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Neuropathological and clinical correlates of Lewy body disease survival by race and ethnicity in the National Alzheimer's Coordinating Center

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Abstract

BACKGROUND: Survival and associated clinical and pathological characteristics in Lewy body disease (LBD)-related dementias are understudied. Available studies focus primarily on white non-Hispanic samples.

OBJECTIVE: We investigated demographic, clinical, and pathological correlates of survival by race and ethnicity in an autopsy-confirmed cohort of LBD cases.

METHODS: Using National Alzheimer's Coordinating Center data, we selected participants who self-identified as Black, Hispanic, or white who had neuropathological assessments showing transitional or diffuse LBD pathology. We used Kruskal-Wallis and Pearson χ^2 analyses to investigate group differences in demographic and presenting clinical and pathological characteristics. We used linear regressions to identify predictors of survival with sex, age at symptom onset, education, ethnoracial status, LBD pathology type, and Braak tangle stage included in the model.

RESULTS: Data from 1441 white, 60 Black, and 54 Hispanic participants were available for analysis. Hispanics were more likely to have transitional LBD pathology and had a longer survival than white and Black participants. After controlling for demographic and pathological variables, length of survival did not differ between Hispanics and Black or white participants. Additional key findings demonstrated discrepancies between clinical diagnoses received at last visit and pathological findings, particularly among Black participants.

CONCLUSION: LBD survival differences by race and ethnicity can be accounted for by LBD pathology type and co-occurring Alzheimer's disease pathology. The discrepancies between clinical diagnoses and pathological findings raise concern that dementia with Lewy bodies is underdiagnosed in NACC, especially for Black older adults.

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Keywords

Lewy body disease; cognitive dysfunction; dementia; racial groups; ethnicity; neuropathology

INTRODUCTION

Older adults from marginalized racial and ethnic backgrounds are disproportionately affected by Alzheimer's disease (AD) [1, 2]. Some studies suggest that older adults from minoritized ethnic and racial backgrounds have longer disease duration than white adults, though these data are inconclusive. One study using data from the National Alzheimer's Coordinating Center (NACC) found that African Americans and Latinos with possible/probable AD had longer survival time than white participants despite controlling for age, sex, educational attainment, marital status, living situation, and cognitive test score at first evaluation [3]. A study with autopsy-confirmed AD cases from the Florida Autopsied Multi-Ethnic cohort found that Hispanics had longer disease duration (12 years) than white (9 years) and Black decendents (8 years) [4]. It is possible that survival differences across studies vary as a function of study design, selection bias, timing of diagnosis, comorbidity differences, or underlying sociocultural factors (e.g. lower rate of nursing home placement in minoritized communities). While the exact mechanism of these differences are unknown, racial health inequities are generally driven by intersecting environmental (e.g. access and quality of healthcare, socioeconomic status) and sociocultural factors (e.g., institutional racism, stress) accumulated across the life course that contribute to health conditions associated with increased AD and dementia risk (e.g., cardiovascular disease, diabetes) [1, 5]. Notably, understanding expected disease trajectory and duration has important implications for healthcare providers, patients and their families, and end of life planning.

Unfortunately, factors influencing disease trajectory and duration in non-AD dementias, such as Lewy body disease (LBD)-related dementia, are understudied and available studies focus primarily on white non-Hispanic samples. LBD is associated with aggregations of the alpha-synuclein protein [6] and is the second most common cause of neurodegenerative dementia after Alzheimer's disease (AD) [7, 8]. Clinical presentations of LBD include dementia with Lewy bodies and Parkinson disease with and without dementia. Compared to dementia due to AD, individuals with a clinical diagnosis of dementia with Lewy bodies have shorter survival (4.11 years vs. 5.66 years) [9]. Neuropathological factors associated with shorter disease duration include diffuse LBD pathology (compared to limbic "transitional" LBD), the presence of lacunar stroke, and AD co-pathology (amyloid plaques and tau neurofibrillary tangles) [10, 11]. In addition to shorter survival, co-existing AD and LBD pathology at autopsy is associated with earlier dementia onset [11]. Half of individuals with probable dementia with Lewy bodies and LBD pathology have AD co-pathology at autopsy and up to 60% of individuals with dementia with Lewy bodies have elevated Aβ on amyloid PET scans [12]. Up to 60% of individuals diagnosed with AD demonstrate LBD pathology concomitantly [11, 13]. According to some estimates, Black decedents with AD dementia may be more likely to present with mixed pathology (AD + LBD) than white decedents [14]. Although focused on AD and vascular dementia, a recent systematic review on neuropathology studies in non-Hispanic whites highlights that neuropathology studies

