

Association of Disease Severity and Socioeconomic Status in Black and White Americans With Multiple Sclerosis

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Abstract

Objective

To compare clinical and imaging features of multiple sclerosis (MS) severity between Black Americans (BAs) and White Americans (WAs) and to evaluate the role of socioeconomic status.

Methods

We compared BA and WA participants in the Multiple Sclerosis Partners Advancing Technology Health Solutions (MS PATHS) cohort with respect to MS characteristics, including self-reported disability, objective neurologic function assessments, and quantitative brain MRI measurements, after covariate adjustment (including education level, employment, or insurance as socioeconomic indicators). In a subgroup, we evaluated within-race, neighborhood-level indicators of socioeconomic status (SES) using 9-digit zip codes.

Results

Of 1,214 BAs and 7,530 WAs with MS, BAs were younger, had lower education level, and were more likely to have Medicaid insurance or to be disabled or unemployed than WAs. BAs had worse self-reported disability (1.47-fold greater odds of severe vs mild disability, 95% confidence interval [CI] 1.18, 1.86) and worse performances on tests of cognitive processing speed (−5.06 fewer correct, 95% CI −5.72, −4.41), walking (0.66 seconds slower, 95% CI 0.36, 0.96), and manual dexterity (2.11 seconds slower, 95% CI 1.69, 2.54). BAs had more brain MRI lesions and lower overall and gray matter brain volumes, including reduced thalamic (−0.77 mL, 95% CI −0.91, −0.64), cortical (−30.63 mL, 95% CI −35.93, −25.33), and deep (−1.58 mL, 95% CI −1.92, −1.23) gray matter volumes. While lower SES correlated with worse neuro-performance scores in WAs, this association was less clear in BAs.

Conclusion

We observed a greater burden of disease in BAs with MS relative to WAs with MS, despite adjustment for SES indicators. Beyond SES, future longitudinal studies should also consider roles of other societal constructs (e.g., systemic racism). Such studies will be important for identifying prognostic factors; developing optimal treatment strategies among BAs with MS is warranted.

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Glossary

ADI = area deprivation index; BA = Black American; MS = multiple sclerosis; MS PATHS = Multiple Sclerosis Partners Advancing Technology Health Solutions; PDDS = Patient Determined Disease Steps; WA = White American.

Clinical observations and emerging studies suggest that Black Americans (BAs) with multiple sclerosis (MS) tend to fare worse than their White American (WA) counterparts. Previous studies have suggested that BAs with MS have a greater burden of disease relative to WAs.^{1,2} Studies have reported BAs to have greater disability accumulation,³ earlier progression to requiring ambulatory assistance,⁴ faster lesion accumulation on brain MRI,^{5,6} faster brain and retinal tissue loss,⁷ and increased loss of high-contrast visual acuity after optic neuritis compared to WAs.⁸

Despite these reports, the published studies have created some gaps in knowledge, partially due to limitations in study design and methods. The larger studies were primarily retrospective and focused on global measures of disability (i.e., Expanded Disability Status Scale, Multiple Sclerosis Severity Score), semiquantitative scales that predominantly assess ambulatory function.^{1,9} Many of the studies evaluating other outcomes, particularly brain or retinal atrophy, had a small sample of BAs or were single-center studies,^{6-8,10,11} such that the precision of the estimates and the representativeness of the patients studied were concerns. Furthermore, the intersection of race with socioeconomic status, a known strong determinant of health¹² as it relates to MS outcomes, has not been well described in US-based populations. Here, to address these gaps in the rigor of prior research, we sought to compare a comprehensive set of neuroperformance and imaging measures of disease severity in a large, multicenter cohort of BA and WA people with MS in the United States and to evaluate interactions between race and socioeconomic status with respect to these measures.

