Diverse Populations In Multiple Sclerosis

Understanding the African American Experience in MS

Welcome

- Q & A Instructions
- House Keeping
- Claiming Your CME/CE

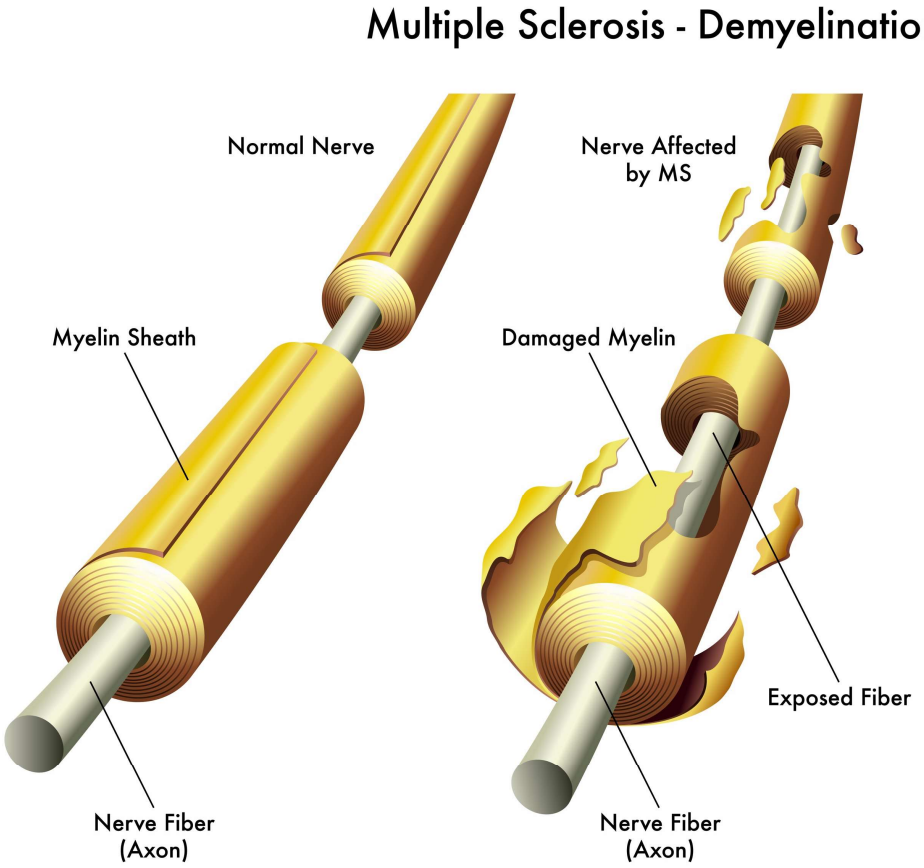
Introduction

(insert speaker bio)

Outline

- Epidemiology
- Phenotype
- Clinical Measures of Disease Activity
- Research Data

What is MS?



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What is MS?

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MOU2

The Face of MS

Worldwide: MS is primarily a disease of young women of Northern European descent

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Slide 7

MOU2 Generally MS is thought of as a disease of young white women

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MOU3

The Face of MS

In the US, several studies report that the incidence of MS highest in African Americans and risk may be 47% higher primarily in African American women.

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MOU3 Data suggests AA may be at higher risk and possibly have worsened course of disease

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The Gulf War era multiple sclerosis cohort: age and incidence rates by race, sex and service.

Wallin MT, Culpepper WJ, Coffman P, Pulaski S, Maloni H, Mahan CM, Haselkorn JK, Kurtzke JF; Veterans Affairs Multiple Sclerosis Centres of Excellence Epidemiology Group, *Brain*, Volume 135, Issue 6, 1 June 2012, Pages 1778–1785

Average annual incidence rates per 100 000 population by sex and major race groups in Gulf War era multiple sclerosis cohort, Department of Defense

Sex/race group	Multiple sclerosis cases total, Department of Defense	Average annual population at risk	Average annual incidence rate per 100 000 (95% CI—Poisson)[a]
Total males	1740	1 321 514	7.31 (6.98–7.67)
Total females	898	202 044	24.69 (23.10–26.36)
Total all groups[b]	2638	1 523 563[c]	9.62 (9.26–9.99)
White males	1245	950 100	7.28 (6.88–7.69)
White females	547	117 846	25.79 (23.67–28.04)
Total whites	1792	1 067 946	9.32 (8.90–9.76)
Black females	293	61 789	26.34 (23.41–29.54)
Total blacks	651	298 293	12.13 (11.21–13.09)
Other race males[d]	137	134 906	5.64 (4.74–6.67)
Total other race	195	157 309	6.89 (5.95–7.92)
Hispanics 2000–07			
Hispanic males	57	108 083	6.59 (4.99–8.54)
Hispanic females	26	19 072	17.04 (11.13–24.97)
Total Hispanic	83	127 155	8.16 (6.50–10.12)

