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Authors

Radzik, Anne
Amezcua, Lilyana
Anderson, Annika
et al.

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Disparities by Race in Pregnancy Care and Clinical Outcomes in Women With Multiple Sclerosis

A Diverse Multicenter Cohort

Anne Marie Radzik, BS, Lilyana Amezcua, MD, Annika Anderson, BA, Serena Gilmore, BS, Sophie Ahmad, MS, Rachel Brandstadter, MD, Michelle T. Fabian, MD, Edith L. Graham, MD, Sophia Hodgkinson, Lindsay Horton, MD, Dina A. Jacobs, MD, Ilana B. Katz Sand, MD, Amit Kohli, MD, Libby Levine, MS, AGNP-BC, Monica McLemore, PhD, Annette F. Okai, MD, Jasmin Patel, MD, Shane Poole, BS, Claire Riley, MD, Sammita Satyanarayan, MD, Lauren Tardo, MD, Elizabeth Verter, MD, Veronica Villacorta, BA, Vanessa Zimmerman, MSN, Leah Zuroff, MD, Mitzi J. Williams, MD, Maria K. Houtchens, MD, and Riley Bove, MD, MMSc

Correspondence
Dr. Bove
riley.bove@ucsf.edu

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Abstract

Background and Objectives

Racial disparities exist in both neurologic and obstetric populations, underscoring the importance of evaluating pregnancy outcomes in diverse women with multiple sclerosis (MS). The objective of this multicenter retrospective study was to compare pregnancy care and outcomes between Black and Hispanic (underrepresented) and White women with MS.

Methods

Demographic and clinical data were extracted from medical records of 9 US MS centers for women with MS/clinically isolated syndrome who delivered live births between 2010 and 2021. Sites identified at last 15 consecutive Black/Hispanic women and a matching number of White women. Socioeconomic factors, pregnancy, and MS care/outcomes were compared between groups (underrepresented and White and then Black and Hispanic) using Wilcoxon rank sum (U statistic and effect size r reported), χ^2, t tests and logistic regressions as appropriate to data type. Multiple imputation by chained equation was used to account for missing data.

Results

Overall, 294 pregnancies resulting in live births were analyzed (81 Black, 67 Hispanic, and 146 White mothers). Relative to underrepresented women, White women lived in areas of higher median (interquartile range [IQR]) Child Opportunity Index (79 [45.8] vs 22 [45.8], U = 3,824, r = 0.56, p < 0.0001) and were more often employed (84.9% vs 75%, odds ratio [OR] 2.57, CI 1.46–4.50, p = 0.0008) and privately insured (93.8% vs 56.8%, OR 11.6, CI 5.5–24.5, p < 0.0001) and more received a 14-week ultrasound (98.6% vs 93.9%, OR 4.66, CI 0.99–21.96, p = 0.027). Mode of delivery was significantly different between the three groups ($X^2(10,294)$ = 20.38, p = 0.03); notably, Black women had the highest rates of emergency cesarean deliveries, and Hispanic women highest rates of uncomplicated vaginal deliveries. Babies born to underrepresented women had lower median (IQR) birthweights than babies born to White women (3,198 g [435.3 g] vs 3,275 g [412.5 g], U = 9,255, r = 0.12, p = 0.04) and shorter median (IQR) breastfeeding duration (4.5 [3.3] vs 6.0 [4.2] months, U = 8,184, r = 0.21, p = 0.003). While underrepresented

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From the University of California San Francisco (A.M.R.); Department of Neurology (L.A.), University of Southern California, Los Angeles; Department of Neurology (A.A., S.P., R. Bove), UCSF Weill Institute for the Neurosciences, and Department of Neurology (S.G.), University of California San Francisco; Department of Neurology (S.A., E.L.G.), Northwestern University, Chicago, IL; Department of Neurology (R. Brandstadter, D.A.J., V.Z., L.Z.), Hospital of the University of Pennsylvania, Philadelphia; Corinne Goldsmith Dickinson Center for MS (M.T.F., I.B.K.S., A.K., J.P., S.S., E.V.), Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY; Brigham and Women's Hospital (S.H., M.K.H.), Boston, MA; University of Texas Southwestern Medical Center (L.H., L.T.), Dallas; Center for Translational and Computational Neuroimmunology and Multiple Sclerosis Center (L.L., C.R.), Department of Neurology, Columbia University Irving Medical Center, New York, NY; Family Health Care Nursing Department (M.M.), School of Nursing, University of California San Francisco; North Texas Institute of Neurology and Headache (A.F.O.), Frisco; University of Southern California (V.V.), Los Angeles; and Joi Life Wellness Group (M.J.W.), Multiple Sclerosis Center, Smyrna, GA.

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Glossary

ARR = annualized relapse rate; **CIS** = clinically isolated syndrome; **COI** = Child Opportunity Index; **DMT** = disease-modifying treatment; **EDSS** = Expanded Disability Status Scale; **EHR** = electronic health record; **Gd+** = gadolinium enhancing; **IQR** = interquartile range; **IRB** = institutional review board; **MS** = multiple sclerosis; **OR** = odds ratio; **UCSF** = University of California San Francisco.

women were younger than White women (mean [SD] 30.9 [4.8] vs 33.8 [4.0], $t = 1.97$, CI 1.96–3.98, $p < 0.0001$), their median (Q1–Q3, IQR) Expanded Disability Status Scale was higher (1.5 [1–2.5, 1.5] vs 1 [0–1.5, 1.5], $U = 7{,}260$, $r = 0.29$, $p < 0.0001$) before pregnancy. Finally, medical records were missing more key data for Black women (19.7% missing vs 8.9% missing, OR 2.54, CI 1.25–5.06, $p = 0.008$).

Discussion

In this geographically diverse multicenter cohort, underrepresented women entered pregnancy with higher disability and fewer health care resources. Pregnancy represents a pivotal window where structural factors affect maternal and fetal health and neurologic trajectories; it is a critical period to optimize care and health outcomes.

Introduction

The pregnancy period represents a critical focus of research in neurologic diseases due to the need to optimize prenatal and maternal treatments and maternal/fetal outcomes and to understand the biology of disease-relevant factors during gestation. Women represent three-quarters of people with multiple sclerosis (MS) and are most often diagnosed during their reproductive years.[1] After the immunotolerant state of pregnancy, postpartum MS relapse risk[2] is influenced by both disease-related factors (disability before pregnancy and relapse rate)[3] and treatment-related[3,4] and breastfeeding[5] practices. Therefore, quality and type of care could influence MS outcomes.

Health disparities and health inequities disproportionately affect underrepresented and minoritized people with MS in the United States and elsewhere.[6,7] Black and African American (herein referred to as Black) women and Hispanic and Latinx (herein referred to as Hispanic) women have an earlier age at onset, higher risk of early and total disability, greater neurodegeneration,[8,9] and lower overall survival at 5 years[10] when compared with White individuals. There are also marked race and ethnic disparities in pregnancy care, experiences, and outcomes in the general US population.[11-17] To date, in the United States and Europe, most research on MS pregnancy outcomes has focused on White women, and consideration of relevant socioeconomic factors is generally lacking.

The goal of this multicenter retrospective analysis was to evaluate differences in prenatal and pregnancy care of Black and Hispanic women (as a cohort referred to as underrepresented women) with White women with MS. The following hypotheses were tested: underrepresented women would have lower socioeconomic opportunities, worse pregnancy care and outcomes, and worse MS care and outcomes compared with their White counterparts.

