BMJ Open

Survival among the older adults with clinical signs of Lewy body dementia in 40 Swedish nursing homes: a 6-year follow-up study

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ABSTRACT

Objectives To investigate survival among elderly residents of Swedish nursing homes (NHs), with specific focus on those with two or more signs of Lewy body dementia (LBD).

Design Prospective observational study.

Setting NHs in Malmö, the third largest city in Sweden.

Participants The study population was older adults (aged ≥65 years) living in the 40 NHs in Malmö. Clinical data were collected with a customised questionnaire assessing core clinical LBD signs. Patients were categorised based on 0–1 or 2–4 LBD signs. The head nurse at each NH collected the study data: LBD questionnaires, electronic medication lists and electronic medical records from 2012 to 2013.

Main outcome measures 80-month mortality.

Results Five hundred and fifty-eight (96%) of the residents were deceased at follow-up; among these, mean (95% CI) overall survival time was 29 (28–31) months. Mean survival differed between the LBD groups; those with 0–1 LBD signs lived 8 months longer than those with 2–4 LBD signs. Mortality risk for residents in the LBD 2–4 group was also significantly higher. HR adjusted for age and sex was HR (95% CI) 1.60 (1.30 to 1.97). Mortality risk was also significantly higher in residents with signs of fluctuating cognition 1.36 (1.15 to 1.62), rapid eye movement sleep behaviour disorder 1.49 (1.11 to 1.98), balance problems 1.36 (1.14 to 1.61) or rigidity 1.41 (1.18 to 1.68).

Conclusions This large, longitudinal study shows the important survival effects of identifying and diagnosing older adults NH residents who have two or more LBD signs.

Strenghts and limitations of this study

► Complete coverage of all 40 nursing homes (NHs) in a relatively large geographic region.
► A strength of this study was that it investigated all NHs in a large Swedish city with data from 96% of the residents, including observational data, electronic medical and medication records.
► A long follow-up of 6 years is a strength of this study.
► No formal Lewy body dementia (LBD) diagnoses were made within the present study. However, data on existing LBD diagnoses were collected from the computerised medical records.
► A limitation is the cross-sectional nature of the initial data collection. In addition, the participants were at different stages of their disease and data on severity of dementia, comorbidity and function was lacking.

BACKGROUND

Dementia is one of the most common diagnoses among the older adults; it contributes to major disabilities and is followed, in many cases, by a relatively rapid onset of need for nursing care and even nursing home (NH) admission.[1 2]

Today, over 35 million people live with dementia—a number expected to double every 20 years.[3 4] The majority of these patients suffer from Alzheimer's disease (AD), followed by vascular dementia and Lewy body dementia (LBD); dementia with Lewy bodies (DLB) and Parkinson disease dementia.[5] These dementia diseases cause clinical symptoms that may be difficult to differentiate.[5–7]

Individuals with LBD have a more rapid and aggressive course of dementia, especially if they also have AD pathology with difficult symptomatology and core signs (according to the 2017 LBD criteria) such as visual hallucinations, parkinsonism, fluctuating cognition and rapid eye movement sleep behaviour disorder (RBD).[8–10]

Furthermore, according to Muller *et al* some prognostic factors may be the increased prevalence and early emergence of neuropsychiatric symptoms (NPSs) in LBD patients.[11]

These patients' neuroleptic sensitivity is also important to consider; this condition is due to a failure to upregulate dopamine D2 receptors or reduced dopaminergic innervation after treatment with antipsychotics.[12]

Studies of the epidemiological prevalence of LBD are scarce, most likely because this condition presents a challenging psychological and neurological symptom profile and is

not generally well understood among medical staff across specialities, including primary care.[7 13] NPSs with a prevalence of >80%, such as agitation, aggression, hallucinations, depression and apathy, are common in dementia NHs.[14 15]

Treatment of NPSs is divided into pharmacological and non-pharmacological strategies, with growing encouragement from professional organisations such as the European Medicines Agency and the Swedish National Board of Health and Welfare (NBHW), as well as opinion-leading clinical research groups, for the use of non-pharmacological treatments.[16–21]

Unfortunately, pharmacological treatments for NPSs consist of different antipsychotic medication, which lead to adverse reactions and events including extrapyramidal symptoms, rigidity, higher risk for cerebral vascular insults, further cognitive decline, orthostatism and shorter survival.[22–26] It is of note that some of these effects are also a part of the LBD symptom profile.

