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Race and Ethnicity in Lewy Body Dementia: A Narrative Review

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Abstract

Lewy body dementia is the third most common and costliest type of dementia. It is an umbrella term for dementia with Lewy bodies and Parkinson's disease dementia, both of which place a substantial burden on the person and society. Recent findings outline ethnoracial differences in dementia risk. Delayed and misdiagnosis across ethnoracial groups contribute to higher levels of burden. In this context, we aimed to summarize current knowledge, gaps, and unmet needs relating to race and ethnicity in Lewy body dementia. In this narrative review, we provide an overview of studies on Lewy body dementia focusing on differences across ethnoracial groups and outline several recommendations for future studies. The majority of the findings comparing different ethnoracial groups were from North American sites. There were no differences in clinical prevalence and progression across ethnoracial groups. Compared to people identifying as non-Hispanic White, co-pathologies were more common and clinical diagnostic accuracy was lower for people identifying as Black. Co-morbidities (e.g., diabetes, hypertension) were more common and medication use rates (e.g., antidepressants, antiparkinsonian agents) were lower for people identifying as Black or Hispanic compared to people identifying as White. More than 90% of clinical trial participants identified as non-Hispanic White. Despite increasing efforts to overcome disparities in Alzheimer's disease and related dementias, inclusion of individuals from minoritized communities in Lewy body dementia studies continues to be limited and the findings are inconclusive. Representation of diverse populations is crucial to improve the diagnostic and therapeutic efforts in Lewy body dementia.

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CONFLICT OF INTEREST

Dr. Armstrong serves on the Data and Safety Monitoring Boards for the Alzheimer's Therapeutic Research Institute/Alzheimer's Clinical Trial Consortium and the Alzheimer's Disease Cooperative Study. She has provided educational content for Medscape. The authors have no other conflict of interest to report.

Keywords

Alzheimer's disease; dementia; diversity; equity; ethnicity; inclusion; Lewy body disease; racial groups

INTRODUCTION

Lewy body (LB) dementia, an umbrella term for Parkinson's disease dementia (PDD) and dementia with Lewy bodies (DLB), is the second most common neurodegenerative dementia following Alzheimer's disease (AD) [1]. DLB accounts for 4.2% of all dementia in community-based dementia populations and 7.5% of dementia cases in clinical populations [2]; PDD accounts for 3.6% of all dementia cases with a point prevalence of 25–30% in people with Parkinson's disease [3, 4]. Heterogeneity of clinical presentations in LB dementia contributes to the mis- and under-diagnosis, with potentially more than half of cases missed [5]. Currently, diagnosis relies on clinical features and there are no diagnostic biomarkers [6, 7]. Recent advances in biomarkers (e.g., seeded aggregation assays for alpha-synuclein and immunohistochemical detection of pathologic alpha-synuclein) are promising [8], although lack of diversity in study cohorts limits the generalizability of the findings.

LB dementia poses a significant burden on affected individuals, their care partners, and broader support systems, with substantial negative economic effects both personally and societally [9–13]. In fact, despite being the third most common overall dementia type following AD and vascular dementia, LB dementia is the costliest form of dementia in the United States (US) [14]. Compared to the US average health care spending of $11,462 per person in 2019, medical costs were $18,309 one year before the diagnosis and $29,174 one year after the diagnosis per person with LB dementia [9]. Motor and non-motor symptoms in LB dementia such as falls, urinary incontinence or infection, depression, anxiety, dehydration, and delirium were associated with these high costs [14]. Available treatments are only symptomatic and provide limited benefit. There is an urgent need to develop effective management strategies, but it is challenging to identify large and diverse samples of LB dementia with adequate power for longitudinal studies and clinical trials [15].

Race and ethnicity in dementia

Prevalence of dementia and AD is often reported to be higher in underrepresented racial and ethnic groups compared to people identifying as White [16]. These differences are largely explained by variations in health conditions (e.g., diabetes, cardiovascular disease), socioeconomic risk factors, health-related behaviors, and life experiences [16, 17]. Socioeconomic risk factors commonly relate to disparities resulting from structural racism, including higher rates of poverty, less access to quality education, increased exposure to environmental hazards, and greater exposure to discrimination and adversity in minoritized populations [16]. Cumulative burden of chronic stress and life events is associated with cognitive decline and contributes to racial disparities [18,19]. Other factors include cultural norms and attitudes regarding aging and dementia, lack of trust in healthcare, health literacy, and implicit and explicit bias [20, 21].

Individuals in the US with AD and dementia identifying as Asian, Black, or Hispanic are more likely to live in urban areas and areas with higher poverty and less access to education, timely care, mental health care, and dementia specialists. They also have more difficulty communicating with their healthcare professionals than people identifying as White [22–24]. People identifying as Black or Hispanic with dementia are less likely to receive and more likely to discontinue antidementia drugs, have higher hospital mortality rates, and are less likely to have advanced care planning, more likely to reside in nursing homes with lower quality of care, less likely to enroll in hospice, and have markedly higher end-of-life inpatient expenditures compared to people identifying as White with dementia [25].

