Title

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Journal

The journals of gerontology. Series A, Biological sciences and medical sciences, 78(7)

ISSN

1079-5006

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Publication Date

2023-07-01

DOI

10.1093/gerona/glad016

Peer reviewed

THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2023, Vol. 78, No. 7, 1258–1268
https://doi.org/10.1093/gerona/glad016
Advance Access publication January 16, 2023

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Research Article

Ethnicity and Parkinson's Disease: Motor and Nonmotor Features and Disease Progression in Latino Patients Living in Rural California

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Received: September 9, 2022; Editorial Decision Date: December 28, 2022

Decision Editor: Jay Magaziner, PhD, MSHyg

Abstract

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder among older adults worldwide. Currently, studies of PD progression rely primarily on White non-Latino (WNL) patients. Here, we compare clinical profiles and PD progression in Latino and WNL patients enrolled in a community-based study in rural Central California.

Method: PD patients within 5 years of diagnosis were identified from 3 counties between 2001 and 2015. During up to 3 visits, participants were examined by movement disorders specialists and interviewed. We analyzed cross-sectional differences in PD clinical features severity at each study visit and used linear mixed models and Cox proportional hazards models to compare motor, nonmotor, and disability progression longitudinally and to assess time to death in Latinos compared to WNL patients.

Results: Of 775 patients included, 138 (18%) self-identified as Latino and presented with earlier age at diagnosis (63.6 vs 68.9) and death (78.6 vs 81.5) than WNL. Motor (hazard ratio [HR] = 1.17 [0.71, 1.94]) and nonmotor symptoms did not progress faster in Latino versus WNL patients after accounting for differences in baseline symptom severity. However, Latino patients progressed to disability stages according to Hoehn and Yahr faster than WNL (HR = 1.81 [1.11, 2.96]). Motor and nonmotor symptoms in Latino patients were also medically managed less well than in WNL.

Conclusions: Our PD study with a large proportion of Latino enrollees and progression data reveals disparities in clinical features and progression by ethnicity that may reflect healthcare access and structural socioeconomic disadvantages in Latino patients with PD.

Keywords: Cohort study, Disease progression, Ethnic differences, Minority aging, Motor decline

Parkinson's disease (PD) is the second most common neurodegenerative disorder among older adults in the world, after Alzheimer's disease (1). While PD is more widely known for its motor signs that include mainly tremor, slowness of movements, and rigidity, the disease manifests clinically in a variety of motor and nonmotor symptoms, which present and progress heterogeneously. In fact, heterogeneity is a central aspect of clinical PD, stifling attempts at prognosing and understanding contributors to progression, even though more and more studies are aiming to identify predictors among genetic, environmental, and lifestyle factors (2–6). Emerging evidence (7) suggests that ethnicity is one key determinant of heterogeneity in PD epidemiology, clinical manifestations, and mortality.

However, Hispanic or Latino ethnicity or origin encompasses a variety of factors that may contribute to disease heterogeneity, including geographical origin, cultural, socioeconomic and lifestyle aspects, and possibly biologic responses to the environment (8).

People of Latino or Hispanic ethnicity or origin (henceforth, Latino) constitute the largest minority ethnic group in the United States, comprising almost 20% of the country's and 40% of the California state population from 2010 to 2020 (9,10). California is the U.S. state with the highest concentration of the Latino population, followed by Texas and Florida, but the Latino population across the United States is a diverse group regarding Latin American origin and race identification. While in California and Texas, people who identify as Latino are largely of Mexican origin, in Florida and New York, the most common origin is Central America, including Cuba, Puerto Rico, and the Dominican Republic. In California, the Latino population tends to be younger on average than the state's non-Latino population. However, the age difference is projected to narrow in the next few decades as the Latino population is also one of the fastest growing aging populations in the United States, increasing more than twice as fast as the total California state older population from 1990 to 2020 (10). Additionally, according to an analysis of data from 2010 to 2014, people of Latino ethnicity in California tended to earn less income than those who do not identify as Latino, and thus, are underrepresented among higher and overrepresented in lower income brackets, and are also more likely to live in poverty (10).

Current knowledge about PD relies primarily on clinical and epidemiological studies enrolling predominantly or solely people who are White non-Latino (WNL) (11). Some multiethnic studies have started to report contrasts in prevalence or incidence of PD rates across ethnicities; however, results are not consistent, with some reporting higher incidence of PD in Latinos compared to WNL (12,13) and others finding a similar or even lower prevalence of PD in Latinos compared to the general U.S. population (14,15). As the population ages, particularly the Latino population in the United States, a substantial rise in disease burden related to PD is to be expected. Thus, understanding ethnicity-related disparities of PD clinical progression in the multiethnic population of the United States is central to providing insights into clinical care and developing health policies that address disparities arising from socioeconomic aspects, including discrimination. While some large consortia were set up to study genetic factors contributing to the etiology of PD in Latin Americans (16,17), the clinical phenotype is only minimally explained by genetic differences (18). To our knowledge, no studies have described clinical features and progression of PD among U.S. Latinos in the context of ethnicity-related cultural, lifestyle, and socioeconomic factors.

Understanding whether there is PD heterogeneity in terms of clinical features and progression related to Latino ethnicity may help reduce disparities in health outcomes, namely, factors related to the quality of clinical care such as timely diagnosis and treatment. Here we compare clinical progression in Latino to WNL patients in a community-based study of PD conducted in a rural region of Central California.

Method

The UCLA Institutional Review Board approved all phases of the study protocol, and participants were informed of all procedures and their rights and provided written informed consent.

Study Design

The Parkinson's Environment and Genes Study (PEG) identified PD cases at baseline from 2001 to 2007 (PEG 1) and from 2011 to 2017 (PEG 2), from the entire population of 3 Central California counties; study design details are provided elsewhere (6,19). Briefly, in PEG 1 recruitment of cases, we used public service announcements and word-of-mouth advertising at community organizations and support groups, as well as active recruitment at medical clinics and offices serving PD patients throughout the 3 target counties. In PEG 2, we mainly used the information provided by the pilot program for a PD registry in the 3 counties, a program that also had targeted clinics and other healthcare facilities, and we also conducted some community outreach. Both phases attempted to enroll new-onset patients, up to the first 3 and then 5 years after diagnosis. However, 3% of participants were accepted after 10 or more years since diagnosis because they would have been eligible for PEG 1, but were only identified during PEG 2 recruitment. PEG 1 and 2 participants were seen at baseline and again at up to 2 follow-up visits, the first on average 3.3 years after baseline and the second on average 2.3 years after the first follow-up. At all visits, patients were examined at a local clinic by PEG study movement disorder neurology specialists (J.B. and A.M.K.), who confirmed the PD diagnosis according to the established criteria (19). Self-reported race or ethnicity information on all subjects screened for the study was collected as required by the study funder (National Institute of Environmental Health Sciences [NIEHS]). Here, we restricted our study sample to PD patients who self-identified as Latino, Hispanic, or White (N = 775), that is, comprising 93% of all patients enrolled originally at baseline (N = 832).

