Global Barriers to the Diagnosis of Multiple Sclerosis

Data From the Multiple Sclerosis International Federation Atlas of MS, Third Edition

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Abstract

Background and Objectives

Recent data suggest increasing global prevalence of multiple sclerosis (MS). Early diagnosis of MS reduces the burden of disability-adjusted life years and associated health care costs. Yet diagnostic delays persist in MS care and even within national health care systems with robust resources, comprehensive registries, and MS subspecialist referral networks. The global prevalence and characteristics of barriers to expedited MS diagnosis, particularly in resource-restricted regions, have not been extensively studied. Recent revisions to MS diagnostic criteria demonstrate potential to facilitate earlier diagnosis, but global implementation remains largely unknown.

Methods

The Multiple Sclerosis International Federation third edition of the Atlas of MS was a survey that assessed the current global state of diagnosis including adoption of MS diagnostic criteria; barriers to diagnosis with respect to the patient, health care provider, and health system; and existence of national guidelines or national standards for speed of MS diagnosis.

Results

Coordinators from 107 countries (representing approximately 82% of the world population), participated. Eighty-three percent reported at least 1 "major barrier" to early MS diagnosis. The most frequently reported barriers included the following: "lack of awareness of MS symptoms among general public" (68%), "lack of awareness of MS symptoms among health care professionals" (59%), and "lack of availability of health care professionals with knowledge to diagnose MS" (44%). One-third reported lack of "specialist medical equipment or diagnostic tests." Thirty-four percent reported the use of only 2017 McDonald criteria (McD-C) for diagnosis, and 79% reported 2017 McD-C as the "most commonly used criteria." Sixty-six percent reported at least 1 barrier to the adoption of 2017 McD-C, including "neurologists lack awareness or training" by 45%. There was no significant association between national guidelines pertaining to MS diagnosis or practice standards addressing the speed of diagnosis and presence of barriers to early MS diagnosis and implementation of 2017 McD-C.

Discussion

This study finds pervasive consistent global barriers to early diagnosis of MS. While these barriers reflected a lack of resources in many countries, data also suggest that interventions designed to develop and implement accessible education and training can provide cost-effective opportunities to improve access to early MS diagnosis.

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Glossary

GOF = Goodness of Fit; **McD-C** = McDonald criteria; **MS** = multiple sclerosis; **MSIF** = Multiple Sclerosis International Federation; **OR** = odds ratio; **WB** = World Bank; **WHO** = World Health Organization.

Introduction

Recent data suggest an increasing global prevalence of multiple sclerosis (MS).[1-6] Revisions to the MS diagnostic criteria[7] over the past 2 decades have facilitated earlier diagnosis,[8-10] by obviating the need to wait for a second clinical event to diagnose MS. For example, in a cohort of 785 persons with MS from 9 European centers, the median time to diagnosis was 58.5 months based on a second clinical event, 13.0 months based on the 2010 McDonald diagnostic criteria, and 3.2 months based on the 2017 McDonald criteria (McD-C).[11] Expedited diagnosis consequentially has resulted in earlier treatment, even based on differences in the 2010 and 2017 criteria,[8] which is associated with improved clinical outcomes for people with MS.[12-15] Earlier diagnosis of MS carries the potential to ease the high global burden[1] associated with this disease through a reduction in disability-adjusted life years and associated health care cost.

Despite the importance of rapid diagnosis, diagnostic delays persist in MS care[16-19] and even within national health care systems with robust resources, comprehensive registries, and MS subspecialist referral networks.[20-22] A variety of contextual factors related to the affected individual, the health system, and policy likely contribute to delays between symptom onset and confirmed diagnosis of MS. The Anderson model of total patient delay[23] suggests that an individual needs to recognize bodily changes and appraise symptoms as warranting a need for care and then to obtain an appointment. That health care provider needs to appraise the individual and determine that investigations and referrals are needed. The specialist (neurologist) must be accessible and may need to complete additional investigations to confirm diagnosis.

The global prevalence and characteristics of barriers within this diagnostic pathway that prevent expedited MS diagnosis, particularly in resource-restricted regions, have not been extensively studied. Moreover, the success of global dissemination and implementation efforts surrounding revisions to MS diagnostic criteria particularly remains largely unknown. Scant "real-world" data limited to the United Kingdom and the United States continue to highlight miscomprehension and lack of implementation of contemporary criteria.[24-26]

This study aimed to synthesize novel global data focused on MS diagnosis collected as part of the recently completed Multiple Sclerosis International Federation's (MSIF) third edition of the Atlas of MS—a worldwide study of the epidemiology of MS and the global availability and accessibility of diagnostic and clinical resources for people with MS. We reported data focused on barriers to MS diagnosis, including the implementation of contemporary MS diagnostic criteria, which had been incorporated into the Atlas of MS for the first time (Figure 1). We further analyzed the influence of World Bank (WB) category, World Health Organization (WHO) region, the presence of national standards surrounding MS diagnosis, and the presence of national guidelines focused on MS diagnosis on barriers to diagnosis. These data from 107 countries representing 82% of the world's population carries the potential to inform future clinical, educational, and health care policy—derived interventions aimed to improve early and accurate diagnosis of MS.

Methods

This cross-sectional study conforms to CROSS reporting guidelines.

Setting

The aim of the Atlas was to provide a comprehensive understanding of the global burden of MS. These open-source data are intended as a tool to highlight disparities and inequalities, raise disease awareness, encourage improvements in surveillance systems and service provisions, inform and evidence advocacy efforts, and support the development of public policy to optimize the quality of life of people living with MS. The first edition of the Atlas of MS was published in 2008 in collaboration with the WHO. Data were updated by the MSIF in 2013 (second edition), and the third edition was launched in 2020–2022. Data were collected by questionnaire. The third edition surveyed key epidemiologic findings and barriers and inequalities in relation to diagnosis, access to disease-modifying therapies, and rehabilitation and symptom management.

