. For this purpose, a binary logistic regression model was applied to evaluate the differences observed in the prevalence of different comorbidities between the DLB and AD groups adjusted for the baseline confounders. Afterwards, the adjusted odds ratio (OR) and its corresponding 95% confidence interval (CI) for each comorbidity were calculated. For the comorbidities that occurred before the date of referral for dementia, type of dementia (DLB vs. AD) was considered the dependent variable. If the comorbid event happened after dementia diagnosis, the comorbidity was defined as the dependent variable and the type of dementia as a predictor in the multivariable model. In all analytical procedures, two-tailed P < 0.05 was considered to show statistically significant difference. Data were analyzed using SPSS software version 22 (IBM Co., Chicago, IL USA).

Ethical issues
The regional Ethical Committee of Stockholm approved data collection (Dnr. 2013/147-31/2), as well as the merging and the analytical procedures performed in this study. The patients were informed orally and in writing about SveDem and could decline participation. Data were coded and anonymized before statistical analysis.

Results
Baseline characteristics
A total number of 634 individuals with DLB and 9,161 AD patients were recruited. The DLB group consisted of 382 (60.3%) males and 252 (39.7%) females with a mean age of 76.5 (SD = 7.1) years. The AD group comprised 3,188 (34.8%) males and 5,973 (65.2%) females with a mean age of 77.6 (SD = 8.3) years at the time of dementia diagnosis. Results of the Pearson chi-square test and the independent-samples t test revealed that there were significantly more males (P < 0.001) and fewer old patients (P < 0.001) in the DLB group. Other baseline, demographic and medication characteristics of the two study groups are presented and compared in Table 1. The mean of the baseline MMSE score was quite similar in the DLB (21.4 (SD = 5.0)) and AD (21.5 (SD = 5.0)) groups (P = 0.593). However, in the DLB group the proportion of patients in nursing homes was larger than that in the AD group (11.8% vs. 5.6%, P < 0.001).

DLB patients were under treatment with a significantly higher number of medications (4.7 (SD = 3.0)) compared with the AD group (3.7 (SD = 2.9)). A multivariate Poisson regression model showed that DLB patients received a higher number of drugs (B = 0.268 (95% CI = 0.230 to 0.307), P < 0.001) after adjustment for sex and age. While a similar proportion of patients were treated with cholinesterase inhibitors in both the DLB (73.6%) and AD (72.7%) groups (P = 0.272), N-methyl D-aspartate antagonists (15.0% vs. 9.9%), antidepressants (34.8% vs. 26.3%), antipsychotics (16.3% vs. 4.9%) and anxiolytics (13.3% vs. 8.2%) were significantly more often prescribed among the DLB group.

International Classification of Diseases version 10 chapters
Table 2 summarizes the comorbidity profile of the DLB and AD patients based on the chapters of the ICD version 10 coding system. ‘Mental and behavioral disorders’ (66.1%) and ‘diseases of the eye and adnexa’ (57.9%) were the most common categories recorded for the DLB group apart from the ‘diseases of the nervous system’; while among the AD patients ‘diseases of the eye and adnexa’ (47.9%), ‘diseases of the musculoskeletal system and connective tissue’ (40.7%) and ‘diseases of the circulatory system’ (40.3%) were most commonly recorded as comorbid conditions. ‘Mental and behavioral disorders’, ‘diseases of the nervous system’, ‘diseases of the eye and adnexa’, diseases of the ‘circulatory’, ‘respiratory’, ‘digestive’ and ‘genitourinary’ systems and the ‘diseases of the skin
and subcutaneous tissue’ occurred more commonly in the DLB group based on the univariate comparisons. As shown in Table 2, all univariate significant differences remained statistically significant after multivariate adjustment except for the ‘diseases of the digestive system’. Moreover, DLB patients suffered more from the ‘diseases of the musculoskeletal system and connective tissue’ after adjustment for age and sex (adjusted OR = 1.19 (95% CI = 1.01 to 1.41)). The greatest between-group differences in the ICD version 10 disease categories were observed in ‘mental and behavioral disorders’ (66.1% vs. 38.7%, adjusted OR = 3.14 (95% CI = 2.63 to 3.75)), ‘diseases of the nervous system’ (88.0% vs. 71.0%, adjusted OR = 2.78 (95% CI = 2.15 to 3.58)) and ‘diseases of the eye and adnexa’ (57.9% vs. 47.9%, adjusted OR = 1.69 (95% CI = 1.42 to 2.01)), all of which were more common in the DLB group.

Further subgroup analysis was performed to assess how patients’ gender, level of cognition and living place might affect the differences in the comorbidity profile between the DLB and AD groups. As summarized in Table 3, some comorbidity categories such as ‘mental and behavioral disorders’ and ‘diseases of the nervous system’ were significantly more common in the DLB group among all of the subgroups regarding gender, cognition and living place (all \( P < 0.05 \)). On the other hand, ‘diseases of the circulatory system’ was significantly more prevalent in the DLB patients who were female (46.8% vs. 38.6%, \( P = 0.009 \)), had MMSE < 22 (49.6% vs. 39.1%, \( P = 0.001 \)) and live in their own house (46.3% vs. 40.2%, \( P = 0.005 \)). Furthermore, ‘diseases of the respiratory system’ was more commonly recorded in the DLB patients with both MMSE ≥ 22 (\( P = 0.043 \)) and MMSE < 22 (\( P = 0.018 \)), with regard to gender and living place the difference was significant only among the males (27.7% vs. 20.5%, \( P = 0.001 \)) and those who live in their own houses (22.9% vs. 18.0%, \( P = 0.004 \)). Furthermore, ‘diseases of the digestive system’ (38.9% vs. 30.3%, \( P = 0.003 \)) and ‘diseases of the musculoskeletal system and connective tissue’ (45.6% vs. 38.5%, \( P = 0.022 \)) were significantly higher in the DLB group compared with the AD group only among the subgroup with MMSE < 22 at the time of diagnosis.