are limited and results are mixed, reflecting small sample sizes, heterogeneity within and across ethnic and racial groups, recruitment strategies, cohort inclusion/exclusion criteria, and center biases [15]. Despite the increasing attention to LBD risk factors and predictors of progression [16], as well as AD neuropathology research with U.S. minoritized ethnic and racial groups [15], critical gaps remain in understanding health disparities in LBD disease duration and clinicopathological correlates.

The purpose of the current study was to investigate survival length among Black/African American (B/AA), Hispanic/Latino (H/L), and white participants with autopsy-confirmed LBD within NACC. We also investigated demographic, clinical and pathological (i.e., diffuse vs. transitional LBD, AD co-pathology) correlates of survival, considering that whether the disease trajectory varies between ethnically and racially diverse individuals with LBD is unknown.

METHODS

Data source

Data were obtained from the NACC Neuropathology Data Set and Uniform Data Set for visits conducted from September 2005 to the December 2020 data freeze [17, 18]. NACC is composed of longitudinal data that comprised of over 40,000 participants at the time we received our file [17]. NACC recruitment and data collection has been described previously [17, 19–21]. Study approval was obtained from the Institutional Review Board (IRB) for each participating NACC site. According to the University of Washington Human Subjects Division, the NACC database is exempt from IRB review/approval because it does not meet criteria for human subjects research. The University of Florida IRB confirmed that the current analysis met exempt criteria (IRB202200252).

Participants

Participants were included in the current study if they 1) self-identified as Black/African American non-Hispanic (hereafter referred to as B/AA), white non-Hispanic (hereafter referred to as white), or H/L ethnicity and 2) had neuropathological assessments showing transitional or diffuse LBD pathology. Participants with amygdala-predominant or nigral-predominant LBD pathology were excluded from this study.

Clinical Assessment

Self/informant-reported demographic variables included age at initial and last visit, educational attainment, sex, primary reason for ADRC initial visit, and first-degree family member with cognitive impairment. Comorbidities included self/informant-report of recent or remote history of diabetes, stroke, hypertension, and hypercholesterolemia. NACC clinician-assessed variables included age at death and age when cognitive decline began, time from last visit to death, apolipoprotein E e4 (APOE- ε4) status along with presence of visual hallucinations, cognitive fluctuations, and REM Sleep Disorder (RBD) at last study visit. Survival from cognitive onset was calculated using age of symptom onset subtracted from the age of death.

Cognitive functioning at last study visit was evaluated using the CDR® Dementia Staging Instrument [22] Sum of Boxes score (0–18). Cognitive status (normal, impaired-not-Mild Cognitive Impairment [MCI], MCI, and dementia) at the last visit before death was extracted from the NACC UDS clinician diagnosis form. NACC describes individuals without dementia who are cognitively impaired but do not meet criteria for MCI as "impaired-not-MCI." For each participant we noted the NACC primary and contributing diagnoses of AD, LBD, and Parkinson's disease (a subset of LBD).

