

# Advancing Care and Outcomes for African American Patients With Multiple Sclerosis

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## Abstract

Multiple sclerosis (MS) has historically been underdiagnosed and undertreated among African Americans. Recent evidence suggests that African Americans with MS have a different clinical presentation, increased disease incidence and burden, and worse long-term outcomes vs their White counterparts. Due to limited data available for African Americans in MS clinical trials, it is difficult to make informed, generalizable conclusions about the natural history, prognosis, and therapeutic response in this population. In this narrative review, we highlight the nature and magnitude of the health disparities experienced by African Americans with MS and underscore the pressing need to increase knowledge about and understanding of MS disease manifestations in this group. In addition, we describe the mission and objectives of the recently established National African Americans with Multiple Sclerosis Registry, which is intended to be a platform to advance the care of African Americans with MS and address health disparities they may experience.

## Introduction

Multiple sclerosis (MS) is an autoimmune demyelinating disorder of multifactorial etiology, involving a complex interplay of genetics, environmental factors, and sex.<sup>1</sup> Social determinants of health, including ethnic/racial disparities and inequities, socioeconomic status, healthcare access, and health literacy, can also affect MS care and treatment outcomes.<sup>2-4</sup> The current understanding of the effect of race and ethnicity on MS incidence, pathogenesis, disease course, and treatment response is limited, which may be attributable to the underrepresentation of minority populations in clinical trials.<sup>5</sup>

Historically, MS has been considered to be more common in White people of northern European ancestry vs other ethnic groups.<sup>6</sup> However, there is increasing evidence of the importance of the disease in minority populations. As will be discussed in this review, higher MS risk and incidence, more severe disease at diagnosis, more aggressive disease course, and limited treatment response have been suggested, particularly in the Black or African American population compared with other racial groups in the United States. Despite the unique challenges and unmet needs of Blacks or African Americans with MS (AAwMS), clinicians have limited ability to draw informed, generalizable conclusions about the natural history, prognosis, and therapeutic response in this population given the paucity of available clinical data. Findings of a PubMed literature search (performed in February 2022) highlight the paucity of and need for published literature/data in this patient population: a search of “*black african american multiple sclerosis*” found 49 results in the last 5 years and 69 results in the last 10 years, whereas a search of “*multiple sclerosis united states*” found 3,965 results in the last 5 years and 7,141 results in the last 10 years.

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## Glossary

**AAwMS** = African Americans with MS; **DMTs** = disease-modifying therapies; **EDSS** = Expanded Disability Status Scale; **MS** = multiple sclerosis; **MSSS** = Multiple Sclerosis Severity Scale; **NAAMSR** = National African Americans with Multiple Sclerosis Registry.

In this narrative review, we provide an overview of the limited clinical data published in the literature on the nature and magnitude of MS disease experienced by Black/AAwMS and underscore the pressing need to increase knowledge about and understanding of MS in this patient population. In addition, we describe the mission and objectives of the recently established National African Americans with Multiple Sclerosis Registry (NAAMSR), which is intended as a platform to advance the care of AAwMS and address the health disparities they experience.

## Disparities in Clinical Outcomes and Healthcare Access

The incidence of MS in the United States has historically been thought to be lower in Black or African American people than in White individuals; however, there is increasing evidence to the contrary. A retrospective study of a multiethnic US cohort newly diagnosed with MS between 2008 and 2010 (N = 486, >9 million person-years of observation) found the incidence of MS per 100,000 person-years to be highest in the Black subgroup (regardless of ethnicity) (10.2) when compared with the non-Hispanic White (6.9), Hispanic White (2.9), and Asian or Pacific Islander (1.4) subgroups. MS risk in this study was found to be 47% higher in the Black subgroup (vs non-Hispanic White). This difference was driven by a higher risk in Black women than in non-Hispanic White women (risk ratio 1.59, 95% CI 1.27–1.99;  $p = 0.0005$ ), whereas MS risk in men was similar in both racial groups (risk ratio 1.04, 95% CI 0.67–1.57;  $p = 0.87$ ).<sup>7</sup> A recent retrospective analysis (2010–2016) of a multiethnic US cohort (N = 3,286) reported similar findings of highest age-adjusted MS incidence in non-Hispanic Black patients compared with non-Hispanic White, Hispanic, and other minority groups, with highest prevalence in non-Hispanic Black women.<sup>8</sup> MS prevalence in African Americans has been shown to be higher than that in native Africans with no European ancestry, and lower than those of European ancestry, possibly due to the effects of genetic admixture.<sup>9,10</sup> There is substantial variation in the proportion of genomes of European and African ancestry in African Americans in the United States.<sup>11,12</sup> Of note, race and ethnicity are patient reported in the majority of studies evaluating differences in clinical outcomes described below.

