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Causes and outcomes of hospitalization in Lewy body dementia: A retrospective cohort study

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ABSTRACT

Introduction: Understanding hospitalization in Lewy body dementia (LBD) is a known knowledge gap. We aimed to identify common causes, medication profiles, complications, and outcomes of hospitalization in LBD.

Methods: A retrospective cohort study investigated details of academic medical center hospitalizations over a two-year period for patients with LBD. Data collected included demographics, home medications, pre-hospital living status, reason for admission, admission service, inpatient medications, complications, and discharge status. Non-parametric statistics assessed associations between variables and length of stay. Odds of a change in living situation based on admission variables was calculated.

Results: The study included 178 hospitalizations (117 individuals). Neuropsychiatric symptoms were the most common admission reason (40%), followed by falls (24%) and infection (23%). Patients were usually admitted to medicine services; neurology or psychiatric consultations occurred less than 40% of the time. Antipsychotics were administered during 38% of hospitalizations. Use of antipsychotics other than quetiapine or clozapine was associated with longer length of stay and increased odds of discharge to a higher level of care. One-third of hospitalizations resulted in transition to a higher level of care; 15% ended in hospice care or death.

Conclusion: The most common reasons for hospitalization in LBD are potentially modifiable. Opportunities for improved care include increased involvement of neurological and psychiatric services, delirium prevention strategies, and reduced antipsychotic use. Clinicians should counsel patients and families that hospitalizations in LBD can be associated with end of life. Research is needed to identify strategies to prevent hospitalization and optimal standards for inpatient care.

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1. Introduction

Lewy body dementia (LBD) – the second most common neurodegenerative dementia following Alzheimer disease (AD) – consists of dementia with Lewy bodies and Parkinson disease (PD) dementia. Lack of data regarding hospitalization is a known knowledge gap [1]. Emergency room visits are common: in a survey of caregivers of individuals with LBD, 64% reported a crisis in the prior year and they sought help in a hospital emergency room 73% of the time [2].

Individuals with LBD, frontotemporal dementia, and unspecified dementia are at a higher risk of hospitalization than individuals with AD, vascular dementia, or mixed dementia, likely because neuropsychiatric symptoms are the main predictor of dementia hospital admissions [3]. Hospital admission rates are significantly higher for individuals with dementia with Lewy bodies compared to AD and a catchment population [4]. Individuals with dementia with Lewy bodies have longer hospital stays than those with AD [4–6] and overall higher costs of care [4,7]. In one study, the most common reason for admission for individuals with "parkinsonism-related dementia" was acute delirium (41%), followed by pneumonia (20%), stroke (19%), urinary tract infection (UTI) (7%), and fall-related hip fracture (3%) [6]. In another study, the most common hospital discharge diagnoses for individuals with dementia with Lewy bodies were infections (23%), falls (7%), circulatory illness (7%), dementia (6%), and senility/

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disorientation (5%) [4].

While little is known regarding hospital outcomes in LBD, hospitalization in PD is a known source of worsened function [8]. Hospitalization of individuals with AD is associated with increased risks of death and institutionalization, with hospital delirium associated with even higher risks of death, institutionalization, and cognitive decline [9]. Multiple studies show that individuals with AD experiencing delirium – often in the context of hospitalization – subsequently have faster cognitive progression [9–11] beyond what can be attributed to the pathology itself [12]. Given that over 40% of hospitalized individuals with dementia receive antipsychotics [13] and the morbidity and mortality associated with antipsychotic use in LBD [14,15], occurrence of hospital delirium in LBD likely carries additional risks of antipsychotic-induced complications.

To address knowledge gaps regarding LBD and hospitalization, we performed a retrospective cohort study to identify common causes, complications, medication profiles, and outcomes of hospitalization for individuals with LBD.

2. Methods

2.1. Study design

A retrospective cohort study investigated the causes, experiences, and outcomes of individuals with LBD hospitalized at an academic medical center over a two-year period (1/1/2014–12/31/2015). After institutional review board approval for the chart review (IRB201600391), an honest broker queried records for any hospitalization in the 2-year period including a diagnosis code for LBD (ICD-9 331.82, ICD-10 G31.83) in the admitting diagnoses or on the inpatient problem list.