Data Collected

At all visits, trained research assistants interviewed participants in English or Spanish to collect demographics, including self-reported race or ethnicity with specific geographic origin and subgroups, lifestyle, and medical history, and conducted cognitive and mood assessments, with the Mini-Mental State Examination (MMSE) and Geriatric Depression Scale (GDS), respectively. At follow-up visits, participants were evaluated with the complete Movement Disorders Society—Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Patient Questionnaire.

Study neurologists examined patients and scored motor symptoms and disability using the Unified Parkinson's Disease Rating Scale (UPDRS, later MDS-UPDRS), parts III (UPDRSm) and IV, and Hoehn and Yahr staging (H&Y), respectively. Motor exams were preferably conducted with patients in a functional off-state from PD medications with an overnight withdrawal (>90% of exams were in off-state). Patients also reported current PD medication use and dosing, which we summarized into a total daily levodopa equivalent dose (LED) (20). UPDRSm scores were corrected for missing items that could not be evaluated (such as arising from chair in paraplegic patients), or when an exam was performed in an on-medication state, as previously described (5). For those on medication, we summed to the total score a correction factor equal to the mean difference of "off" and "on" scores in all patients. For missing items due to disability, we used the average of the whole sample for the respective item. We adopted the MDS version of the UPDRS-III in 2016, thus, scores derived from this revised scale were corrected to be equivalent to the previous UPDRS-III version (21). We also derived UPDRSm sub-scores as sums of items corresponding to signs of tremor (total, postural, and rest), rigidity, limb bradykinesia

(finger tapping, hand grip, hand rapid movements, and leg agility), and axial symptoms (22). PD motor subtypes of postural instability and gait dysfunction (according to speech, facial expression, arising from a chair, posture, postural stability, gait, and body bradykinesia), tremor dominance, or indeterminate phenotypes were calculated as ratios of UPDRSm sub-scores (6). Information on the date of diagnosis was obtained through self-report at screening for baseline enrollment and at neurological exam and was confirmed whenever possible with data obtained from the California PD registry (for the PEG 2 cohort). Information on mortality (date of death) was obtained from systematic vital record searches and from contact with relatives during attempts to schedule follow-up visits as late as 2021.

Statistical Analysis

We tested for cross-sectional differences in PD clinical features at each study visit between Latinos and WNL using linear, binomial, or multinomial regression models with continuous, binary, and categorical measures, respectively. Models for differences in H&Y stage, UPDRSm, LED, and GDS were adjusted for age at PD diagnosis, PD duration at each visit, and sex; models for MMSE were further adjusted for years of education.

We assessed associations between PD medication dose (total LED) and UPDRSm or H&Y scores as well as PD duration and age by ethnicity, using linear mixed models with random intercept and slope, and plotting predicted LED linear trends for Latino and WNL groups, adjusted for sex and—when appropriate—for PD duration and age. To assess the longitudinal progression of motor symptoms and disability, we used 2 analytical approaches, both based on years elapsed since the baseline visit as the time measure. We employed Cox proportional hazards models to estimate time-to-event hazard ratios (HRs) for motor and disability outcomes comparing Latinos to WNL. Linear mixed models with random intercept and slope coefficients were also used to predict UPDRSm and H&Y means in Latinos and WNL.

Motor symptom severity and disability progression outcome events were defined, respectively, as time (number of years since baseline visit until visit when the UPDRS was measured) until they had reached a UPDRSm score of 35 or higher (UPDRSm 35+), or an H&Y stage 3 or greater (H&Y 3+), as previously done (6,23), and all models were adjusted for sex, age at baseline, and PD duration at baseline. These models were restricted to patients without the event at baseline and with a maximum of 10 years between baseline and last follow-up (because none of the Latino and only 2 WNL patients reached a total follow-up time greater than 10 years); in these models with up to 10 years of follow-up, the HRs were constant over time for Latinos and WNL, that is, the proportional hazards assumption held. To address loss to follow-up that may result in selection bias, we used Inverse Probability of Censoring Weighting (IPCW) and created weights based on the probability of remaining in the patient cohort for at least 1 follow-up. Weights accounted for age at baseline, PD duration at baseline, sex, PEG 1/2 wave, and smoking (pack years).

All-cause mortality was modeled in time-to-death Cox proportional hazards models with the date of death as the outcome (known for everyone who died), in 2 different models in terms of adjustment variables. Time was modeled as integer years from the date of baseline interview until the date of death for those deceased, and censoring time was determined as integer years from the baseline interview date until the last known date alive when contacted for a follow-up visit. Data analyses were conducted with SAS 9.4 version statistical software (SAS Institute, Cary, NC).

Results

Of the 775 PD patients included here, 138 (18%) self-identified as having Hispanic/Latino ethnicity, 41% ($N = 56$) of whom were foreign born, the majority in Mexico ($N = 52$), and 38% ($N = 53$) were interviewed in Spanish (Supplementary Table 1). Compared to WNL, Latino patients were younger on average at baseline (67 vs 72 years old), were more often men (72% vs 62%), had on average less years of formal education (9 vs 15 years), and more frequently reported as the longest held employment farming-related occupations (31% vs 8%). In terms of comorbidities, Latinos reported more often a diagnosis of diabetes mellitus type 2 than WNL (34% vs 15%), and less frequently used antidepressants (23% vs 32%), despite a similar proportion reporting a depression diagnosis (36% vs 34%).

Both groups had similar proportions of loss to follow-up between baseline and follow-up 1 (41%), but Latino patients were lost slightly more often between follow-up 1 and 2 (53% vs 47% for WNL). The main reason for loss to follow-up in both groups was death (46% of Latinos vs 59% for WNL), followed by not being able to be recontacted (30% of Latinos vs 11% of WNL) or by refusal to continue participation (7% of Latinos vs 16% of WNL).