Questionnaire Development

The Atlas questionnaire was designed through an iterative process by an Atlas working group composed of MSIF members (MS organizations from 12 countries) and a panel of 16 Atlas expert advisors from 15 countries. These 2 groups included representation from all 6 WHO regions,[15] all 4 WB economy income categories,[27] and specific expertise for the data collected. The MSIF International Working Group on Access and the MSIF International Medical and Scientific Board provided a further review of the questionnaire. These groups were composed of a range of stakeholders including clinicians, researchers, epidemiologists, volunteers/staff of MS organizations, and people affected by MS. Epidemiologists from McKing Consulting Corporation provided consultation regarding methodology, questionnaire design, data collection, and analyses.

Initially, important issues potentially affecting MS diagnosis and care in each region were identified by the Atlas working

Figure 1 Potential Patient–Related, Health Professional–Related, and Health Care System–Related Barriers on the Diagnostic Pathway to MS Assessed by the Third Atlas of MS
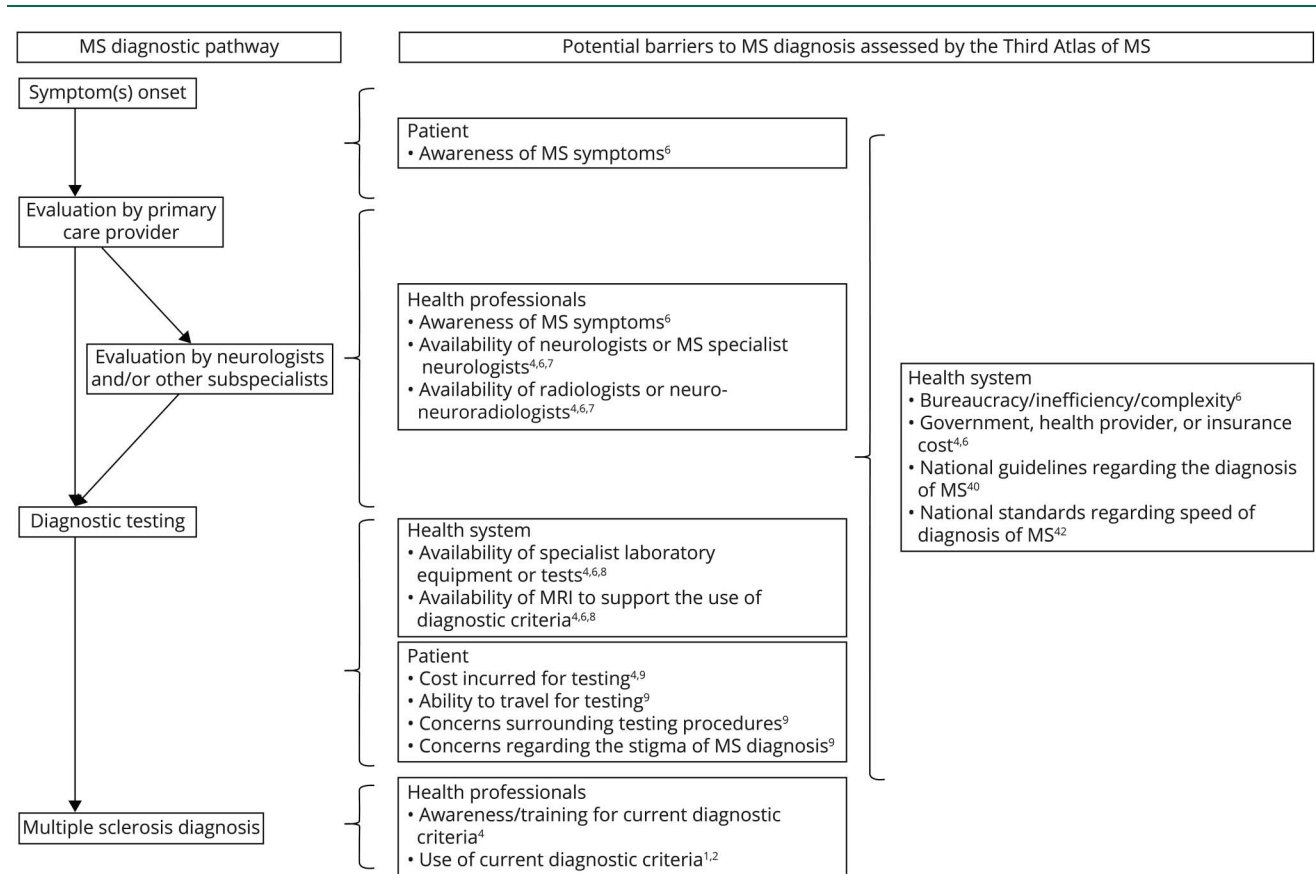
Superscript numbers indicate the Atlas question number that assessed each specific potential barrier to diagnosis. MS = multiple sclerosis.

group. Second, the group reviewed questions from the second edition of the Atlas for relevance to these issues. Relevant questions were retained or modified to conform to the updated priorities of the third edition. Third, the questions, drafted in English, were reviewed for clarity by the MSIF staff and consultants, the Atlas Working Group, Atlas Expert Advisors, and the MSIF International Working Group for Access.

A finalized draft was converted to an online survey tool incorporating skip logic using Surveymonkey.com for pilot testing. The questionnaire was then pilot tested by country coordinators from 5 countries (Argentina, Australia, India, Singapore, and Zambia) representing different WHO regions, WB income groups, and health care systems. No changes were made because of the pilot evaluation.

In collaboration with Guildhawk, a language and technology company, the questionnaire was translated and reviewed by a qualified native-speaking linguist in French and Spanish. An independent linguist proofread the translated files for additional quality assurance, and an additional review by Guildhawk staff was performed to check for accuracy. Each translation provided by Guildhawk was subsequently independently

verified by a native French and a native Spanish speaker drawn from the Atlas working group and its expert advisors. This resulted in minor changes to the translated text before finalization and distribution to country coordinators through an electronic Word document. During this process, the text was not translated back to English from French or Spanish before dissemination.

The final subsection of the questionnaire (eAppendix 1, links. lww.com/WNL/C901) relating to the data presented in this study included 13 questions that assessed the following: the current state of diagnosis including adoption of MS diagnostic criteria; barriers to diagnosis with respect to the patient, health care provider, and health system; and existence of national guidelines or national standards for MS diagnosis (including specifically the speed of diagnosis). A glossary of terms was included within each question. Sources of data reported were also queried.