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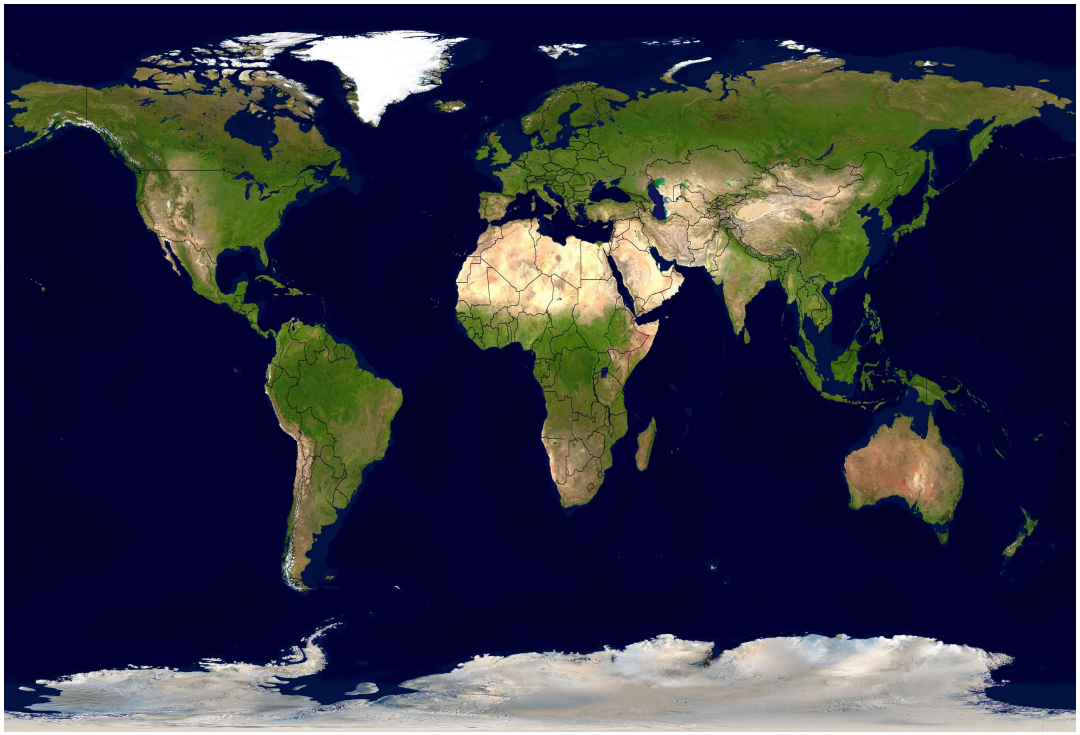
Prevalence of MS



- UK: 90 -190/100,000
- Scandinavia :132/100,000
- Europe: 30-150/100,000
- Canada 60-250/100,000
- USA : 30-150/100,000

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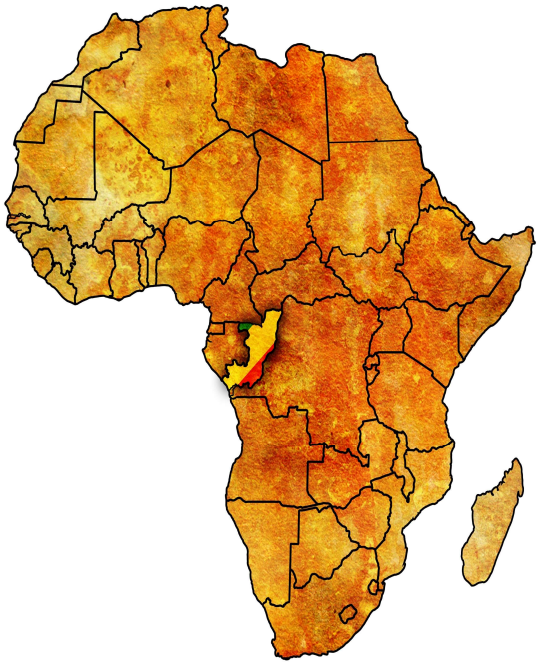
Prevalence of MS

- Africa
  - Arab origins: Libya, Tunisia, Algeria
    - Similar to those of the middle east
  - South Africa:
    - 13/100,000 in White SA
    - 3/100,000 in “colored” SA – mixed genetic background
    - 6 cases in Black SA
  - Rest of continent: occasional cases in black Africans



G. Rosati: Prevalence of MS worldwide. Neurol Sci (2001) 22:117-139

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What does it mean to be African-American?