During chart review, data was extracted from clinical notes and billing summaries in an electronic medical record (EPIC) using a REDCap [16] form that was pilot tested and refined by all co-investigators prior to use. Initial data extraction was performed by 3 investigators (CCS, AB, MJA) to ensure consistency in extraction. CCS and AB extracted the remainder of the charts under the oversight of MJA. Admission data collected included age, gender, medical history, dementia severity, disease duration, comorbidities, home medications, pre-hospital living status, reason for admission, admission service, inpatient medications, hospital complications, discharge status, and number of hospitalizations during the review period. Comorbidity burden was estimated using the Charlson Comorbidity Index (CCI) [17], a shared data instrument in the REDCap library. CCI scores range from 0 to 37 with higher scores indicating more comorbidities; additional points are added for each decade of life over 50. Higher scores predict an increased risk of death within 1 year of hospitalization [17]. Presence of comorbidities was assessed through the chart review. Reason for admission was determined from the admission history and physical documentation and admission and discharge ICD-9 and ICD-10 codes. Extractors selected the reason for admission from a menu (hallucinations or confusion, fall, failure to thrive/family unable to cope, infection, elective surgery, other planned admission, other) and provided additional details where relevant. Extractors also noted the ICD-9 and -10 codes associated with the admission (up to 3; codes were retrieved from the charts and not pre-specified). Multiple reasons for hospitalization were permitted. Patients were identified as having delirium (as a reason for admission or hospital complication) if they had new fluctuating cognitive changes and hallucinations during hospitalization or if their baseline symptoms were acutely worse.

2.2. Participants

Hospitalizations were included if a diagnosis code for LBD (ICD-9 331.82, ICD-10 G31.83) was associated with the inpatient stay. Charts were excluded if there was evidence of parkinsonisms other than LBD.

2.3. Statistical analysis

Baseline subject descriptive data were expressed as means ± standard deviations (SDs) or percents, as appropriate. If an individual had more than one hospitalization during the review period, information for baseline demographics was calculated using details from the first encounter. All other statistics were performed using hospital encounters, with a sensitivity analysis performed using first encounter only (Supplemental File). Length of stay was assessed using median, interquartile range (IQR), and range. The association between LOS and admitting diagnosis was assessed using the Kruskal-Wallis test, the correlations between age and CCI score with length of stay (LOS) were calculated using Spearman's rho, and the associations of gender, home use of medication for dementia (cholinesterase inhibitor, memantine), presence of delirium at admission, hospital complications (hospital delirium, falls, pneumonia) and antipsychotic use with LOS were assessed using Mann-Whitney *U*. The odds of a transition to a higher level of care post-hospitalization were calculated using 2x2 tables for dichotomous variables and binary logistic regression for age at admission and CCI score. Unadjusted odds ratio are presented with 95% confidence intervals (95% CI). Statistical analyses were performed using SPSS version 24 (Armonk, NY) except for 2x2 tables (performed using MedCalc®). Only univariate analyses were performed given the limited sample size and the preliminary nature of this analysis. A p-value of < 0.05 was considered significant.

3. Results

3.1. Demographic and clinical characteristics of participants

The search identified 178 hospitalizations meeting criteria representing 117 individual patients (Table 1). No record demonstrated evidence of a parkinsonism other than LBD. Of the 178 hospitalizations, 125 included diagnosis codes for Parkinson's disease (ICD-9 332.0 or ICD-10 G20) in addition to the codes used to identify individuals with LBD (ICD-9 331.82, ICD-10 G31.83). Eighty-one individuals had a single admission in the 2-year period and 36 individuals had multiple admissions (Table 1). Disease duration was available for only 45 individuals (median 4 years, range 0–24 years). Documentation was insufficient for reliable estimates of dementia severity. Prior to the 178 hospitalizations, 62% of individuals lived at home, 7% were in assisted living, 27% resided in a skilled nursing facility, 2% were at rehab, and 3% were at other or unknown locations (Fig. 1).

3.2. Hospitalization details

Hallucinations and confusion were the most common reasons for hospitalization (Table 2). Of the 2 individuals with 7–8 admissions, one had cancer with increasing complications and one had recurring UTIs complicated by delirium and other symptoms. For 21 (62%) of the 34 individuals with 2–4 admissions, every admission was due to LBD-related symptoms (hallucinations/confusion, failure to thrive, falls, syncope), infection (UTIs, pneumonia, sepsis), or both. Eleven individuals had admissions for general medical concerns in addition to LBD- and infection-related hospitalizations. Two individuals had multiple admissions for medical conditions unrelated to infection or LBD. Hospital admission services included medicine (128, 72%), neurology (21, 12%), surgery (15, 8%), and intensive care (6, 3%). The majority of patients admitted to non-neurological services did not receive neurology or psychiatric consultations during hospitalization (Table 2).