**Charlson comorbidity scoring**

Comorbidity profiles of the DLB and AD patients using the Royal College of Surgeons Charlson categorization

### Table 1 Baseline, diagnostic and medication characteristics of the two study groups: cases suffering from dementia with Lewy bodies versus Alzheimer’s disease patients

| Characteristic                  | Dementia with Lewy bodies (n = 634) | Alzheimer’s disease (n = 9,161) | \( P \) value |
|--------------------------------|-------------------------------------|---------------------------------|---------------|
| Gender                         |                                     |                                 | <0.001\(^a\) |
| Female                         | 252 (39.7%)                         | 5973 (65.2%)                    |               |
| Male                           | 382 (60.3%)                         | 3188 (34.8%)                    |               |
| Age (years)                    | 76.5 (7.1)                          | 77.6 (8.3)                      | <0.001\(^b\) |
| MMSE score                     | 21.4 (5.0)                          | 21.5 (5.0)                      | 0.593\(^b\)   |
| Body mass index (kg/m\(^2\))   | 24.4 (4.1)                          | 24.3 (4.1)                      | 0.565\(^b\)   |
| Living place                   |                                     |                                 | <0.001\(^b\) |
| Own house                      | 559 (88.2%)                         | 8627 (94.4%)                    |               |
| Nursing home                   | 75 (11.8%)                          | 512 (5.6%)                      |               |
| Co-resident                    |                                     |                                 | <0.001\(^b\) |
| Yes                            | 218 (36.0%)                         | 3879 (44.0%)                    |               |
| No                             | 387 (64.0%)                         | 4938 (56.0%)                    |               |
| Medication (at the time of diagnosis) |                                 |                                 |               |
| Cholinesterase inhibitors      | 465 (73.6%)                         | 6598 (72.7%)                    | 0.272\(^a\)   |
| NMDA antagonist                | 95 (15.0%)                          | 895 (9.9%)                      | <0.001\(^b\) |
| Antidepressants                | 220 (34.8%)                         | 2382 (26.3%)                    | <0.001\(^b\) |
| Antipsychotics                 | 103 (16.3%)                         | 447 (4.9%)                      | <0.001\(^b\) |
| Anxiolytics                    | 84 (13.3%)                          | 747 (8.2%)                      | <0.001\(^b\) |
| Hypnotics                      | 106 (16.8%)                         | 1292 (14.2%)                    | 0.065\(^a\)   |
| Cardiovascular drugs           | 365 (57.8%)                         | 4825 (53.2%)                    | 0.054\(^a\)   |
| Total number of drugs          | 4.7 (3.0)                           | 3.7 (2.9)                       | <0.001\(^b\) |

Data presented as number (%) or mean (standard deviation). Statistically significant differences (\( P < 0.05 \)) in bold. MMSE, Mini-Mental State Examination; NMDA, \( N \)-methyl D-aspartate. \(^a\)Pearson chi-square statistic. \(^b\)Independent-sample \( t \) test.
| Chapter | Blocks | Title                                                                 | DLB  | AD     | Unadjusted OR (95% CI) | P value<sup>a</sup> | Adjusted OR (95% CI) | P value<sup>b</sup> |
|---------|--------|----------------------------------------------------------------------|------|--------|------------------------|---------------------|----------------------|---------------------|
| I       | A00 to B99 | Certain infectious and parasitic diseases                            | 87 (13.7) | 1,064 (11.6) | 1.21 (0.96 to 1.53)     | 0.111            | 1.25 (0.98 to 1.59)   | 0.069               |
| II      | C00 to D48 | Neoplasms                                                            | 203 (32.0) | 2,733 (29.8) | 1.11 (0.93 to 1.32)     | 0.245            | 1.06 (0.88 to 1.27)   | 0.541               |
| III     | D50 to D89 | Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 29 (4.6) | 433 (4.7) | 0.97 (0.66 to 1.42)     | 0.861            | 1.01 (0.68 to 1.49)   | 0.976               |
| IV      | E00 to E09 | Endocrine, nutritional and metabolic diseases                        | 79 (12.5) | 1,088 (11.9) | 1.06 (0.83 to 1.35)     | 0.661            | 1.16 (0.90 to 1.49)   | 0.239               |
| V       | F00 to F99 | Mental and behavioral disorders                                      | 419 (66.1) | 3,543 (38.7) | 3.09 (2.61 to 3.66)     | <0.001           | 3.14 (2.63 to 3.75)   | <0.001               |
| VI      | G00 to G99 | Diseases of the nervous system                                       | 558 (88.0) | 6,508 (71.0) | 2.99 (2.34 to 3.82)     | <0.001           | 2.78 (2.15 to 3.58)   | <0.001               |
| VII     | H00 to H59 | Diseases of the eye and adnexa                                       | 367 (57.9) | 4,390 (47.9) | 1.49 (1.27 to 1.76)     | <0.001           | 1.69 (1.42 to 2.01)   | <0.001               |
| VIII    | H60 to H95 | Diseases of the ear and mastoid process                              | 96 (15.1) | 1,462 (16.0) | 0.94 (0.75 to 1.18)     | 0.586            | 0.97 (0.77 to 1.22)   | 0.810               |
| IX      | I00 to I99 | Diseases of the circulatory system                                   | 293 (46.2) | 3,693 (40.3) | 1.27 (1.08 to 1.49)     | 0.003            | 1.29 (1.08 to 1.52)   | 0.004               |
| X       | J00 to J99 | Diseases of the respiratory system                                   | 146 (23.0) | 1,663 (18.2) | 1.35 (1.11 to 1.63)     | 0.002            | 1.30 (1.06 to 1.59)   | 0.010               |
| XI      | K00 to K93 | Diseases of the digestive system                                     | 237 (37.4) | 2,966 (32.4) | 1.25 (1.05 to 1.47)     | 0.009            | 1.17 (0.98 to 1.39)   | 0.082               |
| XII     | L00 to L99 | Diseases of the skin and subcutaneous tissue                         | 155 (24.4) | 1,918 (20.9) | 1.22 (1.01 to 1.47)     | 0.036            | 1.27 (1.05 to 1.54)   | 0.016               |
| XIII    | M00 to M99 | Diseases of the musculoskeletal system and connective tissue         | 273 (43.1) | 3,732 (40.7) | 1.10 (0.93 to 1.29)     | 0.250            | 1.19 (1.01 to 1.41)   | 0.040               |
| XIV     | N00 to N99 | Diseases of the genitourinary system                                 | 233 (36.8) | 2,984 (32.6) | 1.20 (1.02 to 1.42)     | 0.030            | 1.24 (1.04 to 1.47)   | 0.015               |
| XV      | O00 to O99 | Pregnancy, childbirth and the puerperium                             | 1 (0.2) | 2 (0.0) | –                      | –                | –                    | –                   |
| XVI     | P00 to P96 | Certain conditions originating in the perinatal period               | 0 | 0 | –                      | –                | –                    | –                   |
| XVII    | Q00 to Q99 | Congenital malformations, deformations and chromosomal abnormalities | 5 (0.8) | 57 (0.6) | 1.27 (0.51 to 3.18)     | 0.609            | 1.55 (0.61 to 3.98)   | 0.358               |
| XVIII   | R00 to R99 | Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | 460 (72.6) | 5,896 (64.4) | 1.46 (1.22 to 1.75)     | <0.001           | 1.44 (1.19 to 1.73)   | <0.001               |
| XIX     | S00 to T98 | Injury, poisoning and certain other consequences of external causes  | 369 (58.2) | 4,679 (51.1) | 1.33 (1.13 to 1.57)     | 0.001            | 1.54 (1.30 to 1.83)   | <0.001               |
| XX      | V01 to Y98 | External causes of morbidity and mortality                           | 0 | 1 (0.0) | –                      | –                | –                    | –                   |
| XXI     | Z00 to Z99 | Factors influencing health status and contact with health services   | 523 (82.5) | 6,718 (73.3) | 1.71 (1.39 to 2.11)     | <0.001           | 1.73 (1.39 to 2.16)   | <0.001               |