However, clinicopathological studies of LBD have shown an association between visual hallucinations and a cholinergic innervation deficit explaining potential benefits of cholinesterase inhibitor treatment in LBD individuals who also suffer from visual hallucinations.[27–30]

The study aim were to determine the survival rates and duration among the older adults living with dementia in NHs in the third largest Swedish city, in relation to core LBD signs. Our hypothesis was that survival in older adults in NHs is influenced by the LBD and thereby possibly of the reported clinical signs of LBD.

METHODS
Study design
The study was designed to include all NH residents in Malmö, Sweden's third largest city with over 320 000 inhabitants. This study is a cross-sectional study with data used according to the official registry, there were 40 dementia NHs in Malmö during the study period (2012–2013), all of which were included. The participants were at different stages of their diseases.

The study population was all residents aged ≥65 years whose core LBD signs, electronic hospital records and electronic medication lists were available during 2012–2013 (figure 1). Date of death, used to analyse survival, was collected 6 years after the study was begun (January 2012–August 2018).

Procedures
The main source of clinical data was a questionnaire specifically designed to assess clinical signs of LBD. This questionnaire was compatible with the clinical consensus DLB criteria at the time and with the diagnostic form LBD diagnostic symptoms by the Lewy Body Dementia Association.[31 32] We chose four main LBD signs, which are equivalent to the four core clinical criteria in the recently updated DLB consortium report.[8]
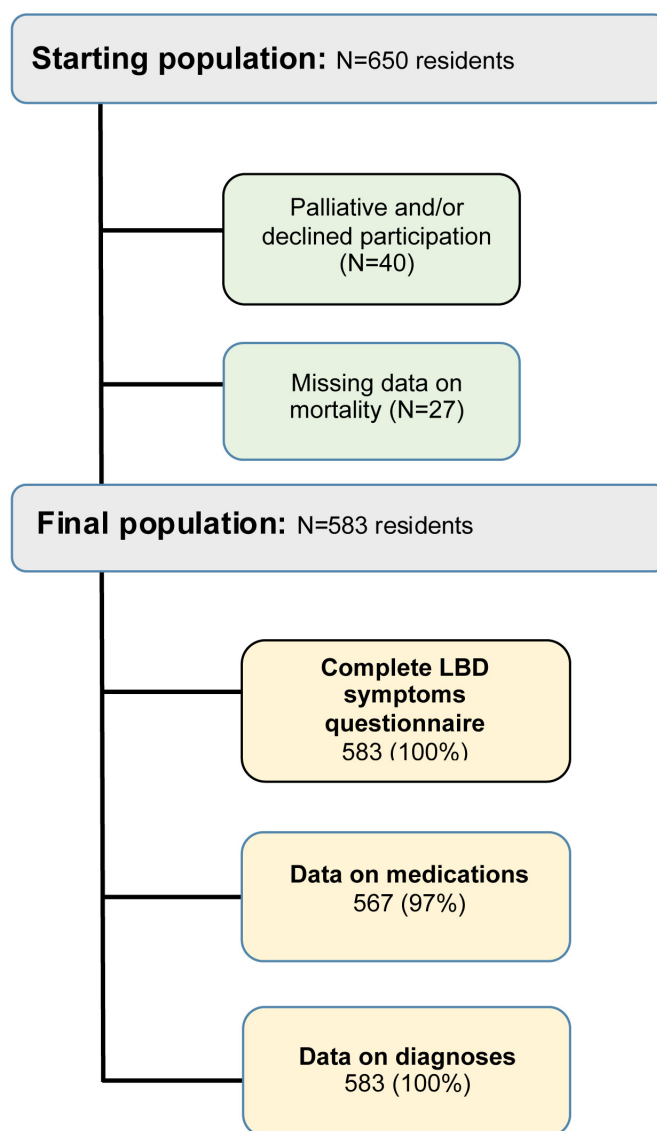

Figure 1 Flowchart of the study population from 40 nursing homes presenting the specific size of the collected data. Age: ≥65 years. LDB, Lewy body dementia; N, number.