So far, anxiety, depression, stroke, hypertension, diabetes, and hyperlipidemia have been associated with a higher risk of LB dementia (Table 1) [26–31]. Prevalence of these medical conditions, health care access, and outcomes for these conditions seem to differ across ethnoracial groups [32]. Within AD, clinical profile, progression rate, risk factors, and prevalence of biomarkers differ across ethnoracial groups [33, 34]. Whether such differences exist in LB dementia needs investigation. For example, research is needed on the degree to which educational attainment, vascular comorbidities, and mood disorders may contribute to potential differences in LB presentations between groups [24, 26, 35]. Environmental factors likely also contribute to the risk and manifestation of LB dementia [26, 36] and may be different between ethnoracial groups. Geography (rather than race) may be a driver; people identifying as Black or African-American in the US had a higher prevalence of Parkinson's disease than people identifying as Black or African in sub-Saharan Africa [37, 38]. This likely relates to various considerations including diagnostic rates and life expectancy. However, Parkinson's disease prevalence can differ across regions within a single country or rural and urban areas within a single region [39, 40], which may interact with race and ethnicity [24]. The effect of urban or rural living has not been studied extensively in LB dementia and should be considered when assessing ethnoracial differences for prevalence.

Education is suggested to be a protective factor against PDD and cardiovascular diseases, which are associated with higher LB dementia risk [28, 41]. Compared to people identifying as White, people identifying as Black or Hispanic can have lower educational attainment and lower quality of education [42]. A recent review showed that disparities between people identifying as Black and White with dementia can be reduced by about half by equalizing the education quality [43]. This supports that potential ethnoracial disparities for LB dementia can be overcome if determined and addressed.

Race and ethnicity terminology

When investigating ways to improve diagnosis and treatment in LB dementia, considering race and ethnicity can reveal important disparities in care and inform generalizability of findings to all affected people. Race, ethnicity, and ancestry are often used synonymously, although they have different meanings. Race is defined as "a group of people connected by common descent or origin", and ethnicity is defined as "membership of a group regarded as ultimately of common descent or having a common national or cultural tradition" [44, 45]. They are social constructs without biological meanings. The terms ancestry (referencing a

person's lineage or region of origin) or genetic admixture (describing a person's genetic background from different ancestries) likely better reflect disease risk than race and ethnicity, but race and ethnicity still have important social meanings and implications for health research [26]. Recent publications highlight the importance of precise terminology for race and ethnicity in healthcare research [26]. Use and classification of race and ethnicity should be consistent and self-reported rather than assigned by an observer [46]. Categories should not be viewed as absolute as people may identify with more than one race or ethnicity. The Inclusive Language section of the AMA Manual of Style can be used for guidance and clarification about the correct up to date terminology [26].

Association of ethnicity and race with overall health and disease states is due to complex relationships between ancestry, heritage, demographic, socioeconomic, cultural, structural, institutional, and other factors [47–50]. Therefore, race and ethnicity should not be reported in isolation but instead accompanied by sociodemographic factors and social determinants of health. Although definitions and categories can change over time, place, and context, lack of information on race and ethnicity can lead to neglection of social stratification, injustices, inequities, and health [47, 48]. As social factors play an important role in cognitive decline and dementia [51], inclusion of diverse populations and a closer look at underrepresented ethnoracial groups in dementia research can help advance diagnostic and therapeutic efforts.

Approach to the narrative review

The majority of the studies in LB dementia come from Japan, the United Kingdom, and the US; 79% of the authors for the most recent DLB diagnostic criteria were working in these countries [15]. This challenges the applicability of current literature across different populations. As the European population is expected to shrink and the sub-Saharan African population is expected to double in the coming decades [52], generalizability of the available data on dementia will decrease even further.

In this review, we aimed to underscore the current knowledge and gaps to raise awareness and outlined recommendations for future research in LB dementia to advance efforts for diversity, equity, and inclusivity. We present and discuss the available findings for differences across ethnoracial groups in LB dementia, stratifying for DLB and PDD when possible, with a focus on risk, prevalence, progression, clinical and neuropathological features, treatment options, and clinical trials. In the US, the National Institutes of Health (NIH) standard for classification of race includes the options of "American Indian or Alaska Native", "Asian", "Black or African American", "Native Hawaiian or Other Pacific Islander", "White", "More than one race", or "Unknown". Classification of ethnicity includes the options of "Hispanic or Latino", "Not Hispanic or Latino", or "Unknown" [53]. Recent studies from US tend to follow these standards. However, these categories reflect US-based populations and not ethnic and racial groups globally. Therefore, we outline the racial and ethnic groups as reported in the included studies or report the country of origin when such data are not disclosed.

PREVALENCE

International

There are several systematic reviews focusing on the prevalence of DLB and PDD [2, 3, 54, 55]. Studies from broad geographic areas, including North and South America, Europe, and Asia, are represented in these systematic reviews; however, data across studies were averaged to overall prevalence rates of 5% for DLB and 3.5% for PDD of all dementia cases. Differences across ethnoracial groups within included countries were not evaluated in these studies. In a separate study, higher age-standardized Parkinson's disease prevalence rates were reported in North America with lower rates in Africa [56]. Although there are currently no studies investigating ethnoracial differences for LB dementia prevalence on a global scale, there are efforts to combine LB dementia cohorts from different regions [15]. Such initiatives will enable future efforts to compare prevalence and incidence of LB dementia based on ancestry, ethnicity, and race.

Geographical differences can be important for LB dementia and contribute to potential ethnoracial differences. Prevalence and clinical correlates of genetic factors (e.g., *GBA*, *LRRK2*), social determinants of health (e.g., education), medical conditions (e.g., cardiovascular disease), and exposure to environmental factors (e.g., smoking) are associated with different risk for LB dementia and these can differ across regions [26–28, 38, 57].