Standard Protocol Approvals, Registrations, and Patient Consents

The Atlas of MS study methodology and questionnaire was not reviewed or approved by an institutional review board—this study surveyed health care professionals.

Figure 2 Countries That Provided Clinical Management Data for the Atlas of MS Third Edition
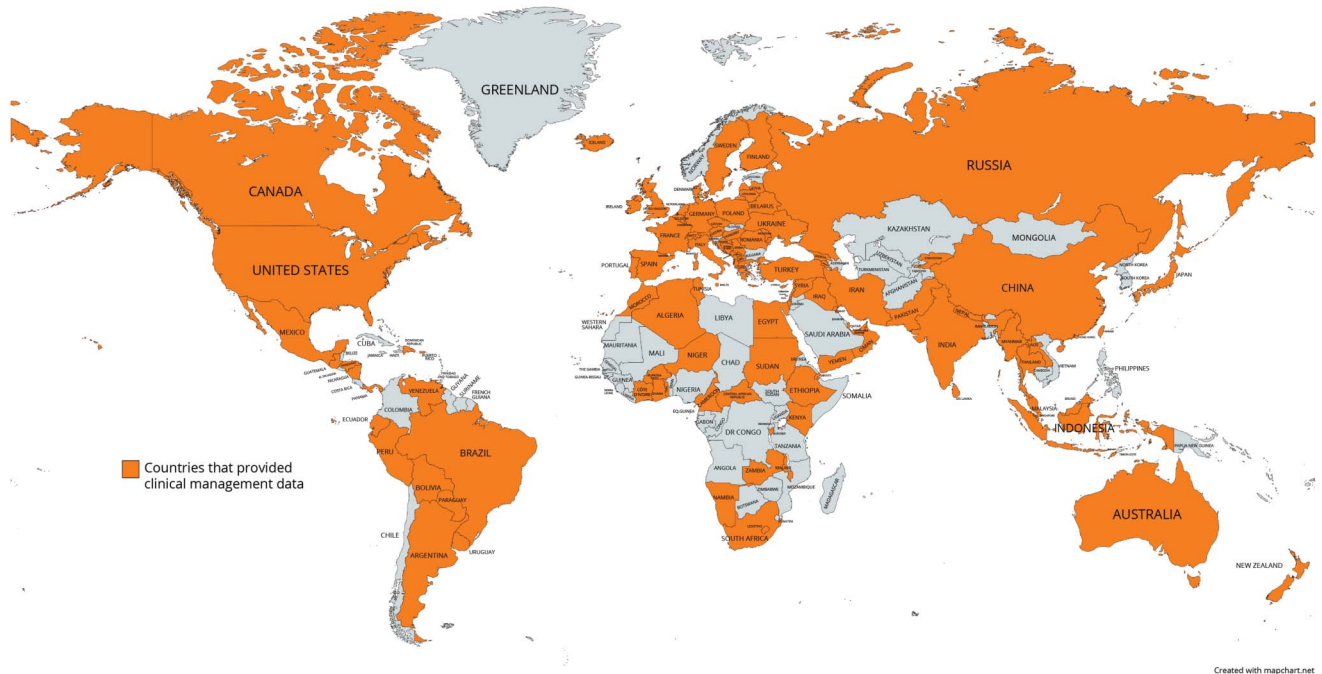
MS = multiple sclerosis.

Questionnaire Distribution

International contacts were identified through MSIF's network of MS organizations, the MSIF International Medical and Scientific Board, International Working Group on Access, previous Atlas contacts, the World Federation of Neurology, the Atlas working group and expert advisors, and regional International Committees for the Treatment and Research in Multiple Sclerosis and from scientific literature. Country coordinators, typically representatives from MS organizations, neurologists, epidemiologists, or researchers, were identified in each country and subsequently asked to complete the questionnaire while making use of all possible sources of information available to them including collaborating with other experts in the country where possible or necessary. Country coordinators were identified for 138 countries and were queried regarding preferred questionnaire language; 123/138 (89.1%) requested English, 9 requested French, and 6 requested Spanish.

Data were collected between October 2019 and April 2020 through the online survey tool, and country coordinators were provided electronic PDF or Word documents to allow collaboration and verification of data with other experts.

Analysis

Descriptive statistics are reported. For analyses WB high-income and upper middle-income categories were merged to create a high/upper middle-income category, and lower middle-income and low-income were combined to create a lower middle/low-income category due to sample size limitations.

The independent variables of interest were as follows: (1) Use of 2017 McD-C (yes/no, not sure excluded); (2) most commonly use 2017 McD-C (yes/no, not sure was excluded); and (3) the presence of at least 1 major barrier to early diagnosis of MS (yes/no, not sure was excluded). The outcomes of interest were as follows: (1) any national standards or targets set relating to the diagnosis, treatment, or monitoring of patients with MS in the country (yes/no); (2) any national guidelines for diagnosis, treatment, or living with MS? (yes/no); and (3) speed of diagnosis as a standard (yes/no).

We conducted a Fisher exact test to test the association between the survey responses for these variables and WB income categories or WHO regions and the unadjusted association between 2 survey responses. We used a series of multivariable logistic regression models to test the associations between the independent variables and outcomes of interest while adjusting for WB income and WHO region. We reported the generalized variance inflation factor[28] to test the multicollinearity of WB income and WHO regions, c-statistics to test discriminating ability, and p value of Hosmer-Lemeshow Goodness of Fit (GOF) test to test the model fit (eTable 1, links.lww.com/WNL/C903).[29] A c-statistic of 0.5 indicates the model is no better than chance at predicting the outcome, and 1.0 indicates perfect classification. A p value for the GOF test of >0.05 indicates a good fit.