Methods

Data Collection

This cross-sectional study used data from US sites in the Multiple Sclerosis Partners Advancing Technology Health Solutions (MS PATHS) network, which is sponsored by Biogen, Inc (Cambridge, MA). MS PATHS is a collaboration among 10 MS centers; 7 are located in the United States. During routine clinic visits, standardized patient data are collected from patients with MS and clinically isolated syndrome, including the MS Performance Test, an iPad-based application requiring minimal assistance from staff.¹³ The MS Performance Test collects sociodemographic characteristics, including self-reported race, as well as clinical and disease information (including the Patient Determined Disease Steps [PDDS], which correlates well with the neurologic examination-based Expanded Disability Status Scale¹⁴), and objective assessments of walking speed, manual dexterity, and cognitive processing speed. These neuroperformance

measures were designed to capture components similar to those of the MS Functional Composite (Timed 25-Foot Walk, 9-Hole Peg Test) and the validated Symbol Digit Modalities Test, commonly used outcome measures in MS clinical trials.¹⁵ MS PATHS participants who undergo clinical brain MRIs at the participating institutions agree to share their images with the network. At all sites, 2 standardized MRI acquisition sequences (3-dimensional T1 magnetization prepared rapid acquisition with gradient echo and 3-dimensional fluid-attenuated inversion recovery) on Siemens 3T scanners (Malvern, PA) were incorporated into routine MS brain MRI protocols.¹³ A software prototype (MS PATHS Image Evaluation) developed within the network is used for automated calculation of brain volumes, total T2 lesion volume, and new T2 lesion counts.¹⁶

Standard Protocol Approvals, Registrations, and Patient Consents

This study was reviewed and approved by the Johns Hopkins Medicine Institutional Review Board, an ethics standards committee on human experimentation for any experiment using human participants. As detailed comprehensively in a prior publication, patients provide informed consent for the sharing and use of their data, and MS PATHS has an established governance structure such that academic sites oversee their own scientific work using the data.¹³

Data Analysis

For the current analysis, we included first visit data from US MS PATHS participants with self-reported BA or WA race who were enrolled between September 2016 and September 2019. European participants were excluded due to differences in social and economic factors that might introduce heterogeneity in analyses that would be hard to interpret, as well as differences in privacy laws among countries that prevent the collection of race and ethnicity data.

We computed basic descriptive statistics on each of the groups and performed univariate tests for differences between the 2 groups using generalized linear models. Variables serving as proxies for socioeconomic status included education level, employment status, and insurance status. We classified participants self-reported disability as follows: mild (PDDS score <2), moderate (PDDS score 2–4), and severe (PDDS score >4). We then computed multivariate-adjusted odds ratios of moderate vs mild and severe vs mild disease in BAs relative to WAs. We also compared the multivariate-adjusted mean differences in neurologic performance outcomes, including the Walking Speed Test, Manual Dexterity Test, and Processing Speed Test (cognitive performance), as well as in quantitative brain MRI measurements (T2-weighted lesion volumes;

periventricular, juxtacortical, and infratentorial lesions; and volumes of thalamic, cortical gray matter, deep gray matter, and brain compartments). Generalized linear models were used throughout. Models for PDDS, neuroperformance outcomes, and quantitative MRI data were adjusted for age, sex, disease subtype and duration, current disease-modifying therapy administration route, body mass index, smoking status, employment, education, and insurance status (Medicaid vs other).

Because education level is only 1 indicator of socioeconomic status in people with MS¹⁷ and cross-sectional measures of insurance type or employment status might reflect outcomes of MS-related disability,¹⁸ for MS PATHS participants who are followed up locally at Johns Hopkins, we used available 9-digit zip codes associated with participant addresses to incorporate additional measures of socioeconomic status that are derived from Census block-level data; zip codes are not available as part of the MS PATHS dataset. For these analyses, we restricted to patients who are geographically close to the center (e.g., residing in Maryland, Delaware, Pennsylvania, Virginia, and the District of Columbia) to minimize potential referral bias. Additional indicators of socioeconomic status include the median household income by 9-digit zip code and the area deprivation index (ADI). The ADI is an established composite index incorporating 17 different measures of socioeconomic status that is derived from the 9-digit zip code, and nationwide indices range from 0 (least disadvantaged) to 100 (most disadvantaged).^{19,20} We then assessed whether the association between race and MS outcomes was modified by these more detailed measures of socioeconomic status in this subset of participants using similarly adjusted generalized linear models.

Data Availability

MS PATHS data are currently available only to qualified investigators and collaborators of participating institutions.

Results

Demographic Characteristics

Among the participants in MS PATHS who were included in the analysis, 1,214 (14%) self-identified as BAs and 7,530 (86%) self-identified as WAs. Several demographic differences between the groups were notable (table 1). Relative to WAs, BAs at the time of the analysis were younger, had lower education level, and were less likely to be employed. BAs were also more likely to have Medicaid or Medicare insurance, to self-report progressive MS, and to be currently treated with higher-efficacy (infusion) medications (table 1). MS PATHS participants followed up locally at Johns Hopkins did not differ from the larger MS PATHS cohort with respect to demographic and clinical characteristics.