Immigration status represents another social determinant of health that can interact with ethnicity and race [58]. A study in Belgium compared DLB prevalence across their clinical cohort including people born in Belgium and first-generation immigrants (including people born in North Africa, Sub-Saharan Africa, Europe, and Latin America) [59]. DLB prevalence was significantly higher in people born in North Africa (6.3% out of all born in North Africa, total $n = 205$) and Latin America (19.0% out of all born in Latin America, total $n = 21$) compared to people born in Belgium (5.2% out of all born in Belgium, total $n = 2,011$). However, the number of first-generation immigrants was much smaller than people born in Belgium.

US-based

For the general demographics of the US population 65 years and older (total estimate = 52,888,621), American Community Survey 5-year estimates from 2021 note 0.5% of people identify as American Indian and Alaska Native, 4.8% as Asian, 9.2% as Black, 0.1% as Native Hawaiian and Other Pacific Islander, 79.8% as White, 3.0% as two or more races; 8.6% Hispanic and 75.7% as non-Hispanic White [60].

Despite the fact that most LB dementia studies reflect primarily non-Hispanic White populations, the frequency of DLB-related diagnosis codes was similar across ethnoracial groups amongst Medicare fee-for-service beneficiaries over the age of 68 as of December 31, 2013 in the US (total $n = 21,624,228$) [61]. Among all beneficiaries with a claim for dementia ($n = 3,110,654$), 4.0% of people identifying as non-Hispanic Black, 4.4% of people identifying as American Indian or Alaska Native, 5.4% of people identifying as Asian or Pacific Islander, 5.5% of people identifying as non-Hispanic White and 6.1% of people identifying as Hispanic were diagnosed with DLB [61]. DLB prevalence was

lower in people living in rural (4.5%) compared to urban areas (5.2–5.5%). Although rural living has been associated with increased Parkinson's disease risk, potentially as a result of agricultural pesticide or other environmental factors [62], higher Parkinson's disease prevalence in urban areas is also reported [40]. Higher DLB prevalence in urban areas may reflect bias of more diagnoses made among populations living closer to academic/specialized care centers or areas with higher density of clinicians trained in diagnosing these disorders.

DIAGNOSIS AND CLINICAL FEATURES

Clinical diagnostic accuracy is limited in DLB, with pathological confirmation required for the definite diagnosis of both DLB and PDD [6, 7, 63]. In the US-based National Alzheimer Coordinating Center (NACC) database including standardized clinical and neuropathological research data from centers across the US [64–66], age of onset for cognitive decline and functional status were similar across people identifying as Hispanic (n = 122), non-Hispanic Black (n = 130), and non-Hispanic White (n = 1,782) clinically diagnosed with mild cognitive impairment (MCI) or dementia associated with a LB disorder [67]. Compared to people identifying as non-Hispanic White, people identifying as non-Hispanic Black or Hispanic were more likely to be female, single, and living alone; had fewer years of education; and were more likely to have a history of diabetes and hypertension. Depression frequency and severity were higher for people identifying as Hispanic compared to people identifying as non-Hispanic Black or non-Hispanic White. People identifying as Hispanic were more impaired on attention and language tests; people identifying as Black were more impaired on executive function, attention, and language tests compared to people identifying as White after adjusting for sex, education, hypertension, diabetes, and cognitive severity. Although these findings suggest an ethnoracial difference for risk factors, cognitive profile, and clinical features, the need for culturally-sensitive test batteries was also emphasized. Caution is also needed given that NACC is not population-based and recruitment biases could affect results.

The majority of the literature guiding the diagnostic criteria for DLB came from research in people identifying as White or studies from Asia, Europe, and North America [15]. It is uncertain whether this might affect diagnostic accuracy in other populations. In individuals with limbic or neocortical LB pathology in NACC (including 61% with intermediate/high likelihood of a DLB phenotype), only 28.6% had a clinical diagnosis of LB disease at their last visit (n = 1,555) [68]. While every group had a lower rate of clinical diagnosis than pathological diagnosis, the gap was significantly wider for people identifying as Black. A clinical LB disease diagnosis was less common for people identifying as Black (15% of all identifying as Black, total n = 60 versus 24.1% of all identifying as Hispanic, total n = 54 and 30.4% of all identifying as White, total n = 1,441) despite 70% of people identifying as Black having an intermediate or high likelihood of a DLB phenotype based on pathology (versus 40.8% of all identifying as Hispanic and 61.4% of all identifying as White). In a separate study of individuals with LB and/or AD neuropathology in NACC, as dementia worsened over time, clinical diagnostic accuracy increased in people identifying as White, whereas accuracy declined in people identifying as Black [69]. Reasons for this are uncertain and may reflect performance of the clinical diagnostic criteria in different ethnic

and racial groups, clinician or center biases in diagnosis (e.g., many centers participating in NACC are focused on AD), or other factors.

PROGRESSION

Overall, LB dementia is associated with over three-times higher mortality rates than the general population. DLB is associated with a faster cognitive and functional decline as well as shorter survival compared to AD [70–74]. Studies suggest similar rates of cognitive decline and mortality for PDD and DLB [73, 75, 76]. However, Parkinson's disease mortality can differ across ethnoracial groups. Across 138,728 US Medicare beneficiaries with Parkinson's disease identified in 2002 and followed through 2008, compared to people identifying as White (total n = 125,660; 64.6%), the death rate was higher for people identifying as Black (total n = 8,527; 66.4%) and lower for people identifying as Hispanic (total n = 3,036; 55.4%) or Asian (total n = 1,505; 50.8%) [77]. Dementia was also associated with higher risk of death and PDD was diagnosed more often in people identifying as Black (78.2%) and Hispanic (73.1%) compared to people identifying as White (69.0%) or Asian (66.8%) [77].

