Published Ahead of Print on April 5, 2023 as 10.1212/WNL.0000000000207247

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The Official Journal of the American Academy of Neurology

AMERICAN ACADEMY OF NEUROLOGY®

Neurology Publish Ahead of Print
DOI:10.1212/WNL.0000000000207247

Racial and Ethnic Differences in Health-Related Quality of Life for Individuals with Parkinson Disease Across Centers of Excellence

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Figure Count:
1

Table Count:
3

Search Terms:
[52] All epidemiology, [345] Equity, Diversity, and Inclusion (EDI), [165] Parkinson's disease/Parkinsonism

Acknowledgment:

Study Funding:
Parkinson’s Foundation, Parkinson’s Outcomes Project

Disclosures:
D.G. Di Luca reports no disclosures relevant to the manuscript. S. Luo receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee. H. Liu reports no disclosures relevant to the manuscript. M. Cohn reports no disclosures relevant to the manuscript. T. Davis receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee. A. Ramirez-Zamora receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee. M. R. Rafferty receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee. N. Dahodwala receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee. A. Naito is an employee of the Parkinson’s Foundation. M. Neault receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee. J. Beck is an employee of the Parkinson’s Foundation. C. Marras receives honorarium for participation in the Parkinson’s Foundation Parkinson’s Outcomes Project Steering Committee.

Preprint DOI:

Received Date:
2022-07-28

Accepted Date:
2023-02-16

Handling Editor Statement:
Submitted and externally peer reviewed. The handling editor was Associate Editor Peter Hedera, MD, PhD.

Abstract

Background and objectives: Racial and ethnic minorities have been underrepresented in Parkinson's disease (PD) research, limiting our understanding of treatments and outcomes across all non-White groups. The goal of this research is to investigate variability in health-related quality of life (HRQoL), and other outcomes in patients with PD across different races and ethnicities.

Methods: This was a retrospective, cross-sectional and longitudinal, cohort study of individuals evaluated at PD Centers of Excellence. A multivariable regression analysis adjusted for sex, age, disease duration, Hoehn and Yahr (H&Y) Stage, comorbidities and cognitive score was used to investigate differences between racial and ethnic groups. A multivariable regression with skewed-t errors was performed to assess the individual contribution of each variable to the association of PDQ-39 with race and ethnicity.

Results: A total of 8,514 participants had at least one recorded visit. The majority (90.2%) self-identified as White (n=7,687), followed by 5.81% Hispanic (n=495), 2% Asians (n=170), and 1.9% African American (162). After adjustment, total PDQ-39 scores were significantly higher (worse) in African Americans (28.56), Hispanics (26.62) and Asians (25.43) when compared to White patients (22.73, $p<0.001$). This difference was also significant in most PDQ-39 subscales. In the longitudinal analysis, the inclusion of cognitive scores significantly decreased the strength of association of PDQ-39, race/ethnicity for minority groups. A mediation analysis demonstrated that cognition partially mediated the association between race/ethnicity and PDQ-39 scores (proportion mediated 0.251, $p <0.001$).

Discussion: There were differences in PD outcomes across racial and ethnic groups, even after adjustment for sex, disease duration, HY stage, age and some comorbid conditions. Most notably, there was worse HRQoL among non-Whites when compared to White patients, which was partially explained by cognitive scores. The underlying reason for these differences needs to be a focus of future research.

Introduction

Parkinson's disease (PD) is a common movement disorder that affects around 1 million people in the United States (US) [1]. PD is associated with significant motor and nonmotor symptoms that affects people of different ethnicities, races, and socioeconomic backgrounds [2, 3]. Even though limited data suggests the racial distribution of PD may not be homogenous, the inclusion of underrepresented minorities in PD research has been disproportionately low. Currently, little is known about the natural history, clinical management, and outcomes across different racial and ethnic groups with PD, especially for African American (AA) and Hispanic patients [4-7]. Studies have suggested that AA individuals with PD might have less access to specialists, overall delayed diagnosis, and less access to appropriate treatments [8, 9]. Additionally, Hispanic and AA patients also are thought to have a different disease trajectory when compared to White patients, including higher rates of dementia [10].

Recently, researchers have recognized health-related quality of life (HRQoL) as an important patient-reported outcome in PD [11-13]. One study suggested that AA patients with PD might have worse HR-QoL scores, however, these findings have not been yet confirmed in larger, population-based studies [14]. Additionally, the explanations for any differences remain unclear, and to our knowledge, there are no data that examine HR-QoL in other underrepresented minorities with PD, including Hispanic and Asian patients.

The evaluation of practice patterns and underlying reasons behind HRQoL differences in underrepresent minorities is crucial to improve care to all patients. Therefore, our current study aims to

explore potential treatment and outcome differences among White, Hispanic, AA, and Asian individuals with PD in a large population-based sample of patients.