Methods

Study Setting and Sample Selection

This retrospective chart review includes data from 9 geographically diverse MS centers across the United States. Institutions were chosen from academic and private MS centers whose clinical populations were representative of the ethnoracial diversity in the United States to support generalizability of the findings. This included regions with high and low proportions of Hispanic and/or Black individuals. Some sites had prior pipelines for extracting pregnancy data for patients with MS.[18-20] For other sites and to enrich these procedures, an electronic health record (EHR) search was conducted using billing diagnosis code of MS (G35) for female patients aged between 18 and 50 years. This group was then screened for billing diagnosis codes related to pregnancy and fertility.

Inclusion criteria were derived both from the demographic section of the EHR (female sex, 18–50 years, self-reported race: Black or African American or White, and/or ethnicity: Hispanic or Latina or Latinx) and from the clinical sections (MS/clinically isolated syndrome [CIS] diagnosis according to 2017 McDonald Criteria[21] and received MS care at the participating Center during a postdiagnosis pregnancy between January 2010 and December 2021). Individuals who self-identified as both Black and Hispanic in the EHR were for the current analyses categorized as Black (n = 13). Patients were presumed to be cis-women (herein referred to as women), given their female biological sex and ability to get pregnant, but gender identity was not specifically or systematically collected in the EHR. Each institution was asked to contribute data from a minimum of 15 Black or Hispanic patients and 15 White patients. This sample size of approximately 150 underrepresented women was chosen to ensure the study had enough power to detect significant differences in relapses and new lesions preconception to postpartum because a sample of approximately 100 women was previously sufficient to detect such

differences.[19] White women from each Center were included to account for possible regional or MS Center–specific effects (for example, if comparing MS outcomes from Black women in an academic New York clinic with Hispanic women in a private Texas practice). The most chronologically recent consecutive cases that fit the inclusion criteria were identified and extracted by each coinvestigator to reduce possible investigator recall bias.

Standard Protocol Approvals, Registrations, and Patient Consents

Deidentified data from the participating coinvestigators were sent to University of California San Francisco (UCSF) for statistical analysis. The UCSF Institutional Review Board (IRB) approved the statistical analysis of UCSF EHR data and the analysis of external data with no patient contact. Each contributing MS center received approval by local IRBs as warranted for extraction of deidentified EHR data. A Data Usage Agreement governed the sharing of deidentified patient data with UCSF.

Data Collection

Clinically acquired data were extracted from the EHR between April and July 2022 at each participating site for each pregnancy, for the 12 months before conception to the 12 months post delivery. A minimal dataset for inclusion in analysis was specified, and pregnancies missing these data were not shared with the analyzing team.

Demographic Data

Minimum dataset data were race, ethnicity, insurance status, and age at conception. Additional data were zip code used to calculate the Child Opportunity Index (COI); COI metrics but not zip code were shared alongside the patient's clinical data. The COI is a composite index measured at the census tract level that captures in a single metric, neighborhood resources and conditions that matter for a child's healthy development. It is based on 29 indicators spanning the 3 domains of education, health, and socioeconomic status.[22] This measure was used as a proxy to estimate socioeconomic opportunity of the mother-child pair.

Pregnancy-Related Data

Minimum dataset data were as follows: outcome, that is, live birth or pregnancy loss; complications, that is, gestational hypertension, gestational diabetes, infections, or preeclampsia; and breastfeeding status. Additional data were as follows: use of fertility treatments, 14-week ultrasound, birth weight, gestational age at delivery, infant complications, maternal postpartum complications, and route of birth (cesarean, vacuum, and natural). Newborns were categorized as small for gestational age if their birth weight was <2,500 g.

MS-Related Data

Minimum dataset data were MS onset and MS type and relapses in the 12 months before to 12 months after pregnancy. Additional data were MRI dates and reports, Expanded Disability Status Scale (EDSS), and disease-modifying treatment (DMT) use during this time frame. The year postpartum was broken down into 4 time intervals: 0–3, 3–6, 6–9, and 9–12 months. Clinical relapses were defined as new or worsening neurologic symptoms for at least 24 hours without fever or infection, as documented by the treating neurologist. When EDSS was not included in the EHR, it was extrapolated by the site's MS expert collaborator from the treating neurologist's note as previously validated.[23] Disability progression was measured comparing the pre-pregnancy EDSS with the last available EDSS within 12 months of delivery using the following criteria: for a baseline score of 0: 1.5-point increase; baseline score 1.0–5.5: 1.0 point increase; baseline score ≥6: 0.5 point increase.[24] MRI reports for the brain and spinal cord (thoracic and cervical) performed during the 12 months before conception and 12 months after delivery were reviewed by each site investigator for the presence of T2-weighted hyperintense lesions that were new relative to the most recent past imaging and/or gadolinium enhancing (Gd+) lesions with administered contrast. DMT use was categorized as therapeutic during conception if patients received rituximab or ocrelizumab in the prior 6 months; dimethyl fumarate, glatiramer acetate, or interferon treatment through the menstrual cycle before conception; or alemtuzumab in the past 5 years. Natalizumab and S1P modulators were considered therapeutic only if they were continued throughout the pregnancy because their discontinuation can result in rebound relapse.[4,25]

Statistical Analyses

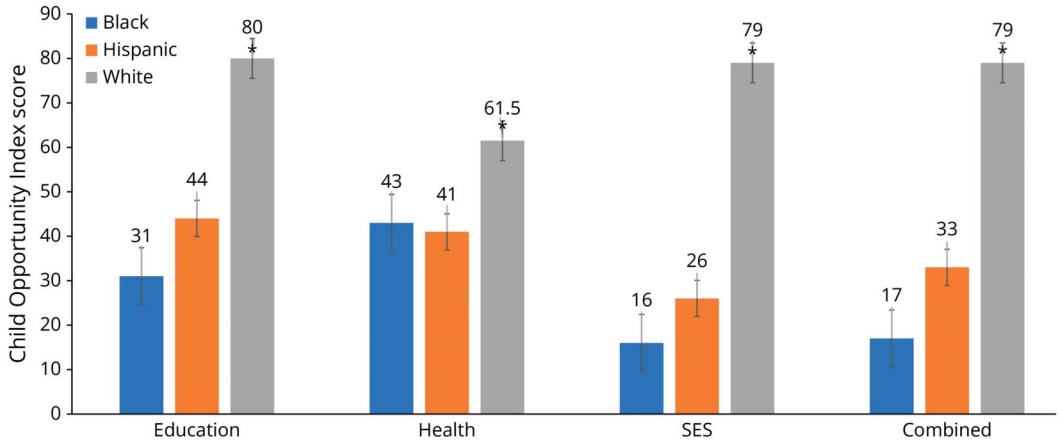
Outcomes Selected

Because of possible biases in pregnancy ascertainment and in pregnancy outcome documentation and because of our focus on postpartum trajectories, only pregnancies resulting in live births were analyzed. From the variables evaluated, primary outcomes for each category were selected. The primary demographic characteristic was the COI composite scale; others were maternal age, employment, insurance status, education, and COI individual scales. The coprimary pregnancy-related measures were use of 14-week ultrasound and duration of breastfeeding. The International Society of Ultrasound in Obstetrics and Gynecology recommends a 14-week ultrasound to provide early detection of fetal abnormalities, confirms viability, and an accurate gestational age.[26,27] Others were obstetric complications, gestational age, newborn birth weight, and newborn small for gestational age. The coprimary MS-related outcomes were therapeutic DMT use during conception and annualized relapse rate (ARR) in the 3 months postpartum. Others were EDSS worsening, postpartum MRI activity and relapses for other time points (3-month increments in the year before, during, and post pregnancy).