Post-mortem Pathological Evaluation

We used the fourth Dementia with Lewy Bodies Consortium consensus report to assess the effects of co-existing LBD-AD pathology [23, 24]. This approach uses Braak neurofibrillary tangles (NFT) degeneration stages [25] in conjunction with LBD pathology (i.e. diffuse or transitional) to estimate the likelihood that the pathological findings were associated with a typical dementia with Lewy bodies syndrome during life. A typical dementia with Lewy bodies syndrome is characterized by progressive cognitive dysfunction interfering with daily activities (i.e., attention, executive function, and visual processing deficits relative to memory and naming) and core clinical features (e.g., fluctuations, visual hallucinations, parkinsonism, REM sleep behavior disorder) with or without accompanying indicative biomarkers [23]. In line with these criteria [23], low-likelihood of dementia with Lewy bodies was categorized by the presence of transitional Lewy pathology and Braak NFT stage V-VI. Intermediate likelihood of dementia with Lewy bodies was categorized by 1) transitional Lewy pathology and Braak NFT stage III-IV, or 2) diffuse Lewy pathology and Braak NFT stage V-VI. Diffuse or transitional LBD pathology in combination with Braak NFT stage 0-II was characterized as high-likelihood of dementia with Lewy bodies. Vascular co-pathology was extracted using NACC derived variables for the presence of one or more vascular pathology present, as well as presence for hemorrhages/microbleeds and infarcts/lacunes.

Statistical analyses

We summarized continuous and categorical variables with medians (with full ranges) and proportions, respectively. For between-group comparison of demographic and clinical variables, we used Kruskal-Wallis analyses and Pearson χ^2 analyses. Significant main effects were adjusted for multiple comparisons using Bonferroni correction.

We used hierarchical linear regressions to investigate group differences in survival (i.e., time from symptom onset to death). Survival was adjusted for sex (reference group: male), age at symptom onset, education (continuous), and ethnoracial status (reference group: H/L). LBD pathology type (reference group: transitional) and Braak NFT stage (reference group: low) were added as predictors in a second model. Normality in survival was achieved after the removal of 12 outliers (values 3 standard deviations from the mean; 1 B/AA, 3 H/L; 8 white participants) and a Blom transformation [26]. Multicollinearity was checked for all study variables by using correlations, tolerances, and variance inflation factors (VIF). Correlations were sufficiently low, tolerance scores were greater than 0.1, and VIF scores were below 2. All statistical analyses were performed using R. Alpha was set at $p \leq 0.05$.

RESULTS

Sample characteristics

Data from 1441 white, 60 B/AA, and 54 H/L participants from 36 Alzheimer's Disease Research Centers (ADRC) were available for analysis. Demographic characteristics for the entire sample and each ethnoracial cohort are listed in Table 1. B/AA participants were more likely to be female than white participants. White participants had more years of education relative to B/AA and H/L participants. Approximately 81% of B/AA participants reported history of hypertension compared to 51% of white and 57% of H/L participants. Diabetes was more common among H/L participants relative to white participants (26.2% vs. 9.7%). B/AA participants were more likely to present with an APOE- ε4 allele (74.5%) compared to H/L (45.5%) and white (55.9%) participants. Group differences in median age at onset were not statistically significant (p=0.06).

Clinical findings

Most participants were considered to have dementia at their last study visit (Table 2). Cognitive severity staging was highest for H/L compared to white participants. After excluding participants with normal cognition at their last study visit (i.e., focusing on individuals diagnosed with cognitive impairment), most participants received an AD clinician-diagnosis. AD was more commonly the primary cause of cognitive impairment for H/L and B/AA participants compared to white participants. B/AA participants were less likely to have a clinical diagnosis of LBD as the primary cause of cognitive impairment, particularly when compared to white participants. The frequency of visual hallucinations (χ^2 (2) = 2.849, p = .241), delusions (χ^2 (2) = 3.375, p = .185), and REM sleep disorder (χ^2 (2) = 5.406, p = .067) at last visit was not significantly different between groups. Median survival for the full cohort was 9 years (full range 0–31). Despite similar median ages at initial visit, onset of symptoms, and death, H/L participants had significantly longer survival (median 14 years, full range 3–28 years) compared to white (median 9 years, full range 0–31 years) and B/AA (9 years, full range 2–25 years) participants.