Methods

Data Source

The study data originated from the Parkinson Foundation Parkinson's Outcomes Project (PF-POP), which includes data from Parkinson's Foundation Centers of Excellence. Patients with a clinical diagnosis of PD are invited to participate without exclusions. The database contains detailed information from patients over the preceding year. Considering the significant cultural differences between participating countries, and overall inconsistency in racial and ethnic designations, the analysis was restricted to sites in the US only.,

All study visits were held approximately 10–18 months apart, with participants automatically withdrawn if they went 24 months without a subsequent return visit scheduled. The diagnosis of PD was confirmed by the clinical judgement of the treating movement disorders expert considering all available information. Inclusion criteria to be part of study required the presence of a diagnosis of PD, and the only exclusion criteria was unwillingness or inability to provide informed consent at the time of recruitment. Translated versions of the PDQ-39 form were available to all centers (including Spanish, French, Hebrew, and Italian). All statistical analyses were performed by a POP statistician (LS).

Study design and variables

A retrospective cross-sectional analysis was performed when examining baseline characteristics, including medication management and use of therapies. For the evaluation of longitudinal PDQ-39 data, a retrospective cohort design was used. The primary outcome measure of our study was HRQoL as measured by the 39-item PD questionnaire (PDQ-39) [15, 16]. Secondary variables of interest included patient demographics including age, sex, level of education. Additionally, we evaluated clinical management variables and outcomes, including medication characteristics, exercise program, use of physical occupational and speech therapies, deep brain stimulation placement, and cognitive scores. For the purposes of the analysis, exercise program was defined as a binary variable representing self-report of participating in any type or duration of physical activity. Cognition was measured as Z-scores based on the combination of immediate 5-word recall, verbal fluency (animal category) and delayed 5-word recall, with higher scores indicating better cognitive performance. Detailed methods have been previously described [17, 18].

The most widely accepted classification of race/ethnicity by the US Office of Management and Budget (OMB) described in the Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity was used [19]. Participants were divided in four groups, comprising White non-Hispanic, AA non-Hispanic, Asian non-Hispanic and Hispanic patients. Underrepresented minorities were considered those other than non-Hispanic white patients. Race and ethnicity were determined by self-identification.

Statistical analysis

No sample size calculations were done when the registry was conceived due the hypothesis-free nature of the data collection. Due to the retrospective and broad exploratory nature of these analyses no specific power analysis was performed. Sample characteristics, therapies and outcomes were compared between the four racial/ethnic categories. Differences in means were tested using analysis of variance (ANOVA) and differences in categorical variable were analyzed using Chi Square or Fisher's exact tests.

Multivariable regression analyses were performed to compare differences in clinical management and PDQ-39 scores at baseline between racial and ethnic groups with adjustment for sex, age, cognitive score, PD duration and H&Y Stage, heart disease, diabetes, cancer, and hypertension. Adjustment variables were selected based on difference and distribution across racial/ethnic groups and or clinical relevance.

For evaluation of associations with longitudinal measurements of quality of life, linear mixed models with random intercept and random slope of time were used with the continuous PDQ-39 being the response variable. Due to the skewness of this variable, models based on skew-normal and skew-t distributions, instead of normal distributions, were adopted [20]. The base model included as covariates race/ethnicity (4 categories with white non-Hispanic patients being the reference group), age at baseline, sex, PD duration at baseline, H&Y stage at baseline (stages 1-1.5, 2-2.5, 3, 4, 5, using stage 1 as the reference group), heart disease, diabetes, cancer and hypertension. Based on the model selection criteria, skew-t linear mixed model had the lowest Akaike's Information Criteria (AIC) and Bayesian Information Criteria (BIC), therefore it was selected as the final model. Statistically significant variables were further analysed for pairwise differences using White patients as the reference group within the multivariable model. P-values were adjusted for multiple comparisons using the Bonferroni method.

We conducted a mediation analysis to understand the extent to which each covariate would influence the association of race/ethnicity and PDQ-39 scores. With this framework, mediating variables were a step in the chain of events between race/ethnicity and different HR-QoL scores, partially accounting for this association. With PDQ-39 score as the dependent variable, a multivariable mixed linear regression model with skewed-t errors was used, adding each potentially mediating variable to the mixed linear model including follow-up time in years, race, sex, age at baseline, PD duration at baseline, PD HY stage at baseline, cognitive score, baseline presence of cancer, heart disease, diabetes, and hypertension.

A likelihood ratio test was used to compare models with/without each potentially mediating variable. In the case of any marked change in beta-coefficients and statistical significance, the target variable ("mediator variable") was then included in an additional mediation analysis to calculate the average causal mediation effects (ACME), the average direct effect (ADE), and the proportion of mediation using using the "mediation" package (version 4.5.0) in R software (version 4.1.0) [21]. A p-value <0.05 was considered significant. Statistical analysis was performed using R statistical program (version 4.1.0).