Comparisons Performed

First, group demographic characteristics were described for each subset of patients: Black, Hispanic, and White women. Then, pregnancy and MS outcomes were compared by race and ethnicity using the Student t test, Wilcoxon rank sum (U statistic and effect size r reported), χ^2, and logistic regression. Given the heterogeneous ways in which race and ethnicity have

Figure 1 Comparison of COI in Patient's Zip Code, Between Black and Hispanic (Underrepresented) and White Women With MS



The COI 2.0 is a composite index measured at the census tract level that captures neighborhood resources that matter for a child's healthy development in a single metric. It is based on 29 indicators spanning the 3 domains of education, health, and SES.[22] The median scores by race and ethnicity for each scale were compared through the Wilcoxon rank sum test ($p < 0.001$ for all measures). COI = Child Opportunity Index; MS = multiple sclerosis; SES = socioeconomic status.

been reported to influence both pregnancy and MS outcomes, the groups were compared in several ways. The first evaluated for possible "White privilege" by comparing outcomes for White women with those for Black and Hispanic women, that is, underrepresented, women. Then, if a significant difference was found, the groups of Black and Hispanic women were further compared. Finally, to ensure other important differences were not missed, 3-way comparisons were secondarily performed (eTable 1, links.lww.com/WNL/D360). Statistical analyses were performed using the JMP Pro 17 statistical software package and R. All missing data values were estimated using multivariate imputation by chained equations in the R statistical package. Statistical significance threshold was set at $p < 0.05$.

Data Availability

Deidentified data and statistical analysis plan will be shared with qualified investigators on reasonable request to the corresponding author.

Results

Sociodemographic and Clinical Characteristics of Study Cohort

A total of 294 live births among 81 Black, 67 Hispanic, and 146 White women were included in the current analyses. A further 16 pregnancies collected for the analyses were excluded; 13 resulted in pregnancy loss (6 Black, 4 Hispanic, and 3 White women), and 3 occurred in women ultimately categorized as a race and ethnicity other than Black, Hispanic, or White. Each center contributed approximately 25% Black, 25% Hispanic, and 50% White patients to the cohort, with exact proportions varying by site as influenced by local demographics (eTable 1, links.lww.com/WNL/D360); collectively, they were managed by an estimated 61 neurologists during their pregnancy. There was no difference in the proportion of pregnancies by race and ethnicity that occurred between 2010 and 2015 (Black women = 21.0%, Hispanic women = 20.9%, and White women = 18.5%), 2016 and 2019 (Black women = 48.2%, Hispanic women = 52.2%, and White women = 48.0%), and 2020 onward (Black women = 30.9%, Hispanic women = 26.9%, and White women = 33.6%, $\chi^2(4,294) = 1.1$, $p = 0.90$).

Sociodemographic Characteristics

On the primary demographic measure, the COI, White women lived in zip codes with significantly higher COI scores than underrepresented (Black and Hispanic) women, for the combined scale (median [interquartile range (IQR)] 79 [45.8] vs 22 [45.8], $U = 3{,}824$, $r = 0.56$, Figure 1) and each of the 3 individual measures analyzed (education, health, and socioeconomic opportunity, Figure 1). Compared with Hispanic women, Black women lived in zip codes with significantly lower scores on the combined scale (median [IQR] 17 [28.5] vs 33 [50.0], $U = 2{,}155$, $r = 0.13$) and the socioeconomic opportunity measure (median [IQR] 16 [32.5] vs 26 [57.0], $U = 2{,}139$, $r = 0.13$).

There were striking differences across most other demographic characteristics. White patients were older than underrepresented women (mean [SD] 33.8 [4.0] vs 30.9 [4.8], $t = 1.97$, CI 1.96–3.98) and had significantly more opportunities across all measures (Table 1). White women had significantly greater odds of the following: completing a college degree (52.7% vs 22.3%, odds ratio [OR] 3.9, CI 2.35–6.45), completing post–college education (20.6% vs 4.7%, OR 5.2, CI 2.21–12.29), being employed (84.4% vs 67.6%, OR 2.5, CI 1.46–4.51), and being employed full-time (72.6% vs 56.1%, OR 2.0, CI 1.27–3.38) when compared with underrepresented counterparts. There was no significant difference between Black and Hispanic women for these measures.

Table 1 Demographic and Clinical Features of Cohort at Conception, by Race and Ethnicity

					White vs Black + Hispanic		Black vs Hispanic	
	Black	Hispanic	White	Total	*p* Value	CI or *r*[a]	*p* Value	CI or *r*[a]
N (%)	81 (27)	67 (23)	146 (50)	294 (100)				
Age, y, mean (SD)[b]	31 (4.9)	30 (4.6)	34 (4.0)	32 (4.7)	<0.0001	1.96–3.98	0.14	-1.56×10^{-5}, 3.00
Sociodemographic features								
Childhood Opportunity Index Composite score, median, IQR (range)[c]	17, 29 (1–95)	33, 50 (1–100)	79, 44 (5–100)	52, 64 (1–100)	<0.0001	*0.56*	0.03	*0.13*
Education, n (%)[d]					<0.0001	0.48–11.14	0.92	0.48–11.14
Did not complete HS	1 (1.2)	1 (1.5)	0 (0)	2 (0.7)				
HS/GED	36 (44.4)	25 (37.3)	24 (16.4)	85 (28.9)				
College	14 (17.3)	12 (17.9)	47 (32.2)	73 (24.8)				
Post college	4 (4.9)	3 (4.5)	30 (20.6)	37 (12.6)				
Unknown	26 (32.2)	26 (38.8)	45 (30.8)	97 (33.0)				
Employed, n (%)[d]	56 (69.1)	55 (65.7)	124 (84.9)	224 (76.2)	0.0008	1.46–4.50	0.65	0.43–1.7
Employment type[d]					0.02	0.83–12.83	0.3	0.83–12.83
Full-time	47 (58.0)	36 (53.7)	106 (72.6)	189 (64.3)				
Part-time	10 (12.4)	9 (13.)	20 (13.7)	39 (13.3)				
Disability	2 (2.5)	1 (1.5)	2 (1.4)	5 (1.7)				
Student	6 (7.4)	1 (1.5)	3 (2.1)	10 (3.4)				
Unemployed	12 (14.8)	11 (16.4)	8 (5.5)	31 (10.5)				
Unknown	4 (4.9)	9 (13.4)	7 (4.8)	20 (6.8)				
Insurance type[d]					<0.0001	0.22–9.35	0.42	0.22–9.35
Public	37 (45.7)	24 (35.8)	9 (6.2)	70 (23.8)				
Private	42 (51.9)	42 (62.7)	137 (93.8)	221 (75.2)				
Charity	1 (1.2)	0 (0)	0 (0)	1 (0.3)				
Unknown	1 (1.2)	1 (1.5)	0 (0)	2 (0.7)				
MS features								
Disease course[d]					0.30	0.22–9.35	0.03	0.22–9.35
CIS/RR	76 (93.9)	67 (100)	144 (98.6)	287 (97.6)				
PP/SP	5 (6.1)	0 (0)	2 (1.4)	7 (2.3)				
Disease duration, y, median, IQR (range)[c]	6, 5 (0–21)	6, 5 (0–16)	6, 5 (0–19)	6, 5 (0–21)	0.96	*0.05*	0.64	*0.03*
EDSS, median, IQR (range)[c]	1.5, 2 (0–6.5)	1.5, 1 (0–6)	1, 1.5 (0–6.5)	1.5, 1.5 (0–6.5)	<0.0001	*0.29*	0.45	*0.04*
DMT preconception, n (%)[d]								
First line self-injectable	18 (22.2)	16 (23.9)	43 (29.5)	77 (26.2)	0.50	0.48–11.14	0.58	0.48–11.14
Infusion	35 (43.2)	35 (52.2)	62 (42.5)	132 (44.9)				
Oral	16 (19.8)	7 (10.5)	24 (16.4)	47 (16.0)				
HSCT	11 (13.6)	8 (11.9)	13 (8.9)	32 (10.9)				
None	1 (1.2)	1 (1.5)	4 (2.7)	6 (2.0)				