Neuropathological studies suggest that neocortical LB pathology (versus limbic) and AD co-pathology are associated with shorter survival in LB diseases [78–81]. Across 41 participants with AD identifying as Black and 81 participants with AD identifying as White in the Rush Alzheimer's Disease Clinical Core, mixed LB and AD pathology was more likely in people identifying as Black [82], which may suggest a higher risk for shorter survival. Nevertheless, this higher likelihood of mixed LB and AD pathologies in people identifying as Black was not replicated in another cohort of people with limbic or neocortical LB pathology in the NACC [68]. In this NACC study, people identifying as Hispanic (n = 54) had longer unadjusted survival compared to people identifying as Black (n = 60) or White (n = 1,441). However, this significant difference did not survive adjustment for age at symptom onset, sex, education, LB pathology type (limbic versus neocortical), and Braak neurofibrillary tangle stage. Thus, the limited available data in the literature are inconclusive in terms of progression and mortality rates across US-based ethnoracial groups in LB dementia.

NEUROPATHOLOGY

Autopsy confirmation of LB pathology remains the gold standard for diagnosis of both DLB and PDD [6, 7]. Level of substantia nigra neuron loss and LB pathology as well as the prevalence and level of co-pathologies (e.g., AD and cerebrovascular pathologies) are associated with the clinical phenotype and can differ for PDD and DLB [83, 84]. In US-based cohorts, studies examining LB pathology tend to show higher rates of co-pathology in minoritized populations. In the Rush AD Clinical Core, people with clinical diagnoses of AD identifying as Black (n = 41) had a higher likelihood of LB pathology and/or more severe vascular pathology accompanying AD pathology when compared to a matched sample of individuals identifying as White (n = 81) [82]. In a NACC study of individuals with a clinical diagnosis of dementia at last visit, people identifying as Black (n = 110) had more frequent co-pathologies, including LB pathology, AD pathology, frontotemporal

lobar degeneration with tau and TDP-43 inclusions, and various vascular findings compared to people identifying as White (n = 2,500) [85]. Compared to people identifying as White, people identifying as Black were more likely to have LB pathology as a contributing neuropathological diagnosis associated with their dementia. In a NACC study focused on individuals with limbic or neocortical LB pathology, people identifying as Black (n = 60), Hispanic (n = 54), or White (n = 1,441) who died at similar ages had similar levels of Braak tau staging. However, the Black cohort had more women, hypertension, neocortical LB pathology, and infarcts/lacunes. The Hispanic cohort had a higher ratio of people with diabetes, limbic LB pathology and hemorrhages/microbleeds [68].

While most studies report more co-pathology in minoritized populations, one study utilizing multiple US-based aging cohorts found that the frequency of LB pathology and co-morbid degenerative or vascular pathology was largely similar between individuals identifying as Black (n = 81) and a matched sample of individuals identifying as White (n = 154) [86]. This sample included individuals with normal cognition, MCI, and dementia. Clinical diagnoses of DLB (one person identifying as Black, one person identifying as White) and Parkinson's disease (four people identifying as Black, seven people identifying as White) were uncommon, and PDD was not mentioned [86]. Across brain regions, the LB count only differed in the anterior cingulate cortex (higher count for people identifying as Black). The association between LB pathology and cognition and olfaction was similar across racial groups, despite a lower smell test score for people identifying as Black. People identifying as Black had a stronger association between LB pathology and parkinsonism.

TREATMENT AND CLINICAL TRIALS

Available treatment options for DLB and PDD offer limited symptomatic relief and there is an urgent need for effective disease-modifying strategies. For a cohort of people with LB dementia or MCI in NACC, people identifying as White (n = 1,782) were significantly more likely to use an antiparkinsonian drug at the time of the visit compared to people identifying as Hispanic (n = 122) or non-Hispanic Black (n = 130) despite similar reported levels of parkinsonism [67]. Report of antidepressant and AD medication use at the time of the visit also differed across the ethnoracial groups, with lowest rates seen in people identifying as non-Hispanic Black and highest rates in people identifying as White, although these differences did not persist after multiple comparison correction.

Centers in Japan, US, and Europe have been the main drivers of clinical trials in LB dementia [15]. As of February 7, 2023, ClinicalTrials.gov listed 14 completed clinical trials with a total of 1,676 participants with DLB, PDD, or LB dementia across studies (Table 2). Four studies were conducted in Asia (n = 415, 24.8% of total participants in all trials), seven in North America (n = 718, 42.8%) and three had sites in North America and Europe (n = 543, 32.4%). Of the seven studies reporting detailed race data (n = 873, four in North America, three in North America and Europe), 96.1% of the participants identified as White (Fig. 1). Of the five studies reporting detailed ethnicity data (total n = 819), 92.8% of the participants identified as non-Hispanic with only 6.5% identifying as Hispanic (two in North America, three in North America and Europe).