Pathology Findings

Diffuse LBD pathology was more common among B/AA than white and H/L participants (Table 3). In contrast, H/L participants were more likely to have transitional LBD pathology compared to white and B/AA participants. Overall, few participants had low Braak NFT staging, especially B/AA participants (0%) compared to white participants (13.2%). High Braak NFT staging was common (66.2%). Roughly a quarter of the total sample had a high likelihood of a typical dementia with Lewy bodies syndrome (Table 3). A greater proportion of H/L participants had a low likelihood for meeting criteria for a typical dementia with Lewy bodies syndrome compared to white and B/AA participants. Frequency of intermediate likelihood of a dementia with Lewy bodies syndrome was similar among B/AA and white participants. While most participants demonstrated one or more type of vascular co-pathology, specific patterns emerged among B/AA and H/L participants. Hemorrhages/microbleeds were most commonly observed in H/L participants compared to white participants, while infarcts/lacunes were most common among B/AA participants.

Variables Associated with Survival

Regression model results are summarized in Table 4. Model 1 accounted for roughly 10% of the variance in survival. Younger age of onset and female sex were associated with longer survival. H/L participants had significantly longer survival than white and B/AA participants, respectively. In Model 2, LBD pathology and Braak staging were added as predictors of survival. Results of Model 2 showed that age at onset and sex remained statistically significant. Adding LBD pathology and Braak staging increased the amount of variance explained by the model by 4%. After adjusting for Braak staging and demographic variables, diffuse pathology was associated with a significantly shorter survival. Compared to those with low Braak NFT staging, survival was significantly longer for those with high Braak NFT staging. After controlling for demographic and pathological variables, H/L no longer had significantly longer survival than B/AA or white participants.

DISCUSSION

Summary of Key Findings

In the present study, we used NACC data to investigate demographic, clinical, and neuropathological characteristics in H/L, B/AA, and white participants with autopsy-confirmed LBD. Approximately 94% of the sample had a dementia diagnosis at last follow-up. Whereas only 28.6% of the sample had a primary or contributing clinical LBD diagnosis at their last visit, 61% had pathological post-mortem findings that suggested an intermediate- to high-likelihood of a typical dementia with Lewy bodies presentation during life. H/L participants had the highest frequency of transitional LBD pathology. Only 15% of B/AA participants received a clinical diagnosis of LBD as a primary or contributing cause of their dementia syndrome (versus 30.4% white). Yet 70% of B/AA had an intermediate to high likelihood of a typical dementia with Lewy bodies presentation per pathological findings (versus 40.8% H/L). The discrepancies between clinical diagnoses and pathological findings raise the possibility that dementia with Lewy bodies was underdiagnosed across all groups, but especially for B/AA older adults. In a model accounting for approximately 10% of survival variance, younger age of onset and female sex were associated with longer survival and H/L participants had longer survival versus white and B/AA populations. After controlling for demographic and neuropathological variables, survival did not differ between racial-ethnic groups.

Survival in Individuals with LBD from Diverse Backgrounds

H/L participants had a longer unadjusted survival from symptom onset to death than white and B/AA participants and had significantly worse cognitive severity staging at their last visit compared to white participants. Survival remained significantly longer for H/L compared to white and B/AA participants after accounting for sex, age at cognitive symptom onset, and educational attainment. Prior research using NACC identified that in individuals with dementia due to LBD, H/L ethnicity was associated with longer survival. That study used a clinical cohort, however, without pathologic confirmation or variables [27]. Several other studies consistently show that individuals identifying as H/L have longer survival than individuals identifying as B/AA or white in the context of dementia generally [28, 29] or AD [4]. Similar findings are described in Parkinson disease, where individuals who were women

and identified as Hispanic or Asian had longer survival than white men [30]. In our analysis, however, the longer survival of individuals identifying as H/L became non-significant once adjusting for LBD and AD pathology. Given that H/L had a higher frequency of transitional LBD pathology compared to white and B/AA participants, it is not surprising survival was longer among H/L since diffuse LBD pathology is associated with shorter survival time compared to transitional LBD pathology [10]. Why H/L participants in the current cohort had different pathology, though, remains uncertain. It is possible recruitment biases relating to the focus of ADRC sites recruiting H/L populations accounts for some portion of the finding, but differences in the progression of underlying neuropathological disease process cannot be excluded. Our findings highlight the importance of including pathological data to explain group differences that might otherwise go unexplained, particularly when cohorts are derived from a clinical diagnosis. Findings also underscore the importance of additional research to investigate differences in Lewy body dementia pathology between racial-ethnic groups.