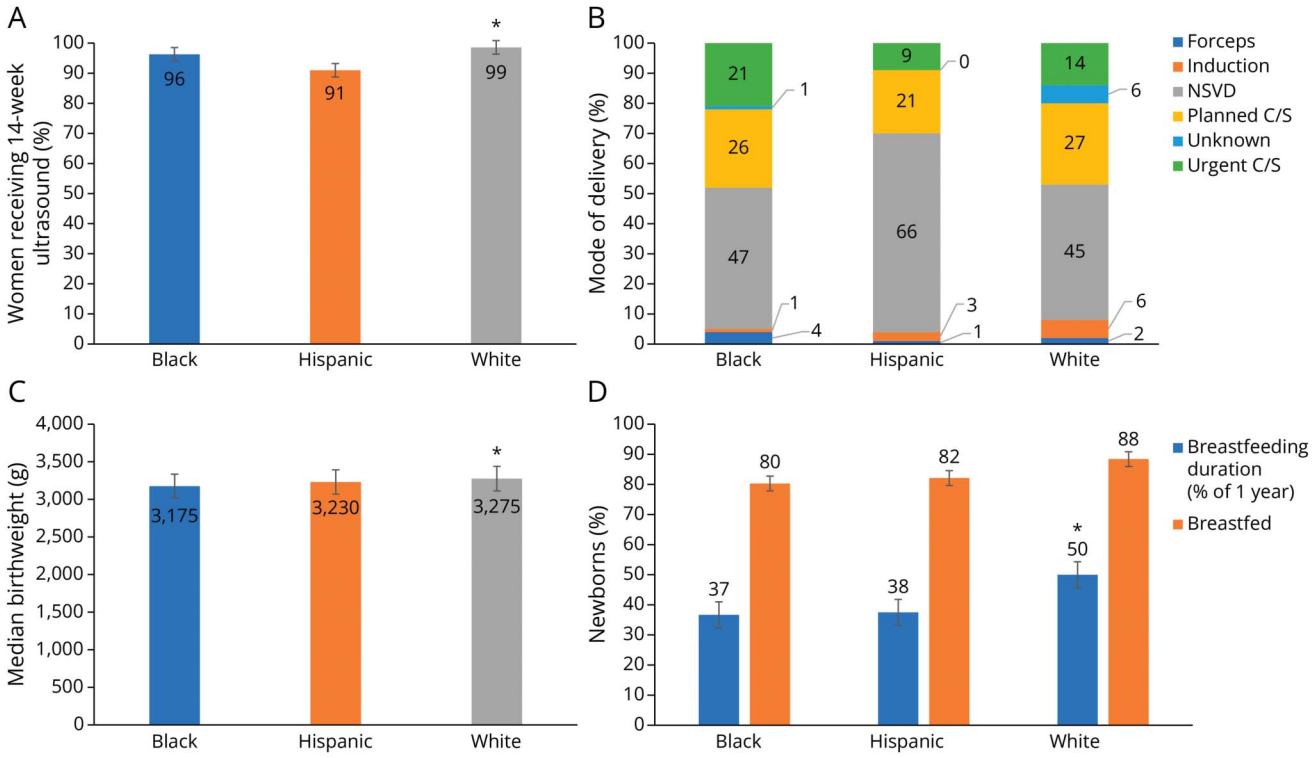
Continued

Table 1 Demographic and Clinical Features of Cohort at Conception, by Race and Ethnicity *(continued)*

	Black	Hispanic	White	Total	White vs Black + Hispanic		Black vs Hispanic	
					p Value	CI or *r*[a]	*p* Value	CI or *r*[a]
Rebound risk, yes, n (%)[d]	14 (17.3)	11 (16.4)	12 (15.1)	47 (16.0)	0.67	0.47–1.63	0.89	0.40–2.23
Pregnancy features								
Gravidity, median, IQR (range)[c]	2, 2 (0–7)	2, 1 (0–7)	1, 2 (0–9)	1, 2 (0–9)	0.0002	*0.21*	0.30	*0.06*
Parity, median, IQR (range)[c]	1, 2 (0–4)	1, 1 (0–5)	1, 1 (0–6)	1, 1 (0–6)	<0.05	*0.11*	0.45	*0.04*

Abbreviations: DMT = disease-modifying treatment; CIS = clinically isolated syndrome; EDSS = Expanded Disability Status Scale; GED = general educational development; HS = high school; HSCT = hematopoietic stem cell transplant; IQR = interquartile range; MS = multiple sclerosis; PP = primary progressive; RR = relapsing-remitting; SP = secondary progressive.
For all: Black women = 81, Hispanic women = 67, White women = 146.
[a] *r* = measure of effect size for Wilcoxon rank sum displayed as a single value in italics; *r* = 0.10–<0.3 (small effect), 0.30–<0.5 (moderate effect), and ≥0.5 (large effect).
[b] *t* test.
[c] Wilcoxon rank sum.
[d] Chi-square.

Figure 2 Comparison of Key Pregnancy Outcomes Between Black and Hispanic (Underrepresented) and White Women With MS



Panel A depicts the percentage of women who received a 14-week ultrasound. Panel B depicts the mode of delivery. Panel C depicts median birth weights. Panel D depicts the percentage of newborns classified as low birth weight (<2,500 g). Finally, panel E depicts breastfeeding duration and proportion of pregnancies where a mother breastfed. Data availability: For all: Black women = 81, Hispanic women = 67, White women = 146. Newborns were categorized as low birth weight if they weighed less than 2,500 g. C/S = cesarean; NSVD = normal spontaneous vaginal delivery.