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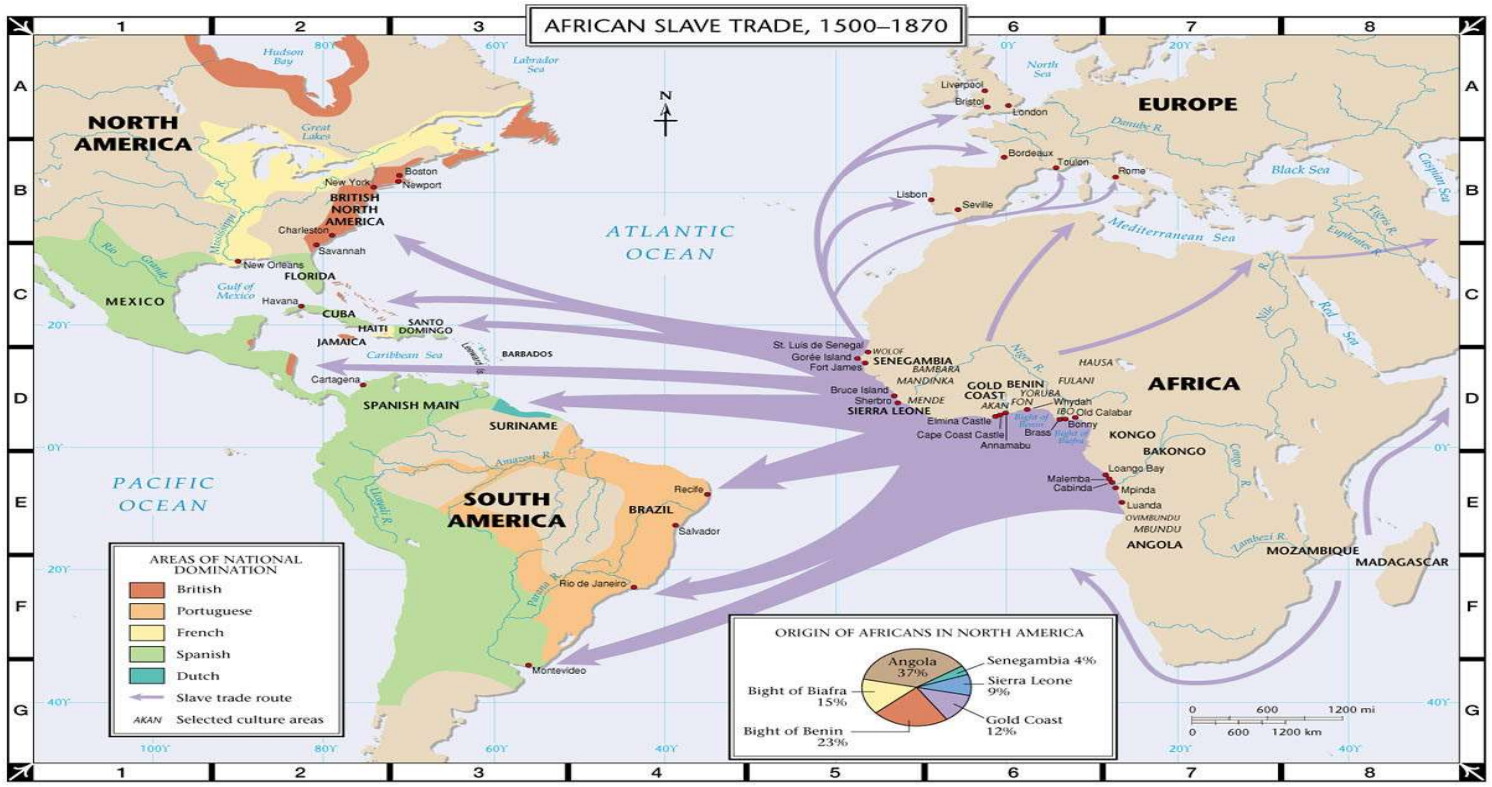
The Slave Trade



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Genetic Factors

- African-American ethnicity is determined by self-identification.
- Generally AA are predicted to have between 70 – 80% African ancestry and up to 20% European ancestry.
- Admixture of genes may explain some of the differences in susceptibility, but environmental factors may also play a role.