Figure 3 Use of MS Diagnostic Criteria

A. MS diagnostic criteria used: N (%)
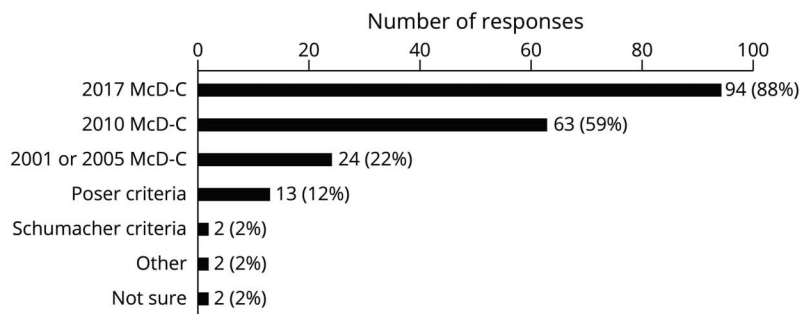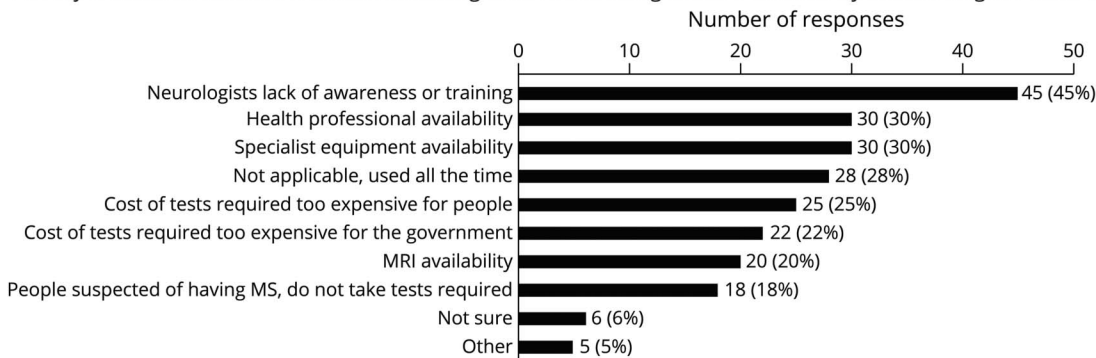

B. Single MS diagnostic criteria most commonly used: N (%)
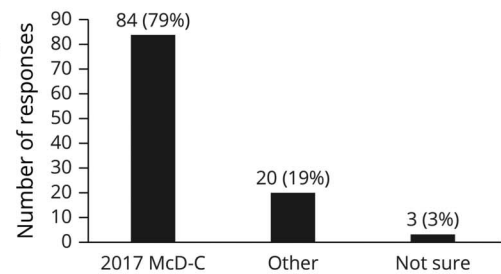
C. Why is the 2017 McDonald criteria not being used or not being used all the time by all neurologists in the country?: N (%)

(A) Responses to the query for all MS diagnostic criteria currently used by providers (may select more than 1 response). (B) Responses to a second question querying the single "most commonly" used MS diagnostic criteria by providers, demonstrating the proportion indicating 2017 McDonald criteria. (C) Responses regarding why 2017 McDonald criteria is not being used or not being used all the time by providers in the country (may select more than 1 response). MS = multiple sclerosis.

All statistical analyses were conducted in R version 4.0.2. Data are available on request to the MSIF.

Results

Coordinators representing 107 countries (approximately 82% of the world population) participated in the section of the Atlas questionnaire focused on MS diagnosis (Figure 2, and eTables 2 and 3, links.lww.com/WNL/C904 and links.lww.com/WNL/C905). Descriptive open-source data are available from the MSIF (atlasofms.org). Data generated by each country coordinator completing the survey comprise the reported results from each country.
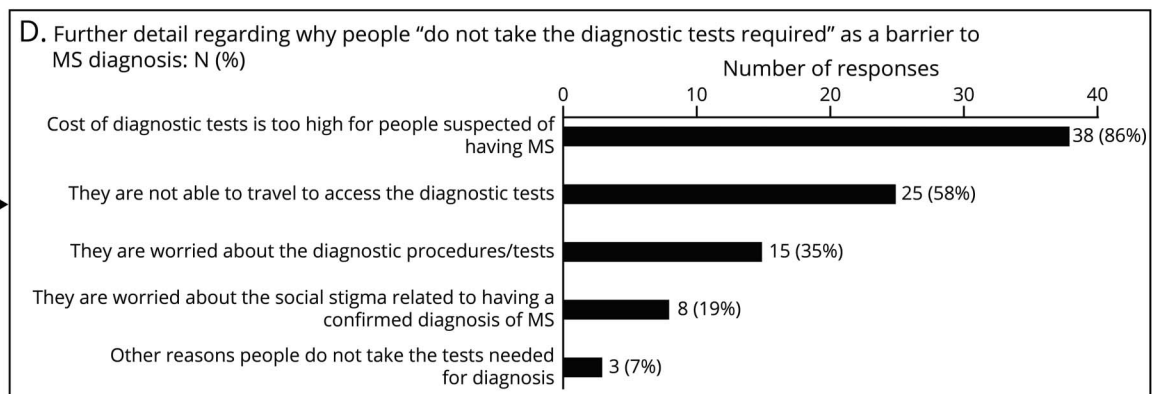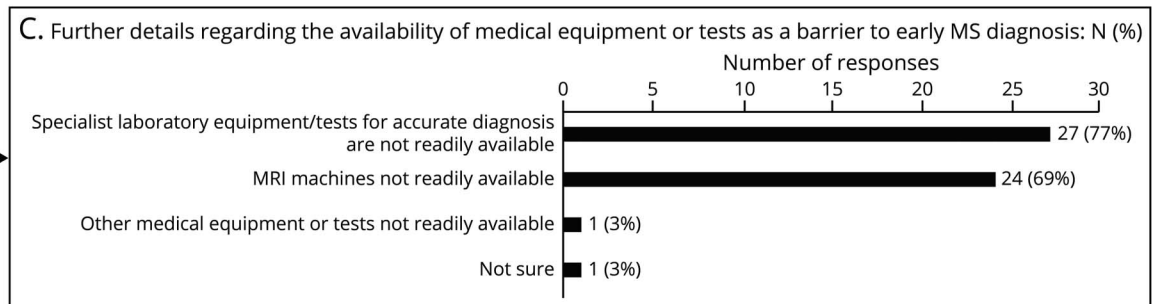
Current State of MS Diagnosis