The nursing staff at each NH collected data at their institution. Swedish NH staff usually include a physician, a head nurse and several assistant nurses who care for an average of 15 residents. A seminar on the study for staff members at each NH was held and was led by a physician and study author (IZ). The seminar included information and instructions about scoring the presence/absence of clinical LBD signs: LBD 0–1; zero or one core sign of LBD, LBD 2–4: two more signs of LBD (parkinsonism, visual hallucinations, fluctuating cognition and RBD). A more detailed description of the questionnaire has been previously published.[33]

The head nurse completed the study questionnaires and collected each resident's computerised medical record and medication list from the Swedish National Medication Dispensing System (NMDS).

Dementia diagnoses are usually made by a physician from primary care, who is also responsible for most NH

residents' treatments. We must presume that the dementia diagnoses collected for this study were made according to a 'basal dementia investigation', in accordance with the Swedish NBHW.[34] The basal dementia investigation consists of cognitive testing, relevant laboratory tests, CT and/or MRI (evaluated by a radiologist) and a structured anamnestic interview of the patient and/or family members by the physician.

The first diagnostic level determines whether dementia is present and at the second level, the etiological dementia diagnosis is specified. In our study, formal etiological diagnoses were found from computerised medical records in 433 (74%); dementia None - other specified (NOS) (27%), AD (27%), AD-mix (22%), vascular dementia (VaD) (19%) and DLB/PDD (5%).

Swedish NHs are conducted by the municipality and for a NH placement they require that elderly have dementia at the first or second diagnostic level.

Medical data

Collection of data from the NMDS included formal dementia diagnosis (yes/no), treatment information and deceased patients' dates of death.[35] The Anatomical Therapeutic Chemical (ATC) Classification System was used to categorise medication antipsychotics (N05A) and antidementia medicines (N06D). We initially intended to analyse survival effects of medication (antidementia and antipsychotics) but decided not to due to inadequate power and the cross-sectional nature of the data collection.

Patient and public involvement

Patients were not involved in the design of the study. However, the patients were involved in the study in the sense that they gave their informed consent to participate.

Statistical analysis

For statistical analyses, we used IBM SPSS for Windows V.22.0.

NH residents were divided into dichotomous groups: according to number of LBD signs (0–1/2–4). Data are presented as mean (95% CI) unless otherwise noted. Kaplan-Meyer curves were constructed to show the survival distribution for all residents and log rank tests were used to compare survival between groups. Multivariate Cox regression analysis was performed to identify possible covariates of survival. In the Cox regression analysis, we controlled for age and sex. A $p < 0.05$ was considered statistically significant.

RESULTS

Study population characteristics are presented in table 1. All patients had dementia at the first diagnostic level 558 (100%) and 433 (74%) had a formal dementia diagnosis (second diagnostic level) registered in the electronic data system. These were our available data. Survival data were collected 6 years after the study was initiated (January 2012–August 2018), at which time 558 (96%) of the residents were deceased. Among the deceased residents, mean survival time was 29 (28–31) months. In an earlier study of the same population, we reported that 20% of the residents had 2–4 LBD core signs.[33]

Twenty-one per cent of the residents were treated with antipsychotics and 33% with antidementia medication (table 1).

Survival based on LBD group

The mean survival time differed between the LBD groups, with residents in LBD 2–4 living 8 months shorter than those with LBD 0–1 (p=0.0004).

Table 1 Demographics

	Study population
	N (%), 583 (100)
Deceased*	558 (96)
Sex, female	444 (76)
Age, years, ≥86	333 (57)
Formal dementia diagnosis†	433 (100)
Dementia NOS	115 (27)
Alzheimer	115 (27)
Alzheimer-mix	96 (22)
Vascular dementia	85 (19)
DLB/PDD	22 (5)
Study groups‡	583 (100)
LBD 0–1	467 (80)
LBD 2–4	116 (20)
Clinical LBD signs§	
Parkinsonism	39 (7)
Fluctuating cognition	214 (37)
Visual hallucinations	118 (20)
RBD	52 (9)
Balance problems	233 (40)
Rigidity	182 (31)
Medication¶	
Antipsychotics	122 (21)
Antidementia medicine	185 (33)