Other predictors of longer survival in the current study are consistent with prior findings, including younger age at cognitive symptom onset and female sex [10, 31]. The finding of longer survival with high AD pathology (i.e., Braak NFT stage) is somewhat surprising and may reflect cohort selection and the complex interaction of clinical and pathological considerations in LBD and AD. Prior studies have found that individuals with probable dementia with Lewy bodies and AD pathology have a higher mortality risk than individuals with probable dementia with Lewy bodies without positive AD biomarkers [32]. However, a study published in 2016 using NACC and a pathologically-defined LBD cohort did not find an association between survival and Braak staging after adjusting for age at onset, sex, and APOE-ε4 [10]. Differences between the 2016 study and the present study include a much larger sample size (1525 vs. 807) and a larger percentage of individuals with transitional LBD (51.8% vs. 42.6%) in the present study. Whether these differences account for contrasting results is unknown. It is possible that some of the included cases in the current study reflected a more AD-like picture with comorbid LBD rather than a Lewy body dementia picture with comorbid AD. In this circumstance, the finding that more AD pathology was associated with longer survival may reflect the fact that individuals with AD have a decreased risk of mortality and longer survival when compared to individuals with pathologically-defined Lewy body dementia [33].

Demographic and Health Differences between Cohorts

Our results are consistent with prior studies demonstrating health disparities in ethnically and racially minoritized communities, including lower educational attainment and more cardiovascular disease risk factors in B/AA and H/L than white older adults [34–36]. Regarding vascular co-pathology, consistent with our results, prior studies show that microbleeds and lacunar infarctions are more common among B/AA and H/L than white individuals [37–39], with hypertension being one of the most frequent risk factors [39]. We also found that B/AA participants were more likely to present with an APOE-ε4 allele compared to H/L and white participants, which is consistent with prior studies [34]. Although results are inconclusive, some data suggest that APOE-ε4 is a stronger risk factor for AD in white compared to B/AA samples [40, 41]. More work is needed to recruit larger,

more diverse cohorts to analyze how co-pathology, as well as cardiovascular disease and genetic risk factors interact with LBD pathology across different race-ethnic groups.

Sex differences dramatically varied by ethnoracial background, with females representing approximately 57% of the B/AA cohort relative to 37% of H/L and 38% of the white cohort. We previously found that B/AA and H/L were more likely to be female compared to white participants using NACC data from a clinician-diagnosed LBD sample [42]. Our findings contrast from clinical and pathological LBD cohorts with predominantly white populations that describe LBD as more common in males than females [7, 43]. Given the high proportion of AD co-pathology in our sample, it is possible that our findings are influenced by the inclusion of all cases with neuropathological assessments showing transitional or diffuse LBD pathology, irrespective of co-pathology (i.e. AD pathology). Additionally, higher prevalence of females among the B/AA cohort may reflect the commonly encountered sampling bias in AD/ADRD research where males from minoritized communities are underrepresented. While several factors may be influencing observed sex differences in the NACC, identifying contributors is limited by the underrepresentation of racially/ethnically minoritized communities in dementia research in general, particularly among non-AD subtypes, such as LBD.

Clinical-Pathological Differences Between Cohorts

We found significant diagnostic evaluation differences, particularly among B/AA participants. B/AA participants were less likely to receive a clinical diagnosis of LBD at their last visit (versus white participants). Yet B/AA were more likely to present with diffuse LBD pathology (than both cohorts) and with a neuropathological profile consistent with an intermediate-high likelihood of a typical dementia with Lewy bodies syndrome (versus H/L participants). Together, these results reflect the discrepancy between pathological findings and clinical diagnosis was largest among B/AA participants. Our results are consistent with a similar NACC analysis by Wei and colleagues (published as a pre-print) that found that non-white participants (B/AA and “other race/ethnicity”) were less likely to receive a clinical diagnosis concordant with their post-mortem neuropathology findings (AD, LBD, or AD+LBD) [44]. While our analysis did not specifically investigate diagnostic accuracy by sex due to small sample size, it is possible our B/AA cohort had the largest diagnosis discrepancy based on the over-representation of females. Recent studies suggest that men present earlier with core Lewy body dementia features, such as RBD, [45, 46] and that women are more likely to be under or misdiagnosed [44, 47]. However, the frequency of core Lewy body dementia symptoms did not significantly differ between our study cohorts (Table 2). Our findings highlight possible disparities in clinical diagnostic practices in minoritized communities that warrant attention. Future efforts with larger samples should examine whether LBD presents similiarly across racial and ethnic groups in conjuction with sex differences.