Table 1 describes PD-related characteristics by ethnicity, at baseline and follow-up visits. Latinos compared to WNL were on average 5 years younger at PD diagnosis, having more frequently young onset PD (age at PD diagnosis <50), as well as longer average PD duration at baseline and at follow-up. The distributions of age at PD diagnosis are shown for both ethnicity groups in Supplementary Figure 1.

Latino patients were clinically worse off than WNL at baseline and follow-up visits, measured by both H&Y and UPDRSm differences adjusted for age at diagnosis, PD duration, and sex (Table 1). The differences (Latino minus WNL sub-scores) were greater for rigidity, limb bradykinesia, and axial sub-scores in adjusted models (Supplementary Table 3). Despite Latino patients being on average clinically worse off, PD medication-use frequency and dose were similar in both groups at baseline and follow-up visits (in adjusted models, Table 1 and Supplementary Table 2). In Figure 1, we show plots of adjusted longitudinal predictions of total LED, by ethnicity, according to 4 scales: PD duration, age, UPDRSm, and H&Y progression (model estimates are displayed in Supplementary Table 4). Total LED is positively associated with PD duration in both groups, though Latino patients reported slightly lower LED averages than WNL at the same PD duration, with the differences increasing over time (panel A), that is, the slopes were slightly different even though the interaction term (PD duration × Latino) was not formally statistically significant. On the other hand, age was negatively associated with LED in both groups (panel B), with Latino patients having a statistically significantly greater negative slope (interaction term age × Latino). For UPDRSm score progression and LED, the slope was positive for WNL, but null for Latino patients (panel C), yet the interaction term (UPDRSm × Latino) was again not formally statistically significant. For H&Y progression and LED, linear predictions showed similar positive associations for both Latinos and WNL, but WNL reported slightly higher average LED doses at the same H&Y stage compared with Latino patients (panel D).

In models adjusted for sex, PD duration at baseline, and age at PD diagnosis, the rate of progression to UPDRSm 35+ was faster

Table 1. Comparison of Parkinson's Disease-Related Characteristics by Ethnicity (Latino and White non-Latino), at Baseline and Follow-up, PEG Study

	Baseline			Follow-up 1			Follow-up 2		
	WNL	Latino	*p* Value	WNL	Latino	*p* Value	WNL	Latino	*p* Value
Total	634 (82.1)	138 (17.9)		374 (87.3)	81 (18.9)		198 (83.9)	38 (16.1)	
Follow-up time, years	0	0		3.38 ± 1.67	3.30 ± 1.57		2.34 ± 1.01	2.34 ± 0.94	
Age at PD diagnosis	68.90 ± 10.20	63.58 ± 11.34	<.0001*						
Median [min, max]	70 [34,89]	65 [23, 85]							
Early-onset PD, <50 years old	27 (4.2)	16 (11.6)	.001†						
Primary relative with PD	103 (16.4)	19 (14.1)	.508†						
PD duration, years	2.92 ± 2.61	3.68 ± 2.81	.002*	6.19 ± 3.13	6.87 ± 2.96	.066[a]	7.96 ± 2.76	8.93 ± 3.33	.038*
Median [min, max]	2 [0, 18]	3 [0, 14]		6 [1, 24]	7 [2, 15]		8 [2, 18]	9 [4, 18]	
Motor phenotype, subtypes									
Tremor dominant	161 (25.4)	26 (18.8)		97 (26.1)	11 (13.6)		23 (11.6)	5 (13.2)	
PIGD	389 (61.3)	93 (67.4)	.261†	236 (63.6)	65 (80.2)	.016†	149 (75.3)	29 (76.3)	.887†
Indeterminate	85 (13.4)	19 (13.8)		38 (10.2)	5 (6.2)		26 (13.1)	4 (10.5)	
Hoehn and Yahr stage, categories									
0–2	418 (66.7)	79 (59.0)		193 (53.6)	28 (34.6)		44 (31.2)	6 (25.0)	
2.5–4	198 (31.6)	50 (37.3)	.124‡	155 (43.1)	50 (61.7)	.008‡	86 (61.0)	17 (70.8)	.62‡
4.5–5	11 (1.8)	5 (3.7)		12 (3.3)	3 (3.7)		11 (7.8)	1 (4.2)	
Hoehn and Yahr stage, 3+	109 (17.4)	27 (20.1)	.120§	88 (24.4)	31 (38.3)	.00§	53 (37.6)	13 (54.2)	.040§
UPDRS motor total score	20.66 ± 10.47	26.00 ± 13.40	<.000‖	25.05 ± 12.19	30.69 ± 13.84	<.000‖	29.13 ± 12.91	36.48 ± 13.28	.00‖
Median [min, max]	19 [2, 66]	24 [4, 67]		24 [3, 65]	28 [8, 71]		28 [1, 81]	35 [12, 77]	
UPDRS motor total score, 35+	74 (11.7)	41 (29.7)	<.000§	84 (22.5)	27 (33.3)	.029§	29 (14.6)	11 (28.9)	.028[d]
Total LED/day, mg	409 ± 336	437 ± 375	.469‖	902 ± 825	899 ± 707	.383‖	838 ± 576	803 ± 500	.244‖
Median [min, max]	340 [0, 2 300]	388 [0, 2 100]		747 [0, 9 100]	796 [0, 3 600]				

Notes: *N* (%) are shown for categorical measures and crude mean ± *SD* for continuous measures, and *p* values are from adjusted models. LED = levodopa equivalent dose; PD = Parkinson's disease; PIGD = postural instability and gait dysfunction; UPDRS = Unified Parkinson's Disease Rating Scale; WNL = White non-Latino.

*p Value obtained from t test comparing means for Latino versus WNL groups.

†p Value obtained from chi-square comparing distribution for Latino versus WNL groups.

‡p Value obtained from multinomial regression models comparing Latino versus WNL groups and adjusted for sex, PD duration at visit, and age at PD diagnosis.

§p Value obtained from binomial regression models comparing Latino versus WNL groups and adjusted for sex, PD duration at visit, and age at PD diagnosis.

‖p Value obtained from linear regression models comparing Latino versus WNL groups and adjusted for sex, PD duration at visit, and age at PD diagnosis.