The type of source consulted by country coordinators to provide information on diagnostic criteria included a published academic paper or poster: 51/107 (48%), patient data: 54/107 (50%), personal opinion: 72/107 (67%), opinion of others: 45/107 (42%), and other: 3/107 (3%). Figure 3 details responses to the 3 questions surrounding MS diagnostic criteria. Schumacher (1965), Poser (1983), and McD-C and its revisions (2001, 2005, 2011, 2017) all currently remained in use. Thirty-six (34%) countries reported using only 2017 McD-C for diagnosis. WB high/upper middle-income countries were more likely (n = 31, 42%) than lower middle/low-income countries (n = 5, 16%) ($p = 0.007$) to report using only 2017 McD-C for diagnosis compared with any McD-C, while there was no difference by WHO region ($p = 0.13$). Two countries (Burundi, Morocco) reported not using any McD-C criteria.

The 2017 McD-C were reported as the "most commonly used criteria" to diagnose MS in 84 (79%) countries, and this was more likely in WB high/upper middle-income countries than WB lower middle/low-income countries (66 [90%] vs 18 [58%], $p < 0.001$) but did not differ by WHO region ($p = 0.31$).

Procedures reported as used for the diagnosis of MS included neurologic examination by 106/106 (100%), MRI by 103/106 (97%), spinal tap by 96/106 (91%), evoked potentials by 69/106 (65%), optical coherence tomography by 40/106 (38%), and other by 5/106 (5%). MRI was not reported as a procedure used to diagnose MS in 3 (3%) countries (Brundi, Central African Republic, and Malawi).

Figure 4 Major Barriers to Early MS Diagnosis

A. Major barriers preventing early MS diagnosis: N (%)

Number of responses

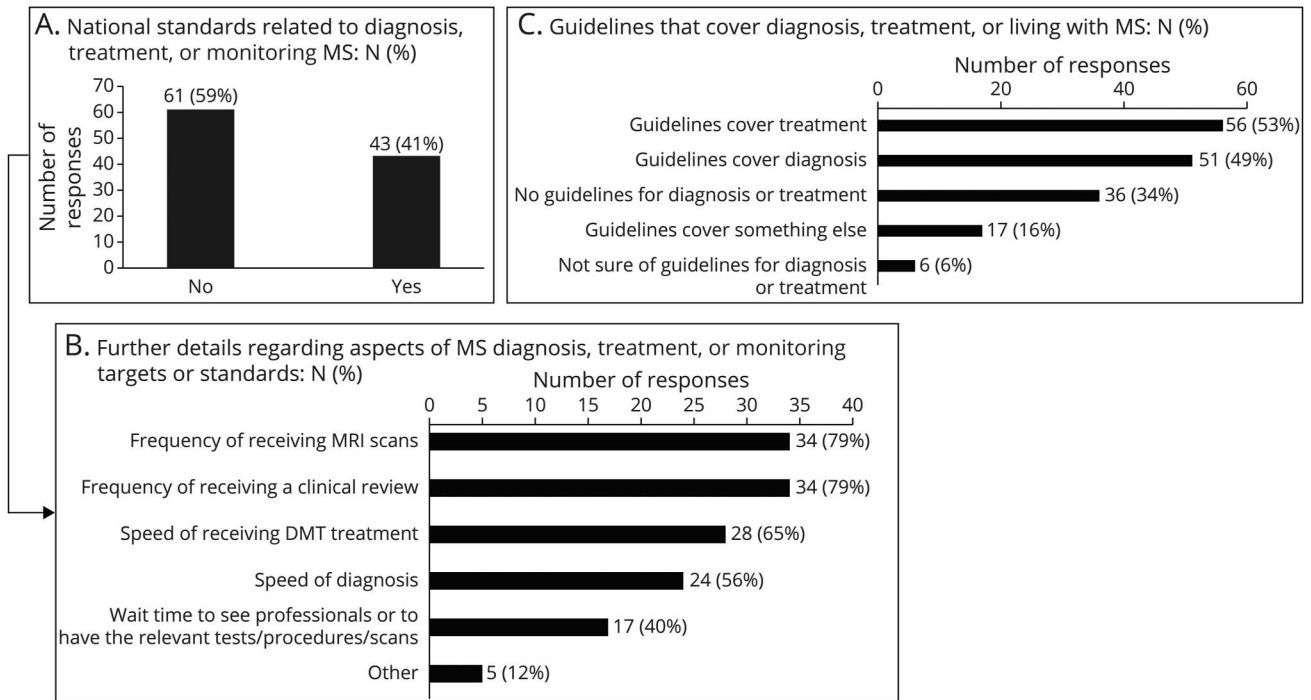|	
Lack of awareness of MS symptoms among the general public	72 (68%)
Lack of awareness of MS symptoms among health care professionals	63 (59%)
Health care professionals with the knowledge to diagnose MS not available	47 (44%)
People suspected of having MS do not take the diagnostic tests due to costs, travel, or other reasons	43 (41%)
Specialist medical equipment or diagnostic test not available	36 (34%)
Bureaucracy/inefficiency/complexity in health system	29 (27%)
Cost too expensive for the government, health provider, or insurance provider	28 (26%)
No major barriers to early diagnosis	17 (16%)
Other	1 (10%)
Not sure	1 (10%)

B. Further details regarding barriers concerning the availability of healthcare professionals with specialist knowledge: N (%)

Number of responses

Specialist MS neurologists not readily available	38 (88%)
Neurologists not readily available	26 (60%)
Radiologists/neuro-radiologists not readily available	26 (60%)
Other staff not readily available	3 (7%)

C. Further details regarding the availability of medical equipment or tests as a barrier to early MS diagnosis: N (%)

Number of responses

Specialist laboratory equipment/tests for accurate diagnosis are not readily available	27 (77%)
MRI machines not readily available	24 (69%)
Other medical equipment or tests not readily available	1 (3%)
Not sure	1 (3%)

D. Further detail regarding why people "do not take the diagnostic tests required" as a barrier to MS diagnosis: N (%)

Number of responses

Cost of diagnostic tests is too high for people suspected of having MS	38 (86%)
They are not able to travel to access the diagnostic tests	25 (58%)
They are worried about the diagnostic procedures/tests	15 (35%)
They are worried about the social stigma related to having a confirmed diagnosis of MS	8 (19%)
Other reasons people do not take the tests needed for diagnosis	3 (7%)

(A) Responses to query regarding major barriers that prevent early diagnosis of MS (may indicate more than 1), and further responses obtained in a follow-up question if barriers involving the (B) availability of "health care professionals with subspecialist knowledge," (C) "medical equipment or tests," or (D) "people do not take the diagnostic tests," were selected. MS = multiple sclerosis.