Table 2 Comparison of MS-Related Care and Outcomes, by Race and Ethnicity

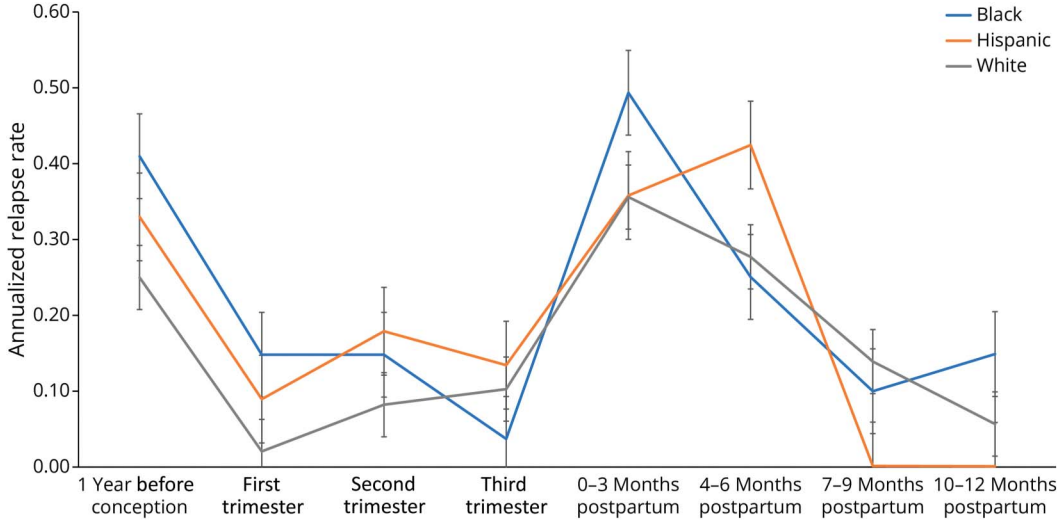
				Black + Hispanic vs White			Black vs Hispanic		
	Black	Hispanic	White	*p* Value	OR or *U*	CI or *r*[a]	*p* Value	OR or *U*	CI or *r*[a]
Before/during pregnancy									
DMT considered therapeutic at conception, yes, n (%)[b]	58 (71.6)	49 (73.1)	111 (76.0)	0.46	1.22	0.72–2.05	0.84	1.08	0.52–2.23
ARR preconception, median, IQR (range)[c]	0, 1 (0–3)	0, 1 (0–3)	0, 0 (0–2)	0.11	*9,909*	*0.04*	0.46	*2,560*	
Depression in year preconception, n (%)[b]	20 (24.7)	14 (20.9)	21 (14.4)	0.06	0.56	0.31–1.03	0.58	0.81	0.37–1.75
DMT interrupted during pregnancy, n (%)[b]	74 (91.4)	64 (95.5)	132 (90.4)	0.37	0.68	0.29–1.59	0.32	2.02	0.50–8.13
MRI preconception done, n (%)[b]	60 (74.0)	49 (73.3)	113 (77.4)	0.45	1.23	0.72–2.09	0.90	0.95	0.46–1.99
Gd+ lesions before conception, n (%)[b]	12 (14.8)	14 (20.9)	20 (13.7)	0.36	0.74	0.40–1.40	0.33	1.52	0.65–3.55
New T2 lesions before conception, n (%)[b]	16 (19.8)	12 (17.9)	30 (20.6)	0.73	1.11	0.62–1.97	0.78	0.89	0.39–2.03
Postpartum									
ARR in first 3 mo postpartum, median, IQR (range)[c]	0, 0 (0–4)	0, 0 (0–4)	0, 0 (0–1)	0.34	*10,458*	*0.07*	0.51	*2,621*	*0.03*
Percent patients with relapse in first 3 mo postpartum[b]	12.4	9.0	7.5	0.33	0.67	0.30–1.50	0.51	0.70	0.24–2.03
Depression in year postpartum, n (%)[b]	19 (23.5)	17 (25.4)	31 (21.2)	0.53	0.84	0.49–1.45	0.79	1.11	0.52–2.36
Weeks to start DMT postpartum, median, IQR (range)[c]	17.0, 13.6 (0–68.6)	17.8, 13.9 (0–161)	18.6, 12.8 (0–157)	0.08	*9,526*	*0.10*	0.87	*2,670*	*0.01*
Weeks to first MRI postpartum, median, IQR (range)[c]	28.1, 7.4 (0–160.4)	28.7, 11.4 (2.4–87.9)	27.7, 8.3 (3.6–184.1)	0.11	*9,651*	*0.09*	0.68	*2,607*	*0.02*
EDSS postpartum, median, IQR (range)[c]	1.5, 2.0 (0–6.5)	1.5, 1.5 (0–6.5)	1, 2 (0–7)	<0.0001	*2,474*	*0.05*	0.52	*2,546*	*0.04*
EDSS 1 y postpartum, median, IQR (range)[c]	2, 2 (1–6.5)	2, 1.5 (0–6.5)	1, 1 (1–6.5)	0.0005	*8,330*	*0.20*	0.35	*2,474*	*0.05*
EDSS change pre/post pregnancy, median, IQR (range)[c]	0, 0 (−3.5, 4)	0, 1 (−2.5, 6.5)	0, 0 (−2.5, 4)	0.74	*10,587*	*0.02*	0.10	*2,321*	0.09
Clinically meaningful increase in EDSS, n (%)[b]	4 (4.9)	3 (4.5)	10 (6.9)	0.44	1.48	0.55–4.00	0.90	0.90	0.19–4.18
Gd+ lesions postpartum, n (%)[b]	11 (13.6)	11 (16.4)	17 (11.6)	0.42	0.75	0.38–1.49	0.63	1.25	0.50–3.09
New T2 lesion postpartum, n (%)[b]	23 (28.4)	16 (23.9)	44 (30.1)	0.47	1.21	0.72–2.00	0.53	0.79	0.38–1.66

Abbreviations: ARR = annualized relapse rate; DMT = disease-modifying treatment; EDSS = Expanded Disability Status Scale; Gd+ = gadolinium enhancing; IQR = interquartile range; MS = multiple sclerosis; OR = odds ratio.
For all: Black women = 81, Hispanic women = 67, White women = 146.
[a] *r* = measure of effect size for Wilcoxon rank sum displayed as a single value in italics; *r* < 0.3 (small effect), 0.30–<0.5 (moderate effect), and ≥0.5 (large effect).
[b] *t* test.
[c] Wilcoxon rank sum.

MS Characteristics Before Pregnancy

There were fewer differences in most preconception MS characteristics. Overall, almost 94.9% patients had relapsing-onset MS or CIS, and the cohort median MS duration was 6 years (IQR 3–8). Based on available data, in terms of DMT, in 98.0% pregnancies (288/294), the patient was treated with a DMT in the year before conception (mostly self-injectables and monoclonal antibodies). Despite similarities in DMT usage and MS duration, and despite their older age, White women had significantly lower median (Q1–Q3, IQR) EDSS (1 [0–1.5, 1.5] vs 1.5 [1–2.5, 1.5], U = 7,260, r = 0.29) and lower gravidity (median [IQR] 1 [2] vs 2 [2], U = 8,195, r = 0.21) and parity (median [IQR] 1 [1] vs 1 [1.8], U = 9,482, r = 0.11) at conception than underrepresented women. These variables did not differ significantly between Black and Hispanic women (Table 1).

Figure 3 Comparison of Annualized Relapse Rate Between Black and Hispanic (Underrepresented) and White Women With MS Before, During, and After Pregnancy



For all: Black women = 81, Hispanic women = 67, White women = 146. *p = 0.05. MS = MS = multiple sclerosis.

Pregnancy Care and Outcomes

Pregnancy care and outcomes varied significantly by race and ethnicity. The key findings are presented graphically in Figure 2, and individual analyses are detailed in eTable 2 (links.lww.com/WNL/D360).