Limitations

Limitations in this study include small sample sizes for the B/AA and H/L cohorts. Available biomarker data are limited, particularly among minoritized ethnic and racial groups in ADRD research [15]. The lack of participants from diverse racial and ethnic

backgrounds in contrast to the number of white non-Hispanic participants in NACC is stark, undermining the ability to truly understand LBD across different groups. Additionally, NACC may not accurately represent the general U.S. population, particularly racially and ethnically minoritized communities [48], and results are influenced by location site, ADRC specialization, and additional recruitment factors across sites. Many ADRC sites focus on AD so there are relatively fewer participants with LBD and other neurodegenerative diseases in NACC. Comparing groups based on self-reported race and ethnicity does not capture more meaningful social factors connected to ADRD health disparities, such as quality of education, neighborhood and built environment, public health and health care, and other markers of disadvantage [49, 50]. Given low autopsy rate in minoritized communities, it is possible that the B/AA and H/L decedents in our analysis reflect a highly select and motivated group of people agreeing to autopsy. We also did not measure other pathologies and had limited data on core and supporting LBD features (e.g., neuropsychiatric features, RBD), restricting our ability to detect subtle differences in clinical presentation. Given the limited sample size, we were unable to explore potentially important interactions (i.e., age by sex by ethnoracial group interactions in survival) that should be investigated in future studies. Finally, clinical data were collected largely through self or informant report, which is subjective. For instance, how participants responded to age of cognitive decline, or how NACC clinicians judged this age, may be variable. Despite limitations, this study also had strengths. Use of pathologically-confirmed cases of LBD rather than clinician diagnosis is a study strength, given that LBD is a diagnosis that is often misdiagnosed [51]. NACC also provides an opportunity for large sample sizes than are commonly unavailable through other resources, particularly when using neuropathological results.

Conclusions

To our knowledge, this is the first study to compare survival, along with clinical and pathological characteristics, of B/AA, H/L and white participants with autopsy-confirmed LBD. This study demonstrated differences in the pathology composition in NACC's LBD autopsy-confirmed cases that varied by ethnicity and race. Results suggested that survival length was similar across ethnoracial groups after controlling for LBD pathology type and co-occurring AD pathology. Given these findings, it is important to consider pathology when investigating survival and disease trajectory differences in LBD, along with other ADRDs. Future research should investigate factors contributing to neuropathology differences between ethnoracial groups, and how these neuropathological differences might relate to differences in clinical symptoms and/or disease progression. Additionally, more efforts are needed to engage and recruitment diverse populations to yield representative and adequately powered sample sizes for analyses.

Our results also revealed discrepancies between clinical diagnoses and pathological findings, raising concern that LBD-related dementias are underdiagnosed in NACC, especially among B/AA older adults. If LBD is underdiagnosed among ethnically/racially minoritized older adults, in NACC specifically or more broadly, caution is warranted when using a clinically-derived sample to make ethnic and racial comparisons. Overall, more efforts are needed in identifying, understanding, and addressing disparities in LBD research and clinical care.

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Conflicts of Interest/Disclosure Statement:

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Table 1.