Figure 5 National Standards or Guidelines Relating to MS

A. National standards related to diagnosis, treatment, or monitoring MS: N (%)

61 (59%)
43 (41%)
No / Yes

C. Guidelines that cover diagnosis, treatment, or living with MS: N (%)

Number of responses

Guidelines cover treatment — 56 (53%)
Guidelines cover diagnosis — 51 (49%)
No guidelines for diagnosis or treatment — 36 (34%)
Guidelines cover something else — 17 (16%)
Not sure of guidelines for diagnosis or treatment — 6 (6%)

B. Further details regarding aspects of MS diagnosis, treatment, or monitoring targets or standards: N (%)

Number of responses

Frequency of receiving MRI scans — 34 (79%)
Frequency of receiving a clinical review — 34 (79%)
Speed of receiving DMT treatment — 28 (65%)
Speed of diagnosis — 24 (56%)
Wait time to see professionals or to have the relevant tests/procedures/scans — 17 (40%)
Other — 5 (12%)

Proportion of responses indicating (A) national standards related to MS diagnosis, (B) national standards focused on the speed of diagnosis of MS, or (C) the presence of national guidelines that cover diagnosis of MS. MS = multiple sclerosis.

Barriers to Diagnosis

Sources consulted by country coordinators surrounding barriers to diagnosis included published academic articles or posters: 30/106 (82%), patient data: 57/106 (54%), personal opinion: 81/106 (76%), opinion of others: 54/106 (51%), and other: 3/106 (3%).

More than 80% (n = 88) of countries reported at least 1 "major barrier" to early MS diagnosis (Figure 4). From the patient perspective (of symptom appraisal and care seeking), the most frequently reported barrier was lack of awareness of MS symptoms among "general public" by 72 (68%). From the health care provider perspective, the most commonly reported barrier was "lack of awareness of MS symptoms among health care professionals" (n = 63, 59%). This barrier was closely related to a lack of availability of "health care professionals with knowledge to diagnose MS" (n = 47, 44%). Of the countries reporting a lack of knowledgeable health professionals, 38 (88%) reported specialist MS neurologists are "not readily available" and 26 (60%) reported neurologists are "not readily available." This problem was compounded by a lack of "specialist medical equipment or diagnostic tests" in one-third of countries (n = 36). Of those countries, 24 (69%) reported MRI machines, and 27 (77%) reported "specialist laboratory equipment/tests for accurate diagnosis" are "not readily available."

WB lower middle/low-income countries reported at least 1 major barrier preventing early MS diagnosis more frequently than WB high/upper middle-income countries (31 [94%] vs 57 [78%], $p = 0.05$), while there were no significant differences between WHO regions ($p = 0.09$).

Sixty-six (66%) countries reported at least 1 barrier to the adoption of 2017 McD-C, most often that "neurologists lack awareness or training" (n = 45, 45%). WB lower middle/low-income countries reported at least 1 barrier to the adoption of 2017 McD-C more often than WB high/upper middle-income countries (29 [88%] vs 37 [51%], $p < 0.001$). Europe (19 [46%]) and Eastern Mediterranean (9 [50%]) WHO regions were less likely to report at least 1 barrier to the adoption of 2017 McD-C compared with all other regions (Africa: 13 [87%], America: 13 [76%], Western Pacific: 7 [78%], South East Asia: 5 [83%]) ($p < 0.001$).

Guidelines or National Standards

Fifty-one (49%) countries reported having national guidelines that cover the diagnosis of MS (Figure 5). WB high/upper middle-income countries reported national guidelines covering the diagnosis of MS more often than WB lower middle/low-income countries (45 [63%] vs 6 [18%], $p < 0.001$). Europe and Eastern Mediterranean WHO regions were more likely to report national guidelines covering the diagnosis of MS than all other WHO regions (33 [56%] vs 18 [36%], $p < 0.001$).

Forty-three (41%) countries reported national standards pertaining to MS care, and of those, 24 (56%) countries

Table 1 Odds Ratios (95% CIs) for Associations Between Use of the 2017 McD-C and National Standards or Diagnostic Guidelines for MS Before and After Adjustment for World Bank Income and World Health Organization Region

	National standards[a]		Diagnostic guidelines[b]		Speed of diagnosis standard[c]	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Only use McD-C 2017[d]	0.68 (0.27–1.68)	0.24* (0.07–0.68)	0.78 (0.32–1.89)	0.37 (0.13–1.01)	1.39 (0.31–6.75)	2.71 (0.59–14.04)
Most commonly use McD-C 2017[e]	1.77 (0.56–6.27)	0.74 (0.18–2.89)	1.40 (0.46–4.47)	0.38 (0.08–1.49)	0.60 (0.05–4.76)	0.27 (0.005–4.80)
At least 1 barrier to diagnosis[f]	0.50 (0.15–1.57)	1.09 (0.34–3.50)	0.72 (0.22–2.23)	1.23 (0.38–3.93)	0.46 (0.07–2.49)	0.35 (0.006–1.75)