Standard Protocol Approvals, Registrations, and Patient Consents

Detailed data regarding the study design can be found on ClinicalTrials.gov under the study identifier NCT01629043 (Parkinson's Foundation Quality Improvement Initiative). All participants were required to provide written informed consent prior to study enrollment. Independent ethics approval was obtained at each clinical site).

Data Availability

Data not provided in the manuscript due to space limitation, although anonymized and de-identified POP data are available upon request.

Results

Patient Characteristics

At the time of analysis, 13,174 participants from 31 centers had been included in the project database. 4,660 patients were excluded for the following reason: 3,864 patients outside the US, 796 patients with missing baseline data on race and ethnicity. A total of 8,514 participants from 19 centers

were included in the final analysis. All participants were evaluated at least once between July 14, 2009, and February 20, 2020. For the longitudinal analysis, patients with at least one visit during the above period (2009-2020) were included. A total of 69.3% (5902 out of 8514) participants had at least two visits.

Participating patients were White (90.28%) followed by 5.81% Hispanics, 1.99% Asians, and 1.90% AA. The characteristics of the individuals included in our study are described in Table 1. Overall, in our cohort, White patients had greater years of educational attainment, compared to AA, and Hispanic patients but fewer than Asians. White, Hispanic and Asian patients were more likely to have a regular care partner when compared to African Americans individuals.

Regarding comorbidities, African American individuals had the highest rate of heart conditions (32.1%) followed by White (27.7%), Asian (25.3%) and Hispanic patients (18.8%). On the other hand, Asians had higher rates of diabetes (15.3%), followed by African Americans (11.1%), Hispanic (9.9%) and White patients (8.7%) (Table 1).

Disease characteristics

A summary of detailed disease characteristics is shown in Table 1. Most patients had a H&Y stage between 2-2.5. There was no significant difference in disease duration across racial and ethnic groups. Dyskinesias and wearing-off symptoms were more prevalent in Asian patients, although limiting or bothersome dyskinesias were more frequent in AA patients. Cognitive scores were higher in White when compared to other racial and ethnic groups as measured by Z-scores (0.08±0.74 vs. -0.2±0.74 in AA, -0.11±0.77 in Asians and -0.07±0.73 in Hispanics).

Management

Adjusted analysis of treatment characteristics at baseline according to race and ethnicity are shown in Table 2. Across all racial/ethnic groups, more than 80% were on a form of levodopa. The mean levodopa equivalent daily dose (LEDD) was significantly higher in Asian and Hispanic patients (260 ± 707 and 206 ± 404 respectively) compared to White (148 ± 364) and AA patients (129 ± 316). White patients were significantly more likely to be prescribed dopamine agonists when compared to AA patients (41% vs. 28.7% respectively). White patients were also significantly more likely to be prescribed antidepressant medications (32.1% vs. 23% in AA, and 21.9% in Asian patients). This was also similar when evaluating patients with higher emotional subscore in the PDQ-39 (>=10), among which the rate of antidepressant treatment was higher in White patients (52.1% vs. 35.6% in AA, 35.9% in Asians and 41.5% in Hispanic patients). Hispanic patients had the highest MAO-B inhibitor prescription rate (36.1% vs. 26.4% in White patients)

Regarding other forms of treatments, there were differences among groups in nonpharmacologic management. Speech and physical therapies use was lower in Hispanic patients when compared to other racial and ethnic groups (10.7% vs. 15.5% in White patients). Additionally, Asian patients had a higher enrollment in exercise programs (83.9% vs. 72.3% in White individuals). There were also differences in social worker counseling, with Asian patients having the lowest proportional number of enrollments (2.4% vs. 7.4% in White individuals).

Health-Related Quality of Life

Total baseline PDQ-39 scores were significantly higher (worse) in minority groups when compared to White non-Hispanic patients ($p<0.001$) after adjusting for sex, age, cognitive scores, PD duration and HY stage and presence of cancer, heart disease, diabetes, and hypertension at baseline (Table 3). Individual PDQ-39 subscales mobility, ADL, emotional well-being, stigma, social support, and pain scores were worse among underrepresented minorities.

In our longitudinal analysis, follow-up time, race, sex, age at baseline, H&Y stage, cancer, heart problem and diabetes were significantly associated with PDQ-39 total scores (eTable1). A marked decrease in significance between race/ethnicity and PDQ-39 was found following further adjustment for cognitive score (eTable 2). Prior to adjusting the model for baseline cognitive scores variable, p-values were highly significant (<0.01) for AA, Asian and Hispanics when compared to White patients. Following inclusion of cognition to the model, beta coefficients markedly decreased, and p-values increased for AA (2.406 to 1.626 and p-values 0.003 to 0.043) and Asian individuals (2.279 to 1.743 and p-values 0.009 and 0.045, respectively). Adding other patient characteristics, comorbidities or management variables to the model including LEDD, did not significantly change the results (eTable 2). A subsequent mediation analysis evaluating the impact of each individual covariate on HRQoL demonstrated that cognition partially mediated the relationship between PDQ-39 scores and race/ethnicity (ACME 0.922, p<0.001; proportion mediated 0.251, p <0.001) (Figure and eTable 3).