Adjustment is made for age, sex, and Mini-Mental State Examination score. The AD group is considered the reference group. Statistically significant ORs (P<0.05) in bold. AD, Alzheimer’s disease; CI, confidence interval; DLB, dementia with Levy bodies; OR, odds ratio.<sup>a</sup>Chi-square statistics.<sup>b</sup>Binary logistic regression model.
Table 3 Comorbidity profile of patients with dementia with Lewy bodies ($n = 634$) versus Alzheimer’s disease patients ($n = 9,161$) within different subgroups regarding gender, cognitive level at the time of diagnosis and living place using the chapters of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision

| Title | Gender | DLB (%) | AD (%) | P value | Cognition | DLB (%) | AD (%) | P value | Living place | DLB (%) | AD (%) | P value |
|-------|--------|---------|--------|---------|-----------|---------|--------|---------|--------------|---------|--------|---------|
| Certain infectious and parasitic diseases | Male | 14.9 | 12.5 | 0.183 | MMSE ≥ 22 | 16.3 | 11.2 | 0.005 | Own house | 14.3 | 11.4 | 0.038 |
| | Female | 11.9 | 11.1 | 0.703 | MMSE < 22 | 11.9 | 12.2 | 0.855 | Nursing home | 9.3 | 15.0 | 0.188 |
| | Male | 35.6 | 33.8 | 0.494 | MMSE ≥ 22 | 32.8 | 31.6 | 0.652 | Own house | 32.4 | 30.1 | 0.259 |
| Neoplasms | Female | 26.6 | 27.7 | 0.701 | MMSE < 22 | 31.9 | 27.9 | 0.169 | Nursing home | 29.3 | 25.4 | 0.467 |
| Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | Male | 5.2 | 4.8 | 0.687 | MMSE ≥ 22 | 3.6 | 4.5 | 0.447 | Own house | 4.7 | 4.6 | 0.967 |
| | Female | 3.6 | 4.7 | 0.403 | MMSE < 22 | 5.9 | 4.8 | 0.414 | Nursing home | 4.0 | 6.8 | 0.457 |
| Endocrine, nutritional and metabolic diseases | Male | 12.8 | 10.9 | 0.262 | MMSE ≥ 22 | 10.5 | 11.7 | 0.526 | Own house | 12.3 | 11.8 | 0.700 |
| | Female | 11.9 | 12.4 | 0.819 | MMSE < 22 | 15.9 | 11.8 | 0.046 | Nursing home | 13.3 | 13.5 | 0.973 |
| Mental and behavioral disorders | Male | 67.3 | 37.4 | <0.001 | MMSE ≥ 22 | 65.7 | 40.8 | <0.001 | Own house | 65.5 | 38.8 | <0.001 |
| | Female | 64.3 | 39.3 | <0.001 | MMSE < 22 | 66.7 | 36.0 | <0.001 | Nursing home | 70.7 | 36.5 | <0.001 |
| Diseases of the nervous system | Male | 91.4 | 72.8 | <0.001 | MMSE ≥ 22 | 89.5 | 75.5 | <0.001 | Own house | 88.7 | 72.2 | <0.001 |
| | Female | 82.9 | 70.1 | <0.001 | MMSE < 22 | 86.3 | 66.8 | <0.001 | Nursing home | 82.7 | 52.3 | <0.001 |
| Diseases of the eye and adnexa | Male | 56.5 | 44.2 | <0.001 | MMSE ≥ 22 | 60.2 | 49.0 | <0.001 | Own house | 58.3 | 47.7 | <0.001 |
| | Female | 59.9 | 49.9 | 0.002 | MMSE < 22 | 55.6 | 47.0 | 0.007 | Nursing home | 54.7 | 52.0 | 0.660 |
| Diseases of the ear and mastoid process | Male | 15.4 | 17.2 | 0.383 | MMSE ≥ 22 | 17.5 | 17.1 | 0.857 | Own house | 15.7 | 16.2 | 0.790 |
| | Female | 14.7 | 15.3 | 0.794 | MMSE < 22 | 14.1 | 14.6 | 0.819 | Nursing home | 10.7 | 12.9 | 0.588 |
| Diseases of the circulatory system | Male | 45.8 | 43.5 | 0.391 | MMSE ≥ 22 | 43.7 | 40.8 | 0.296 | Own house | 46.3 | 40.2 | 0.005 |
| | Female | 46.8 | 38.6 | 0.009 | MMSE < 22 | 49.6 | 39.1 | 0.001 | Nursing home | 45.3 | 41.2 | 0.499 |