Clinical Outcomes

Adjusted for covariates as detailed above, BAs with MS performed more poorly on the self-administered neuroperformance

scales with greater global disability scores (table 2). Furthermore, patient performance with respect to walking speed (mean 0.66 seconds slower in BAs [95% confidence interval 0.36, 0.96]), manual dexterity (mean 2.11 seconds slower in BAs [95% confidence interval 1.69, 2.54]), and cognitive processing speed (mean 5.06 fewer correct responses in BAs [95% confidence interval -5.72, -4.41]).

In multivariate analyses of brain MRI measures, BAs had 0.31 mL (95% confidence interval 0.25, 0.38) greater T2 lesion volume than WAs. In the evaluation of the location of lesions between races, this finding appears to be driven largely by greater volumes of periventricular and infratentorial lesions in BAs (table 3 and figure). Overall, brain volumes were also lower in BA patients. Furthermore, BAs had markedly lower gray matter volumes, including lower overall (gray matter fraction) and gray matter subcompartment volumes. BAs averaged lower volumes of cortical gray (-30.63 mL [95% confidence interval -35.93, -25.33]), deep gray (-1.58 mL [95% confidence interval -1.92, -1.23]), and thalamic (-0.77 mL [95% confidence interval -0.91, -0.64]) volumes (table 3 and figure).

Effect Modification by Socioeconomic Status in the Johns Hopkins Cohort

In the Hopkins-only multivariate analysis, we explored more thoroughly the intersection between race and socioeconomic status in relation to the MS-related clinical and MRI measures herein. Among WA individuals, lower median household income was associated with slower cognitive processing and walking speeds, while a worse score on the ADI was associated with slower cognitive processing and manual dexterity speeds. On the other hand, among BA patients, lower median income was associated only with slower manual dexterity performance, and worse ADI scores were not meaningfully associated with differences in cognitive processing or walking or manual dexterity speeds (table 4). Relatively consistent findings were observed in the overall MS PATHS cohort when we used less-detailed general indicators of socioeconomic status (e.g., education status).

Discussion

In this large cross-sectional cohort, our results indicate that BAs with MS have consistently greater disease burden as measured in the domains of cognitive processing, walking, and manual dexterity than WAs, even after adjustment for relevant covariates. We also affirm findings from prior studies that MS in BAs is associated with greater overall disability (PDDS score) and greater burden of disease as measured by MRI (lesion volumes, gray matter volumes). These results provide confirmatory evidence that at the group level, BAs with MS fare worse than their WA counterparts across multiple clinical and imaging domains. The brain and gray matter volume findings in particular are noteworthy because in healthy cohorts BAs have greater brain volumes than WAs²¹;

Table 1 Demographics and Disease Characteristics Between BA and WA Patients With MS