Discussion

The analysis of this large cohort evaluating more than 8000 PD patients identified the characteristics, management and clinical outcomes of patients evaluated at specialized US tertiary care centers. Overall, minorities reported worse HRQoL when compared to White non-Hispanic patients, which was not explained by disease duration, H&Y stage, sex, age, or the presence of clinically relevant comorbidities. However, cognition appeared to partially mediate the differences between minority groups and White non-Hispanic patients. Previous studies have demonstrated that underrepresented minorities may have limited access to neurologists, medications, and other therapies. Our study reveals that some health disparities and management differences persist even with ongoing expert neurologist care. Despite the racial diversity in the communities of many of the included sites in PF-POP, the vast majority of included patients in US sites to date remain White and non-Hispanic. This constitutes a stark underrepresentation of non-White individuals in this research study, mirroring the lack of inclusion of non-White individuals in health research. Nevertheless, to our knowledge, this is the largest cohort describing the detailed clinical features and outcomes of underrepresented minorities with Parkinson's disease, and one of the few to provide data on HRQoL.

Regarding differences in PD course, minorities, including AA and Hispanic patients had overall lower cognitive scores. This is in keeping with the literature, where AA and Hispanic individuals with PD have been shown to perform worse in cognitive testing [10]. Although the underlying etiology for lower cognitive scores in minority groups is unclear, several hypotheses have been considered, including co-pathology. AA patients having a higher probability of mixed pathologies on postmortem examination [22], as well as a higher prevalence of cardiovascular risk factors which might contribute to the underlying dementia [23, 24]. Our results corroborate some of these findings, with AA patients having the highest prevalence of self-reported heart conditions.

Previous studies have also considered the contribution of life-long social experiences, including lower socioeconomical status, education and other psychological stressors that may be associated with worse cognitive scores in this population [25]. In our cohort, AA and Hispanic patients had slightly lower years of education, although we were not able to assess quality of education. Racism and discrimination have also been hypothesized as a potential contributor to lower cognitive scores in AA and Hispanic patients, although not clearly observed in Asian individuals [26-29]. Previous Medicare data analyses have found higher rates of dementia in AA patients with PD, and more frequent prescribing of specific drug therapies for dementia [10, 30]. Additionally, AA patients have been frequently shown to be at higher risk for dementia and Alzheimer's disease (AD) [31, 32], including a higher cumulative risk in first-degree relatives of AA with AD when compared to white individuals with AD [33]. Finally, cultural biases have also been shown to potentially influence the results of cognitive testing, and these may account for some of the observed differences [34].

All groups had a similar rate of levodopa prescription. However, despite having similar disease duration and H&Y stages, AA and Hispanic patients were also less likely to be prescribed anti-depressant medications when compared to White patients despite higher scores on the emotional well-being subscale of the PDQ-39. The differences observed in our cohort are in partial agreement with previous studies, which demonstrated that AA patients are less likely to receive any PD medication, or to have depression treatment when compared to white patients [8, 9, 35, 36]. Differences in depression treatment have been reported between racial and ethnic groups without PD, possibly due to lower levels of acceptance by minorities [37, 38]. We do not have information on the reason underlying such differences in our cohort, although it is also possible that there were additional contraindications to higher levodopa doses (such as worse cognition), or other specific medications.

Underrepresented racial and ethnic groups had worse HRQoL as observed by PDQ-39 scores ranging from 2.7 to 5.83 units higher when compared to White patients. Although no clinically relevant difference has been defined for comparison between independent groups, the thresholds for minimally clinically important difference (MCID) for the PDQ-39 total score has been suggested to be –4.72 and +4.22 among individuals with PD followed over time [39]. In our cohort, worse PDQ-39 scores in non-White racial and ethnic groups were also observed across several PDQ-39 subscales. For instance, mobility, activities of daily living (ADL), stigma and social support sub-scores were particularly higher for AA patients. Although previous retrospective studies have described worse outcomes for AA patients with PD [8, 40], the evaluation of HR-QoL in underrepresented minorities with PD has been less explored. A recent study reported that in a cohort of 24 AA and 25 White individuals with PD, AA patients had significantly higher PDQ-39 scores, and in the subscales of mobility, ADL, cognition, and body discomfort [14]. Similar findings have also been reported in the context of stroke, where African American and Hispanic patients were found to have worse quality of life following stroke recovery when compared to White patients [41]. There are also reports of increased non-motor symptom burden in underrepresented minorities which likely contribute to reduced HRQoL [42]. Our current dataset does not allow us to explore the prevalence of non-motor symptoms in detail.