| Diseases of the respiratory system | Male | 27.7 | 20.5 | 0.001 | MMSE ≥ 22 | 22.0 | 17.6 | 0.043 | Own house | 22.9 | 18.0 | 0.004 |
| | Female | 15.9 | 16.9 | 0.677 | MMSE < 22 | 24.4 | 18.6 | 0.018 | Nursing home | 24.0 | 20.1 | 0.438 |
| Diseases of the digestive system | Male | 41.6 | 37.0 | 0.079 | MMSE ≥ 22 | 36.7 | 34.3 | 0.357 | Own house | 37.7 | 32.7 | 0.013 |
| | Female | 31.0 | 29.9 | 0.721 | MMSE < 22 | 38.9 | 30.3 | 0.003 | Nursing home | 34.7 | 27.9 | 0.229 |
| Diseases of the skin and subcutaneous tissue | Male | 24.3 | 20.2 | 0.057 | MMSE ≥ 22 | 25.3 | 22.5 | 0.230 | Own house | 24.7 | 21.1 | 0.043 |
| | Female | 24.6 | 21.3 | 0.217 | MMSE < 22 | 24.1 | 19.3 | 0.056 | Nursing home | 22.7 | 18.6 | 0.397 |
| Diseases of the musculoskeletal system and connective tissue | Male | 39.8 | 36.1 | 0.157 | MMSE ≥ 22 | 41.3 | 42.9 | 0.555 | Own house | 42.9 | 41.0 | 0.371 |
| | Female | 48.0 | 43.2 | 0.132 | MMSE < 22 | 45.6 | 38.5 | 0.022 | Nursing home | 44.0 | 37.5 | 0.280 |
| Diseases of the genitourinary system | Male | 36.4 | 32.1 | 0.093 | MMSE ≥ 22 | 38.0 | 33.6 | 0.108 | Own house | 38.3 | 32.6 | 0.005 |
| | Female | 37.3 | 32.8 | 0.138 | MMSE < 22 | 35.6 | 31.1 | 0.132 | Nursing home | 25.3 | 32.6 | 0.205 |
| Pregnancy, childbirth and the puerperium | Male | – | – | – | MMSE ≥ 22 | 0.3 | 0 | 0.062 | Own house | 0.2 | 0 | 0.601 |
| | Female | 0.4 | 0 | 0.117 | MMSE < 22 | 0 | 0 | 1 | Nursing home | 0.4 | 0 | 1 |
| Certain conditions originating in the perinatal period | Male | 0 | 0 | – | MMSE ≥ 22 | 0 | 0 | – | Own house | 0 | 0 | – |
| | Female | 0 | 0 | – | MMSE < 22 | 0 | 0 | – | Nursing home | 0 | 0 | – |
| Congenital malformations, deformations and chromosomal abnormalities | Male | 1.0 | 0.6 | 0.300 | MMSE ≥ 22 | 0.9 | 0.6 | 0.464 | Own house | 0.7 | 0.5 | 0.545 |
| | Female | 0.4 | 0.6 | 1 | MMSE < 22 | 0.7 | 0.4 | 0.349 | Nursing home | 1.3 | 2.1 | 1 |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | Male | 72.8 | 66.9 | 0.020 | MMSE ≥ 22 | 74.1 | 67.2 | 0.010 | Own house | 72.3 | 64.5 | <0.001 |
| | Female | 72.2 | 63.0 | 0.003 | MMSE < 22 | 71.5 | 61.3 | 0.001 | Nursing home | 74.7 | 62.7 | 0.043 |
| Injury, poisoning and certain other consequences of external causes | Male | 50.8 | 45.1 | 0.034 | MMSE ≥ 22 | 59.6 | 49.2 | <0.001 | Own house | 58.3 | 50.2 | <0.001 |
| | Female | 69.4 | 54.3 | <0.001 | MMSE < 22 | 56.7 | 53.5 | 0.312 | Nursing home | 57.3 | 64.8 | 0.206 |
of the ICD version 10 codes are presented in Table 4. Cerebrovascular diseases were more common in the DLB group after adjustment for age and sex (16.2% vs. 10.0%, adjusted OR = 1.74 (95% CI = 1.38 to 2.19)). As illustrated in Figure 1, 12.7% of the AD patients had a zero score according to the Charlson scoring of the comorbidities, while only 3.3% of the DLB patients showed this condition. The proportion of individuals with one, two and three or more comorbidity categories of Charlson scoring was higher in the DLB group (P < 0.001). Moreover, DLB patients had a significantly higher mean for the total Charlson score (1.52 (SD = 0.85) vs. 1.33 (SD = 0.89)). This difference remained significant even after multivariate adjustment (OR = 1.22 (95% CI = 1.12 to 1.33)).