Clinical characteristics of African Americans vs Caucasian Americans with multiple sclerosis

B.A.C. Cree, MD, PhD, MCR; O. Khan, MD; D. Bourdette, MD; D.S. Goodin, MD; J.A. Cohen, MD; R.A. Marrie, MD; D. Glidden, PhD; B. Weinstock-Guttman, MD; D. Reich, PhD; N. Patterson, PhD; J.L. Haines, PhD; M. Pericak-Vance, PhD; C. DeLoa, BS; J.R. Oksenberg, PhD; and S.L. Hauser, MD

Abstract—*Background:* African American (AA) individuals are thought to develop multiple sclerosis (MS) less frequently than Caucasian American (CA) individuals. *Objective:* To compare the clinical characteristics of AA and CA patients with MS. *Methods:* The clinical features of MS were compared in a large retrospective cohort of AA (n = 375) and CA (n = 427) subjects. *Results:* The proportion of women to men was similar in AA and CA subjects (81% [AA] vs 77% [CA]; $p = 0.122$). There were no differences in the proportions of subjects with relapsing–remitting, secondary progressive, primary progressive, and progressive relapsing MS. The median time to diagnosis was 1 year after symptom onset in AA subjects and 2 years after symptom onset in CA subjects ($p = 0.0013$). The age at onset was approximately 2.5 years later in AA than CA subjects (33.7 vs 31.1 years; $p = 0.0001$). AA subjects presented with multisite signs and symptoms at disease onset more often than CA subjects ($p = 0.018$). Clinical involvement restricted to the optic nerves and spinal cord (opticospinal MS) occurred in 16.8% of AA patients compared with 7.9% of CA patients ($p < 0.001$). Transverse myelitis also occurred more frequently in AA subjects (28 vs 18%; $p = 0.001$). Survival analysis revealed that AA subjects were at higher risk for development of ambulatory disability than CA subjects. After adjusting for baseline variations and differences in therapeutic interventions, AAs were at 1.67-fold greater risk for requiring a cane to ambulate than CA patients ($p < 0.001$). There was a trend suggesting that AAs were also at greater risk for development of wheelchair dependency ($p = 0.099$). Adjusted Cox proportional hazard models showed that this effect was in part attributable to the older age at onset in AAs ($p < 0.001$). *Conclusions:* Compared with multiple sclerosis (MS) in Caucasian Americans, African American patients with MS have a greater likelihood of developing opticospinal MS and transverse myelitis and have a more aggressive disease course.

NEUROLOGY 2004;63:2039–2045

MS Phenotypes

Table 1. Demographic and Clinical Characteristics of a Cohort of Patients With MS

Clinical Characteristic	Patients, No. (%)		*P* Value
	White (n=717)	African American (n=673)	
Sex, F/M, No.	556/161	539/134	.12
Age at onset, mean (SD), y	29.9 (8.6)	32.8 (9.7)	<.001
Disease duration, mean (SD), y	9.9 (8.4)	9.7 (7.8)	.62
Disease type			
RRMS	71.6 (513)	59.7 (402)	.001
SPMS	155 (21.6)	182 (27.0)	
PPMS	33 (4.6)	46 (6.8)	
PRMS	6 (1.5)	24 (1.8))	
Unknown course[a]	5 (0.7)	17 (4.6)	
Time from disease onset to diagnosis, median (mean), y	1 (3.4)	1 (3.1)	.33
MSSS, mean (SD)	4.47 (2.6)	5.6 (2.8)	<.001
HR for time to cane dependency[b]		1.96	<.001
Opticospinal MS	53 (7.4)	72 (11.0)	.02
Transverse myelitis	84 (11.7)	180 (27.0)	<.001
Motor onset	138 (19.2)	209 (31.0)	<.001
Seropositive for anti—aquaporin 4	3 (4.2)	8 (6.2)	.55

Abbreviations: HR, hazard ratio; MS, multiple sclerosis; MSSS, Multiple Sclerosis Severity Score; PPMS, primary progressive multiple sclerosis; PRMS, progressive relapsing multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

[a] Patients could not be classified into 1 of the preceding categories.

[b] Expanded Disability Status Scale score=6.

Cree, B. A. C. et al. Arch Neurol 2009;66:226-233.

