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Global access to diagnostic paraclinical testing incorporated in the 2024 revised McDonald criteria: disparities and opportunity.

Andrew J. Solomon*[1], Magd Zakaria[2], Deanna Saylor[3], Shanthi Viswanathan[4], Dominika Czarnota-Szałkowska[5], Brenda L. Banwell[6], Timothy Coetzee[7], Xavier Montalban[8], Noah Hillman[9], Russel T. Shinohara[9] Nick Rijke[10], Anne Helme[10] Rachel King[10]

*Corresponding author: Andrew J. Solomon, andrew.solomon@uvm.edu
1 South Prospect Street, Burlington, VT 05401, phone: 802-847-4589
fax: 802-847-4918

Affiliations:

1. Department of Neurological Sciences, Larner College of Medicine at the University of Vermont, Burlington, Vermont, United States.
2. Department of Neurology, Ain Shams University, Cairo, Egypt.
3. Department of Neurology, University of North Carolina, Chapel Hill, North Carolina, United States and Department of Internal Medicine, University Teaching Hospitals - Adult Hospital, Lusaka, Zambia.
4. Department of Neurology, Tunku Abdul Rahman Neuroscience Institute, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia.
5. Polish Multiple Sclerosis Society (Polskie Towarzystwo Stwardnienia Rozsianego - PTSR), Warsaw, Poland.
6. Department of Pediatrics, Johns Hopkins School of Medicine, Baltimore, Maryland, United States.
7. National Multiple Sclerosis Society, New York, NY, United States.
8. Department of Neurology-Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitario Valld'Hebron, Barcelona, Spain.
9. Penn Statistics in Imaging and Visualization Center, Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, United States
10. Multiple Sclerosis International Federation (MSIF), London, United Kingdom.

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“Take-home points”

1. Global access to paraclinical testing (i.e. MRI, CSF evaluation, optical coherence tomography, evoked potentials) incorporated in multiple sclerosis diagnostic criteria is largely unknown.
2. No single paraclinical test was available across all 122 countries reporting data, all ten tests were available in only 41% of countries, and some countries reported lack of availability of all testing. Testing availability did not guarantee access for the diagnostic evaluation for MS in many countries.
3. Barriers such as cost and lack of expertise for performance and interpretation often precluded use of paraclinical testing use in routine care. Barriers to access were more common in countries categorized by the World Bank as Low Income, yet barriers were also prevalent and present in High Income Countries.

Abstract:

Background and Objectives: Paraclinical testing incorporated within multiple sclerosis (MS) diagnostic criteria over time have facilitated earlier diagnosis, yet global implementation is largely unknown. Lack of "specialist medical equipment or diagnostic tests" was a barrier to early diagnosis of MS endorsed by a third of 107 countries surveyed in the recent Multiple Sclerosis International Federation (MSIF) Atlas of MS Third Edition. The present study assessed global access to paraclinical testing incorporated in MS diagnostic criteria.

Methods: Survey development included stakeholders with varied expertise and perspectives from all World Health Organization regions and World Bank (WB) country economy income categories. The survey assessed availability, routine use, and barriers to routine use of MRI, CSF testing, evoked potentials, optical coherence tomography, and serum AqP4-IgG and MOG-IgG antibody testing. Opinions regarding anticipated 2024 criteria revisions and preferences regarding the dissemination of MS guidelines were surveyed. The survey was available from April 11, 2024, to September 2, 2024.

Results: 122/149 (82%) of country coordinators participated. No paraclinical test was available across all countries. All ten tests were available in only 41% of countries. Availability of paraclinical testing did not guarantee routine use in the diagnostic evaluation for MS. Cost and lack of expertise for performance or interpretation were frequent barriers to routine use. Such barriers were present even in WB high income countries (HIC), but low and low middle income countries (LLMIC) reported significantly more limited availability of paraclinical testing and significantly diminished routine use to aid diagnosis of MS.

Discussion: This study highlights worldwide barriers and disparities in access to paraclinical testing that can expedite the diagnosis of MS. Creative approaches are urgently needed to address cost and required expertise for these paraclinical tests to improve worldwide access. Our data suggest that targeted educational efforts surrounding 2024 McDonald criteria revisions can reduce barriers to implementation. There was enthusiasm that the incorporation of these new approaches to paraclinical testing within the criteria would improve access to early MS diagnosis. This study will provide valuable baseline data to inform future assessments of global access to paraclinical testing for the diagnosis MS.