Antipsychotic medications were administered during 68 of the 178 hospital admissions (38%), usually quetiapine (25% of admissions), followed by risperidone (7%), haloperidol (7%), and clozapine (2%). Antipsychotics were continued unchanged from home prescriptions in 35 hospitalizations (20%), started in 25 (14%), added/increased in 8 (5%), and reduced or omitted in 11 (6%). In the 25 hospitalizations

Table 1
Characteristics of hospitalized patients with a diagnosis code for Lewy body dementia.

Variable[a]	Value (n = 117)
Age (years) (mean [SD, range])	78 (8, 58–97)
Sex (n, % male)	69 (59%)
Number of admissions in the 2-year period	
1	81 (69%)
2	23 (20%)
3	10 (9%)
4	1 (1%)
7	1 (1%)
8	1 (1%)
Charlson Comorbidity Index score (mean [SD])	6 (2)
Antipsychotics: home medications at admission[b]	41 (35%)
Quetiapine	19 (16%)
Risperidone	9 (8%)
Aripiprazole	4 (3%)
Haloperidol	3 (3%)
Olanzapine	3 (3%)
Clozapine	2 (2%)
Anti-parkinsonian medications: home medications at admission[b]	
Carbidopa-levodopa immediate release	58 (50%)
Dopamine agonist	12 (10%)
Carbidopa-levodopa controlled release	5 (4%)
Entacapone	5 (4%)
Rasagiline	4 (3%)
Amantadine	2 (2%)
Cognitive enhancing medications: home medications at admission[b]	
Donepezil	30 (26%)
Memantine	19 (16%)
Rivastigmine	14 (12%)
Galantamine	1 (1%)
Benzodiazepines: home medications at admission[b]	
Clonazepam	14 (12%)
Lorazepam	8 (7%)
Alprazolam	6 (5%)
Diazepam	1 (1%)
Temazepam	1 (1%)
Anticholinergic medications: home medications at admission[b]	
Tolterodine	3 (3%)
Oxybutinin	3 (3%)
Benztropine	2 (2%)
Tricyclic antidepressant	2 (2%)
Trihexphenidyl	1 (1%)

[a] All statistics are the "n" and percent of the cohort unless otherwise noted.
[b] Subgroup medication values indicate use (yes/no) and are not mutually exclusive; some patients were prescribed more than one medication within a category.

where antipsychotics were started in patients not receiving them prior to admission, the most common choices were quetiapine (48%), haloperidol (32%), and risperidone (28%). Benzodiazepines were administered during 50 hospitalizations (28%), most commonly lorazepam (31, 17%). Anticholinergics were administered during 24 hospitalizations (13%), most commonly oxybutynin (8, 5%) and diphenhydramine (7, 4%).

3.3. Hospital outcomes: complications, length of stay, and discharge disposition

There were 134 recorded complications during the 178 hospitalizations (Table 2). Median LOS was 5 days (IQR 8, range 1–72 days). Reason for admission was not significantly associated with LOS ($p = 0.42$). Age (Spearman's correlation coefficient −0.060, $p = 0.43$), gender (median for males 4.0 [IQR 6] vs females 5.0 [IQR 5], $p = 0.28$), CCI score (Spearman's correlation coefficient −0.052, $p = 0.49$), and home use of medication for dementia (median for individuals taking anti-dementia medication 5.0 [IQR 4] vs not, 5.0 [IQR 5], $p = 0.53$) were not associated with LOS. LOS was longer for individuals with delirium present at admission (median 6 days [IQR 6] vs 3 days [IQR 5], $p = 0.002$) and those experiencing complications including delirium (6 days [IQR 6] vs 3 days [IQR 3], $p < 0.001$), in-hospital pneumonia (6 days [IQR 8] vs 4 days [IQR 5], $p = 0.007$), and in-hospital falls (8 days [IQR 13] vs 4 days [IQR 4], $p = 0.011$). Hospitalizations involving antipsychotic administration (any type) did not have a significantly longer LOS (median for individuals receiving any antipsychotic 6 days [IQR 7] vs not, 4 days [IQR 4], $p = 0.088$). However, hospitalizations involving administration of antipsychotics other than quetiapine or clozapine were longer than hospitalizations involving no antipsychotics or only quetiapine or clozapine use (median 7.5 days [IQR 9] vs. 4 days [IQR 4], $p = 0.001$). Results were similar when evaluating only first hospitalizations (Supplemental File).