ARCHIVES OF NEUROLOGY

MOU33

Clinical characteristics of Multiple Sclerosis in African Americans

- Similar proportion of MS subtypes
- More aggressive course of disease
- Shorter time to walking disability
- More optic nerve impairment

1. Cree et al. Neurology 2004;63:2039–45.

Slide 17

MOU33 This picture is fine for this slide

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Brain and retinal atrophy in African-Americans versus Caucasian-Americans with multiple sclerosis: a longitudinal study

- Progression was significantly faster in black MS patients in both brain and retinal measures.
- MRI scans showed whole brain, gray and white matter atrophy twice as fast in the African-Americans than in Caucasian-Americans.
- Black MS patients also showed faster atrophy of the thalamus, which could be linked to cognitive impairment.

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Natalia Gonzalez Caldito et al. *Brain*, Volume 141, Issue 11, 1 November 2018, 3115–3129

Multiple Sclerosis Mortality by Race/Ethnicity, Age, Sex, and Time Period in the United States, 1999–2015.

- In a population with MS listed as the primary cause of death:
  - White people and females are overall more likely to die from MS
  - African Americans are dying from MS at an earlier age; suggests that MS burden weighs unequally by race
  - Further investigation into these trends may provide additional evidence into risk or protective factors within each group

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Amezcua L, Rivas E, Joseph S, Zhang J, Liu L: Neuroepidemiology 2018;50:35-40.

MOU4

Clinical Trial Experience

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MOU4 Briefly discuss the low numbers of enrollment in clinical trials

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African Americans in Clinical Trials

- Interferon:
  - EVIDENCE STUDY: 36
- Natalizumab:
  - AFFIRM: 10
  - SENTINEL: 39
- Fingolimod:
  - FREEDOMS : 52
  - TRANSFORMS: 10
- Teriflunomide:
  - TEMSO: 24
- Dimethyl Fumarate:
  - CONFIRM & DEFINE: 29
- Alemtuzumab:
  - CARE MS I & 2: 55

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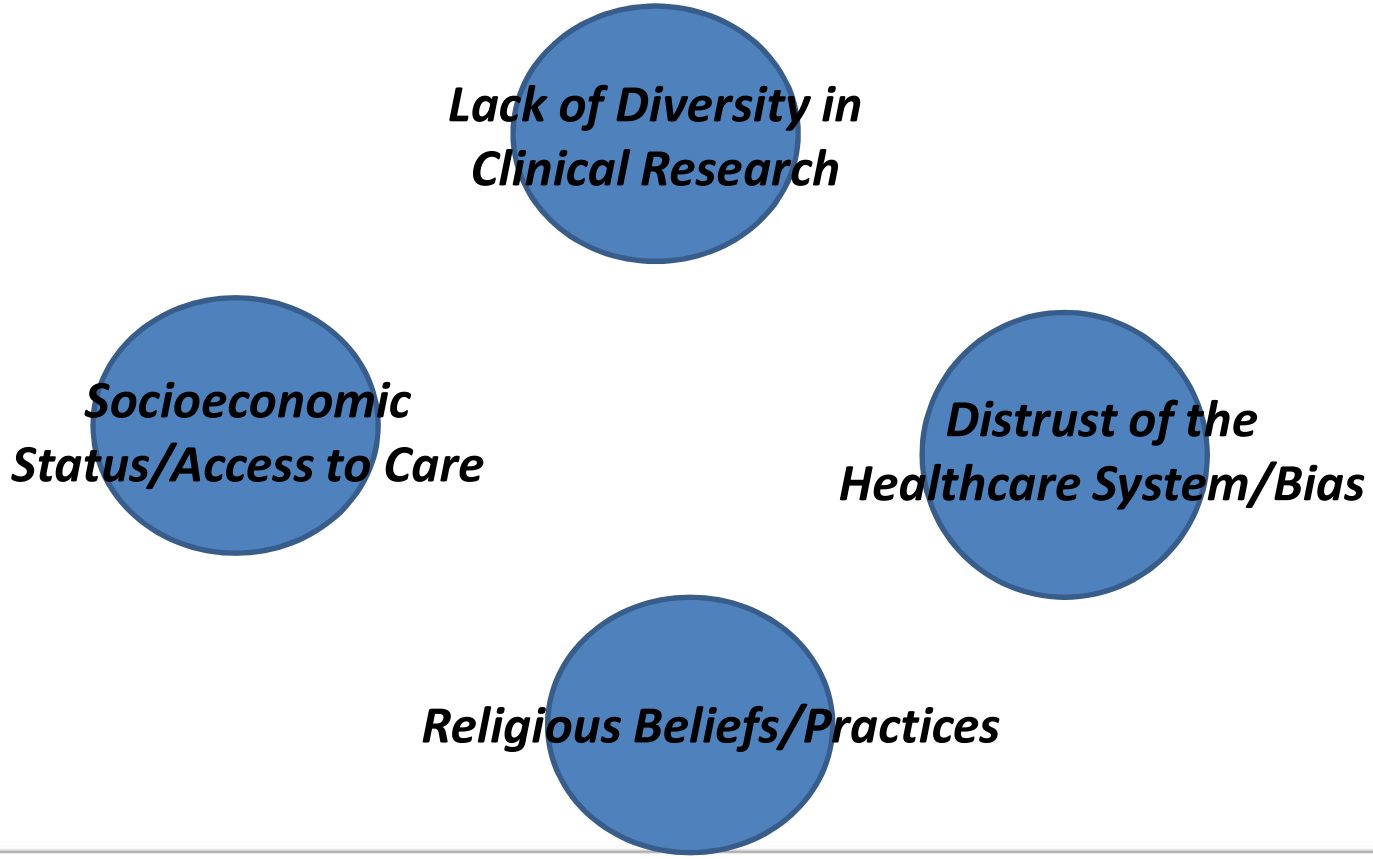
Factors Affecting the Care of Patients of African Descent with MS