### Neuropsychiatric comorbidities

Considering the date of registration in SveDem and the Swedish National Patient Registry, occurrence of the selected neuropsychiatric comorbidities was determined as either before or after dementia diagnosis. As presented in Table 5, depression was the most common neuropsychiatric comorbidity before the diagnosis of dementia in both groups (6.0% in DLB and 3.0% in AD). Among strokes, cerebral infarction was more common in the DLB group than in the AD group, while the frequency of cerebral hemorrhages did not differ between the AD and DLB groups. According to univariate comparisons (Table 5), depression (P < 0.001), behavioral disorders (P = 0.012), stroke (P = 0.002) and migraine (P = 0.028) were all more frequent in individuals with DLB compared with the AD group.

### Table 3 Comorbidity profile of patients with dementia with Lewy bodies (n = 634) versus Alzheimer’s disease patients (n = 9,161) within different subgroups regarding gender, cognitive level at the time of diagnosis and living place using the chapters of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (Continued)

| External causes of morbidity and mortality | Male | Female | Male | Female |
|--------------------------------------------|------|--------|------|--------|
| Age at diagnosis                           | 0    | 0      | 0    | 0      |
| Sex                                         | 0    | 0      | 0    | 0      |
| Cognitive level at the time of diagnosis   | MMSE ≥ 22 | 0 | MMSE < 22 | 0 |
| Living place                               | Own house | 0 | Own house | 0 |
| Nursing home                               | 0    | 0      | 0    | 0      |

| Factors influencing health status and contact with health services | Male | Female | Male | Female |
|--------------------------------------------------------------------|------|--------|------|--------|
| Age at diagnosis                                                   | 81.4 | 73.0   | 84.1 | 73.5   |
| Sex                                                                 | 0.001 | 0.001  | 0.001 | 0.001  |
| Cognitive level at the time of diagnosis                           | MMSE ≥ 22 | 84.3 | MMSE < 22 | 81.1 |
| Living place                                                        | Own house | 76.8 | Own house | 69.8 |
| Nursing home                                                        | 0    | 0      | 0    | 0      |

Statistically significant differences (P < 0.05) in bold. Univariate comparisons were performed using either the chi-square or Fisher’s exact test wherever appropriate.

AD, Alzheimer's disease; DLB, dementia with Lewy bodies; MMSE, Mini-Mental State Examination.

### Table 4 Comorbidity profile of the patients with dementia with Lewy bodies versus Alzheimer’s disease patients based on the Royal College of Surgeons Charlson Score indicating International Classification of Disease, 10th revision codes for 14 disease categories

| Disease category               | DLB (n = 634) | AD (n = 9,161) | Unadjusted OR (95% CI) | P value | Adjusted OR (95% CI) | P value |
|-------------------------------|---------------|----------------|------------------------|---------|----------------------|---------|
| Myocardial infarction         | 34 (5.4)      | 532 (5.8)      | 0.92 (0.64 to 1.31)    | 0.643   | 0.85 (0.59 to 1.22)  | 0.372   |
| Congestive cardiac failure    | 38 (6.0)      | 458 (5.0)      | 1.21 (0.86 to 1.70)    | 0.270   | 1.21 (0.85 to 1.73)  | 0.282   |
| Peripheral vascular disease   | 15 (2.4)      | 271 (3.0)      | 0.79 (0.47 to 1.34)    | 0.392   | 0.77 (0.45 to 1.31)  | 0.335   |
| Cerebrovascular disease       | 103 (16.2)    | 912 (10.0)     | 1.75 (1.40 to 2.19)    | <0.001  | 1.74 (1.38 to 2.19)  | <0.001  |
| Chronic pulmonary disease     | 27 (4.3)      | 480 (5.2)      | 0.80 (0.54 to 1.20)    | 0.281   | 0.88 (0.59 to 1.31)  | 0.525   |
| Rheumatological disease       | 12 (1.9)      | 286 (3.1)      | 0.60 (0.33 to 1.07)    | 0.081   | 0.64 (0.35 to 1.19)  | 0.160   |
| Liver disease                 | 4 (0.6)       | 48 (0.5)       | 1.20 (0.43 to 3.35)    | 0.578   | 1.13 (0.40 to 3.19)  | 0.818   |
| Diabetes mellitus             | 26 (4.1)      | 481 (5.3)      | 0.77 (0.52 to 1.15)    | 0.206   | 0.73 (0.48 to 1.11)  | 0.145   |
| Hemiplegia or paraplegia      | 0             | 19 (0.2)       | –                      | 0.631   | –                    | 0.998   |
| Renal disease                 | 11 (1.7)      | 98 (1.1)       | 1.63 (0.87 to 3.06)    | 0.123   | 1.57 (0.83 to 2.97)  | 0.167   |
| Any malignancy                | 94 (14.8)     | 1283 (14.0)    | 1.07 (0.85 to 1.34)    | 0.565   | 0.96 (0.75 to 1.21)  | 0.707   |
| Metastatic solid tumor        | 2 (0.3)       | 74 (0.8)       | 0.39 (0.09 to 1.59)    | 0.239   | 0.42 (0.10 to 1.74)  | 0.235   |
| AIDS/HIV infection            | 0             | 1 (0.0)        | –                      | –       | –                    | –       |
| Total Charlson score          | 1.52 (0.85)   | 1.33 (0.89)    | 1.25 (1.15 to 1.36)    | <0.001  | 1.22 (1.12 to 1.33)  | <0.001  |

Data presented as mean (standard deviation). Adjustment is made for age, sex, and Mini-Mental State Examination score. The AD group is considered the reference group. The dementia category of the original Charlson scoring is not reported here because the whole study population is dementia patients in our study. Statistically significant ORs (P < 0.05) in bold. AD, Alzheimer’s disease; CI, confidence interval; DBL, dementia with Lewy bodies; OR, odds ratio. *Chi-square statistics. **Binary logistic regression model.
group. However, the other types of headache were not significantly different between the two groups (3.2% in DLB and 3.4% in AD, OR = 0.92 (95% CI = 0.58 to 1.45), P = 0.713).