One-third of hospitalizations (58/178) resulted in a transition to a higher level of care (Fig. 1); 15% (27/178) resulted in death or transition to hospice care. Only inpatient antipsychotic use other than quetiapine or clozapine was significantly associated with an increased odds of transition to a higher level of care, but confidence intervals were often too wide to exclude or confirm an important association (Table 3). Results were similar when using only first hospital encounters, but in that cohort, use of any antipsychotic was associated with an increased odds of transition to a higher level of care (OR 2.43, 95% CI 1.11–5.33) and the association with inpatient antipsychotics other than quetiapine and clozapine was of borderline significance (OR 2.44, 95% CI 0.98–6.12) (Supplemental File).

4. Discussion

This retrospective cohort study identified that hallucinations and confusion were the most common reasons for hospitalization for individuals with LBD, followed by falls and infection. Most patients (88%) were hospitalized on inpatient teams other than neurology and did not receive neurology or psychiatry consultations. Antipsychotic medications were administered during 38% of hospitalizations and these were new prescriptions or increased doses in 19% of hospitalizations. While quetiapine was the most commonly used antipsychotic, individuals with LBD also received other antipsychotics including haloperidol and risperidone. Inpatient use of antipsychotics other than quetiapine or clozapine was associated longer LOS and an increased odds of discharge to a higher level of care. Fifteen percent of the time, hospitalizations resulted in death or transition to hospice care.

The finding that delirium/confusion was the most common reason for hospitalization is consistent with a prior study reporting acute delirium as the most common reason for hospitalization in "parkinsonism-related dementia" (41%). The high rates of hospitalization for falls (24%) and infection (23%) were also largely consistent with prior findings of high rates of infection [4,6] and falls [4] in similar cohorts. Median LOS (5 days, IQR 8, range 1–72 days) was shorter than that described for a similar cohort (17.4 ± 16.5 days) [6] and less than estimated hospital days/year for this population (approximately 10 days/year) [4,5].

Unsurprisingly, almost half of hospitalizations in this cohort were complicated by delirium. Delirium has known overlap with LBD symptoms and may be a prodromal feature of dementia with Lewy bodies [18]. While this overlap makes assessment more challenging, it is critical to diagnose delirium in individuals with LBD to guide assessment and treatment [19]. Delirium was associated with a longer LOS in this study, consistent with other series of individuals with dementia linking delirium to longer hospital LOS and poorer functional outcomes [20,21]. Delirium was not associated with an increased odds of transition to a higher level of care, but precision was insufficient to exclude the possibility of an important effect.

Frequency of antipsychotic use in this cohort was similar to the 40% described for hospitalized patients with dementia in general [13]. Despite the known risk of antipsychotics [14,15], antipsychotics other than quetiapine and clozapine – those generally considered safest in LBD, though not without risks – were administered during 30 (17%) of reviewed hospitalizations. Consistent with findings in PD [22],