In addition to higher MS risk and incidence, Black/AAwMS have earlier mortality compared with patients with MS in other minority groups in the United States. Based on findings of an analysis of 16 years of data (1999–2015) from the

Centers for Disease Control and Prevention's Data for Epidemiologic Research system, non-Hispanic Black people with MS were found to have the highest mortality rate in patients younger than 55 years of age relative to non-Hispanic White, Asian or Pacific Islander, American Indian or Alaska Native, and Hispanic people with MS. Mortality rates were highest for non-Hispanic Black patients in the 55- to 64-year-old age group compared with 65–74 years for non-Hispanic White patients.<sup>13</sup> These data demonstrating higher mortality risk at a younger age in Black people with MS compared with their White counterparts suggest variability in the burden of disease by race/ethnicity in the United States that may be attributed to differences in comorbidities, access to care, and MS disease progression in these patient populations.<sup>13</sup>

Black/AAwMS may experience more severe disease at baseline, with a significantly greater frequency of multifocal involvement at initial clinical presentation.<sup>14</sup> They may also experience higher Expanded Disability Status Scale (EDSS) scores vs their White counterparts at diagnosis (2.9 vs 1.8;  $p = 0.0002$ ) and through  $\geq 5$ -year follow-up (5.6 vs 4.1;  $p = 0.0001$ ).<sup>15</sup> Moreover, Black/AAwMS may experience faster clinical progression and poorer clinical outcomes than their White counterparts. In a retrospective cohort study of 375 AAwMS, African American patients (mean disease duration of 9.8 years) had a significantly shorter median time to ambulation with a cane (16 vs 22 years;  $p < 0.0001$ ) and wheelchair dependency (30 vs 38 years;  $p = 0.05$ ), a 1.67-fold greater risk of requiring a cane for ambulation ( $p < 0.001$ ), and a trend toward a shorter median conversion time to secondary progressive MS (18 vs 21 years;  $p = 0.051$ ) vs White Americans (n = 427; mean disease duration of 11.4 years). The faster disability accumulation observed among African Americans was thought to be partly attributable to their older age at disease onset (33.7 vs 31.1 years;  $p = 0.0001$ ),<sup>14</sup> a factor that has been associated with a poorer prognosis.<sup>16</sup> The lower frequency of the *HLA-DRB1\*15* allele is thought to contribute to the later age of disease onset seen in AAwMS.<sup>17</sup>

In an analysis of patient- and physician-reported data of 419 Black/AAwMS and 5,809 non-Hispanic White Americans living with MS (of similar age at disease onset and diagnosis) in the New York State Multiple Sclerosis Consortium database, median Multiple Sclerosis Severity Scale (MSSS) score (an algorithm relating MS disability to disease duration) was higher in Black/AAwMS (6.0 vs 4.8;  $p = 0.0001$ ), suggesting a more rapidly disabling disease course. Black/AAwMS were overrepresented in the 2 most severe MSSS categories (41.5% vs 29.3%) and underrepresented in the 2 least severe categories

(23.4% vs 35.4%; overall  $p < 0.001$ ). In addition, they had a 2.6-fold higher prevalence of “malignant” (or rapidly progressing) MS (7.3% vs 2.9%;  $p < 0.001$ ).<sup>17,18</sup>

MRI and optical coherence tomography studies suggest that AAwMS experience neurodegeneration and loss of brain and retinal tissue that is different from and more rapid than their White counterparts.<sup>19-23</sup> AAwMS experience atrophy of gray matter ( $-0.9\%/year$  vs  $-0.5\%/year$ ;  $p = 0.02$ ), white matter ( $-0.7\%/year$  vs  $-0.3\%/year$ ;  $p = 0.04$ ), and nuclear thalamic tissue ( $-1.5\%/year$  vs  $-0.7\%/year$ ;  $p = 0.02$ ) at rates twice that of White patients of similar age and disease duration. Atrophy rates of retinal nerve fiber layer ( $-1.1\%$  vs  $-0.8\%$ ;  $p = 0.02$ ) and ganglion cell inner plexiform layer ( $0.7\%/year$  vs  $-0.4\%/year$ ;  $p = 0.01$ ) were faster in African American patients.<sup>24</sup> Findings of these imaging studies corroborate the more rapid disease progression observed in African Americans as described above. These variations in MS disease expression observed among African Americans may be influenced by genetic factors. African origin within the *HLA* locus has been implicated in disability progression, and genotyping of the *HLA-DRB1\*15* allele suggests that the increased incidence of opticospinal disease among African Americans may be related to the lower frequency of the allele in this population (37.6% vs 53.3% in White Americans living with MS).<sup>17</sup> African Americans have a significantly higher risk of neuromyelitis optica spectrum disorder, with earlier onset and more severe attacks, compared with White and Asian patients.<sup>25</sup>