Demographic information by ethnoracial group

	W (N=1441)	B/AA (N=60)	H/L (N=54)	Total sample (N=1555)
Female, n (%)	553 (38.4%)[a]	34 (56.7%)[b]	20 (37%)[ab]	607 (39%)
Education, years [range]	16 [2, 26][a]	14 [4, 20][b]	12 [3, 27][b]	16 [2, 27]
Age, years [range]				
Onset of symptoms	70 [34, 102]	70.5 [48, 96]	66 [36, 87]	70 [34, 102]
Initial visit	75 [35, 102]	76 [52, 101]	75 [40, 93]	75 [35, 102]
Last visit	78 [39, 108]	80.5 [52,102]	78 [42, 93]	78 [39, 108]
Death	80 [39, 109]	82 [52, 103]	79 [44, 95]	80 [39, 109]
Time from last visit to death, months [range]	12 [0, 161]	12 [0, 114]	12.5 [1, 97]	12.0 [0, 161]
Hypertension	541 (51%)[a]	39 (81.3%)[b]	24 (57.1%)[a]	604 (52.5%)
Diabetes	103 (9.7%)[a]	8 (16.7%)[ab]	11 (26.2%)[b]	122 (10.6%)
Stroke	68 (6.4%)	5 (10.4%)	4 (9.5%)	77 (6.7 %)
Hypercholesterolemia	586 (55.8%)	27 (57.4%)	17 (40.5%)	630 (55.3%)
APOE-ε4 allele present	713 (55.9%)[a]	35 (74.5%)[b]	20 (45.5%)[a]	768 (56.2%)
Primary reason for initial visit				
Research	959 (66.6%)	41 (68.3%)	37 (68.5%)	1037 (66.7%)
Clinical	454 (31.5%)	17 (28.3%)	16 (29.6%)	487 (31.3%)
Both	28 (1.9%)	2 (3.3%)	1 (1.9%)	31 (2.0%)
Relative with cognitive impairment	828 (63.3%)	31 (60.8%)	31 (72.1%)	890 (63.4%)

W: White non-Hispanic, B/AA: Black/African American non-Hispanic, H/L: Hispanic/Latino

Missing data (White; Black/African American; Hispanic/Latino): education (n=13; n=0; n=0), hypertension (n=381; n=12; n=12); diabetes (n=379, n=12, n=12), stroke (n=381, n= 12, n=12), hypercholesterolemia (n=390, n=13, n=12), APOE-ε4 (n=166, n=13, n=10), relative with cognitive impairment (n=132, n =9, n=11)

Note: Proportions with different alphabetic superscript are statistically significant using post hoc Bonferroni-correction. Identical alphabetic superscript means no significant difference between groups.

Table 2.

Clinical characteristics at last study visit, by ethnoracial group

	W (N=1441)	B/AA (N=60)	H/L (N=54)	Total sample (N=1555)
CDR Sum at last visit [range]	12 [0,18][a]	14.5 [3,18][ab]	18 [2,18][b]	12 [0,18]
Cognitive status, %				
Normal	5 (0.3%)	0 (0%)	0 (0%)	5 (0.3%)
Impaired-not MCI	9 (0.6%)	0 (0%)	0 (0 %)	9 (0.6%)
MCI	72 (5%)	0 (0%)	1 (1.9%)	73 (4.7%)
Dementia	1355 (94%)	60 (100%)	53 (98.1%)	1468 (94.4%)
Primary cause				
AD	947 (65.7%)[a]	53 (88.3%)[b]	46 (85.2%)[b]	1046 (67.3%)
LBD	330 (22.9%)[a]	5 (8.3%)[b]	7 (13%)[ab]	342 (22%)
Contributing cause				
AD	85 (5.9%)	2 (3.3%)	0 (0%)	87 (5.6%)
LBD	94 (6.5%)	3 (5%)	6 (11.1%)	103 (6.6%)
Parkinson's disease*	122 (11.7%)	3 (6.52%)	3 (7.14%)	128 (11.3%)
Visual hallucinations	368 (26.3%)	17 (29.3%)	19 (36.5%)	404 (26.8%)
Delusions	301 (21.8%)	17 (29.8%)	15 (28.8%)	333 (22.3%)
REM sleep disorder	217 (18.3%)	3 (6.3%)	6 (12.8%)	226 (17.6%)
Survival, years [range]	9 [0, 31][a]	9 [2, 25][a]	14 [3, 28][b]	9 [0, 31]

W: White non-Hispanic, B/AA: Black/African American non-Hispanic, H/L: Hispanic/Latino

Missing data (White; Black/African American; Hispanic/Latino): Parkinson's disease (n=399, n=14, n=12), Visual hallucinations (n=44, n=2, n=2), Delusions (n=58, n=3, n=2), REM sleep disorder (n=255, n=12, n=7)

Note: Proportions with different alphabetic superscript are statistically significant using post hoc Bonferroni-correction. Identical alphabetic superscript means no significant difference between groups.