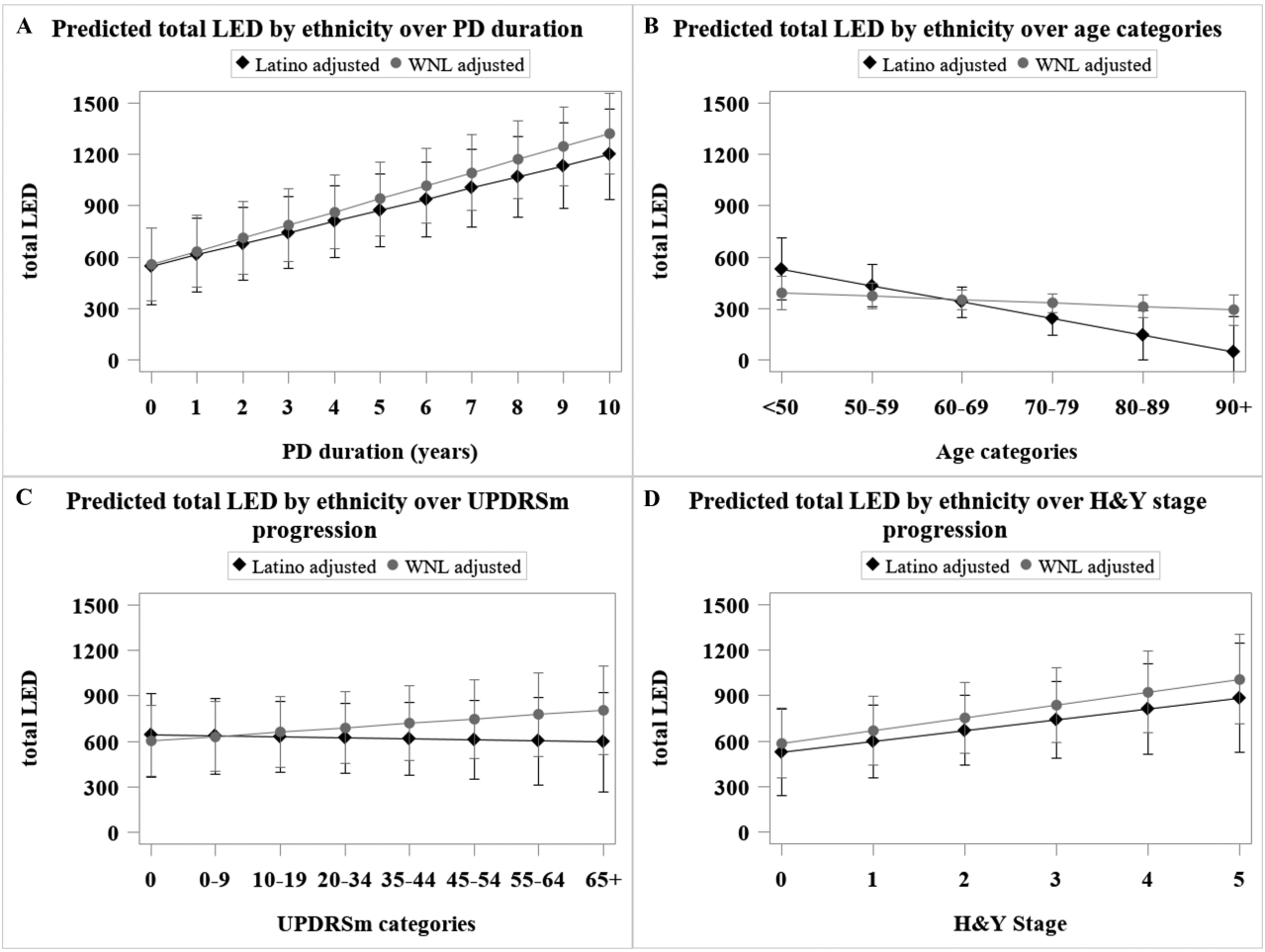

Figure 1. Linear mixed models predictions for total LED means, by ethnicity, using 4 different progression measures (PD duration, age, UPDRSm, and H&Y). Total *N* in models = 773. Panel A model adjusted for sex and age. Panel B adjusted for sex and PD duration. Panels C and D models adjusted for sex, PD duration, and age. Model estimates are shown in Supplementary Table 4. H&Y= Hoehn and Yahr stage; LED = levodopa equivalent dose; PD = Parkinson's disease; UPDRSm = Unified Parkinson's Disease Rating Scale motor exam scores; WNL = White non-Latino.

in Latinos than WNL (Figure 2, panel A), with an estimated HR of 1.63 [1.00, 2.66] for a total N of 405 patients included in our model. However, when we further accounted for the baseline UPDRSm score (panel B), there was no difference in the rate of progression to UPDRSm 35+ for Latinos versus WNL, HR = 1.17 [0.71, 1.94]. Progression to an H&Y stage 3+ was also faster in Latinos compared to WNL patients, HR = 2.18 [1.35, 3.51] (panel C), and this rate remained faster (albeit weakened) in Latinos when we included baseline H&Y stage in the models, HR = 1.81 [1.11, 2.96], *N* = 380 (panel D). In sensitivity analyses with IPCW accounting for differential loss to follow-up in these models, the magnitudes of effect estimates were very similar (results not shown), but estimates were less precise.

Plotting crude and adjusted predicted UPDRSm for Latinos versus WNL throughout follow-up showed that Latino PD patients have higher scores on average than WNL at baseline and throughout follow-up, but similar slopes (Figure 3, panels A and B). This was confirmed in the linear mixed models that adjusted for sex, age, PD duration, PEG cohort, and smoking. Specifically, the predicted UPDRSm score was statistically significantly different by ethnicity at baseline ($p < .0001$), but not the interaction of ethnicity and time ($p = .898$, Supplementary Table 5). Results were similar for the H&Y outcome (Figure 3, panels C and D).