Figure 2 illustrates the forest plots of adjusted OR for each neuropsychiatric comorbidity in DLB with AD as the reference group. With respect to the timing of the events, depression (adjusted OR = 2.12 (95% CI = 1.49 to 3.03)) and migraine (adjusted OR = 3.65 (95% CI = 1.48 to 9.0)) were more commonly recorded before the diagnosis of dementia in the DLB group (Figure 2B). As shown in Figure 2C, ischemic stroke (adjusted OR = 1.89 (95% CI = 1.21 to 2.96)) was the only significant comorbid condition that was more likely to happen among the DLB patients compared with the AD population after the onset of dementia.

Further subgroup analysis was performed regarding gender, cognitive level and living place. As summarized in Table 6, depression and stroke were more common in the DLB group compared with AD patients among both males and females (all P < 0.05), whereas the higher prevalence of anxiety in DLB patients was statistically significant only among the males (3.4% vs. 1.8%, P = 0.031). With respect to level of cognition, depression, stroke and migraine were significantly more common in DLB patients compared with the AD group only among those with MMSE < 22 (all P < 0.05). Depression, sleep disorders and stroke were more commonly occurred in the DLB patients compared with the AD group among those who were living in their own house (all P < 0.05), while migraine was more prevalent in DLB patients who lived in nursing homes (2.7% vs. 0.2%, P = 0.045).

**Discussion**

In this study we investigated selected risk factors and comorbidities in patients suffering from DLB in comparison with AD. There were more males in the DLB group, which is in line with previous studies [21]. At the time when dementia diagnosis was set, DLB patients were younger, and, despite similar level of cognitive impairment, lived more frequently in nursing homes and received more psychiatric medication and a higher total number of drugs. This indicates a worse health profile at the time when dementia was diagnosed and suggests that DLB patients may have been affected by a larger number of diseases before they developed dementia compared with the AD subjects. Patients with DLB were more frequently affected with depression, stroke and cerebrovascular infarctions and migraine.

**Medication**

There were some interesting differences in the use of medication. Cholinesterase inhibitors were used in the majority of DLB and AD patients. Although these drugs are indicated for AD and Parkinson’s disease with dementia, but not formally for DLB, there is good evidence that they are also useful in DLB [22,23]. Memantine was prescribed for 15% of DLB patients and 10% of AD patients, although the evidence is less conclusive for DLB. However, there are some indications that memantine may in fact be useful also for DLB [24], including meta-analysis data [23].

**Depression**

Depression was more frequent in both men and women in the DLB group compared with AD, particularly in
### Table 5 Occurrence and timing for different neuropsychiatric comorbidities in patients with dementia with Lewy bodies versus Alzheimer’s disease patients

| Comorbidity                  | Dementia with Lewy bodies (n = 634) | Alzheimer’s disease (n = 9,161) | P valuea |
|-----------------------------|-------------------------------------|--------------------------------|----------|
| Depression                  |                                     |                                | <0.001   |
| None                        | 587 (92.7)                          | 8,736 (95.5)                   |          |
| Before dementia diagnosis   | 38 (6.0)                            | 277 (3.0)                      |          |
| After dementia diagnosis    | 8 (1.3)                             | 130 (1.4)                      |          |
| Anxiety                     |                                     |                                | 0.508    |
| None                        | 612 (96.7)                          | 8,905 (97.4)                   |          |
| Before dementia diagnosis   | 16 (2.5)                            | 172 (1.9)                      |          |
| After dementia diagnosis    | 5 (0.8)                             | 66 (0.7)                       |          |
| Behavioral disorders        |                                     |                                | 0.012    |
| None                        | 612 (96.7)                          | 8,964 (98.0)                   |          |
| Before dementia diagnosis   | 9 (1.4)                             | 107 (1.2)                      |          |
| After dementia diagnosis    | 12 (1.9)                            | 72 (0.8)                       |          |
| Bipolar affective disorder  |                                     |                                | 0.258    |
| None                        | 628 (99.2)                          | 9,100 (99.5)                   |          |
| Before dementia diagnosis   | 5 (0.8)                             | 36 (0.4)                       |          |
| After dementia diagnosis    | 0                                   | 7 (0.1)                        |          |
| Sleep disorders             |                                     |                                | 0.093    |
| None                        | 616 (97.3)                          | 9,001 (98.4)                   |          |
| Before dementia diagnosis   | 14 (2.2)                            | 116 (1.3)                      |          |
| After dementia diagnosis    | 3 (0.5)                             | 26 (0.3)                       |          |
| Syncope                     |                                     |                                | 0.472    |
| None                        | 587 (92.7)                          | 8,486 (92.8)                   |          |
| Before dementia diagnosis   | 35 (5.5)                            | 443 (4.8)                      |          |
| After dementia diagnosis    | 11 (1.7)                            | 214 (2.3)                      |          |
| Stroke                      |                                     |                                | 0.002    |
| None                        | 580 (91.6)                          | 8,665 (94.8)                   |          |
| Before dementia diagnosis   | 28 (4.4)                            | 277 (3.0)                      |          |
| After dementia diagnosis    | 25 (3.9)                            | 201 (2.2)                      |          |
| Cerebral hemorrhage         |                                     |                                | 0.709    |
| None                        | 623 (98.4)                          | 9,015 (98.6)                   |          |
| Before dementia diagnosis   | 6 (0.9)                             | 62 (0.7)                       |          |
| After dementia diagnosis    | 4 (0.6)                             | 66 (0.7)                       |          |
| Epilepsy                    |                                     |                                | 0.291    |
| None                        | 622 (98.3)                          | 9,022 (98.7)                   |          |
| Before dementia diagnosis   | 8 (1.3)                             | 66 (0.7)                       |          |
| After dementia diagnosis    | 3 (0.4)                             | 55 (0.6)                       |          |
| Migraine                    |                                     |                                | 0.028    |
| None                        | 627 (99.1)                          | 9,113 (99.7)                   |          |
| Before dementia diagnosis   | 6 (0.9)                             | 28 (0.3)                       |          |
| After dementia diagnosis    | 0                                   | 2 (0.0)                        |          |