*Primary or contributing diagnosis

Table 3.

Neuropathological comparison by ethnoracial group

	W (N=1441)	B/AA (N=60)	H/L (N=54)	Total sample (N=1555)
LB pathology, %				
Transitional	747 (51.8%)[a]	21 (35%)[b]	37 (68.5%)[c]	805 (51.8%)
Diffuse	694 (48.2%)[a]	39 (65%)[b]	17 (31.5%)[c]	777 (48.2%)
Braak NFT stage, %				
Low	190 (13.2%)[a]	0 (%)[b]	3 (5.6%)[ab]	193 (12.5%)
Intermediate	304 (21.2%)	16 (26.7%)	11 (20.4%)	331 (21.4%)
High	941 (65.6%)	44 (73.3%)	40 (74.1%)	1025 (66.2%)
Dementia due to LBD likelihood, %				
Low	554 (38.6%)[a]	18 (30%)[a]	32 (59.3%)[b]	604 (39%)
Intermediate	492 (34.3%)[ab]	29 (48.3%)[b]	13 (24.1%)[a]	534 (34.5%)
High	389 (27.1%)	13 (21.7%)	9 (16.7%)	411 (26.5%)
Vascular pathology *	1408 (98.6%)	60 (100%)	53 (98.1%)	1521 (98.6%)
Hemorrhages/ Microbleeds	84 (5.98%)[a]	4 (6.78%)[ab]	9 (17.0%)[b]	97 (6.39%)
Infarcts/lacunes	194 (13.6%)[a]	23 (38.3%)[b]	8 (14.8%)[a]	225 (14.6%)

W: White non-Hispanic, B/AA: Black/African American non-Hispanic, H/L: Hispanic/Latino

Missing data (White; Black/African American; Hispanic/Latino): Braak NFT (n=6, n =0, n=0); Dementia due to LBD syndrome likelihood (n=6, n=0,n =0), vascular pathology (n=13, n=0, n=0), hemorrhages/microbleeds (n= 36, n =1, n=1), infarcts/lacunes (n=12, n=0, n=0)

Note: Proportions with different alphabetic superscript are statistically significant using post hoc Bonferroni-correction. Identical alphabetic superscript means no significant difference between groups.

* at least one vascular pathology present

Table 4.

Regression summary on Blom-transformed survival

	Model 1			Model 2		
Predictors	***std. B***	***95%CI***	***p***	***std. B***	***95%CI***	***p***
(Intercept)	.21	−0.05 – 0.48	<0.001	0.16	−0.13 – 0.45	<0.001
Female	0.23	0.13 – 0.33	<0.001	0.15	0.05 – 0.25	0.003
Age at onset	−0.29	−0.34 – −0.25	<0.001	−0.26	−0.31 – −0.21	<0.001
Education	−0.01	−0.06 – 0.04	0.632	−0.01	−0.06 – 0.04	0.635
Black/African American *	−0.38	−0.74 – −0.02	0.037	−0.28	−0.64 – 0.07	0.112
White *	−0.31	−0.58 – −0.04	0.025	−0.25	−0.52 – 0.01	0.059
Diffuse				−0.29	−0.39 – −0.20	<0.001
Intermediate Braak **				−0.04	−0.21 – 0.13	0.652
High Braak **				0.27	0.13 – 0.42	<0.001
Observations	1525			1525		
R^2 / R^2 adjusted	0.099 / 0.096			0.146 / 0.141		

* Hispanic/Latino is reference group,

** Low Braak stage is reference group