We found similarly worse HRQoL when comparing Hispanics and Asians to White non-Hispanic individuals with PD. Specifically, Hispanic patients were more likely to have impairment in mobility, and ADL. Additionally, Asian patients had significantly worse mobility, ADL, stigma, pain and social support scores. To our knowledge, our study is the first to demonstrate worse HRQoL in Asian and Hispanic patients compared to White individuals living with PD.

When examining potential mediating effects, cognitive scores were found to account for some of the differences in PDQ-39 scores among underrepresented minorities. This finding suggests that the difference in HRQoL observed among different racial and ethnic groups might be partially mediated by cognitive differences; and, therefore, additional cognitive screening and treatment might be particularly important when evaluating an ethnically diverse group of patients. In keeping with our results, it has been previously demonstrated that non-motor symptoms, including cognitive impairment, can significantly impact HRQoL in individuals with PD [43-47]. A recent longitudinal study found that patients with baseline PD and mild cognitive impairment (PD-MCI) had worse HRQoL over 36 months, with poor attention being considered a robust predictor of decline [48].

Our study has several limitations. First, it only contains data on patients treated at Parkinson's Foundation Centers of Excellence, which is unlikely to be representative of the overall care provided worldwide. Given the limited access to neurologists and movement disorders specialists, we would expect even larger health care gaps and differences outside dedicated PD centers. The smaller number of individuals in the non-White non-Hispanic groups limits our ability to detect small but potentially important differences. Additionally, despite the availability of detailed clinical characteristics, we do not have comprehensive neuropsychological assessments. Given our findings related to cognition, a more detailed examination of the relationship between cognition and HR-QoL disparities is warranted. We

also do not have full details on the social determinants of health that may impact the care and outcomes of the participants, such as income, profession, and cultural influence. A clustering analysis, taking into account the influence of clinical sites, was considered; however, due to the small sample sizes in certain categories this method was not performed. Finally, we did not adjust our final analysis by level of education, considering the high percentage of missing data. Other variables, such as referral to therapies, also had a high proportion of missing data, which could have impacted our final conclusions.

Conclusion

In summary, in our large cohort evaluating more than 8000 PD patients treated at Parkinson's Foundation Centers of Excellence, we have found that racial and ethnic minorities have worse HRQoL when compared to White, non-Hispanic patients. Our study suggests that some of the quality-of-life differences might be mediated by cognitive status, which varied significantly among different groups. Moreover, our analysis also provides a unique and detailed description of clinical features and differences in the management and outcomes of minorities patients with PD, historically underrepresented in research.

Additional studies should be pursued with a focus on a better understanding of the reasons for treatment and outcome differences in underrepresented populations, including differences in cognitive deficits, non-motor symptoms, clinical care and HRQoL. The inclusion of minorities in large observational research and clinical trials is critical for advancing our understanding of PD across all races and ethnicities, including potential phenotypic or biological differences in the natural PD course. Qualitative research examining approaches and attitudes to treatment from the health care provider and patient perspective are also needed to identify opportunities to improve care in non-White people with PD.

http://links.lww.com/WNL/C718

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Table 1. Baseline demographics and clinical characteristics of PD patients at baseline enrolment divided by race and ethnicity.

Variable		*White Non-Hispanic patients (N = 7,687)*	*African American Non-Hispanic patients (N = 162)*	*Asian Non-Hispanic patients (N = 170)*	*Hispanic patients (N = 495)*	*P value**
Age	Years (mean ± SD) min, max	67.24±9.45 25,95	66.07±10.32 38,90	65.22±9.94 37,86	65.08±10.69 28,93	<0.001
	Missing	18	0	0	2	
Male, N (%)		4866 (63.3)	83 (51.2)	111 (65.3)	311 (63)	0.016
	Missing	1	0	0	1	
Living situation, N (%)	At home	1611 (97.2)	34 (100)	43 (100)	147 (96.7)	0.245
	Skilled care	35 (2.1)	0 (0)	0 (0)	1 (0.7)	
	Other	11 (0.7)	0 (0)	0 (0)	4 (2.6)	
	Missing	6030	128	127	343	
Regular care partner, N (%)	No	1158 (15.1)	42 (25.9)	25 (14.7)	82 (16.6)	<0.001
	Spouse/partner	6050 (78.8)	99 (61.1)	138 (81.2)	373 (75.5)	
	Other relative	301 (3.9)	17 (10.5)	5 (2.9)	32 (6.5)	
	Paid caregiver	127 (1.7)	3 (1.9)	0 (0)	4 (0.8)	
	Other	44 (0.6)	1 (0.6)	2 (1.2)	3 (0.6)	
	Missing	7	0	0	1	
Level of Education, N (%)	Less than High School	47 (1.3)	1 (1.6)	3 (3.7)	23 (7.9)	<0.001
	High School	475 (13.5)	16 (25.8)	7 (8.5)	57 (19.7)	
	Some Post-High School	762 (21.6)	16 (25.8)	16 (19.5)	76 (26.2)	
	Bachelor's Degree	1072 (30.5)	18 (29)	18 (22)	79 (27.2)	
	Graduate Degree (Master's/Professional /Doctoral)	1164 (33.1)	11 (17.7)	38 (46.3)	55 (19)	
	Missing	4167	100	88	205	
Employment Status, N (%)	Outside of Home Full time	301 (18.2)	8 (24.2)	12 (27.3)	34 (22.4)	0.325
	Outside of Home Part Time	157 (9.5)	2 (6.1)	1 (2.3)	15 (9.9)	