Nonmotor outcomes, GDS and MMSE, were statistically significantly worse in Latino ethnicity patients at baseline and first follow-up; that is, in adjusted models, MMSE was on average lower, and GDS on average higher in Latino compared to WNL patients (Table 2). Even though the scores were also worse for Latinos at the second follow-up, the adjusted mean differences did not reach statistical significance. Like UPDRSm and H&Y, in linear mixed models with random intercept and slope (results not shown), ethnicity-specific differences were only seen at baseline for MMSE and GDS, while rates of progression were similar for Latino and WNL, that is, the interaction terms for ethnicity with time (time × Latino) were not statistically significant ($p = .089$ for GDS and $p = .484$ for MMSE). Nonmotor measures for autonomic symptoms and UPDRS part IA (rated by physician, complex behaviors items: cognitive impairment, hallucinations, depressed mood, anxious mood, apathy, features of dopamine dysregulation syndrome) were not different between ethnicity groups (Supplementary Table 2).

At the time of death, Latino patients were younger, on average 78 years of age while WNL patients were on average 82 years ($p = .004$). In Cox models, time to death was not different in Latino and WNL patients (Supplementary Table 6) in models adjusted for sex, age, PD Dx, PD duration, study wave, and smoking, with a total *N* = 770 (HR = 1.05 [0.78, 1.41]).

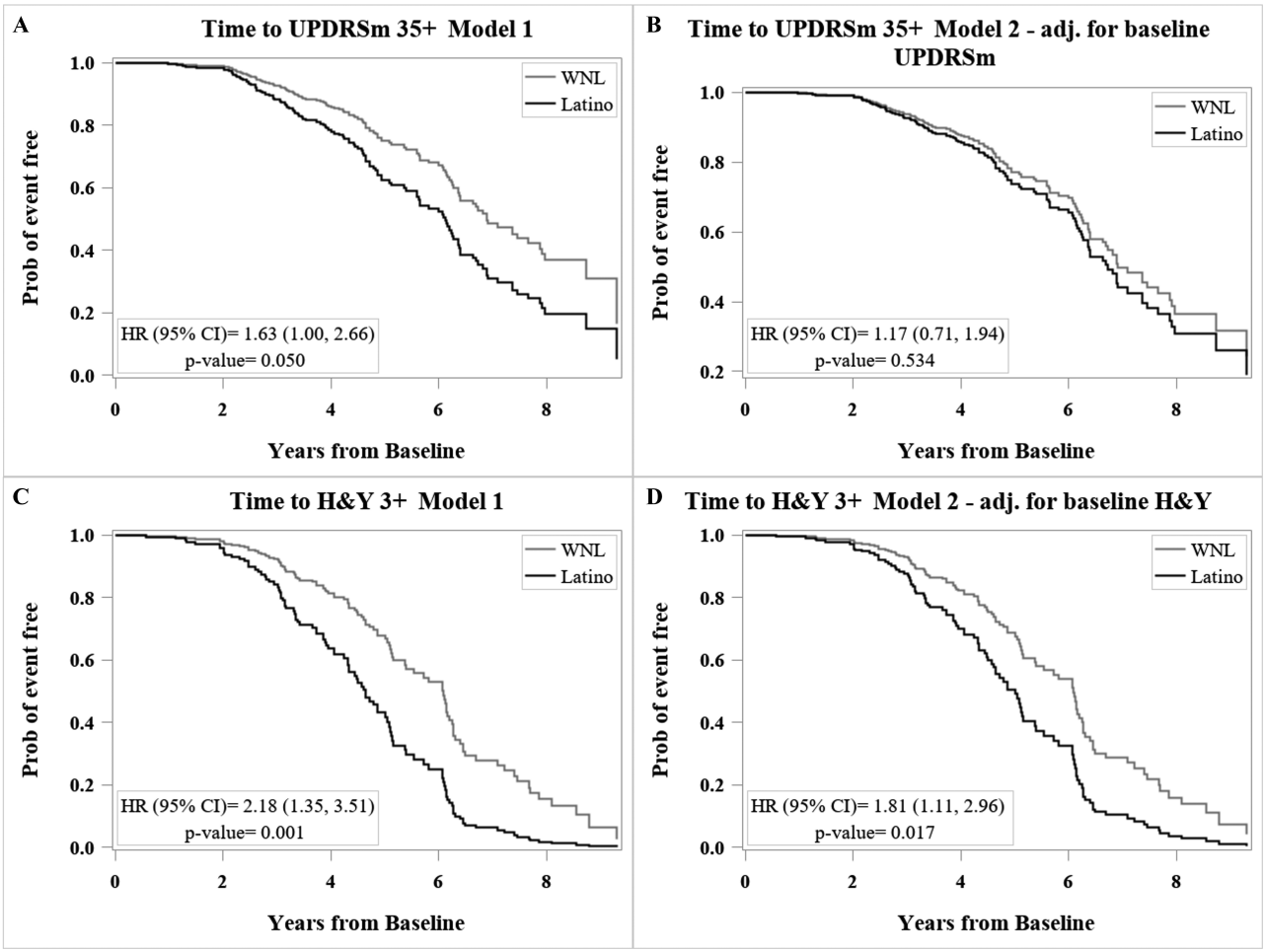

Figure 2. Time to motor progression event models comparing Latino to White non-Latino patients during PEG study follow-up. Model 1 adjusted for age at PD diagnosis, PD duration, sex, PEG Wave 1/2, and smoking. Model 2: adjusted for Model 1 variables + baseline UPDRSm or H&Y. H&Y = Hoehn and Yahr stage; HR = hazard ratio; PD = Parkinson's disease; PEG = Parkinson's Environment and Genes Study; UPDRSm = Unified Parkinson's Disease Rating Scale motor exam scores; WNL = White non-Latino; *N* (%) events and total *N* in models = UPDRSm 35+: Latino 22 (36.7)/WNL 95 (27.5)/total *N* = 405 H&Y 3+: Latino 26 (39.4)/ WNL 81 (25.7)/total N=380

Discussion

In this large community-based study of PD in rural regions of California, Latino patients, compared with WNL, presented at a higher frequency with early-onset PD and worse motor and nonmotor symptom severity throughout study visits. Furthermore, they reported taking suboptimal doses of dopaminergic medication when considering the motor symptom scores and the overall extent of disability, and they were younger at time of death compared with WNL patients. In our study, 18% of PD patients identified as Latino, that is, one of the largest proportions of Latino enrollees in the United States for a PD onset and clinical progression study (11,24). This allowed us to compare a wide range of PD clinical characteristics according to ethnicity. In previous PD studies, ethnicity information has commonly only been treated as a confounding factor, along with race, but ethnicity-specific effects have not been a focus. For instance, a recent analysis of clinical progression in the Parkinson's Progression Markers Initiative (PPMI) dataset did not allow for comparisons based on race/ethnicity, as this study only enrolled 2.8% Latinos among the PD patients (25), and an analysis of clinical features associated with different ages of PD onset in PPMI did not report on ethnicity-specific profiles (26).