Prenatal Care

For the primary pregnancy outcome evaluated, White women were more likely than underrepresented women to receive a 14-week ultrasound (98.6% vs 93.9%, OR 4.7, CI 0.99–21.96); rates in Black and Hispanic women did not significantly differ (96.3% vs 91.0%, OR 0.39, CI 0.09–1.63). There were no differences between underrepresented and White women in the other pregnancy-related outcomes evaluated: rates of gestational hypertension, gestational diabetes, or preeclampsia/eclampsia (eTable 2, links.lww.com/WNL/D360).

Delivery and Postpartum Outcomes

For the primary postpartum outcome evaluated, there was no difference in rates of breastfeeding between groups; however, the median breastfeeding duration was shorter for underrepresented women than for White women (median [IQR] 4.5 [3.3] vs 6.0 [4.2] months, U = 8,184, r = 0.21). When comparing Black and Hispanic women, there was no significant difference in breastfeeding characteristics (eTable 2, links.lww.com/WNL/D360). Route of birth also varied significantly by race and ethnicity ($\chi^2(10,294) = 20.38$, p = 0.03). In this study, due to the distribution of outcomes, 3-way comparison was conducted. Regarding specific delivery mode, Black women had higher rates of emergency cesarean sections (Black/Hispanic/White: 21.0%/9.0%/14.4%, Black vs Hispanic: OR 2.08, CI 1.00–7.30; Black vs White: OR 1.58, CI 0.78–3.21), and Hispanic women had a greater proportion of uncomplicated vaginal births (Hispanic/Black/White: 65.7%/46.9%/44.5%, Hispanic vs Black: OR 2.16, CI 1.11–4.22; Hispanic vs White: OR 2.38, CI 1.31–4.35)." Given the potential for significant differences in gravidity and parity between White and underrepresented women to influence mode of delivery, gravidity and parity were sequentially added to the model, but mode of delivery still differed significantly by race and ethnicity ($\chi^2(5,294) = 11.05$, p = 0.03).

Newborn Characteristics

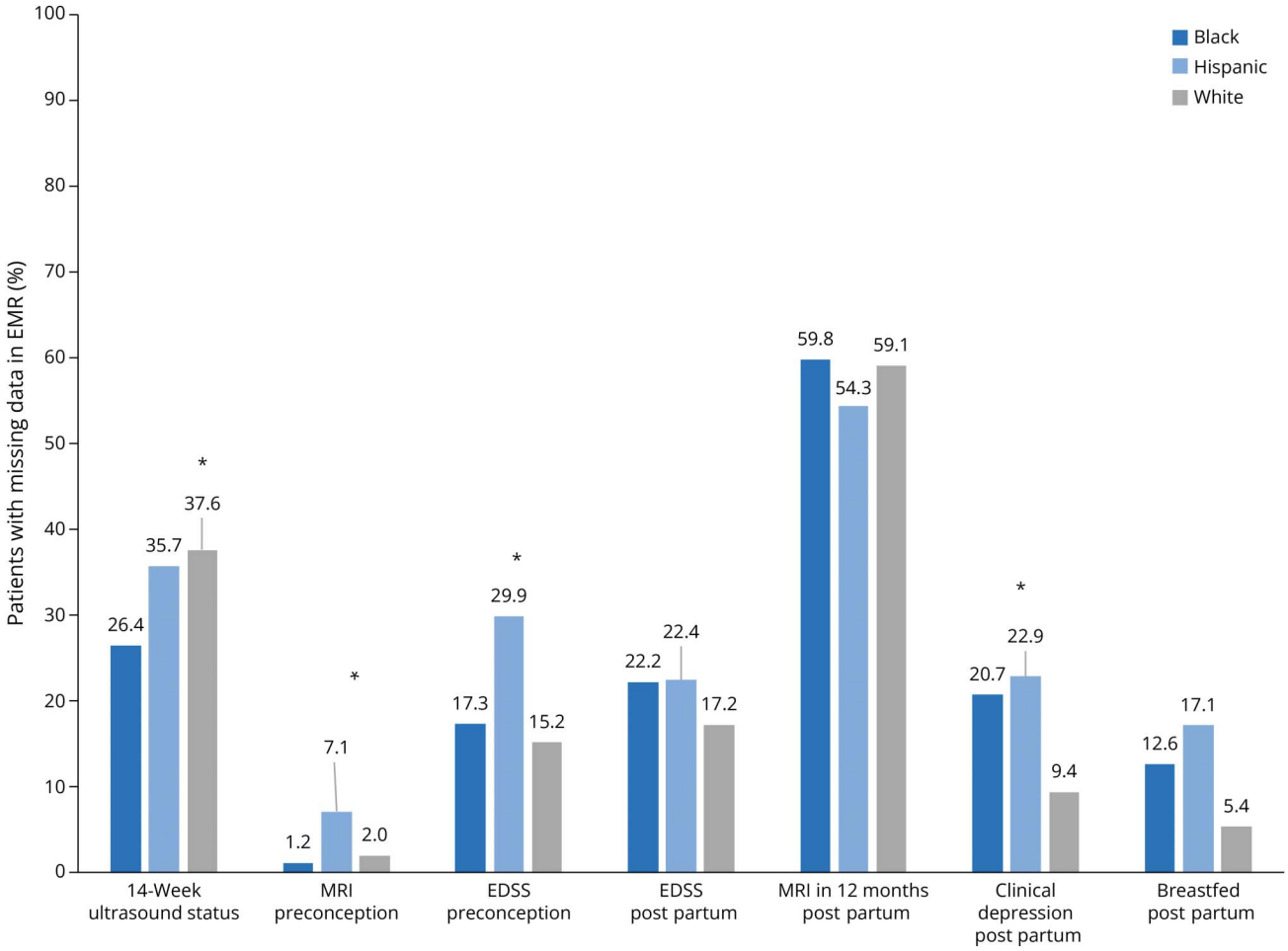
Underrepresented women delivered babies with lower birth weight than White women (median [IQR] 3,198 g [435.3 g] vs 3,275 g [412.5 g], U = 9,255, r = 0.12), although the groups did not differ in the percentage of infants categorized as low birth weight (<2,500 g) (eTable 2, links.lww.com/WNL/D360). When comparing Black and Hispanic women, no Hispanic women had a newborn categorized as low birth weight, while 9.9% of Black women had babies categorized as low birth weight. This difference likely drove the lower birth weight of newborns born among underrepresented women. There were no differences between the groups in gestational age, percentage of preterm deliveries, or infant complications at birth (eTable 2).

MS Care and Outcomes

MS-Related Care

The first primary MS treatment and care variable evaluated was therapeutic DMT during conception. DMT was considered therapeutic in 74.2% pregnancies, and there were no differences between underrepresented and White women (Table 2). There were also no differences in time to DMT resumption postpartum or in the proportion of patients undergoing MRI preconception or a surveillance MRI postpartum (Table 2).

Figure 4 Comparison of Missing Data in the Electronic Medical Record for Key Measures, Between Black and Hispanic (Underrepresented) and White Women With MS



All live births were included in analysis: N = 294 pregnancies; Black women N = 81; Hispanic women N = 67, White women N = 146. Missing Data were compared using a Pearson χ^2 test for significance. *$p < 0.05$. EDSS = Expanded Disability Status Scale; MS = MS = multiple sclerosis.