	Not Employed	1198 (72.3)	23 (69.7)	31 (70.5)	103 (67.8)	
	Missing	6031	129	126	343	
Duration of care at POP center	Years (mean ± SD) (min, max) Cognitive z-score (combined)	6.3±4.8 0,40	5.39±4.67 0,22	6.11±5.21 0,27	4.88±4.26 0,19	<0.001
	Missing	4242	105	93	211	
Disease Duration	Years (mean ± SD) (min, max)	6.70±5.73 0,49	6.73±5.37 0,21	7.06±5.99 0,33	6.65±5.65 0,33	0.867
	Missing	41	1	3	3	
Hoehn and Yahr stage, N (%)	1	872 (12.1)	14 (9.1)	12 (7.9)	55 (11.5)	0.018
	2 – 2.5	4141 (57.5)	80 (51.9)	87 (57.6)	297 (62)	
	3 – 3.5	1755 (24.4)	40 (26)	41 (27.2)	103 (21.5)	
	4	368 (5.1)	20 (13)	10 (6.6)	20 (4.2)	
	5	65 (0.9)	0 (0)	1 (0.7)	4 (0.8)	
	Missing	486	8	19	16	
Cognition (Z-score)	Score (mean ± SD) (min, max)	0.08±0.74 -4.58,2.06	-0.2±0.74 -2.75,1.36	-0.11±0.77 -2.75,1.26	-0.07±0.73 -3.15,1.91	0.001[#]
	Missing	107	1	7	8	
Dyskinesias over the last 30 days, N (%)		473 (28.8)	10 (31.2)	20 (47.6)	47 (31.1)	0.191
	Missing	6043	130	128	344	
Wearing-off, N (%)		709 (43.2)	13 (39.4)	23 (54.8)	75 (49.7)	<0.001
	Missing	6046	129	128	344	
Heart problem		2130/7687 (27.7)	52/162 (32.1)	43/170 (25.3)	93/495 (18.8)	<0.001
Lung problem		82/7687 (1.1)	1/162 (0.6)	4/170 (2.4)	5/495 (1)	0.401
Diabetes		665/7687 (8.7)	18/162 (11.1)	26/170 (15.3)	49/495 (9.9)	0.013
Cancer		1090/7687 (14.2)	12/162 (7.4)	13/170 (7.6)	52/495 (10.5)	<0.001
Osteoarthritis		508/7687 (6.6)	10/162 (6.2)	12/170 (7.1)	40/495 (8.1)	0.632
Depression		500/7687 (6.5)	11/162 (6.8)	10/170 (5.9)	54/495 (10.9)	0.002[#]

High blood pressure		516/7687 (6.7)	16/162 (9.9)	17/170 (10)	57/495 (11.5)	<0.001

**P values from ANOVA for continues variables (ie., age, duration of care at POP center, disease duration, and cognition score), and from chi-square test for other categorical variables. Fisher exact test was used when there were at least cells with expected frequencies are less than or equal to 5.

[#] P value < Bonferroni-corrected p value threshold (0.05/18 = 2.78E-03).

Table 2. Adjusted differences in clinical management at baseline among different races and ethnic groups.