Data presented as number (%). Statistically significant differences (P < 0.05) in bold. *Pearson chi-square statistics.
Patients with a lower cognitive status at the time when dementia was diagnosed. Depression is a common feature of DLB [11], especially in its early stages. Several hypotheses have linked depression to the etiology and pathophysiology of dementia, depression may be a risk factor for DLB [9]. DLB has also been associated with a higher risk of depression [25]. The etiology of depression is probably multifactorial and the relation to dementia is complex. In our study, depression was significantly more often diagnosed in DLB patients before they were diagnosed with dementia. After the dementia diagnosis was set, depression occurrence did not differ between the DLB and AD patients.

It is a matter of dispute whether depression is a risk factor or a prodromal stage of DLB. Nonmotor symptoms and widespread brain pathological changes are believed to occur in DLB before dementia onset [26], so depression may be a sign of underlying pathological changes that are already present in DLB subjects. It would be of interest to investigate whether prevention or treatment of depression could decrease the incidence of DLB or postpone the development of dementia.

Migraine

In our study, migraine was more common in the DLB group before dementia was diagnosed. Furthermore, it occurred more frequently in DLB patients that had a lower MMSE score at the time of diagnosis. Migraine was shown as a risk factor for developing dementia [27] and associated with smaller brain tissue volumes [28]. Recently, headache has been suggested as a risk factor for the development of vascular dementia in a prospective population-based study [29]. However, there are no previous studies investigating migraine in DLB patients. Conditions that are common in DLB patients and subjects suffering from migraine include complex visual hallucination [30] and disorders in olfactory perception [31]. Even though their etiology seems different, further research on these two disorders could provide valuable insights into the relationship between DLB and migraine.

Stroke

Strokes were found to be more common for both men and women in the DLB group compared with the AD group, especially in subjects with lower MMSE scores. The occurrence of cerebrovascular infarctions but not cerebral hemorrhages after dementia diagnosis was significantly higher in the DLB group compared with AD patients. This relationship was not significant before dementia was diagnosed. This finding is surprising as strokes are common predictors for AD [32]. The difference in use of antipsychotics may be an explanation.

Studies on cerebrovascular pathology in DLB patients are not numerous and provide contradictory results. In a
Table 6 Frequency of different neuropsychiatric comorbidities in patients with dementia with Lewy bodies (n = 634) versus Alzheimer’s disease patients (n = 9,161) within different subgroups regarding gender, cognitive level at the time of diagnosis and living place using the chapters of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision

| Title              | Gender | DB (%) | AD (%) | P value | Cognition | DB (%) | AD (%) | P value | Living place | DB (%) | AD (%) | P value |
|--------------------|--------|--------|--------|---------|-----------|--------|--------|---------|--------------|--------|--------|---------|
| Depression         | Male   | 6.3    | 3.8    | 0.020   | MMSE < 22 | 6.3    | 5.2    | 0.350   | Own house    | 7.0    | 4.5    | 0.006   |
|                    | Female | 8.7    | 4.8    | 0.005   | MMSE < 22 | 7.4    | 3.5    | 0.001   | Nursing home | 9.3    | 3.9    | 0.068   |
| Anxiety            | Male   | 3.4    | 1.8    | 0.031   | MMSE < 22 | 3.3    | 2.7    | 0.464   | Own house    | 3.2    | 2.6    | 0.372   |
|                    | Female | 3.2    | 3.0    | 0.901   | MMSE < 22 | 3.3    | 2.7    | 0.528   | Nursing home | 4.0    | 2.8    | 0.469   |
| Behavioral disorders | Male  | 3.4    | 2.6    | 0.381   | MMSE < 22 | 2.4    | 1.9    | 0.471   | Own house    | 2.9    | 1.8    | 0.079   |
|                    | Female | 3.2    | 1.6    | 0.071   | MMSE < 22 | 3.7    | 2.0    | 0.062   | Nursing home | 6.7    | 4.1    | 0.362   |
| Bipolar affective disorders | Male | 0.5    | 0.5    | 0.702   | MMSE < 22 | 0.6    | 0.5    | 0.689   | Own house    | 0.9    | 0.4    | 0.185   |
|                    | Female | 1.2    | 0.5    | 0.129   | MMSE < 22 | 1.1    | 0.4    | 0.105   | Nursing home | 0      | 1      | 1       |
| Sleep disorders    | Male   | 3.9    | 2.5    | 0.094   | MMSE < 22 | 2.7    | 2.0    | 0.339   | Own house    | 2.7    | 1.6    | 0.040   |
|                    | Female | 0.8    | 1.1    | 1       | MMSE < 22 | 2.2    | 1.1    | 0.124   | Nursing home | 2.7    | 1.4    | 0.325   |
| Syncope            | Male   | 7.1    | 6.7    | 0.789   | MMSE < 22 | 6.9    | 7.4    | 0.782   | Own house    | 7.5    | 7.2    | 0.740   |
|                    | Female | 7.5    | 7.4    | 0.950   | MMSE < 22 | 7.8    | 6.9    | 0.579   | Nursing home | 5.3    | 7.7    | 0.471   |
| Stroke             | Male   | 8.7    | 6.0    | 0.043   | MMSE < 22 | 6.9    | 5.3    | 0.193   | Own house    | 8.4    | 5.1    | 0.001   |
|                    | Female | 7.9    | 4.8    | 0.025   | MMSE < 22 | 9.3    | 5.0    | 0.002   | Nursing home | 8.0    | 7.1    | 0.772   |
| Cerebral hemorhage | Male   | 1.8    | 1.6    | 0.732   | MMSE < 22 | 1.2    | 1.2    | 0.547   | Own house    | 1.8    | 1.4    | 0.410   |
|                    | Female | 1.2    | 1.3    | 1       | MMSE < 22 | 1.9    | 1.7    | 0.807   | Nursing home | 0      | 1.8    | 0.613   |
| Epilepsy           | Male   | 1.6    | 1.5    | 0.958   | MMSE < 22 | 1.2    | 1.3    | 1       | Own house    | 1.8    | 1.3    | 0.287   |
|                    | Female | 2.0    | 1.2    | 0.242   | MMSE < 22 | 2.2    | 1.2    | 0.165   | Nursing home | 1.3    | 2.4    | 1       |
| Migraine           | Male   | 0.5    | 0.2    | 0.249   | MMSE < 22 | 0.9    | 0.4    | 0.165   | Own house    | 0.7    | 0.3    | 0.138   |
|                    | Female | 1.6    | 0.4    | 0.580   | MMSE < 22 | 1.1    | 0.2    | 0.034   | Nursing home | 2.7    | 0.2    | 0.045   |