DISCUSSION

In this review, we outlined available findings for diagnosis, progression, clinical profile, neuropathology, and management for LB dementia across ethnoracial groups (Table 3). Despite the high prevalence and burden reported in LB dementia, this review identified a paucity of research investigating racial, ethnic, or ancestral considerations in the epidemiology, clinical presentation, diagnosis, experience, progression, pathology, or treatment of LB dementia. This underscores the importance of health disparities as a research priority as identified by the AD and Related Dementias Summits, hosted most recently in 2022 [87].

Racial, ethnic, and ancestral considerations in LB dementia clinical care

Clinical diagnosis of LB dementia is challenging regardless of the person's background. Medicare and NACC data in this review were mixed on whether race and ethnicity affect identification of LB dementia [61, 67, 68, 77]. Risk of LB dementia misdiagnosis can be higher in a primary care setting than a tertiary care facility [63, 88]. In the US, access to timely care and specialists is significantly lower for people identifying as Asian, Black, or Hispanic in comparison to people identifying as White [24]. Different or delayed diagnosis is common in LB dementia, and leads to uncertainty, fear, worry and concern about the future for both people with LB dementia and their families [10, 89]. Mis- or delayed diagnosis interferes with timely support and treatment, which are top research priorities for people with LB dementia and caregivers [90]. Misdiagnosis can also to inappropriate treatments, such as risky antipsychotic use [91].

Minoritized populations with dementia may be at a higher risk for receiving delayed or insufficient healthcare with less access to new treatment options [92, 93]. Disparities in healthcare access and obtaining accurate diagnoses expand to disparities in access to appropriate treatments, as suggested by different rates of medication use across people with LB dementia or MCI identifying as Black, Hispanic, or White [67].

Racial and ethnic considerations in LB dementia research

While a few studies suggest potential ethnoracial differences in LB pathology and co-pathology, this research is severely limited given small numbers of individuals from minoritized groups, likely reflecting a combination of under-diagnosis and concerns regarding research participation and brain donation [94]. More representation is needed across LB studies, including neuropathological studies but also observational studies and clinical trials. Of clinical trials reporting detailed ethnicity and race data, over 90% of participants with identified as White and non-Hispanic. This likely reflects a complex interplay of barriers to accessing healthcare and historically rooted distrust of clinical research [33, 95]. Although many of these studies are conducted in the US and Europe, the ratio of research participants identifying as White continues to be higher than the ratio of people identifying as White in the population.

Increasing participation of underrepresented groups in clinical trials requires efforts from individuals, institutions and funding agencies involved with research. Research suggests

that minoritized people are interested in participating in trials [96] and are more likely to be recruited from internal sources such as referrals by healthcare providers, community outreach and local research registries [34, 97]. However, healthcare professionals may assume lack of interest or other barriers and not provide information [96]. This can significantly limit the participation of diverse populations in trials. Diversifying the research team and including professionals that can speak the native language of the targeted populations will allow people to feel more comfortable and overcome potential mistrust.

In addition to recruitment challenges, trial inclusion and exclusion criteria may affect enrollment of racial and ethnic minorities. The fact that individuals from underrepresented groups may have more co-morbidities and are more likely to be single (and thus potentially lack convenient study partners) may influence the likelihood of fulfilling trial eligibility criteria [67]. Trials may also use cognitive tools developed and validated in cohorts mostly including people identifying as White to determine eligibility. For instance, people identifying as Black without cognitive impairment may have scores below average or low-average, whereas people identifying as White may have high-average or superior scores, leading to misdiagnosis of cognitive impairment in these groups [98]. Applying ethnically and culturally appropriate tests or test norms can help interpret the level of impairment more reliably to determine eligibility. Additionally, views regarding dementia may vary by culture [99] and this may affect study partner responses to commonly used tools such as the Clinical Dementia Rating Scale [34].

Additional suggested strategies for improving recruitment of individuals from minoritized communities can include providing resources to cover costs associated with participation, expanding research sites to community settings, and incentives from funding agencies to the research teams to encourage recruitment of underrepresented groups [97, 100, 101].

There are established consortia and emerging collaborative initiatives to diversify and expand LB dementia cohorts [15, 102]. Supporting these efforts to reach more diverse populations and harmonization of data across different consortia studies can allow analysis of geographic, social, and other factors driving the ethnoracial differences more reliably. More global research is still needed to incorporate both additional countries and representation of different groups within formal borders.

Recommendations for future research in LB dementia

Improving representation in LB dementia research starts with improving recognition and diagnosis in underrepresented groups (Table 4). This has critical implications for accurate prevalence estimates and for connecting individuals with LB dementia to both clinical care and research. Research into barriers affecting diagnosis and access to dementia care is critical. Diagnosis of LB dementia relies heavily on informant report for core clinical features including symptoms of dementia, REM sleep behavior disorder, visual hallucinations, and cognitive fluctuations [6]. Research outside LB dementia suggests that informant reporting may vary by background in terms of cognitive symptoms [103, 104] and level of functioning [105, 106]. Additionally, the type of caregiver available (e.g., spouse versus child) and whether that caregiver lives with the older adult may vary among racial-ethnic groups [107], which has implications for assessing functionality and symptoms

like dream enactment [106]. Whether LB dementia diagnostic criteria perform well across different people groups also requires further study.

Studies should use culturally sensitive batteries and neuropsychological tests adapted and validated across populations and languages. Prior US-based research, for example, has found that neuropsychological tests were less specific and had higher false-positive error rates for people identifying as Black or Hispanic [108]. Implications relating to primary language and social determinants of health/disparities need to be incorporated into assessments of impairment based on neuropsychological testing, in addition to classically assessed factors such as age, gender, and education [109].