	All US MS PATHS sites			JHU site		
	BAs	WAs	<i>p</i> Value ^a	BAs	WAs	<i>p</i> Value ^a
Total, n	1,214	7,530		282	1,170	
Hispanic or Latino, n (%)	29 (2.3)	181 (2.4)	0.80	1 (0.0)	25 (2.1)	0.07
Male sex, n (%)	220 (28.2)	2002 (26.6)	<0.001	49 (17.4)	291 (24.9)	0.005
Age, mean (SD), y	47.1 (12.6)	50.9 (12.5)	<0.001	45.4 (12.6)	49.35 (12.7)	<0.001
BMI, mean (SD), kg/m²	30.9 (8.0)	28.8 (7.1)	<0.001	30.5 (8.0)	27.6 (6.4)	<0.001
Age at symptom onset, mean (SD), y	32.6 (11.8)	33.7 (11.3)	0.001	32.2 (11.7)	33.9 (11.1)	0.03
Disease duration, mean (SD), y	11.65 (8.7)	13.97 (10.0)	<0.001	10.2 (7.3)	12.3 (9.5)	<0.001
Smoking status, n (%)			<0.001			0.40
Never smoker	753 (63.5)	3,849 (52.4)		188 (6.7)	703 (60.1)	
Former smoker	163 (13.8)	1,333 (18.1)		38 (13.5)	163 (14.0)	
Current smoker	265 (22.4)	2089 (28.4)		45 (16.0)	214 (18.3)	
Status unknown	7 (0.6)	78 (1.1)		6 (2.1)	58 (5.0)	
Education, mean (SD), y	14.2 (2.7)	14.8 (2.6)	<0.001	14.9 (2.8)	15.8 (2.5)	<0.001
Employment status, n (%)			<0.001			0.001
Employed	530 (44.7)	3,633 (49.4)		158 (56.0)	689 (58.9)	
Disabled/unemployed	574 (48.4)	3,055 (41.6)		108 (38.3)	355 (38.3)	
Insurance type, n (%)			<0.001			<0.001
Private insurance	517 (43.6)	4,642 (63.2)		151 (54)	865 (74)	
Medicaid	211 (17.9)	507 (6.9)		29 (10)	21 (2)	
Medicare	326 (27.4)	1,634 (22.2)		66 (23)	184 (16)	
Not insured	13 (1.1)	44 (0.6)		4 (1.4)	3 (0.3)	
Other insurance	112 (9.5)	527 (6.7)		27 (9.6)	62 (5.3)	
Unknown insurance	6 (0.5)	27 (0.4)		0	3	
MS type, n (%)			<0.001			0.04
Relapsing-remitting	662 (55.9)	4,459 (60.7)		159 (56.4)	743 (63.5)	
Secondary progressive	208 (17.5)	1,281 (17.4)		40 (14.2)	169 (14.4)	
Progressive relapsing	139 (11.7)	479 (6.5)		29 (10.3)	65 (5.6)	
Primary progressive	93 (7.8)	542 (7.4)		32 (11.3)	68 (5.8)	
Unsure	83 (7.0)	588 (8.0)		17 (6.0)	93 (7.9)	
Current therapy, n (%)						
Injectable	216 (18.2)	1,554 (21.1)		59 (2.1)	303 (2.6)	0.20
Infusion	279 (23.5)	1,278 (17.1)		61 (21.6)	245 (20.9)	
Oral	320 (27.0)	2081 (27.7)		63 (22.3)	261 (22.3)	
Other therapy	109 (9.2)	592 (10.7)		26 (9.2)	63 (5.4)	
No therapy	261 (22.0)	1,816 (24.2)		68 (24.1)	265 (22.6)	
Unknown therapy	0	25 (3.3)		0	1 (0.1)	
Patient characteristics, n (%)						

Continued

Table 1 Demographics and Disease Characteristics Between BA and WA Patients With MS (continued)

	All US MS PATHS sites			JHU site		
	BAs	WAs	<i>p</i> Value ^a	BAs	WAs	<i>p</i> Value ^a
PDDS score, median (IQR)	2 (0–4)	1 (0–3)	<0.001	2 (0–4)	1 (0–3)	<0.001
Walking speed, mean (SD), s	8.1 (5.0)	7.2 (4.7)	<0.001	7.55 (3.6)	6.35 (3.1)	<0.001
Dexterity, mean (SD), s	29.9 (7.3)	27.7 (6.8)	<0.001	30.0 (7.2)	26.4 (6.4)	<0.001
Processing Speed Test, mean (SD), n questions	43.4 (12.9)	47.6 (12.8)	<0.001	42.4 (12.8)	50.4 (12.2)	<0.001

Abbreviations: BA = Black American; BMI = body mass index; IQR = interquartile range; JHU = Johns Hopkins University; MS = multiple sclerosis; MS PATHS = Multiple Sclerosis Partners Advancing Technology Health Solutions; PDDS = Patient Determined Disease Steps; WA = White American.

^a The *p* values are derived from univariate tests for differences between BAs and WAs using generalized linear models.

furthermore, reductions in gray matter volume have been strongly predictive of longer-term clinical disability in people with MS,^{22–28} suggesting that the results herein are likely to persist in longitudinal studies. This consistency of results, particularly after adjustment for confounders, improves confidence in the findings and demonstrates that BAs face MS-related disability that extends beyond reduced ambulation. The likelihood of selection bias may be reduced by the use of a multicenter cohort and large sample size; the patients studied are more likely to be representative of the broader population of people with MS in the United States than in smaller, single-center studies.