*All residents who were deceased after 80 months from study start.
†Formal dementia diagnosis according to basal guidelines for dementia investigation from the Swedish NBHW, second level where residents had a formal etiological diagnosis 433/583 (74%).
‡LBD 0–1: zero or one sign of LBD, LBD 2–4: two or more signs of LBD.
§Clinical LBD signs according to the study questionnaire.
¶Medication according to ATC coding: antipsychotics (ATC: N05A) and antidementia medication (ATC: N06D). Existing data on medication 567 (100%).
ATC, Anatomical Therapeutic Chemical Classification System; LBD, Lewy body dementia; NBHW, National Board of Health and Welfare.
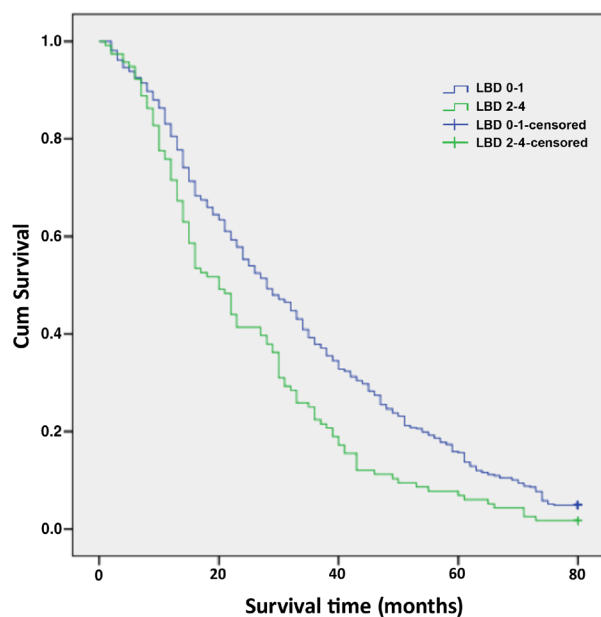
Figure 2 Kaplan-Meier survival curves comparing survival among elderly residents with LBD 0–1 and LBD 2–4 signs. Kaplan-Meier estimates of 80-month survival time from reported time of onset for the two groups (LBD 0–1 and LBD 2–4). Log rank X^2 (df=1, n=583)=14.8, p=0.0001. LBD; Lewy body dementia.

Mortality risk for residents in the LBD 2–4 group was also significantly higher, as shown in the Kaplan-Meier graph in figure 2.

Survival in relation to LBD signs

Examining LBD signs from the study questionnaire, we found that mortality risk was significantly higher among residents with signs of fluctuating cognition, RBD, balance problems and stiffness (table 2).

DISCUSSION

In this NH population-based study, we identified that having two or more core LBD signs was associated with a significant reduction in survival time. Several studies have shown a more rapid decline, lower quality of life

(QoL) and more intensive medical and nursing care needs in LBD patients.[36–38] Our residents did not have formal LBD diagnoses; rather, they were divided into groups based on their number of LBD signs, as reported by NH personnel, and thus may not be comparable to previous studies.

The NH patients in our study with 2–4 LBD signs had increased mortality risk and shorter life expectancy (table 3, figure 2). Therefore, we suggest increased number of LBD signs, as a marker of the severity of the underlying pathophysiology (alfa-synuclein, Lewy bodies and Lewy neurites).

This is in accordance with a neuropathological study by Fujishiro et al[39] showing increased alfa-synuclein pathology with increasing number of LBD core symptoms. In this study, the core symptoms of the consensus criteria from 2005 (parkinsonism, visual hallucinations, fluctuating alertness/cognition) were used complemented with RBD, the same signs which we used in our study.

The fact that the prevalence of LBD signs was the strongest predictive factor for survival suggests that more than the formally LBD diagnosed 5% of the NH residents might have undiagnosed LBD.

A recent study by Savica et al[40] also showed shorter survival among those diagnosed with LBD, among whom death occurred 4 years earlier (based on date of diagnosis), at a median age of 77 years, compared with an age-matched and sex-matched general population group.