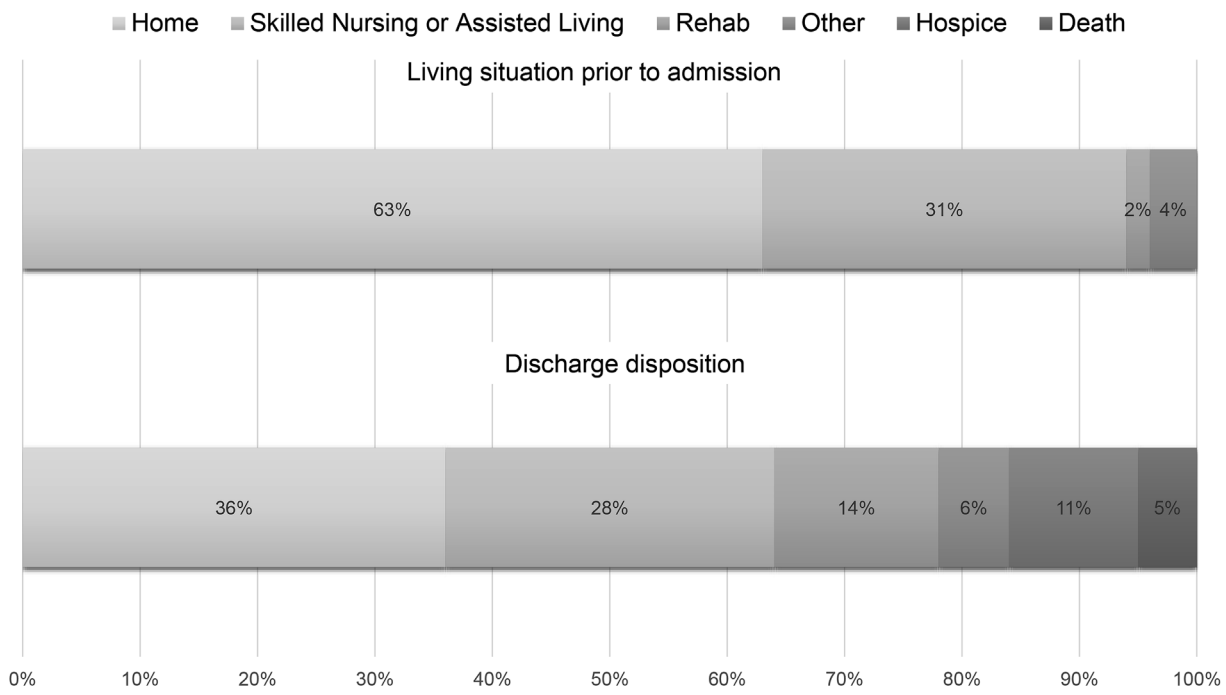

Fig. 1. Change in Living Situation from Baseline (Pre-Admission) to Discharge (n = 178). Caption: Graph demonstrates living situation prior to admission for each of the 178 reviewed hospitalizations and the discharge disposition after hospitalization.

Table 2
Characteristics of hospitalizations of individuals with Lewy body dementia.

Characteristic	N (%) (total n = 178)
Reason for hospital admission	
Hallucinations or confusion	71 (40%)
Falls	43 (24%)
Infection	41 (23%)
Urinary tract infection	19 (11%)
Pneumonia	12 (7%)
Sepsis	10 (6%)
Other infection	5 (3%)
Other	23 (13%)
Gastrointestinal disease	12 (7%)
Cardiac disease	11 (6%)
Respiratory illness	9 (5%)
Failure to thrive, failure to cope	9 (5%)
Genitourinary disorder	5 (3%)
Elective surgery	5 (3%)
Intracranial hemorrhage	4 (2%)
Planned admission (non-surgical)	3 (2%)
Syncope	2 (1%)
Stroke	2 (1%)
Neurology consultation[a]	44 (28%)
Psychiatry consultation[a]	14 (9%)
Neurology or psychiatry consultation[a]	50 (32%)
Hospital complications	
Delirium	88 (49%)
In-hospital pneumonia	30 (17%)
In-hospital fall	8 (5%)
In-hospital death	8 (5%)

[a] For admissions to services other than neurology inpatient (n = 157).

inpatient antipsychotic use other than quetiapine or clozapine was associated with a longer length of stay. Use of antipsychotics other than quetiapine or clozapine during hospitalization was also associated with an increased odds of discharge to a higher level of care. While these are associations and cannot prove causation, known risks of antipsychotic use include adverse reactions [14], additional cognitive decline in individuals with dementia [23], and higher mortality both in populations with PD [15] and dementia [24]. A recent analysis of causes of death in dementia with Lewy bodies reported antipsychotic administration as an immediate contributor in 1% of cases [25]. Antipsychotic use in the current cohort may reflect the fact that antipsychotics are preferred to other pharmacologic treatments for delirium in some circumstances [26] and most of the hospitalizations reviewed occurred on services other than neurology and without neurology or psychiatry input. Alternatively, antipsychotic use could reflect a higher disease severity in these individuals and the higher disease severity could be driving longer length of stay and need for increased levels of care.

A minority of the cohort reported cholinesterase inhibitor or memantine use at baseline. Use of medications for dementia was not associated with a shorter length of stay or a reduced odds of transition to a higher level of care, but precision was insufficient to exclude the possibility of an important effect. Given that hallucinations/confusion were the most common cause of hospital admissions in this cohort and that cholinesterase inhibitors may help neuropsychiatric symptoms in LBD [27], the potential effect of cholinesterase inhibitor use on hospitalization warrants exploration. There is currently no identified role for using cholinesterase inhibitors to treat delirium in older adults [28].