Latino patients in the PEG Study cohort had lower socioeconomic status (SES) compared to WNL according to average years of education and job type, with the most common and longest held occupation being farming. This is consistent with what is known about the workforce of rural California (10). In terms of comorbidities, only the prevalence of type 2 diabetes was higher amongst Latinos, possibly related to lower SES (27,28). A high prevalence of diabetes has been reported in other studies of Latino older individuals (29), and previously, diabetes has been associated with a 38% increase in the risk of developing PD, as reported in a meta-analysis based on 7 observational cohort studies (30).

We found that Latino patients were of younger age at diagnosis than WNL corresponding to a higher frequency of early-onset PD amongst Latinos. No studies have yet reported specifically on age at PD diagnosis in Latinos in the United States; but 1 study focused on Alzheimer's disease age of onset using data from 5 minority health clinics across the United States and found that Latinos had a younger age at the onset of Alzheimer's disease symptoms than WNL (31). In previous clinic-based studies (26,32), early-onset PD was associated with a less severe motor and nonmotor PD phenotype, slower progression of motor symptoms, and less cognitive impairment and

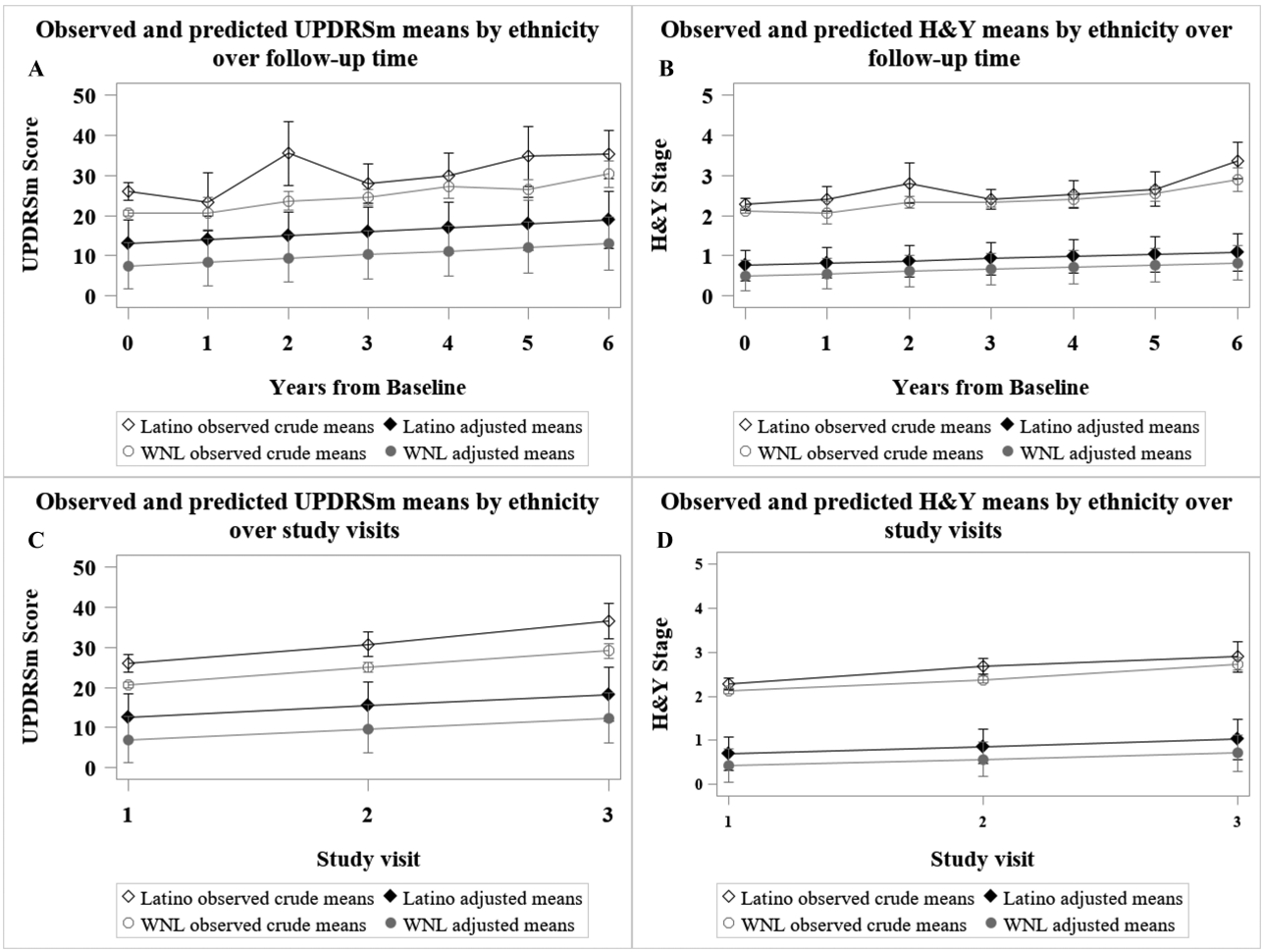

Figure 3. Observed and predicted UPDRSm and H&Y means for Latino and WNL groups using 2 time scales (by study visit and by years from baseline) during PEG Study follow-up (total *N* = 770). Observed are the actual means for each group, Latino and WNL, at each time point (study visit or year). Predicted mean estimates obtained from linear mixed models adjusted for sex, PD duration, age, smoking, PEG Wave 1 or 2. Model estimates are shown in Supplementary Table 5. H&Y = Hoehn and Yahr stage; PD = Parkinson's disease; PEG = Parkinson's Environment and Genes Study; UPDRSm = Unified Parkinson's Disease Rating Scale motor exam scores; WNL = White non-Latino.