Herein, we have found a significantly shorter mean survival time, by 8 months timed from the beginning of the study period, among patients with 2–4 LBD signs. This finding was within a population with a high median age of 87 years, who were thus likely to be at the end stages of their lives.

We also found that the LBD signs of fluctuating cognition, RBD, balance problems and rigidity predicted a significantly shortened life expectancy (table 2). It is, however, hard to make conclusions on the survival effect of these signs without further adjustment for, for example, level of cognitive impairment or comorbidity.

Jellinger et al[41] studied predictors of survival among DLB patients and found similar results in which fluctuating

Table 2 Mortality risk based on clinical signs				
	HR (95% CI)			
Clinical signs from the questionnaire	**Model 1 (crude estimates)**	**P value**	**Model 2 (estimates adjusted for age and sex)**	**P value**
Parkinsonism (no*, yes)	1.20 (0.86 to 1.66)	0.280	1.41 (1.01 to 1.95)	0.043
Fluctuating cognition (no*, yes)	1.36 (1.15 to 1.62)	0.0004	1.35 (1.13 to 1.60)	0.001
Visual hallucinations (no*, yes)	1.10 (0.90 to 1.36)	0.330	1.23 (0.99 to 1.52)	0.052
RBD (no*, yes)	1.49 (1.11 to 1.98)	0.007	1.65 (1.23 to 2.21)	0.001
Balance problems (no*, yes)	1.36 (1.14 to 1.61)	0.0005	1.31 (1.11 to 1.56)	0.002
Rigidity (no*, yes)	1.41 (1.18 to 1.68)	0.0002	1.45 (1.21 to 1.74)	<0.001

*Set reference value.
RBD, rapid eye movement sleep behaviour disorder.

Table 3 Mortality risk based on baseline variables and LBD groups

| | HR (95% CI) | | | |
	Model 1 (crude estimates)	P value	Model 2 (estimates adjusted for age and sex)	P value
Age, years	1.05 (1.03 to 1.06)	≤0.001	1.05 (1.03 to 1.06)	<0.001
Sex N (%) (male*, female)	0.94 (0.78 to 1.15)	0.560	0.80 (0.65 to 0.97)	0.024
LBD sign groups (LBD 0–1, LBD 2–4)	1.49 (1.21 to 1.83)	0.0002	1.60 (1.30 to 1.97)	<0.001

*Set reference value.
LBD, Lewy body dementia; LBD 0–1, zero or one sign of LBD; LBD 2–4, two or more signs of LBD.

cognition was a negative prognostic marker of shorter survival.

Several large studies have shown shorter survival times among residents with dementia treated with antipsychotics; all conclude by encouraging less use of psychotropics, which has also been a consistent message in important clinical guidelines.[16–18 20]

In addition, some have reported survival benefits of treatment with different antidementia medications and further studies are needed to demonstrate if this also is valid for NH populations.[27 42 43]

Our analyses of different antipsychotic and antidementia treatments were not conclusive in this study population of elderly NH patients due to insufficient power.

However, in our previous study, we showed that increased usage of antipsychotics was associated with an increased number of LBD signs.[33]

Strengths and limitations of this study

We identified residents with two or more LBD signs (based on core LBD symptoms described in consensus criteria) and categorised them as at risk for inappropriate treatment due to misdiagnosis.[8] A strength of this study was its large N, with data collected by nurses who followed a consistent questionnaire protocol and a long follow-up of 6 years (80 months). In addition, we used medical records across all 40 NHs with data from 96% of the residents, including observational data, electronic medical and medication records.

A limitation is the cross-sectional nature of the initial data collection. In addition, the participants were at different stages of their disease and data on severity of dementia, comorbidity and function was not possible to collect. Therefore, the Cox regression models were only adjusted for age and gender.

Although our use of a non-validated questionnaire may also be considered a limitation, over 90% (n=13) of the residents with a formal LBD diagnosis, according to computerised medical records, were categorised in the 2–4 LBD group, suggesting that the instrument has face validity.

CONCLUSIONS

The main study finding is that elderly NH patients with two or more LBD signs are at significantly increased mortality risk relative to other elderly NHs residents and therefore are important to identify. The identification of possible LBD is beneficial for a more appropriate medical treatment and nursing care and prevention of unnecessary hospital admissions.

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