This study systematically investigated the experiences of hospitalized individuals with LBD over a two-year period and identified common reasons for admission, inpatient experiences, complications, and hospital outcomes. Study limitations include its retrospective approach, reliance on chart documentation, single center experience, and use of ICD-9 and -10 codes for the diagnosis of LBD (ICD-9 331.82, ICD-10 G31.83). These codes were chosen to emphasize the experiences of those with dementia with Lewy bodies but they can be used for LBD more generally. The diagnostic code F02.3 (dementia in Parkinson's disease or parkinsonism) was not included. Results may not be generalizable to individuals with unrecognized LBD. The relatively small sample size limited the ability to perform multivariable regressions to control for variables such as age and disease duration, a variable for which data was also largely lacking. Most statistical analyses were performed at the encounter level, so patients with different hospitalizations were included more than once, but a sensitivity analysis using only the initial hospitalizations in the date range showed similar results. Statistics reflect associations and do not imply causation; it may be that inpatient antipsychotic use reflected higher dementia severity or more complicated inpatient courses. The association is still of use, as it may

Table 3
Odd ratios of transition to a higher level of care post-hospitalization (n = 178).

Variable	Odds Ratio[a] (95% CI)
Age (per additional year)	1.00 (0.96, 1.03)
CCI score (per additional point)	0.95 (0.79, 1.14)
Male gender	0.98 (0.52, 1.84)
Home cholinesterase inhibitor use	1.22 (0.64, 2.33)
Home antipsychotic use (any)	1.68 (0.86, 3.27)
Home antipsychotic use other than quetiapine, clozapine (versus use of quetiapine, clozapine or no antipsychotic use)	2.02 (0.77, 5.28)
Experience of hospital complication	0.82 (0.44, 1.54)
Experience of hospital delirium	0.84 (0.45, 1.58)
Inpatient antipsychotic use (any)	1.87 (0.98, 3.54)
Inpatient antipsychotic use other than quetiapine, clozapine (versus use of quetiapine, clozapine, or no antipsychotic use)	2.41 (1.06, 5.47)

CCI: Charlson Comorbidity Index.
[a] Unadjusted odds ratios.

reflect an opportunity for improved care or identify patients at higher risk of longer or more complicated hospitalizations, regardless of underlying cause.

Our findings support prior studies suggesting that neuropsychiatric symptoms are a major driver of hospitalization in dementia in general [3] and LBD in particular [4]. While symptomatic care in LBD is challenging, the top two reasons for hospital admission in this study – neuropsychiatric symptoms and falls – are both potentially modifiable, suggesting that improved treatments could potentially reduce hospitalizations. Once patients are hospitalized, opportunities for improved care include increased involvement of neurological and psychiatric services, increased non-pharmacologic and multi-component strategies to prevent hospital-associated delirium [29], and reduced antipsychotic use, particularly for those antipsychotics associated with higher risks in LBD. Physicians providing inpatient care must be aware of the high frequency (15%) with which hospitalizations in LBD are associated with end-of-life, reflecting either inpatient death or transition to hospice, and counsel patients and families appropriately. Burdensome interventions such as hospitalization are common in the last 3 months of individuals with advanced dementia [30] and reducing hospitalization in individuals with LBD at the end of life represents an area for improvement.

Consistent with a recent call for further research regarding prognosis and hospitalization in dementia with Lewy bodies [1], this study highlights areas for improved care for individuals with LBD and the need for additional research regarding strategies to avoid hospitalization in this population, predictors of hospital outcomes, and standards for inpatient care.

Declaration of interest

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Author roles

CCS: Acquisition of data, analysis and interpretation of data, drafting and revising the article, final approval; AB: acquisition of data, analysis and interpretation of data, drafting and revising the article, final approval; EHM: analysis and interpretation of data, revising manuscript critically for important intellectual content, final approval; DMR: conception and design of the study, analysis and interpretation of data, revising article critically for important intellectual content, final approval; LA: conception and design of the study, analysis and interpretation of data, revising article critically for important intellectual content, final approval; MJA: conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content, final approval.

Declarations of interest

CCS: None.
AB: None.
EHM: None.
DMR: None.
LA: Dr. Almeida has received compensation from Medtronic as an educational consultant.

MJA: Dr. Armstrong receives compensation from the AAN for work as an evidence-based medicine methodology consultant and serves on the level of evidence editorial board for Neurology and related publications (uncompensated). She receives research support from ARHQ (K08HS24159), the Michael J. Fox Foundation, a 1Florida ADRC (AG047266) pilot grant, and as the local PI of a Lewy Body Dementia Association Research Center of Excellence. She receives royalties from the publication of the book Parkinson's Disease: Improving Patient Care and she has received honoraria for presenting at the AAN annual meeting (2017) and participating in Medscape CME.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.03.014.

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