Table 2. Comparison of Nonmotor Outcomes, Cognition, and Depression Symptoms, by Ethnicity (Latino and White non-Latino), at 3 PEG Study Visits

	Baseline			Follow-up 1			Follow-up 2		
	WNL	Latino	*p* Value*	WNL	Latino	*p* Value[a]	WNL	Latino	*p* Value*
MMSE total score	27.81 ± 2.46	26.18 ± 3.74	.025	27.90 ± 2.46	26.29 ± 3.94	.048	27.43 ± 3.05	25.54 ± 4.75	.227
Median [min, max]	29 [16, 30]	28 [9, 30]		29 [16, 30]	27 [12, 30]		28 [7, 30]	28 [14, 30]	
GDS total score	3.45 ± 3.08	4.91 ± 3.69	<.0001	3.72 ± 3.24	4.67 ± 3.66	.032	3.62 ± 2.94	4.39 ± 3.93	.523
Median [min, max]	3 [0, 15]	4 [0, 15]		3 [0, 15]	4 [0, 14]		3 [0, 13]	3 [0, 14]	

Notes: Mean ± *SD* are shown for crude means and standard deviations, *p* values are from adjusted models. Latino/WNL numbers for each study visit: Baseline 138/634; Follow-up 1 81/374; Follow-up 2 38/198. GDS = Geriatric Depression Scale; MMSE = Mini-Mental State Examination; PEG = Parkinson's Environment and Genes Study; WNL = White non-Latino.

**p* Value obtained from linear regression models comparing Latino and WNL patients, adjusted for age at PD diagnosis, sex, PD duration at visit, and years of education for MMSE models

decline, which was different from what we found, where Latinos were not only younger at diagnosis, but also exhibited worse (ie, more advanced) clinical symptoms of PD and longer PD duration at study baseline. This finding suggests that despite our study being able to recruit a large proportion of Latino patients, it may have taken them longer to be diagnosed with PD, obtain care, and enroll in our study.

Younger age of PD onset has been associated with a higher likelihood of a genetic predisposition (33–35). Specifically, early-onset

PD has been linked to autosomal recessive mutations in genes associated with monogenic PD, mainly Parkin (PRKN) and PINK1 mutations, while mutations in the LRRK2 gene are the most common genetic variants, with very young onset associated with specific variants of this gene. However, these are reportedly rare in the population of Latin American origin, according to a large consortium on the genetics of PD in this population (36). Latinos in our cohort reported a low (and similar to WNL) proportion of familial PD and, in addition, we were able to check 4 out of 12 known rare pathogenic LRRK2 mutations in our data (rs34637584/rs34410987/rs34778348/rs34594498) and none was present. For the common risk factor SNP (rs76904798) within LRKK2, we estimated a prevalence of 6.2% in the Latino patients (8/130, only 1 was early-onset PD), and of 2% (11/582 and none early-onset PD) in the WNL, a lower prevalence than commonly reported (9%–14%). In sensitivity analysis, we excluded from the sample 2 younger patients with a potentially pathogenic mutation in a PD-related gene, and the results reported here did not change. Though it can be considered a weakness of our study that more extensive genotyping data are not available, the earlier age of PD onset in Latinos in our cohort is likely at least partly due to an accumulation of environmental exposures throughout the life course, including, for example, harmful exposures resulting from more frequently reported farming occupations, and environmental exposures have been shown to contribute to a younger age at PD onset (37).

Latino PD patients had clinically worse PD signs and symptoms rated by our neurologists throughout follow-up (in models adjusted for PD duration, age, and sex) than WNL, but reported similar average doses of LED. Our graphs illustrate this showing a positive linear association of total LED and UPDRSm for WNL, but a flat line for Latino patients, suggesting no adjustment of treatment with worsening symptomatology throughout the disease course. While dopaminergic treatment cannot halt the progression of neurodegenerative processes, it can increase the quality of life throughout the clinical course. With several types of drugs and delivery systems available, adequate pharmacological management of PD symptoms can help prevent other comorbidities resulting, for example, from falls and from loss in activities of daily living that lead to early disability. This suboptimal dopaminergic therapeutic management in Latino patients might be indicative of financial or other types of barriers to accessing health care, including language, timely medical encounters, and access to prescriptions and medication. SES disparities may influence clinical care, and Latinos in the study were of lower SES according to the indicators of education and occupation in our study, but also in California, in general. For example, a study with U.S. nationally representative data from the 2006–2013 Medical Expenditure Panel Survey, found that Hispanic participants with PD were 40% less likely to see an outpatient neurologist (OR 0.61 [0.54–0.69]) than WNL (38). Another study that examined the place of death as an indicator of healthcare utilization quality, found that end-of-life care remained suboptimal for Latino patients with PD, with a low hospice rate as compared to non-Latinos, who had greater access to nursing facilities (39).

Progression of motor symptoms measured by UPDRSm was not faster for Latinos than WNL when we adjusted for the respective baseline values as shown in Cox and repeated-measures longitudinal models. Nevertheless, Latino patients progressed to motor disability with functional impairment measured by an H&Y stage 3+ faster than WNL in models adjusted for baseline values. Our data, thus, suggest compounded disparities, with Latinos diagnosed younger but receiving less optimal pharmacological management of PD that may have resulted in faster time to disability and earlier age at death.

Nonmotor outcomes related to cognition and depression were worse in Latinos throughout our study's follow-up period, though the mean differences were not statistically significant at the last study visit, probably because of the much-reduced sample size for Latino participants (N = 38). There are no previous studies evaluating such nonmotor outcomes in Latinos with PD in comparison to other ethnicities, as discussed in a recent meta-analysis and systematic review reporting on enrollment of minorities in clinical trials that evaluated the treatment of PD neuropsychiatric symptoms (11). The authors found a strikingly low number of studies reporting ethnicity and race, and a low representation of African American and Hispanic/Latino patients in studies reporting on these clinical interventions. However, the literature consistently reported higher rates of cognitive impairment in older Latinos in general compared to WNL (40–43). In a clinic-based study from the National Alzheimer's Coordinating Centers conducted in 32 locations in the United States that enrolled 400 patients and 400 controls, Latino subjects performed worse than non-Latinos in neuropsychological tests (40). In a stratified random sample of 1 152 noninstitutionalized older adults (65 years and older) in El Paso County, Texas, Latino subjects had 2.46 times greater odds of receiving an MMSE score ≤24 than WNL (41). The Sacramento Area Latino Study on Aging, a cohort study of community-dwelling older Latino adults in the Sacramento area of California designed to evaluate metabolic and cardiovascular risk factors for dementia, found the dementia prevalence to be lower in this population than in a study of a Latino population of Caribbean origin in New York City, but similar to the estimated prevalence for the general population of Europe and Canada (42). A study of Medicare Centers for Medicare and Medicaid Services data including N = 268 407 beneficiaries with PD, of which 2.7% were Hispanic, analyzed patterns of dementia drugs prescribed in PD patients, and reported that dementia medications were prescribed to Black and Hispanic beneficiaries more often than for WNL beneficiaries. Specifically, the prescription of memantine (a drug primarily indicated for severe disease) was more frequent in Hispanic patients compared with other ethnicities/races (43). This study also reported that Hispanics were more often subject to prescribing errors for dementia medications, indicating disparities in the quality of care of services available. In our cohort, the finding that Latino PD patients had worse cognitive outcomes than WNL, may also be a result of the notable differences in the average years of education between the groups; that is, even though our models were adjusted for years of education, they do not account for education quality and for other harmful exposures during the life course, for example, poverty (29). Additionally, diabetes is an important established risk factor for cognitive decline and dementia (44), and the Latino patients in our cohort had a much higher prevalence of diabetes. Hence, worse cognitive outcomes in Latino patients as compared to WNL in our cohort may also be due to disparities in SES and clinical care.