Longitudinal studies should assess whether risk factors (e.g., environmental exposures, comorbid vascular conditions) vary between different people groups and how this might affect both diagnosis and progression. Consistent and systematic collection of data for structural and social determinants of health is also critical, ideally using approaches that will allow harmonization of data and findings from different cohorts [110]. Research in AD is mixed regarding whether biomarkers (e.g., cerebrospinal fluid, plasma biomarkers) perform differently based on participant background and medical comorbidities [111–113], suggesting that biomarkers should be validated across diverse LB dementia populations.

There is a critical need to assess whether there are any pathologic differences by background, which will necessitate greater diversity in studies including pathology. Religious beliefs and cultural attitudes, which may vary along with race, ethnicity, and ancestry, play an important role in the decision of brain donation [114]. In one US-based study, however, people identifying as Black were as likely as people identifying as White to be willing to donate their brains once approached by healthcare professionals [115]. From a global standpoint, each country’s own legislation and the attitudes of the ethnic, racial, or religious group in the majority can impact the approach towards brain donation [116, 117]. Barriers to brain donation include lack of knowledge and the approach of healthcare teams when providing education [116–118].

As demonstrated in this review, increased diversity in LB dementia clinical trials is a critical unmet need. Diverse populations are necessary to provide general-izable findings in clinical trials as pharmacokinetics and pharmacodynamics can differ across ethnoracial groups, with implications for both safety and efficacy [119–121]. Barriers to diverse clinical trial participation include LB dementia-specific considerations, such as under-diagnosis, and systemic barriers such as mistrust. A comprehensive review of approaches to improve clinical trial diversity is outside of the scope of this review, but such approaches include engaging diverse research staff (in terms of background and language), study team training regarding communication with diverse communities, designing culturally- and linguistically-appropriate documents using accessible literacy levels, using study materials available in multiple languages, choosing inclusion/exclusion criteria that allow for a broad range of backgrounds (e.g., in terms of language, education, study partner requirements), and sponsor require ments for enrollment of diverse populations [96, 100, 122].

Strengths and limitations of review

This is the first known review focusing on ethnicity and race in LB dementia and it identifies numerous gaps in the existing literature. Limitations include the fact that this is a non-systematic review. Narrative reviews are prone to selection bias compared to systematic reviews. A systematic review with a clearly defined hypothesis, search method using different search engines, predefined selection criteria, data extraction and analysis based on the hypothesis can provide a better summary of existing data than a narrative review [123, 124]. A narrative review, on the other hand, can provide a broad overview of the studies with more emphasis on interpretation and critique [123, 124]. As our primary focus was to discuss current knowledge in order to outline future directions to advance the LB dementia field, we used a narrative review approach. Many of the identified studies are US-based and the majority use NACC, which is not population-based and which has an under-representation of racial and ethnic minorities. It is also uncertain whether the NACC battery is ideally suited to assess individuals from different racial-ethnic and linguistic backgrounds. Furthermore, available US-based studies are limited to groups identifying as Black, Hispanic, or White, with almost no data for other groups including Asian, Pacific Islander, and Native/Indigenous populations.

CONCLUSION

The majority of the published studies in LB dementia do not report race, ethnicity, and ancestry of participants or take social factors into account. Countries with diverse racial and ethnic populations need to increase efforts for inclusion and engagement in research. A more globally inclusive approach should also be implemented to support efforts from countries underrepresented in LB dementia research. There is an urgent need for further investigation on ethnoracial, cultural, social, and environmental differences in DLB and PDD to better identify, understand and adequately serve all communities affected by LB dementia. Approaches will likely need to include education for clinicians to improve cultural competence and a variety of efforts to improve research diversity. Social factors must be considered with ethnicity and race for a better understanding of the directional ity and interplay of risk. Once factors contributing to LB dementia risk, progression, and response to treatment are identified, strategies to overcome barriers in access and care have the potential to significantly improve diagnostic and therapeutic efforts in LB dementia.