Variable	*White Non-Hispanic patients (N = 7,687)*	*African American Non-Hispanic patients (N = 162)*	*Asian (Non-Hispanic) patients (N = 170)*	*Hispanic patients (N = 495)*	*P-value**
Medications before visit					
Any form of Levodopa, N (%)	6396/7651 (83.6)	143/162 (88.3)	144/169 (85.2)	411/492 (83.5)	0.697
Dopamine agonist, N (%)	3100/7561 (41)	46/160 (28.7)	63/169 (37.3)	195/490 (39.8)	0.022
Nominal P-value** Bonferroni corrected P-value**		0.005 0.014	0.354 1.000	0.428 1.000	
MAO-B inhibitor, N (%)	1989/7547 (26.4)	34/161 (21.1)	46/169 (27.2)	176/488 (36.1)	<0.001
Nominal P-value** Bonferroni corrected P-value**		0.955 1.000	0.120 0.360	<0.001 <0.001	
COMT inhibitor, N (%)	1153/7515 (15.3)	20/160 (12.5)	29/169 (17.2)	58/489 (11.9)	0.064
Nominal P-value** Bonferroni corrected P-value**		0.336 1.000	0.599 1.000	0.018 0.053	
Amantadine, N (%)	1154/7514 (15.4)	27/160 (16.9)	32/169 (18.9)	83/488 (17)	0.950
Antidepressant medications, N (%)	2446/7627 (32.1)	37/161 (23)	37/169 (21.9)	139/493 (28.2)	<0.001
Nominal P-value** Bonferroni corrected P-value**		0.002 0.005	0.001 0.003	0.060 0.179	
Antidepressant medications among patients with PDQ-39 emotional subscore >=10, N (%)	747/1443 (52.1)	16/45 (35.6)	14/39 (35.9)	54/131 (41.5)	<0.001
Nominal P-value** Bonferroni corrected P-value**		0.010 0.030	0.060 0.181	0.007 0.020	

Cognitive enhancers, N (%)	603/7610 (7.9)	13/161 (8.1)	7/169 (4.1)	35/493 (7.1)	0.073
Antipsychotic medication, N (%)	45/1612 (2.8)	2/34 (5.9)	2/44 (4.5)	5/151 (3.3)	0.749
Levodopa Equivalent Daily Dose (LEDD), Mean ± SD (Min,max)	148 ± 364 0,3950	129 ± 316 0,1664	260 ± 707 0,4650	206 ± 404 0,2695	<0.001
Nominal P-value** Bonferroni corrected P-value**		0.414 1.000	1.2E-04 3.6E-04	0.053 0.159	
Other treatments					
Physical therapy use, N (%)	2930/7671 (38.2)	58/162 (35.8)	74/170 (43.5)	140/492 (28.5)	<0.001
Nominal P-value** Bonferroni corrected P-value**		0.242 0.727	0.085 0.256	<0.001 0.002	
Occupational therapy use, N (%)	903/7671 (11.8)	22/162 (13.6)	23/170 (13.5)	39/490 (8)	0.049
Speech therapy use, N (%)	966/6236 (15.5)	19/135 (14.1)	22/135 (16.3)	37/347 (10.7)	0.002
Nominal P-value** Bonferroni corrected P-value**		0.202 0.606	0.493 1.000	0.003 0.010	
Exercise program, N (%)	5517/7630 (72.3)	104/159 (65.4)	141/168 (83.9)	350/490 (71.4)	0.005
Nominal P-value** Bonferroni corrected P-value**		0.548 1.000	0.001 0.004	0.439 1.000	
Social worker/ counseling, N (%)	565/7666 (7.4)	12/162 (7.4)	4/170 (2.4)	21/489 (4.3)	0.002
Nominal P-value** Bonferroni corrected P-value**		0.527 1.000	0.016 0.048	0.022 0.065	
Mental health treatment or referral, N (%)	651/7555 (8.6)	11/162 (6.8)	11/169 (6.5)	31/484 (6.4)	0.119

Deep Brain Stimulation, N (%)	881/7630 (11.5)	12/162 (7.4)	19/169 (11.2)	54/493 (11)	0.025
Nominal P-value** Bonferroni corrected P-value**		0.019 0.057	0.194 0.581	0.238 0.715	

Abbreviations: MAO-B inhibitor=Monoamine Oxidase Type B; COMT-inhibitor=catechol-O-methyltransferase, PDQ-39= The Parkinson's Disease Questionnaire.
* P value of likelihood ratio test of the full model (including sex, age, cognitive score, PD duration, Hoehn and Yahr Stage, heart problem, diabetes, cancer, high blood pressure, race) and reduced model (without race).
** Post-hoc Nominal P value and Bonferroni adjusted P value of each subgroup in the multivariable model while using Non-Hispanic White group as reference, for statistically significant variables.

Table 3: Adjusted differences in quality of life at baseline among different races and ethnic groups.