Black/AAwMS may be less responsive to certain disease-modifying therapies (DMTs) than their White counterparts, which may adversely affect their clinical outcomes.<sup>26,27</sup> A retrospective chart review of 67 self-defined African Americans and 67 White Americans living with MS receiving DMTs (interferons, glatiramer acetate, and natalizumab) reported a greater median EDSS difference from baseline through follow-up for African Americans vs White patients (1.0 vs 0;  $p < 0.001$ ) despite a shorter mean disease duration (7.1 vs 15.1 years;  $p < 0.001$ ) and similar age at diagnosis (34.3 vs 36.9;  $p = 0.13$ ). Although the number of patients studied was small, the results suggest a poorer response to at least some DMTs in AAwMS.<sup>27</sup> These findings of increased disability over a shorter disease duration in African Americans are in line with the trend suggested by a post hoc analysis of the EVIDENCE study comparing the response to interferon  $\beta$ -1a treatment in African American ( $n = 36$ ) and White American ( $n = 616$ ) patients. In EVIDENCE, African American patients had more new T2-weighted MS lesions on MRI (2.00 vs 1.10;  $p = 0.04$ ) and were less likely to remain relapse free (47% vs 57%;  $p = 0.24$ ) at 48 weeks. Again, these findings are limited by the small sample size of African American patients included in the study (5.5% of 652 patients).<sup>26</sup> Subgroup analyses of patients from the pivotal phase 3 trials of natalizumab (AFFIRM and SENTINEL) and ocrelizumab (OPERA I/II), and phase 4 studies of fingolimod (PREFERMS) and dimethyl fumarate (ESTEEM), suggest that these therapies can provide clinical and radiographic benefits for Black/African American

patients.<sup>28-31</sup> Although promising, these analyses were hindered by the limited representation of Black/African American patients in the trials (AFFIRM,  $n = 10$  of 942 [1.1%]; SENTINEL,  $n = 39$  of 1,171 [3.3%]; OPERA I/II,  $n = 72$  of 1,656 [4.3%]; PREFERMS,  $n = 141$  of 875 [16.1%]; and ESTEEM,  $n = 187$  of 5,084 [3.7%]),<sup>28-31</sup> highlighting the urgent need for more well-controlled data in this group.

In addition to underrepresentation in clinical trials, social determinants of health<sup>3</sup> can contribute to health disparities and inequities in MS care and clinical outcomes (Figure 1). A recent review noted a paucity of published literature on the effect of social determinants of health on clinical outcomes and racial/ethnic inequities in MS and related disorders such as neuromyelitis optica spectrum disorder for Black or African American patients in the United States, despite their higher risk of disease and mortality compared with White individuals.<sup>32</sup> Lower socioeconomic status (e.g., education level and income) was associated with greater health disparities, including higher disease burden and more cognitive/psychiatric symptoms.<sup>32-37</sup> The reasons for these disparities and inequities are likely multifactorial (Figure 1), including but not limited to gaps between need of and access to medical care and supportive services,<sup>38-40</sup> societal/cultural constructs (e.g., systemic/unconscious bias and racism), and lack of culturally competent care. Further observational, epidemiologic, and long-term longitudinal studies (taking into consideration both the genetic ancestry and social determinants of health) will be important for developing optimal treatment strategies for the Black and African American patient population with MS, with increased efforts to better understand and help alleviate the racial/ethnic disparities and inequities in clinical care in the United States.

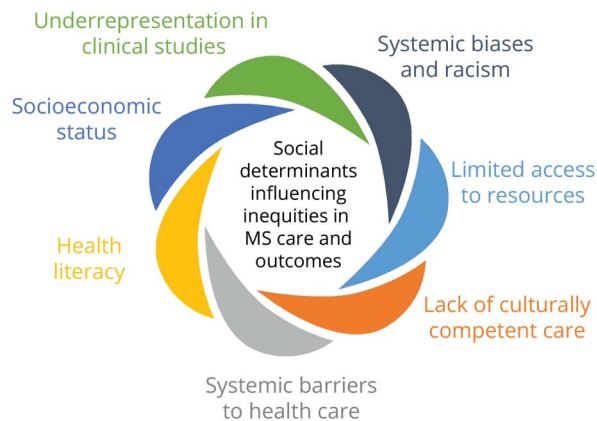
## Further Strategies to Address and Combat Health Inequities for African Americans With MS

As described above, AAwMS may experience increased incidence and disease burden and worsened long-term outcomes compared with their White counterparts. To help address the specific unmet needs of this patient population, there is a compelling need to develop a robust cohort of AAwMS to increase knowledge about and understanding of the disease in this population.