Inflammatory Activity

The second MS treatment and care variable evaluated was ARR, a clinical measure of MS inflammatory activity. This was numerically higher in underrepresented women than in White women at all time points, including in the year preconception, but was not significantly different in the primary time interval, that is, the first 3 months postpartum (Table 2, Figure 3). Altogether, 9.2% of women relapsed in the first 3 months postpartum; this did not differ between the 3 groups. Because breastfeeding, which differed in duration between the 3 groups, is known to attenuate the risk of postpartum relapses, breastfeeding was included in the models, and there was still no difference in the proportion of individuals who relapsed between the groups (OR 0.60, CI 0.23–1.58).

Imaging Outcomes

There was no significant difference between White and underrepresented women in the proportion of brain MRIs with Gd+ lesions or new T2 lesions postpartum (Table 2).

Disease Severity and Progression

There were also significant race and ethnicity differences in overall disability. White women had the lowest EDSS scores before conception, at the first postpartum time point, and at 1 year postpartum (Table 2), and there were no significant differences between Black and Hispanic women at any time point (Table 2). However, there was no pregnancy-related difference between White and underrepresented women in the absolute change in EDSS between the 2 time points (median [Q1–Q3, IQR]: White women= 0 [0–0, 0] vs underrepresented women = 0 [0–0.5, 0.5], $U = 10{,}587$, $r = 0.02$) or in the percentage of patients who experienced clinically meaningful worsening in EDSS scores after pregnancy (White women= 6.9% vs underrepresented women = 4.7%; OR 1.48, CI 0.55–4.0).

Symptoms

Underrepresented women seemed to have numerically higher rates of depression both before pregnancy (22.9% vs 14.4%, OR 0.56, CI 0.31–1.03) and after (24.3% vs 21.2%, OR 0.84, CI 0.49–1.45), but the differences were not significant. Other

indicators of the pregnancy experience such as rates of physical therapy usage were not compared because more than half of all patients had missing data.

Sensitivity Analyses and Missing Data

Because Black and Hispanic women had slightly higher EDSS scores than White women, comparisons were repeated for all primary outcomes found to differ significantly between the 2 groups, with EDSS as a covariate. All outcomes remained significantly different between underrepresented and White women after inclusion of EDSS as a covariate, except for mode of delivery and birth weight. Finally, to gauge whether biases in documentation or data availability within the medical records could have biased the current analyses, the percentage of patients missing data for key variables was calculated. In this study, White women had more missing data for 14-week ultrasounds, and Black and/or Hispanic patients had more missing data across 4 key variables: MRI preconception, EDSS preconception, clinical depression postpartum, and breastfeeding status (Figure 4). These findings point to a possible further racial disparity—that is, missing data in the EHR, which could in turn influence the algorithms and insights generated from such data.

Discussion

In this multicenter retrospective analysis of pregnancies in diverse populations with MS, Black and Hispanic women entered pregnancy with less opportunities and greater MS-related inflammatory activity and disability than White women. Furthermore, they experienced disparities in pregnancy care that could influence both pregnancy outcomes (e.g., 14-week ultrasound) and MS course (e.g., breastfeeding duration) and maternal-infant outcomes (e.g., birth weight and breastfeeding duration). Overall, it seemed that the largest disparities observed were in opportunity, but not so much in measurable aspects of MS-related care. Furthermore, while a rebound in disease activity was observed as expected,[18,19] there did not seem to be differences in risk of relapses based on race and ethnicity. These findings highlight the importance of considering the intersection of race and ethnicity and disability, when evaluating pregnancy outcomes in women with MS. They further suggest that socioeconomic opportunity—perhaps throughout life, rather than specific features of MS-related care, may lay the foundation for disparities in MS outcomes observed in minoritized individuals in the United States and elsewhere.[6-9]

The differences in prenatal care and pregnancy outcomes observed in this study reflect many of those in the general US population. Of note, our analytic focus on live births, chosen because of possible ascertainment biases regarding other pregnancy outcomes (e.g., loss, termination) in the medical record and because of our scientific focus on postpartum outcomes, was not designed to uncover the full spectrum of pregnancy-related disparities, such as fetal mortality, which have been reported in the general US population.[17] In this study, we found that Black and Hispanic women were less likely to receive recommended prenatal care in the form of a 14-week ultrasound. This association had a wide CI, and it is possible that these differences are caused by lack in documentation rather than in disparities in care; however, our observations are consistent with the national trend of Black and Hispanic women being less likely to receive prenatal care compared with White women,[12,28] which can shift utilization from outpatient appointments to emergency department visits for early pregnancy complications.[28] Some reasons for these disparities include transportation, social support, insurance plans, childcare access for existing children, and availability of and access to prenatal appointments.[11,12] Prenatal care is especially important for Black and Hispanic women because of their higher risk of hypertension, diabetes—including gestational, and other chronic diseases that can complicate pregnancies.[29] In terms of birth outcomes, in 2013, Black women were 2 times more likely to have a preterm birth compared with White women, and that gap has only widened in the past decade.[13,30] While Black women in this cohort did not mirror this national trend in preterm birth, Black women in our study were more likely to give birth by emergency cesarean sections, which mirrors the national trend.[14,15] Research has shown that Black and Hispanic women are also more likely to undergo induced labor that they may have not consented to, possibly due to different clinical expectations for these groups of people on the part of their clinicians.[14,31] Newborns born to White women have the highest mean birth weight, and among underrepresented women, infants born to Black women are more likely to be categorized as low birth weight compared with infants born to Hispanic women.[16] In this cohort, similarly, White women had higher mean birth weight; and infants born to Black women appeared more likely to be categorized as low birth weight. Postnatally, disparities in breastfeeding are also reported; while Black, Hispanic, and White women may start breastfeeding at similar rates,[32,33] Hispanic and Black women stop breastfeeding earlier than their White counterparts. In one study, 28% of Black women were still breastfeeding compared with 65% White women at the 6-month mark,[32] and in another, Hispanic mothers were 2.7 times more likely to stop breastfeeding early compared with White mothers.[33] Our findings of shorter breastfeeding duration among Black and Hispanic mothers but similar rates of having breastfed at all reflect this national trend. In this study, our findings could have been confounded by underrepresented women foregoing breastfeeding to resume DMTs due to clinical concerns about postpartum inflammatory activity. Of interest, breastfeeding duration, which can protect against relapses, was shorter in underrepresented women than in White women, and in the Black women, breastfeeding was significantly associated with lower relapse risk.

From the broader literature on both pregnancy and MS, it is clear that minority women bear the brunt of these structural, systemic, and interpersonal racism contribute to worse outcomes for Black and Hispanic women in the United States.[12,34] Race and ethnicity interact with other social determinants of health such as education or neighborhood factors to influence health outcomes. For example, structural racism propagates minorities living with

lower socioeconomic status, correlating with underfunded neighborhoods, underresourced hospitals, and the decline in nearby quality health care.[35] Given the exploratory nature of the current analyses, detailed models evaluating the relative contribution of these factors to the selected outcomes were not conducted. Future prospective research is needed to clarify the association between social factors, such as insurance, unemployment, and health literacy, and neighborhood factors, with pregnancy care and eventually outcomes.