Abbreviations: McD-C = McDonald criteria; MS = multiple sclerosis.
CI of the multivariate logistic regression is calculated using confint function in stats package in R.
*$p < 0.05$.
[a] "Are there any national standards or targets set relating to the diagnosis, treatment or monitoring of MS patients in the country?" Responses are categorized as yes if "yes" and no if "no."
[b] "Does the country have any national health plan(s) or guidelines that cover aspects of diagnosis, treatment or living with MS? Please indicate all that apply." Selection of "yes—diagnosis" are categorized as yes and no if "yes—diagnosis" is not selected. "Not sure" is excluded.
[c] "What aspects of the diagnosis, treatment, or monitoring of MS patients in the country have targets or standards?" Responses are categorized as yes if "speed of diagnosis" is selected and no if "speed of diagnosis" is unchecked.
[d] "Please indicate all the MS diagnostic criteria that you are aware are used in the country?" Responses are categorized as yes if "yes" if "McD-C—2017 version" is selected, and no if "no" if other criteria are selected. "Not sure" is excluded.
[e] "And which 1 criterion do you think is currently the most commonly used to diagnose MS in the country?" Responses are categorized as yes if "McD-C—2017 version" selected and no if other than "McD-C—2017 version" selected. "Not sure" is excluded.
[f] "Please indicate the major barriers in the country that prevent individuals from receiving an MS diagnosis as early as possible. Please indicate all major barriers that apply." Responses are categorized as yes if "yes" and no if "no." "Not sure" is excluded.

reported standards for "speed of diagnosis." WB high/upper middle-income countries also reported national standards more frequently than WB lower middle/low-income countries (36/73 [49%] vs 7/31 [18%], $p = 0.016$). National standards pertaining to MS was also associated with WHO region ($p < 0.001$). Europe and Eastern Mediterranean WHO regions were more likely to report such national standards compared with all other WHO regions (35 [59%] vs 8 [18%], $p < 0.001$)

Countries reporting "only using McD-C 2017" had 77% reduced odds of having "national standards" (odds ratio [OR] 0.23, 95% CI 0.07–0.68, c-statistic = 0.75, Hosmer-Lemeshow GOF p-value = 0.56) and 63% reduced odds of having "guidelines that cover diagnosis" (OR 0.37, 95% CI 0.13–1.01), only after adjusting for WB income category and WHO region (Table 1 and eFigure 1, links.lww.com/WNL/C902). There was no significant association between countries reporting 2017 McD-C as the "most commonly" used criteria and the presence of diagnostic guidelines, before or after adjusting for WB income category and WHO region.

No statistically significant association was identified between countries reporting a "speed of diagnosis" standard and reporting only the use of 2017 McD-C, before or after adjusting for WB income and WHO region (Table 1). There was also no association between countries reporting a "speed of diagnosis" standard and reporting 2017 McD-C as the "most commonly used" criteria, before or after adjusting for WB income and WHO region.

There was no significant association between countries with at least 1 barrier to early diagnosis and guidelines that cover

diagnosis, before or after adjusting for WB income and WHO region. There was no statistically significant association between countries with at least 1 barrier to early diagnosis and the presence of national standards, before or after adjusting for WB income and WHO region (Table 1).

Discussion

We investigated the presence and characteristics of health care system barriers to MS diagnosis in 107 countries. Eight in 10 participating countries reported at least 1 "major barrier" to MS diagnosis and 6 in 10 reported at least 1 barrier to the adoption of 2017 McD-C and frequent concurrent use of prior less sensitive diagnostic criteria. We found that there were barriers to timely diagnosis that were pervasive throughout the entire patient journey—ranging from lack of patient awareness, to lack of health care provider awareness and knowledge/training, to lack of personnel and infrastructure to implement recommendations around diagnosis even if the knowledge and awareness were available.

Barriers to timely MS diagnosis reflected a lack of resources in many countries. This most often included a lack of health care professionals, including neurologists and subspecialty MS neurologists, in particular, and medical equipment or diagnostic tests such as MRI machines and other laboratory equipment, particularly in lower-income settings. In addition, people suspected of having MS often did not complete recommended testing due to cost and/or related required travel, indicating that health care disparities likely play an important role in delayed diagnoses. Compared with 94% of WB high/upper middle-income countries, only 58% of lower middle/

low-income countries reported 2017 McD-C as the most commonly used diagnostic criteria, which may reflect a lack of trained health care professionals or other barriers to implementation at the health system level. WB lower middle/low-income countries were more affected by a lack of resources and were more likely to report at least 1 major barrier preventing early MS diagnosis, with almost every country (94%) reporting such. By contrast, these differences were not found with respect to WHO region. Improving the availability and accessibility of resources in these regions is likely to be complex and challenging, requiring country-specific interventions. However, efforts such as the development of laboratory testing using dried blood spots[30] and portable low-field MRI sensitive to MS lesions[31] show promise to reduce cost and travel-associated barriers to timely evaluation of possible MS diagnoses in resource-limited regions.

Of importance, data also suggest that interventions designed to develop and implement accessible education and training may provide cost-effective opportunities to improve access to early MS diagnosis. Lack of health care provider awareness or training were frequently reported barriers to early MS diagnosis and to the adoption of contemporary McD-C. Interventions leveraging resources already in place may improve access to early diagnosis. For instance, telemedicine may provide accessible and cost-effective opportunities for education, training, and direct care in resource-limited regions. A recent study demonstrated that teleneurology visits were feasible and acceptable for adult patients attending an outpatient neurology clinic in Zambia, while reducing expense and time associated with care.[32] Telemedicine may also be implemented to train regional clinicians in MS diagnosis and care,[33] who can subsequently serve as experts leading educational outreach efforts while providing subspecialist-level telemedicine consultations for local providers in their region. Once such efforts are successful, outreach to increase awareness among primary care providers and other non-neurologist physicians who may first encounter patients with symptoms suggestive of MS (e.g., ophthalmologists) along with the development of efficient referral networks is necessary. In spite of accessible and available care for early MS diagnosis in some regions, a lack of awareness of MS symptoms among the general public was also frequently reported—a barrier also amenable to educational efforts where models from other chronic disease interventions such as engaging mass media, faith-based institutions, and advocacy services may be informative.[34]

Although data support earlier diagnosis and improved outcomes in patients with MS because of revisions to MS diagnostic criteria over the past 20 years, there is scant literature concerning global implementation.[24,25] This study highlights delay in widespread adoption of revised 2017 McD-C approximately 21–27 months after publication. Although most countries reported that 2017 McD-C was the most commonly used criteria, many also reported continued use of prior criteria as part of routine care, suggesting heterogeneous practice in these regions. Persistent utilization of earlier criteria may unnecessarily delay diagnosis in contrast to comparably more sensitive contemporary criteria in a small but significant group of patients.[8] Approximately half WB high/upper middle-income countries reported at least 1 barrier to the adoption of 2017 McD-C, including 10% who did not report that 2017 McD-C was the most commonly used diagnostic criteria. This suggests that resource limitations were not the sole cause of delayed adoption of 2017 McD-C—improved dissemination and parallel education efforts should accompany any future revisions to MS diagnostic criteria to improve global implementation.