Our analysis of how socioeconomic status relates to outcomes between and within racial groups is crucial considering that socioeconomic status is associated with poor health outcomes in a variety of disease states. For example, in another common autoimmune disorder, systemic lupus erythematosus, multivariate models demonstrate that BA race, socioeconomic status, and a specific HLA haplotype are all independently associated with worse outcomes.²⁹ Here, not only do we find that adjusting for socioeconomic status in multivariate models does not attenuate the relation of BA

race to worse outcomes but also, similar to what we have reported with respect to the relation of race and socioeconomic status to health-related quality of life in MS PATHS participants,³⁰ we observe that lower socioeconomic status correlates with worse outcome among WAs, but intriguingly, these associations do not appear to be present among BAs. This pattern of findings is also evident in the MRI analysis that we performed, which is removed from subjective rater or self-reporting bias associated with clinical measures and assesses objective biological differences in the diseases process between BAs and WAs.

There are many potential interpretations of the results. It is likely that there may still be unmeasured confounders related to systematic racism and health outcomes that explain the findings herein. For example, while in the MS PATHS cohort BAs were actually more likely to be treated with higher-efficacy MS medications than WAs, we cannot exclude that differential or biased previous treatment strategies or adherence by race, leading to undertreatment early in the disease course and thus worsened longer-term outcomes in BAs,^{31,32} contributed to the findings herein. Systematic differences in treatment for BAs have been demonstrated for many health conditions, including neurologic conditions.³³ Furthermore, perhaps medical comorbid conditions (vascular comorbid conditions such as hypertension³⁴) or other aspects related to the burden of the cumulative experience of discrimination and racism,³⁵ inside and outside of the health care experience and for which we were not able to adjust, are operative in these populations. Genetic differences could contribute as well. For example, in patients with lupus, a greater load of susceptibility risk alleles was associated with increased risk of childhood-onset lupus, which has a more severe phenotype, among BAs but not WAs.³⁶

Our study has several limitations. This is a cross-sectional study, and as for all cross-sectional studies, one must carefully consider the directionality of the results and in particular whether reverse causality might account for the findings. This is certainly possible here, and longitudinal studies should be performed. That being said, it seems less likely that race and the myriad health and social conditions that differ by race in

Table 2 Multivariate-Adjusted Odds Ratio and Mean Differences for PDDS and Neuroperformance Outcomes

PDDS	Odds ratio ^a (95% CI)	<i>p</i> Value
Moderate vs mild disability	1.04 (0.88, 1.24)	0.64
Severe vs mild disability	1.47 (1.18, 1.86)	<0.001
Neuroperformance outcomes	Mean difference ^a (95% CI)	<i>p</i> Value
Walking speed, s	0.66 (0.36, 0.96)	<0.001
Manual dexterity, s	2.11 (1.69, 2.54)	<0.001
Cognitive performance, n correct	–5.06 (–5.72, –4.41)	<0.001

Abbreviations: CI = confidence interval; PDDS = Patient Determined Disease Steps.

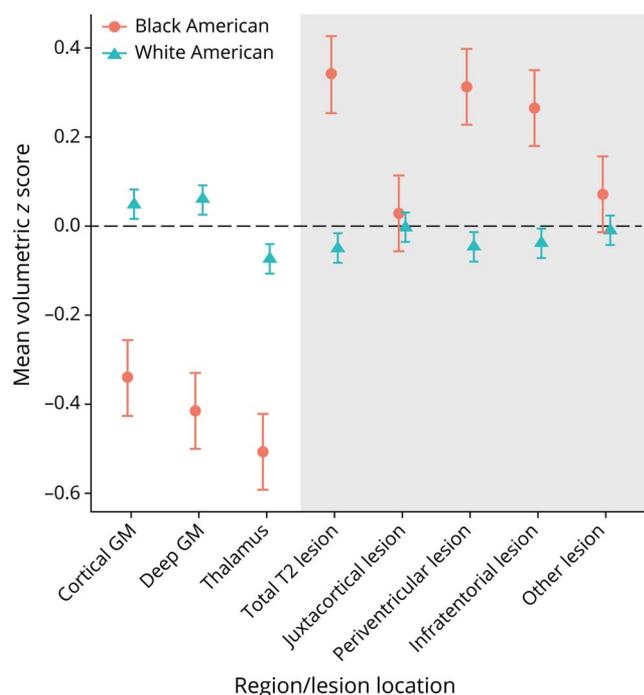
^a Both odds ratios and mean differences are adjusted for age, sex, disease duration and subtype, smoking status, body mass index, insurance status, education level, employment status, and disease-modifying therapy.