Worse depressive symptoms in Latinos than in WNL patients are also supported by a literature that reports racial and ethnic differences in depression (45,46). Recently, a national annual survey included a racially diverse group of adults aged 65 and older who participate in Medicare Advantage (N = 175 956); it operationalized depression using the Patient Health Questionnaire-2 and found that people reporting Hispanic origin had the highest rates of depression among all racial and ethnicity categories (47). In our cohort, the Latino patient group also reported considerably

lower frequency of antidepressant use, despite reporting a similar prevalence of having received a depression diagnosis and—not surprisingly—exhibited higher GDS symptom scores, indicating that nonmotor symptoms are also not well managed therapeutically in this group. This again points to potential disparities in healthcare quality for Latinos; antidepressant use for depression can improve the quality of life and potentially help prevent other comorbidities, including cognitive decline. Older adults with active depression not taking antidepressants have been reported to be at greater risk (73%) of incident cognitive impairment, compared with those without depression and antidepressant use (46). This same study reported a greater risk of cognitive impairment in Latinos compared to WNL even after adjustment for age, education, sex, and APOE ε4 status (46). In addition to other clinical and environmental risk factors for depression, the literature points to discrimination as an important factor that can influence mental health in the Latino population in the United States (45,46,48). In our cohort, Latino patients with PD reporting less medication use for motor and nonmotor symptoms may indicate discrimination compounded with underutilization of health services. Furthermore, timely access to bilingual behavioral health services and treatment is very limited in rural areas.

Besides being younger at PD diagnosis, Latino patients were also on average younger at the time of death than WNL. This may be indicative of the disadvantages that go along with a diagnosis of PD in general leading also to an earlier age at diagnosis as well as death. However, we did not detect a faster time to death (crude or adjusted) in the Latino group than WNL in Cox models accounting for the time between baseline and death or last alive contact. Our result contrasts with a study amongst 131 215 PD Medicare beneficiaries from all over the United States who had sustained hip fractures, which found mortality to be lower in Latino than in WNL PD patients postfracture (HR = 0.87, 95% CI = 0.81–0.95) (49). Apart from being selected for having sustained a hip fracture, this study of Medicare-enrolled PD patients included Latino subjects with higher SES and a higher proportion born in the United States than our cohort.

The most notable strength of our study is that it is the largest population-based study of PD in the United States with progression data and the first study to report on ethnicity-related differences or lack thereof for a wide range of PD motor and nonmotor clinical features and progression, comparing patients reporting Latino ethnicity to those WNL. Importantly, all clinical features were evaluated in a standardized manner by neurologists specializing in movement disorders, who also confirmed the idiopathic PD diagnosis at each visit. Nevertheless, limitations in our study include a slightly higher loss to follow-up rate in the Latino group, which could result in underestimates of mortality and clinical severity in this group because the Latino patients who were lost to follow-up were generally worse off clinically. It has been recommended to disaggregate ethnicity further by origin, sub-group characteristics, and race (47); in our cohort, the majority of Latinos reported Mexican American origin, with sample sizes not allowing sub-group analyses; additionally, we did not collect race information from Latino subjects.

In conclusion, this population-based study of PD found that Latino patients, in comparison to WNL, presented with an earlier age at diagnosis and death, and exhibited worse motor and nonmotor features and disability at younger ages but their symptoms did not progress at faster rates. In addition, motor and nonmotor symptoms in Latino PD patients were medically managed less well than those of WNL patients. While clinicians need to pay attention to these findings, these differences may be driven by healthcare access disparities and structural socioeconomic disadvantages. These factors need to be addressed by systematic policy interventions and may not be amenable to clinical management changes. Future studies need to explore the contribution of such disparities to PD management, possibly employing mediation analyses to assess the role that access and quality of healthcare play.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

Funding

This work was supported by the Michael J. Fox Foundation for Parkinson's Research (grant number MJFF-020971), the National Institute of Environmental Health Sciences (grant numbers: R01ES010544 and 3R01ES031106-02S1), and the American Parkinson Disease Association, Center for Advanced Parkinson Research at UCLA pilot program. C.K. was supported by National Institutes of Health (grant number F32AG063442).

Conflict of interest

None declared.

Acknowledgments

We greatly appreciate all study participants and PEG study staff and volunteers for their time and efforts that allowed us to obtain the data used for this research, especially Dr. Yvette Bordelon, who also conducted neurological examinations.

Author Contributions

A.D.F. analyzed the data and wrote the manuscript. M.E.S.F. provided expert opinion on study results. C.K. conducted data analysis and provided expert opinion. K.C.P. conducted data analysis and provided expert opinion. K.Z. assisted with data analysis. J.B. provided expert opinion and acquired the study funding. B.R. acquired the study funding, designed and conceptualized the study, and provided expert opinion. A.M.K. provided expert opinion and conceptualized the study. A.D.F., I.D.R., E.C., K.Z., C.R., A.M.K., and J.B. acquired the data. All coauthors—M.E.S.F., C.K., K.C.P., I.D.R., K.Z., C.R., E.C., J.B., B.R., and A.M.K.—have reviewed and edited the manuscript.

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