In addition to the structural factors, however, and highly relevant for neurologists guiding diverse patients with neurologic conditions during pregnancy, Black and Hispanic women in the general US population experience direct interpersonal racism when accessing pregnancy-related health care,[36] and this racism is visible to their clinicians.[37] In fact, Black women experience poor outcomes despite socioeconomic status.[38] Mothers exposed to racial discrimination are more likely to experience poor pregnancy care and outcomes,[39] including delaying initiation of prenatal care, experiencing preterm birth, delivering low-birthweight newborns, and receiving inadequate pain management postnatally.[12,40] For example, disparities in breastfeeding rates may partially reflect prenatal care quality and advice from health professionals.[32,41] Furthermore, Black and Hispanic women describe greater levels of peripartum pain but are undertreated relative to their White counterparts,[41] who receive more pharmacologic treatments while in the hospital and at discharge.[40]

This study, while including 294 live births from heterogeneous centers across the mainland United States, was limited by its retrospective nature and likely EHR-related biases including race and ethnicity differences in EHR data availability (itself a novel finding), geographic diversity (most centers included were located in urban areas serving a variable proportion of rural patients), and MS and obstetric care fragmented across multiple health systems. This study design sought to support generalizability by including diverse clinical settings, including community practices and academic centers caring for underserved populations; but it is possible that patients in the general population experience greater disparities in care than appreciated in the current centers where a focus on care equity exists. A large number of exploratory variables were analyzed, and false discovery rate was not used. Pregnancy losses were likely underestimated given the infrequent timing of neurologic evaluations. Furthermore, because individuals' income was not known, the estimates of child opportunity based may underestimate meaningful individual variables. There was likely heterogeneity within individual zip codes for individuals living in high-density areas. In addition, other demographic variables extracted from the EHR were imprecise and subject to bias. Hispanic, a broad term, encompasses a broad range of cultures and ethnicities. Studies further demarcating these differences and examining the experiences of other racial groups such as the sizeable US-based Asian population, are warranted and ongoing. Participants in the current cohort were presumed to be cis-women because there was no specific mention of gender identity in the charts reviewed, but gender identity was not systematically recorded in the EHR, and therefore, the results do not inform outcomes in gender-diverse individuals. Given suboptimal pregnancy outcomes in the US population relative to other developed countries,[42] the goal for better outcomes should extend past that of White women to include all individuals who become pregnant in the United States.

These observations point to several possible approaches to be taken by the field of neurology. To attenuate some of the disparities identified in the current analyses, collaborative care models may help to increase and optimize access to quality prenatal and neurologic care. "Warm hand offs" and/or clearly documented communication between neurologic, obstetric, pediatric, and lactation care team members, available to the patient, emphasizing the importance to MS outcomes of specific factors such as comorbidity management,[43] breastfeeding,[44] and symptom control and developing shared plans to target these goals, could optimize the knowledge and expertise of all parties, enhance a sense of shared responsibility for care management, and on the individual patient level reduce some gaps in care.[45,46] In addition to increased interprofessional collaboration, community engagement and collaboration initiatives present a key opportunity to improve provider-patient trust, utilization of health care services, and potentially decrease inequities and have proven useful in tackling racial disparities in health care, such as those relating to lower breastfeeding among Black women relative to that among White women.[45] In this study, patient stakeholders' voices are critical to the process.[47] Third, there is a need for structured prospective collection of data such as mode of delivery, gestational age and height, complications, and lactation, when caring for women with neurologic conditions during pregnancy. These racial biases in terms of missing data in the EHR in turn could influence the algorithms and insights generated from such data[48] and potentially relative to cohort-based research data.[49] Finally, the initiatives by the American Academy of Neurology and academic institutions to increase the diversity of neurologists are likely to result in increased use of health care, and increased communication with health professionals, by historically underserved populations.[50]

Altogether, these measures may alleviate some of the interpersonal factors contributing to the observed disparities and improve the prenatal care and pregnancy outcomes of racially diverse women living with neurologic conditions.

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Appendix Authors

Name	Location	Contribution
Anne Marie Radzik, BS	University of California San Francisco	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data
Lilyana Amezcua, MD	Department of Neurology, University of Southern California, Los Angeles	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and study concept or design
Annika Anderson, BA	Department of Neurology, UCSF Weill Institute for the Neurosciences, University of California San Francisco	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and analysis or interpretation of data
Serena Gilmore, BS	Department of Neurology, University of California San Francisco	Drafting/revision of the article for content, including medical writing for content
Sophie Ahmad, MS	Department of Neurology, Northwestern University, Chicago, IL	Major role in the acquisition of data
Rachel Brandstadter, MD	Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data
Michelle T. Fabian, MD	Corinne Goldsmith Dickinson Center for MS, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data
Edith L. Graham, MD	Department of Neurology, Northwestern University, Chicago, IL	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data
Sophia Hodgkinson	Brigham and Women's Hospital, Boston, MA	Major role in the acquisition of data
Lindsay Horton, MD	University of Texas Southwestern Medical Center, Dallas	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data
Dina A. Jacobs, MD	Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and study concept or design
Ilana B. Katz Sand, MD	Corinne Goldsmith Dickinson Center for MS, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and study concept or design
Amit Kohli, MD	Corinne Goldsmith Dickinson Center for MS, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY	Major role in the acquisition of data
Libby Levine, MS, AGNP-BC	Center for Translational and Computational Neuroimmunology and Multiple Sclerosis Center, Department of Neurology, Columbia University Irving Medical Center, New York, NY	Major role in the acquisition of data
Monica McLemore, PhD	Family Health Care Nursing Department, School of Nursing, University of California San Francisco	Drafting/revision of the article for content, including medical writing for content; study concept or design; and analysis or interpretation of data
Annette F. Okai, MD	North Texas Institute of Neurology and Headache, Frisco	Major role in the acquisition of data; study concept or design
Jasmin Patel, MD	Corinne Goldsmith Dickinson Center for MS, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY	Major role in the acquisition of data

Appendix *(continued)*

Name	Location	Contribution
Shane Poole, BS	Department of Neurology, UCSF Weill Institute for the Neurosciences, University of California San Francisco	Drafting/revision of the article for content, including medical writing for content; analysis or interpretation of data
Claire Riley, MD	Center for Translational and Computational Neuroimmunology and Multiple Sclerosis Center, Department of Neurology, Columbia University Irving Medical Center, New York, NY	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and study concept or design
Sammita Satyanarayan, MD	Corinne Goldsmith Dickinson Center for MS, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY	Major role in the acquisition of data
Lauren Tardo, MD	University of Texas Southwestern Medical Center, Dallas	Major role in the acquisition of data; study concept or design
Elizabeth Verter, MD	Corinne Goldsmith Dickinson Center for MS, Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY	Major role in the acquisition of data
Veronica Villacorta, BA	University of Southern California, Los Angeles	Major role in the acquisition of data
Vanessa Zimmerman, MSN	Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia	Major role in the acquisition of data
Leah Zuroff, MD	Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia	Major role in the acquisition of data
Mitzi J. Williams, MD	Joi Life Wellness Group, Multiple Sclerosis Center, Smyrna, GA	Drafting/revision of the article for content, including medical writing for content; study concept or design
Maria K. Houtchens, MD	Brigham and Women's Hospital, Boston, MA	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and study concept or design
Riley Bove, MD, MMSc	Department of Neurology, UCSF Weill Institute for the Neurosciences, University of California San Francisco	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

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