Variable		*White Non-Hispanics patients (N = 7,687)*	*African American Non- Hispanic patients (N = 162)*	*Asian (Non-Hispanic) patients (N = 170)*	*Hispanic patients (N = 495)*	*P-value**
PDQ-39 Total Score	Total score (mean ± SD) (min, max)	22.73±15.33 0,93.75	28.56±17.55 0,77.34	26.62±16.66 0,67.45	25.43±17.39 0,95.83	<0.001
	Nominal P[#]		0.013	0.092	<0.001	
	Corrected P[#]		0.039	0.275	0.003	
	Raw $P_{t\text{-}test}$		<0.001	0.002	<0.001	<0.001
	Corrected $P_{t\text{-}test}$		<0.001	0.005	<0.001	
PDQ-39 Subscales						
Mobility	Score (mean ± SD) (min, max)	27.78±26.77 0,100	38.77±30.75 0,100	35.78±27.3 0,100	32.52±28.56 0,100	<0.001
	Nominal P[#]		0.004	0.003	<0.001	
	Corrected P[#]		0.012	0.009	<0.001	
	Raw $P_{t\text{-}test}$		<0.001	<0.001	<0.001	<0.001
	Corrected $P_{t\text{-}test}$		<0.001	<0.001	<0.001	
ADL	Score (mean ± SD) (min, max)	27.61±23.32 0,100	35.7±26.56 0,100	32.25±25.26 0,100	30.82±26.27 0,100	<0.001
	Nominal P[#]		0.023	0.187	<0.001	
	Corrected P[#]		0.068	0.560	<0.001	
	Raw $P_{t\text{-}test}$		<0.001	0.012	0.003	<0.001
	Corrected $P_{t\text{-}test}$		<0.001	0.037	0.010	
Emotional well-being	Score (mean ± SD) (min, max)	23.16±19.06 0,100	26.29±21.06 0,91.67	25.58±21.34 0,100	27.22±22.15 0,100	0.007
	Nominal P[#]		0.755	0.682	<0.001	
	Corrected P[#]		1.000	1.000	<0.001	
	Raw $P_{t\text{-}test}$		0.042	0.112	<0.001	<0.001
	Corrected $P_{t\text{-}test}$		0.126	0.336	<0.001	
Stigma	Score (mean ± SD) (min, max)	17.08±19.6 0,100	24.07±24.96 0,100	21.76±23 0,93.75	20.9±23.78 0,100	0.001
	Nominal P[#]		0.003	0.216	0.014	
	Corrected P[#]		0.009	0.618	0.043	
	Raw $P_{t\text{-}test}$		<0.001	0.003	<0.001	<0.001
	Corrected $P_{t\text{-}test}$		<0.001	0.009	<0.001	

Social support	Score (mean ± SD) (min, max)	9.83±15.35 0,100	16.04±21.2 0,100	12.22±17.11 0,91.67	10.57±16.26 0,91.67	0.002
	Nominal P[#] Corrected P[#]		<0.001 <0.001	0.615 1.000	0.931 1.000	
	Raw $P_{t\text{-}test}$ Corrected $P_{t\text{-}test}$		<0.001 <0.001	0.051 0.153	0.309 0.916	<0.001
Cognition	Score (mean ± SD) (min, max)	24.39±19.28 0,100	28.69±20.19 0,81.25	25.04±19.28 0,81.25	24.19±20.48 0,100	0.563
Communication	Score (mean ± SD) (min, max)	21.71±21.38 0,100	27.07±23.57 0,100	26.05±22.8 0,100	22.29±22.26 0,100	0.054
Pain	Score (mean ± SD) (min, max)	30.61±22.81 0,100	32.92±22.04 0,100	34.29±24.28 0,100	34.87±25.71 0,100	0.003
	Nominal P[#] Corrected P[#]		0.654 1.000	0.167 0.501	<0.001 <0.001	
	Raw $P_{t\text{-}test}$ Corrected $P_{t\text{-}test}$		0.208 0.624	0.042 0.126	<0.001 <0.001	<0.001

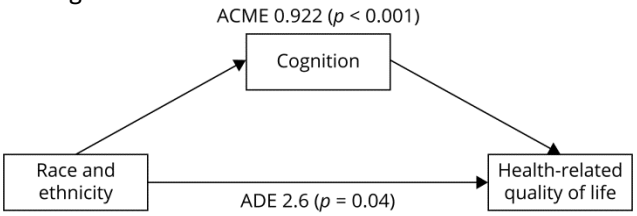
*P value of the likelihood ratio test by comparing the full GLM model and reduced model (including sex, age, cognitive score, PD duration, Hoehn and Yahr Stage, heart problem, diabetes, cancer, and high blood pressure, with/without race).

[#] Nominal P value and Bonferroni adjusted (Corrected) P value of each subgroup in the multivariable model while using "White" group as reference.

Figure. Simplified schematic mediation model for cognition.

Figure Legend:
Mediation analysis model evaluating the influence of cognitive scores on the association of race/ethnicity and health-related quality of life, as measured by PDQ-39 scores.

Abbreviations: ACME Average causal mediation effects; ADE Average direct effect



*Proportion mediated: 0.251 ($p < 0.001$)

Racial and Ethnic Differences in Health-Related Quality of Life for Individuals with Parkinson Disease Across Centers of Excellence

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Neurology published online April 5, 2023
DOI 10.1212/WNL.0000000000207247