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Neurology® Clinical Practice

Multiple sclerosis in US minority populations

Clinical practice insights

Omar Khan, MD
Mitzi J. Williams, MD
Lilyana Amezcua, MD
Adil Javed, MD, PhD
Kristin E. Larsen, PhD
Jennifer M. Smrtka, NP

Podcast

Summary

The heterogeneity of multiple sclerosis (MS) characteristics among various ethnic minority populations is a topic of recent interest. However, these populations are consistently underrepresented in clinical trials, leading to limited data on the effectiveness of treatments in these groups of patients and lack of an evidence-based approach to treatment. In order to achieve optimal disease management in the ethnic minority MS populations, a better understanding of the regional, socioeconomic, and cultural influences that result in underrepresentation of these groups in clinical trials is needed. Furthermore, it would be beneficial to identify the genetic factors that influence disease disparity in these minority populations. Suggestions for the identification and implementation of best practices for fostering the trust of ethnic minority patients with MS and enhancing their participation in clinical trials are offered.

Multiple sclerosis (MS) is a presumed autoimmune disorder of the CNS characterized by inflammatory demyelination and neurodegeneration, affecting approximately 400,000 people across the United States and over 2 million people worldwide.[1,2] Symptoms of MS, a disease typically diagnosed in adult women between the ages of 20 and 50 years, vary tremendously and may comprise diffuse symptoms such as depression, pain, cognitive difficulties, and fatigue, as well as focal

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Racial disparities in neurologic health care access and utilization in the United States

The study found that African-Americans were:

30% less likely to see a neurologist in Clinic

More likely to seek care in an Emergency Room

More likely to have inpatient hospital stays

Faced with higher hospital expenses

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Altaf Saadi, David U. Himmelstein, Steffie Woolhandler, Nicte I.Mejia Neurology Jun 2017, 88 (24) 2268-2275

Why is this important?

- Minorities are underrepresented in clinical trials
- Unique differences in populations due to cultural, environmental, or physiologic factors may be missed.
- Lack of ethnic diversity in clinical research may impact our ability to generalize findings

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Encouraging Participation of Minorities in Research Studies." Annals of Family Medicine vol 10, no. 4 July/August 2012

MS Minority Research Engagement Partnership Network

MS Minority Research Engagement

PARTNERSHIP NETWORK

MS National Multiple Sclerosis Society

Considerations in the Management of African- American MS patients

- Establish a trusting therapeutic relationship
- Direct to culturally appropriate educational materials
- Close observation of those with aggressive disease
- Provide information about clinical trials for the appropriate patients

Summary

- There is a growing body of research over the past decade that points to differences in disease activity and phenotypes in African Americans with MS.
- The true incidence of the disease in this population is unknown, but there are suggested that incidence and risk is highest in African Americans in the US
- Low recruitment in research trials make it difficult to generalize results to populations with different disease characteristics
- Prospective research and more data is needed to determine the roles biology and social determinants of health play in poorer outcomes in this population.

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