This study has limitations. Few peer-reviewed publications exist on the availability of and access to MS diagnosis in many countries, and as a result, this study relied on expert opinion in the absence of such data. These data may therefore also not capture heterogeneity and unmeasured contextual factors that may influence MS diagnosis in each country. Future studies in these regions might pursue evaluation of administrative or direct clinical data to verify and better characterize these findings where possible. However, to improve confidence in these data, collaborations between country coordinators and other experts were requested and the enumeration of data sources consulted if available. Most participating countries referenced the independent evidence consulted (academic papers or patient data such as surveys or registries) rather than reliance on opinion alone. A future Atlas effort may consider directly collecting and assessing the evidence used to inform responses and any barriers to its availability experienced by country coordinators. Funding to support for the development of MS registries in resource-limited regions may expand global representation and increase quantitative country-specific data for future studies evaluating barriers to MS diagnosis. Engagement with regional clinicians, MS advocacy groups, and public awareness campaigns would be needed to aid development and ensure the success of such initiatives. However, efforts toward population surveillance of other diseases[35] in low-income to middle-income countries suggest that single region or country-specific registries alone may be inadequate and that optimal approaches to comprehensive surveillance of MS will likely require leveraging multiple sources of regional health data and international collaboration.

In this study, there was underrepresentation of countries from the African WHO region and countries classified as WB low-income (eTables 2 and 3, links.lww.com/WNL/C904 and links.lww.com/WNL/C905), and these data therefore likely underestimate barriers to early MS diagnosis across these regions. This partly reflects the consequences of a severe lack of neurologists. For example, the number of neurologists in WHO

Africa region is an estimated median of 0.04 per 100,000 people (compared with 6.6 in Europe).[36] Many countries in Africa have 0 or 1–2 neurologists providing care. The resulting burden of patient care, teaching, and administrative responsibilities may make such providers less able to participate in initiatives such as the Atlas of MS. Furthermore, such countries have few if any neurologists with subspecialty MS expertise or capability to focus on MS, given neurologic care necessitated more broadly and by more prevalent neurologic conditions. In regions with few providers of neurologic care, knowledge for neurology is often further limited among non-neurologists, making recognition of symptoms of MS and referral to a neurologist even less likely. As a result, there are scant data concerning MS prevalence and care in Africa.[37]

Methodology used for the Atlas provides an overall estimate of barriers to early MS diagnosis in these regions but limits detailed assessments or conclusions regarding accurate or early diagnosis within or between regions. For instance, as recent data in the United States have highlighted, adoption of McD-C does not necessarily ensure accurate comprehension and application of its key elements.[26] Similarly, despite few diagnostic barriers reported by some countries, social determinants of health and other factors may still create inequalities influencing health care access to facilitate early MS diagnosis for some patients.[38] Further country-specific quantitative data concerning MS diagnosis are needed to better understand the experience of patients in these regions. Of importance, data collection was completed in April 2020 and, as a result, would not have adequately captured any impact of the coronavirus disease 2019 pandemic on MS diagnosis.

This study finds pervasive consistent global barriers to early diagnosis of MS. International expert consensus efforts have repeatedly affirmed optimal diagnostic approaches and the importance of early diagnosis to improve clinical outcomes in MS.[7,39,40] The challenges of dissemination of research findings, practice guidelines, and diagnostic criteria, particularly in resource-limited regions, are well-documented.[41-43] Indeed, this study found little association between national guidelines or standards for MS care and fewer barriers to early diagnosis. The development and improvement of much needed health care system resources required to ameliorate global barriers to MS diagnosis will necessitate difficult policy initiatives. Despite these issues, these data present a key opportunity to improve and expedite diagnosis of MS in many worldwide regions through provider and patient-focused educational interventions. Such approaches, incorporated in policy initiatives such as the recently WHO adopted Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders 2022–2031,[44] optimize clinical resources that are already in place. Models implemented by organizations such as the World Federation of Neurology[45] and others[33,46-49] to assess and develop worldwide neurology-focused educational resources and programs, particularly in resource-limited regions, should be considered.

Disclosure

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Publication History

Appendix Authors

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Andrew J. Solomon, MD	Department of Neurological Sciences, Larner College of Medicine at the University of Vermont, Burlington	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
Ruth Ann Marrie, MD, PhD	Departments of Internal Medicine and Community Health Science, Rady Faculty of Health Sciences, Max Rady College of Medicine, University of Manitoba, Winnipeg, Canada	Drafting/revision of the article for content, including medical writing for content; study concept or design; and analysis or interpretation of data
Shanthi Viswanathan, MD	Department of Neurology, Kuala Lumpur Hospital, Malaysia	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
Jorge Correale, MD	Departamento de Neurologia, Fleni, Buenos Aires; Institute of Biological Chemistry and Physical Chemistry (IQUIFIB), National Council for Scientific and Technical Research/ University of Buenos Aires, Argentina	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
Melinda Magyari, PhD	Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Denmark	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
Neil P. Robertson, MD	Division of Psychological Medicine and Clinical Neuroscience, Department of Neurology, Cardiff University, University Hospital of Wales, United Kingdom	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
Deanna R. Saylor, MD, MHS	Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD; Department of Internal Medicine, University Teaching Hospital, Lusaka, Zambia	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
Wendy Kaye, PhD	McKing Consulting Corporation, Atlanta, GA	Drafting/revision of the article for content, including medical writing for content; study concept or design; and analysis or interpretation of data

Appendix *(continued)*

Name	Location	Contribution
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Anne Helme, PhD	Multiple Sclerosis International Federation, London, United Kingdom	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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