Table 3 Multivariate-Adjusted Mean Differences for Quantitative MRI Outcomes (n = 4,017)

Brain region measurement	Mean (SD)		Mean difference ^a (95% CI)	p Value
	BAs	WAs		
Brain parenchymal fraction	0.849 (0.03)	0.848 (0.03)	-0.002 (-0.004, -0.000)	0.04
White matter fraction	0.380 (0.03)	0.383 (0.03)	0.002 (-0.001, 0.004)	0.13
Gray matter fraction	0.470 (0.024)	0.471 (0.02)	-0.004 (-0.006, -0.002)	<0.001
Cortical gray matter, mL	471.90 (53.71)	503.38 (64.60)	-30.63 (-35.93 -25.33)	<0.001
Deep gray matter, mL	36.58 (4.11)	38.52 (4.13)	-1.58 (-1.92, -1.23)	<0.001
Thalamus, mL	12.32 (1.58)	13.24 (1.61)	-0.77 (-0.91, -0.64)	<0.001
Log (lesion measures), mL				
T2 lesion volume	2.56 (0.80)	2.26 (0.78)	0.31 (0.25, 0.38)	<0.001
Juxtacortical lesion volume	0.87 (0.47)	0.86 (0.45)	-0.01 (-0.06, 0.03)	0.52
Periventricular lesion volume	2.30 (0.94)	1.99 (0.87)	0.34 (0.27, 0.42)	<0.001
Infratentorial lesion volume	0.15 (0.19)	0.10 (0.15)	0.04 (0.03, 0.06)	<0.001
Other lesion volume	0.20 (0.36)	0.18 (0.32)	0.02 (-0.01, 0.05)	0.21

Abbreviations: BA = Black American; CI = confidence interval; WA = White American.

^a Mean differences are adjusted for age, sex, disease duration and subtype, smoking status, body mass index, insurance status, employment status, and disease-modifying therapy.

Figure Difference in Key MRI Outcomes Between Black American and White American MS PATHS Participants

We transformed all brain regions or lesion volumes to have a mean equal to 0 and SD equal to 1 to allow all regions to be plotted on the same scale. Values plotted denote the unadjusted means for each racial group. GM = gray matter; MS PATHS = Multiple Sclerosis Partners Advancing Technology Health Solutions.

the United States, which begin early in life and may extend generationally (before MS onset for a given individual), are a consequence of MS or MS-related disability. Assumptions that employment or insurance type are indicators of socioeconomic status may be too simple; people with MS who are more disabled may be less likely to be employed or to have access to private insurance due to their disability rather than due to socioeconomic status. We also explored education level as a measure of socioeconomic status, but even this may be problematic because the study measured only quantity, not quality, of education, which also does not likely capture racism-based differences between the experiences of BAs and WAs. On the other hand, in our more detailed Hopkins-only analysis, we were able to apply neighborhood-level indicators, including median household income and ADI, as more comprehensive measures of socioeconomic status rather than solely the metrics above. These results should be considered exploratory due to the single-center nature of the study and because the confidence intervals (particularly in the BA subgroup) were wide for some of the estimates. Finally, although some of our results could be affected by type 1 error, we intentionally selected a limited number of hypothesis-driven outcomes to study herein, many of which may be highly related, and thus, findings consistent across models are less likely due to error.

Across the board, BA patients with MS appear to have greater burden of inflammatory and neurodegenerative measures of MS, along with worse neurologic performance. While lower socioeconomic status appears to be correlated with worse neuroperformance measures in WAs, in this cross-sectional

Table 4 Mean Difference in Neuroperformance Outcomes for the Johns Hopkins Cohort