Introduction:

Recent studies suggest a continuous reduction in the time to diagnosis of multiple sclerosis (MS) and a corresponding reduction in risk of disability in tandem with revisions to MS diagnostic criteria over the last four decades.[1-3] While successive criteria revisions have aimed to improve sensitivity to enable earlier diagnosis, diagnostic delay remains a prevalent problem in MS care[4, 5] even in well-resourced healthcare systems[6-9] and carries the risk of long-term disability as a consequence of delayed initiation of disease modifying therapy.[10]

Data supporting the incorporation of paraclinical testing such as CSF evaluation and MRI within MS diagnostic criteria to facilitate earlier diagnosis have in large part driven their revisions over time. Likewise, the 2024 McDonald criteria revisions[11] provide multiple new pathways to diagnosis with promise for further gains in sensitivity that also rely on diagnostic approaches incorporating the results of paraclinical testing including MRI, CSF evaluation, optical coherence tomography, and visual evoked potentials. Yet the global availability and use of paraclinical testing recommended by MS diagnostic criteria is largely unknown and socioeconomic and other disparities may result in barriers to implementation that can contribute to diagnostic delay. In recently reported data, 34% of 107 surveyed countries for the Multiple Sclerosis International Federation (MSIF) Atlas of MS Third Edition reported lack of "specialist medical equipment or diagnostic tests" as a barrier to early diagnosis of MS.[9]

Leveraging the expertise of national MS experts within MSIF's Atlas of MS country coordinator network, this study surveyed global access to paraclinical testing incorporated in MS diagnostic criteria that can aid early diagnosis for MS. The study aimed to characterize barriers to paraclinical testing and opportunities to improve their implementation.

Methods

Setting

The aim of the Atlas of MS[9] is to provide comprehensive understanding of the global burden of MS. This open-source data is intended as a tool to highlight disparities and inequalities, raise disease awareness, encourage improvements in surveillance systems and service provisions, inform and provide evidence for 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 World Health Organization (WHO). The data were updated by MSIF in 2013 (second edition), and in 2020 (third edition).[9] Topical interest surveys developed by MSIF expand on topics covered in the Atlas. This topical interest survey administered in 2024 focused on MS diagnostic testing capabilities in anticipation of the revision of MS diagnostic criteria. Data was collected via a survey.

Survey Development

The survey was designed through an iterative process with input from expert stakeholders ensuring representation from multiple countries and from all World Health Organization regions and all World Bank (WB) economy income categories. Stakeholders included the Atlas working group comprised of MSIF members (MS organizations), a panel of Atlas expert advisors, individuals from the MSIF International Working Group on Access, and the MSIF International Medical and Scientific Board. These contributors to survey development reflected a wide range of international perspectives and expertise from across the MS community and included, clinicians, researchers, volunteers/staff of MS organizations, and people affected by MS.

The survey questions were drafted in English, and the finalized draft was converted to an online survey tool incorporating skip logic using Surveymonkey.com for pilot testing. The survey

was then pilot tested by country coordinators from three countries (Egypt, Malaysia and Poland) representing different WHO regions, WB income groups, and healthcare systems. Minor changes to question wording were implemented following the pilot to improve clarity.

In collaboration with Guildhawk, a language and technology company, the survey 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. During this process the text was not translated back to English from French or Spanish before dissemination.

The survey (**eFigure1**) included questions that assessed availability and routine use of diagnostic tests/procedures for diagnosis of MS, barriers to routine use of these procedures/tests, the potential benefit of the incorporation of the visual system in revised diagnostic criteria, speed of access to MRI scan and results, and preference with regard to the dissemination of updates to MS criteria and guidelines.

Standard Protocol Approvals, Registrations, and Patient Consents

The 2024 Atlas of MS Topical Survey study was not reviewed or approved by an institutional review board - this study surveyed healthcare professionals and MS organization representatives. This cross-sectional survey study conforms to the Consensus-Based Checklist for Reporting of Survey Studies reporting guidelines (**eFigure2**).

Survey 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,

regional International Committees for the Treatment and Research in Multiple Sclerosis, as well as 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 survey 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 identified for 149 countries were queried regarding whether they could accurately complete the survey in English or required another language. 132/149 confirmed they would respond to the English survey, 10 requested French, and 7 requested Spanish versions of the survey.

Data were collected between April 11, 2024, and September 2, 2024 via the online survey tool and country coordinators were provided electronic PDF or Word documents to allow collaboration and verification of the data with other experts. Responses received via completion of the PDF or Word version of survey and emailed were recorded manually into the online survey tool on receipt.

Data Availability

Aggregate data reported in the findings of this study are available from the corresponding author upon reasonable request.