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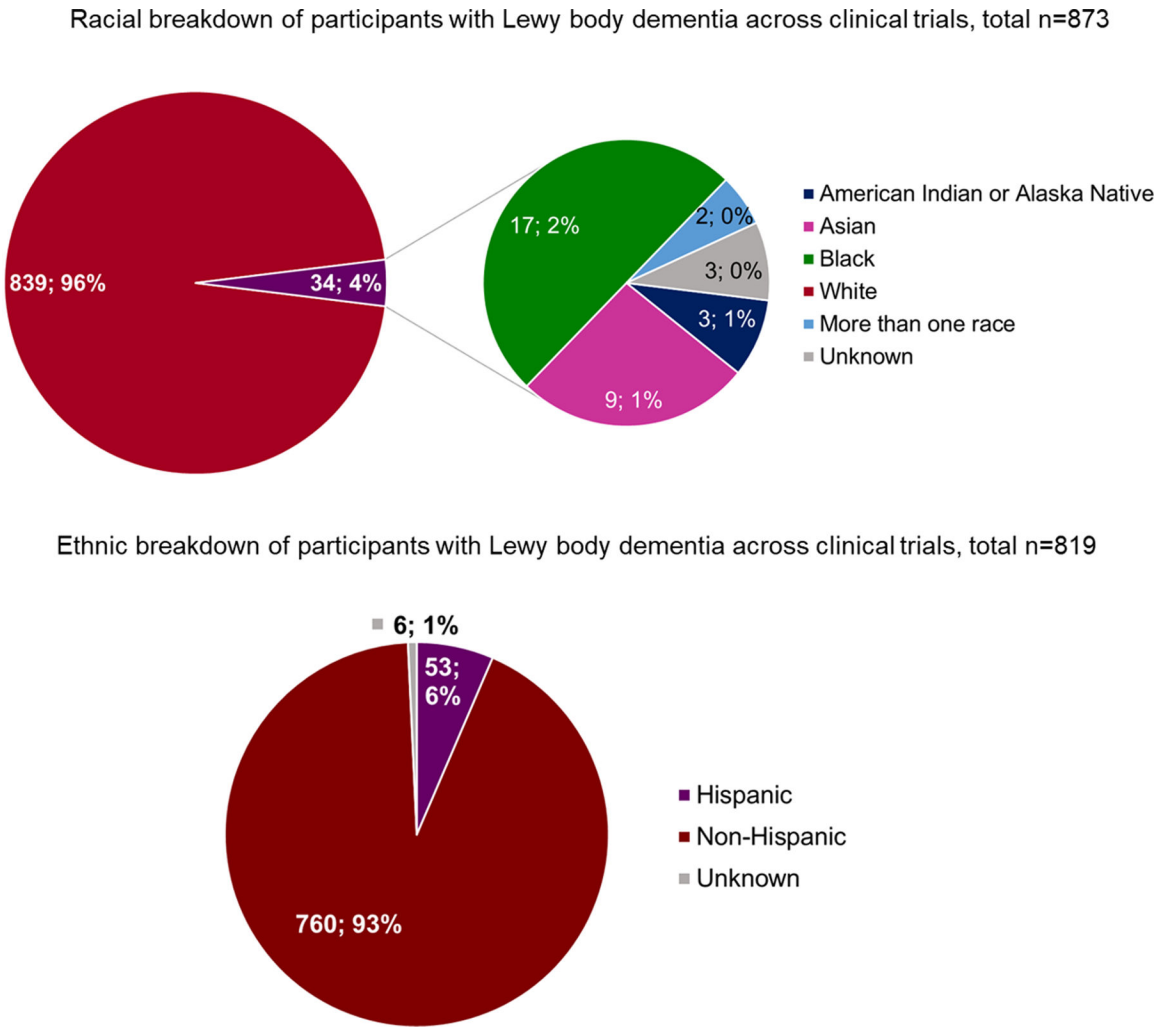

Fig. 1.

Race and ethnic breakdown of participants with Lewy body dementia in clinical trials that reported detailed race and ethnicity data.

Table 1.

Summary of risk factors reported for Lewy body dementia

Dementia with Lewy bodies (DLB) [26,27,31,57]	**Parkinson's disease dementia (PDD) [28–30]**
Male sex	Older age
Low caffeine intake	Male sex
Family history of Parkinson's disease	Low education level
Family history of dementia	Smoking
Hypertension	Hypertension
Hyperlipidemia	Longer Parkinson's disease duration
Diabetes	More severe motor impairment
Stroke	Akinetic-rigid phenotype
Anxiety	Postural instability
Depression	Hallucinations
Genetic factors *(GBA, BIN1, TMEM175, SNCA, APOE)*	REM sleep behavior disorder
	Genetic factors *(GBA1, COMT, MAPT, APOE)*

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Table 2.

Summary of completed studies with available results on ClinicalTrials.gov (n=14)

ClinicalTrials.gov Identifier	Intervention	Phase	Study population	Completion date	Location	Ethnicity and race of study population, %
NCT00294554	Memantine		PDD, n=20	December 2008	Maryland (US)	Race: White- 100%
NCT00543855[125]	Donepezil hydrochloride	2	Probable DLB, n=139	February 2010	Japan	Not reported
NCT00623103[126]	Rivastigmine	3	PDD, n=359	November 2010	Alabama, Arizona, California, Florida, Georgia, Idaho, Illinois, Kansas, New York, Ohio, Pennsylvania, Texas, Utah, Washington (US); Argentina; Australia; Austria; Belgium; Canada; France; Germany; Italy; Netherlands; Spain; Turkey; United Kingdom	Not reported
NCT02708186[127]	Nelotanserin	2	Lewy body dementia with REM sleep behavior disorder, n=34	November 2010	Alabama, Arizona, Arkansas, Colorado, Florida, Georgia, Indiana, Kansas, Nebraska, North Carolina, North Dakota, Ohio, Rhode Island, Tennessee, Texas (US)	Race: Asian- 2.9% White- 97.1%
NCT00598650[128]	Donepezil hydrochloride	2	Probable DLB, n=108	March 2011	Japan	Not reported
NCT00988117	Rivastigmine	4	PD-MCI, n=6 PDD, n=6 Controls, n=15	April 2011	California (US)	Not reported
NCT01023672	Armodafinil	4	Probable DLB, n=17	March 2012	Minnesota (US)	Not reported
NCT01785628[129]	Sarcosine		PDD, n=30	July 2012	Taiwan	Not reported
NCT01278407[130]	Donepezil	3	Probable DLB, n=138	April 2013	Japan	Not reported
NCT02258152	Landipirdine	2	PDD, n=82	October 2017	Alabama, Arizona, California, Florida, Georgia, Illinois, Iowa, Kansas, Maryland, Massachusetts, Minnesota, New Jersey, North Carolina, Pennsylvania, South Carolina, Texas (US)	Ethnicity: Non-Hispanic- 98.8% Unknown- 1.2% Race: Black or African American- 1.2% White- 98.8%
NCT02669433[131]	Intepirdine	2	Probable DLB, n=268	December 2017	Arizona, California, Colorado, District of Columbia, Florida, Georgia, Illinois, Indiana, Kentucky, Massachusetts, Minnesota, New York, North Carolina, Ohio, Oregon, Pennsylvania, Texas, Virginia (US); Canada; France; Italy; Netherlands; Spain; United Kingdom	Ethnicity: Hispanic- 3.7% Non-Hispanic- 95.1% Unknown- 1.1% Race: Asian- 1.5% Black or African American- 1.5% White- 95.5% More than one race- 0.4% Unknown- 1.1%