Univariate comparisons were performed using either the chi-square or Fisher’s exact test wherever appropriate. Statistically significant differences (P < 0.05) in bold. AD, Alzheimer’s disease; DLB, dementia with Lewy bodies; MMSE, Mini-Mental State Examination.
particularly in female patients, those who live in their own house and have a lower cognitive status at the beginning of the diagnostic process. A recent nationwide study in Sweden revealed that 60% of DLB patients were treated with cardiovascular medication, but the use of these drugs was lower in this group compared with AD [47]. However, this difference may be attributed to the fear of side effects in DLB patients; for example, side effects due to autonomic dysfunction. AD patients present the lowest mortality rate compared with other dementia disorders [7] and are therefore considered the healthiest group of dementia patients [50], even though there are some contradictory reports [51,52]. Investigating comorbidities in patients with dementia can provide with valuable insights into dementia disorders and contribute to better understanding of their pathophysiology.

Limitations and strengths

One may criticize that the study is limited by the validity of diagnoses. However, the validity of the Swedish National Patient Registry has been shown to be high for many diagnoses [53]. Nevertheless, the underestimation of comorbidities is inevitable since the Swedish National Patient Registry is based on outpatient or inpatient referrals and those with mild symptoms who did not seek medical help are not recorded. The validity of the data in SveDem has been assessed, especially in memory clinics. The data registered in memory clinics in a random sample of patients were in good agreement with medical records in a validation process [54]. Moreover, although we considered timing for the events, the probability of reverse causation is not completely omitted.

The validity of the diagnosis of dementia disorders has not been examined. It is necessary to acknowledge that the way of diagnosing both dementia types in SveDem reflects clinical practice in Sweden, and biomarkers such as dopamine transporter single-photon emission computed tomography is not available at all centers. Symptoms of DLB and AD overlap, which leads to difficulties in the diagnostic process. Autopsy diagnosis is currently not available but many patients are followed longitudinally, which probably improves diagnostic accuracy. Linking SveDem to autopsy records in future could help assess the accuracy of the clinical diagnoses.

Our study benefits from one of the largest samples of DLB patients in the world. Most of the previous studies have focused either on a single or a small number of comorbidities, while we compared the entire comorbidity profile. Using the exact date of registration for each comorbidity and dementia, we had access to the consecutive timing of the events in order to determine whether comorbidities occurred either before or after dementia diagnosis. Both SveDem and the Swedish National Patient Registry have just a minute proportion of missing values.

The personal registration number makes it possible to follow each individual over time and to connect corresponding information from different registries in Sweden. The number of hospital stays with missing personal registration numbers in the inpatient registry was only 0.6% in 2006 [53].

Conclusions

Our study indicated a worse comorbidity profile in DLB patients, with a higher prevalence of depression, stroke and migraine, compared with the AD population. Deeper knowledge about these differences among the DLB and AD groups is needed. Future studies could explore whether the presented associations are due to different mechanisms of these disorders as well as studying their influence on diagnostics and care.

Abbreviations

AD: Alzheimer’s disease; CI: confidence interval; DLB: dementia with Lewy bodies; ICD: International Classification of Diseases; MMSE: Mini-Mental State Examination; OR: odds ratio; SD: standard deviation; SveDem: Swedish Dementia Registry.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

S-MF was involved in the conception, design and acquisition of data and carried out analysis, interpreted the results and wrote the manuscript. SD contributed to the conception and carried out data mining, analysis and writing of the manuscript. PD participated in the interpretation of the findings, writing of the manuscript and substantial contribution to its content. DA participated in the interpretation of the findings and revised the manuscript critically for important intellectual content. ME conceived of the study, and contributed to its design and coordination and to critical improvement of the manuscript. DR made substantial contributions to conception, design and acquisition of data, participated in the interpretation of the findings and revised the manuscript critically. All authors read and approved the final manuscript.

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Author details

1Division of Clinical Geriatrics, Department of Neurobiology, Care, Sciences, and Society, Center for Alzheimer Research, Karolinska Institutet, Stockholm, Sweden. 2Division of Neurogeriatrics, Department of Neurobiology, Care, Sciences, and Society, Center for Alzheimer Research, Karolinska Institutet, Stockholm, Sweden. 3International Clinical Research Center and St. Anne’s University Hospital, Brno, Czech Republic. 4Centre for Age-Related Diseases, Stavanger University Hospital, Stavanger, Norway. 5Department of Geriatric Medicine, Karolinska University Hospital, Stockholm, Sweden.

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