A platform that was created in response to this need is the National African Americans with MS Registry (NAAMSR),<sup>41</sup> which was launched on September 1, 2020. The objectives and design of the registry are summarized in Figure 2. The NAAMSR aims are as follows: (1) create reliable estimates of the number and geographical distribution of AAwMS in the United States; (2) identify barriers and improve access to MS care; and (3) improve care for AAwMS through patient and healthcare provider education. The registry was founded by



**Figure 1** Social Determinants Influencing Inequities in MS Care and Outcomes



From Okai A et al. National African American Multiple Sclerosis Registry: Advancing Equitable Care and Outcomes for African Americans with Multiple Sclerosis. Poster presented at the American Academy of Neurology (AAN) Virtual Annual Meeting, April 17-21, 2021. MS = multiple sclerosis.

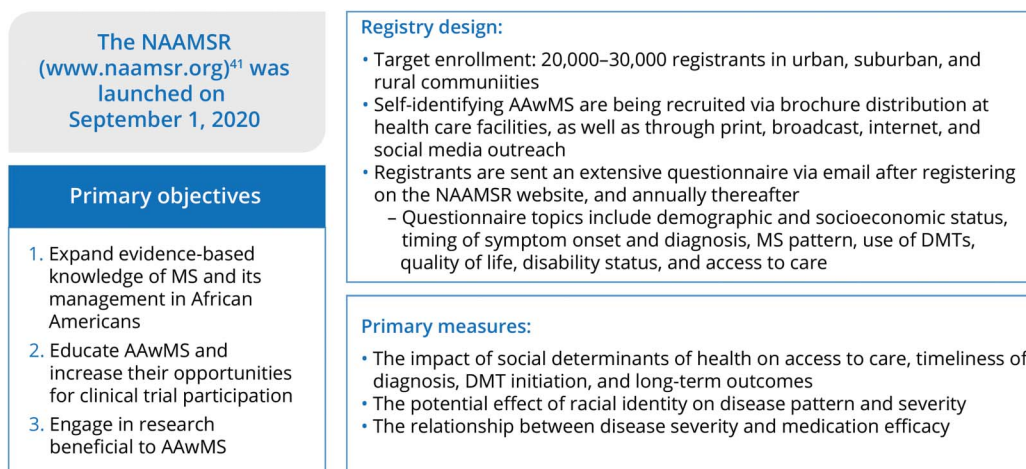
neurologists who specialize in MS care, including leading African American MS neurologists located in different regions of the United States. The registry also aims to increase opportunities for interested African Americans to participate in clinical trials, so that the therapeutic needs of AAwMS are better understood through future research and drug development.

The registry aims to enroll 20,000–30,000 self-identifying AAwMS across urban, suburban, and rural communities in the United States. Those interested in participating will register on the NAAMSR website.<sup>41</sup> They will then be emailed a link to complete a baseline survey. Participants will be sent the link to complete the survey annually. Participation in the registry is

voluntary, and collected information is fully protected and will only be used for research purposes. Unlike other databases, which rely mainly on physician-reported data, the NAAMSR questionnaire collects participant-reported information on topics including demographic and socioeconomic status, timing of symptom onset and diagnosis, MS pattern, use of DMTs, quality of life, disability status, comorbidities, and access to care. The primary measures of the NAAMSR hope to address the following: (1) the effect of social determinants of health on access to care, timeliness of diagnosis, DMT initiation, and long-term outcomes; (2) the potential effect of racial identity on disease pattern and severity; and (3) the relationship between disease severity and medication efficacy. Participants can also opt to receive a lay-friendly newsletter circulated regularly to provide new and relevant educational information on MS and treatment options, increase awareness of clinical trials and other research efforts, and help bridge gaps in health literacy. Outreach efforts to reach both healthcare providers and patients to aid with registry recruitment are ongoing and have included personal communications to academic and private institutions, publicity via social media, podcasts, the National MS Society website, various programs (e.g., National MS Society Black Experience Summit and MS Association of America’s African American Advisory Board), continuing medical education channels, and medical conferences/meetings. Educational outreach to patients and their care team will also be prioritized. The registry also seeks to engage in collaborations/partnerships that advance the care and well-being of AAwMS.

Increased understanding and awareness of the clinical effect of various genetic, environmental, societal, and cultural factors are needed to improve and optimize disease management and treatment outcomes for AAwMS. Through educational efforts targeting patients and their care team, the cultivation of patient trust, and by encouraging participation in research and

**Figure 2** The National African Americans With Multiple Sclerosis Registry (NAAMSR)



From Okai A et al. National African American Multiple Sclerosis Registry: Advancing Equitable Care and Outcomes for African Americans with Multiple Sclerosis. Poster presented at the American Academy of Neurology (AAN) Virtual Annual Meeting, April 17-21, 2021. AAwMS = African Americans with Multiple Sclerosis; DMTs = disease-modifying therapies; MS = multiple sclerosis.

clinical trials, the medical community can better serve the unmet needs of this vulnerable patient population with MS.

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## Appendix (continued)

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