ClinicalTrials.gov Identifier	Intervention	Phase	Study population	Completion date	Location	Ethnicity and race of study population, %
NCT04001517[132]	Neflamapimod	2	Probable DLB, n=91	June 2020	California, Colorado, Florida, Kansas, Massachusetts, Michigan, Minnesota, Nevada, New York, North Carolina, Ohio, Oregon, Pennsylvania, Virginia, Washington (US); Netherlands	Ethnicity: Hispanic- 7.7% Non-Hispanic- 92.3% Race: Black or African American- 1.1% White- 98.9%
NCT03305809[133]	Mevidalen	2	Lewy body dementia, n=344	July 2020	Alabama, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Illinois, Indiana, Kansas, Maine, Massachusetts, Michigan, Missouri, Nevada, New Hampshire, New Jersey, Ney York, North Carolina, Pennsylvania, South Carolina, Texas, Virginia, Washington, Wisconsin (US); Canada; Puerto Rico	Ethnicity: Hispanic- 9.6% Non-Hispanic- 89.8% Unknown- 0.6% Race: American Indian or Alaska Native- 0.6% Asian- 1.2% Black or African American- 3.2% White- 94.8% More than one race- 0.3%
NCT04764669	Irsenontrine	2	Probable DLB, n=21 Probable PDD, n=13	January 2022	Arizona, Florida, Kentucky, New Jersey, New York, Ohio, Oregon (US); Canada	Ethnicity: Hispanic- 8.8% Non-Hispanic- 91.2% Race: American Indian or Alaska Native- 2.9% White- 97.1%

PD-MCI: Parkinson's disease with mild cognitive impairment; PDD: Parkinson's disease dementia; DLB: dementia with Lewy bodies. Individual states are listed for United States, reporting of one country other than United States does not imply a single site study. Ethnicity and race data is presented as reported in ClinicalTrials.gov. For those without available data on ClinicalTrials.gov, ethnicity or race data were also not available on cited publications.

Table 3.

Summary of research studies on ethnoracial differences in LB dementia

Category	Summary of current research on ethnic and racial differences
Prevalence	DLB prevalence higher for immigrants from North Africa and Latin America than natives in Belgium [59], but not different across ethnoracial groups in the United States [61].
Diagnosis and clinical features	In the NACC, clinical diagnostic accuracy is lower in people identifying as Black compared to people identifying as White [69]. Despite more advanced LB pathology stage, diagnosis of LB disease is less common for people identifying as Black compared to people identifying as Hispanic or White [68]. Compared to people identifying as White, higher rates of diabetes, hypertension, depression, female sex, single status, living alone, as well as lower education levels and worse performance on various cognitive tests were observed in people identifying as Black or Hispanic that were clinically diagnosed with MCI or dementia due to a LB disorder [67].
Progression	No significant differences for progression and mortality after accounting for age at onset, sex, education and the level of underlying LB and AD pathology [68].
Neuropathology	Compared to people identifying as White, co-pathology rates (e.g. vascular, AD, frontotemporal lobar degeneration) may be higher in people not identifying as White [82] [85]. Regional pathology burden and clinicopathological correlations can differ; higher LB count in the anterior cingulate cortex, stronger association between LB pathology and parkinsonism in people identifying as Black compared to people identifying as White [86].
Treatment and clinical trials	Antiparkinsonian, antidepressant and Alzheimer's drug use may be higher in people identifying as White compared to people identifying as Black non-Hispanic or Hispanic [67]. More than 9 out of 10 people participating in clinical trials identify as non-Hispanic White (see Table 2).

Table 4.

Recommendations for research in Lewy body dementia relating to race, ethnicity, and ancestral considerations

Category	Considerations
Prevalence	Determine prevalence by geographic reasons and different people groups
Diagnosis	Identify barriers to symptom recognition or reporting Identify and address barriers to accessing healthcare for dementia Determine whether diagnostic criteria perform equally well across groups Develop and implement culturally sensitive neuropsychological test batteries Interpret cognitive testing with consideration of language, social determinants of health
Risk factors	Assess risk factors (e.g. environmental exposures) that may vary by geographic location (e.g. rural/urban) or background (e.g. vascular risk factors)
Observational studies	Include diverse cohorts Collect data on social determinants of health Assess biomarker validity across groups Increase diversity in brain bank studies
Clinical trials	Recruit diverse populations Identify ways to increase access to clinical trials for underrepresented groups (e.g. with regard to travel arrangements, stipends) Use measures with validated versions across different languages Employ culturally sensitive neuropsychological test batteries as outcome measures