	Mean (SD)	Mean difference ^a (95% CI) in neuroperformance outcomes		
		Walking speed	Cognitive performance	Manual dexterity
WA (n = 1,046)				
Median income, \$				
Q1 (lowest SES)	49,836 (10,654)	0.00 (Ref)	0.00 (Ref)	0.00 (Ref)
Q2	76,427 (7,049)	-1.33 (-6.81, 4.48)	1.30 (-0.52, 3.11)	-0.38 (-2.90, 2.14)
Q3	101,875 (8,423)	0.41 (-0.54, 6.39)	1.82 (-0.00, 3.65)	0.31 (-2.57, 3.18)
Q4 (highest SES)	154,182 (32,109)	-6.96 (-12.20, -1.40)	2.09 (0.25, 3.93)	-0.21 (-3.38, 2.96)
ADI, percentile				
Q1 (highest SES)	5.77 (2.58)	0.00 (Ref)	0.00 (Ref)	0.00 (Ref)
Q2	15.15 (2.79)	-1.19 (-3.08, 0.70)	-0.72 (-2.39, 0.95)	0.77 (-0.35, 1.89)
Q3	27.93 (4.86)	-0.60 (-2.32, 1.11)	-1.44 (-3.14, 0.25)	1.32 (0.17, 2.47)
Q4 (lowest SES)	53.21 (14.28)	-0.24 (-1.92, 1.44)	-2.92 (-4.80, -1.04)	1.86 (0.59, 3.12)
BA (n = 288)				
Median income, \$				
Q1 (lowest SES)	46,062 (13,300)	0.00 (Ref)	0.00 (Ref)	0.00 (Ref)
Q2	76,685 (7,268)	-0.96 (-2.29, 0.37)	1.09 (-2.49, 4.67)	-0.47 (-1.69, 0.75)
Q3	100,915 (8,701)	-1.15 (-2.63, 0.33)	1.62 (-2.41, 5.66)	-0.53 (-1.76, 0.70)
Q4 (highest SES)	146,831 (27,723)	-0.48 (-1.20, 2.16)	-3.52 (-7.97, 0.93)	-1.78 (-3.02, -0.54)
ADI, percentile				
Q1 (highest SES)	6.69 (2.56)	0.00 (Ref)	0.00 (Ref)	0.00 (Ref)
Q2	15.34 (2.64)	0.04 (-0.44, 0.51)	3.92 (-1.20, 9.03)	-0.01 (-3.56, 3.54)
Q3	29.41 (4.74)	0.36 (-0.12, 0.85)	2.93 (-1.77, 7.64)	-0.05 (-3.35, 3.25)
Q4 (lowest SES)	62.11 (18.61)	0.15 (-0.39, 0.69)	1.67 (-2.88, 6.22)	-1.06 (-4.25, 2.13)

Abbreviations: ADI = Area Deprivation Index; BA = Black American; Q = quartile; Ref = referent; SES = socioeconomic status; WA = White American.
^a Mean differences are adjusted for age, sex, disease duration and subtype, multiple sclerosis therapy, education, and body mass index.

study, this association is less clear in BAs with MS, at least at a single time point. While this may inspire more robust studies of genetic prognostic factors within BAs with MS,³⁷ it seems more likely that unmeasured confounding (e.g., differences in quality despite apparent similarities in length of education, as discussed above), the relatively smaller size of the BA cohort, cross-sectional design, or all issues contribute to the lack of an association of socioeconomic status within the BA group. Representative cohort studies that longitudinally assess comorbidity or comorbidity management, MS disease activity, and MS therapy use, along with indications for that use of therapy to account for confounding by indication, are needed, and the MS PATHS cohort is expanding its collection to include more robust assessments of many previously unmeasured covariates. The results also reinforce the need for more racially representative phase 3 clinical trials³⁸ and comparative-effectiveness research focusing on treatment

strategies specifically in the BA population to identify whether, for example, certain therapies or more aggressive early treatment will better mitigate long-term disability accrual. Finally, identifying other modifiable prognostic factors within the BA MS population may allow focused efforts on their mitigation that, in turn, will improve outcomes.

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Name	Location	Contribution
Karla Gray-Roncal, MD	Johns Hopkins University, Baltimore, MD	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data
Kathryn C. Fitzgerald, ScD	Johns Hopkins University, Baltimore, MD	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data
Lana Zhovtis Ryerson, MD	NYU Langone Health, New York	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Leigh Charvet, PhD	NYU Langone Health, New York	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Sandra D. Cassard, ScD	Johns Hopkins University, Baltimore, MD	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Robert Naismith, MD	Washington University in St. Louis, MO	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Daniel Ontaneda, MD	Cleveland Clinic, OH	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Kedar Mahajan, MD, PhD	Cleveland Clinic, OH	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Wanda Castro-Borrero, MD	Biogen, Cambridge, MA	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data

Appendix (continued)

Name	Location	Contribution
Ellen M. Mowry, MD	Johns Hopkins University, Baltimore, MD	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data

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