Analysis

Descriptive statistics are reported. Survey responses indicating uncertainty (e.g., "not sure") were excluded when comparing availability and use of paraclinical testing by WB socioeconomic classification. Comparisons were performed using Fisher's exact tests, with WB high-income countries (HIC) compared individually to a combined group of low-income and lower-middle-income countries (LLMIC), and upper-middle-income countries (UMIC). Fisher's exact tests

were performed due to small sample sizes in some income categories, which resulted in low expected cell counts. For comparisons of appointment duration across income levels, p-values were obtained using Mood's median test. Given the exploratory nature of the study, all reported p-values are unadjusted for multiple comparisons.

Results

Coordinators from 122 countries (**Figure 1)** responded to the Topical 2024 survey - a response rate of 81.9% (122/149). The distribution of these countries by WB income category was: High-Income (45), Upper-Middle-Income (33), and Low and Lower-Middle-Income (43), . One country (Venezuela) is currently unclassified by the WB and was excluded from the income group analysis but retained in global-level analysis. Characteristics of participating countries, including population size, MS prevalence (where available), and neurologist workforce density, are summarized in **Table 1**. 121/122 (99.2%) countries reported clinicians, other healthcare professionals, or researchers as the lead country coordinator responding to the survey or as a consulted contributor and 59/122 (48.4%) reported such input from a MS society or patient organization (**eTable1**).

Figure 2 presents responses concerning the availability and routine use of paraclinical tests for the diagnostic evaluation of MS. "Availability" included tests that are accessible either within the country or sent to other countries for processing, while "used routinely" was defined as "for most individuals undergoing MS diagnostic evaluation". **Table 2** reports reasons why specific paraclinical testing was reported as available, but was not routinely used for the diagnosis of MS. 97/119 (81.5%) of country coordinators indicated that once an MRI was ordered it took an average of 1 month or less for the scan to be performed and to receive the results. 14/119 (11.8%) reported

an average of 2-3 months, 1/119 (0.8%) reported 6 months, 3/119 (2.5%) reported 7 or more months and 4/119 (3.4%) were not sure.

Additional questions were focused on available laboratory testing for aquaporin-4-immunoglobulin G (AQP4-IgG) and myelin oligodendrocyte glycoprotein immunoglobulin G (MOG-IgG). 104/122 (85.2%) country coordinators reported that AQP4-IgG testing was available in their country, and they were asked to report all available types of assays. 20/104 (19.2%) reported enzyme-linked immunosorbent assay (ELISA) and/or Tissue Based Assay (TBA) but not Cell Based Assay (CBA) testing, 38/104 (36.5%) reported CBA only, and 23/104 (22.1%) reported CBA and either ELISA or TBA availability while 23/104 (22.1%) were unsure about testing type. 94/122 (77.0%) of country coordinators indicated MOG-IgG testing was available in their country, and they were asked to report all available types of assays. 19/94 (20.2%) reported ELISA and/or TBA but not CBA testing, 37/94 (39.4%) reported CBA only, and 19/94 (20.2%) reported CBA and either ELISA or TBA availability, while 19/94 (22.0%) were unsure about testing type. 54/94 (57.4%) of country coordinators reported that MOG-IgG testing provided a titer, 26/94 (27.7%) reported that testing only provided a positive or negative value, and 14/94 (14.9%) were unsure of how MOG-IgG results were reported. Of note, the survey did not distinguish between live and fixed CBA for either AQP4-IgG or MOG-IgG.

Country coordinators were queried about the consequences of updated diagnostic criteria allowing for confirmation of optic nerve lesions using optical coherence tomography (OCT) or visual evoked potentials (VEP) for fulfillment of dissemination in space for the diagnosis of MS in their country. 13/122 (10.7%) reported no difference, 67/122 (54.9%) reported improved speed of MS diagnosis, 66/122 (54.1%) reported improved accuracy of MS diagnosis, 20/122 (16.4%) endorsed improved access to diagnostic tests for people with MS because OCT and/or VEP are more widely available than MRI, 30/122 (24.6%) reported improved access to diagnostic tests for

people with MS because OCT and/or VEP are more affordable than MRI for either patients or for the health care system, 43/122 (35.2%) reported that inclusion in the criteria could facilitate advocacy to improve access to OCT and/or VEP, 41/122 (33.6%) reported the potential for advocacy to encourage the general public to schedule OCT scans as part of routine eye tests and for optometrists to refer relevant patients to neurology if a neurological condition is suspected, and 7/122 (5.7%) were unsure of the impact of OCT/VEP inclusion.

The approximate average duration of the appointment in which a patient receives their MS diagnosis in their country was queried. 13/122 (10.7%) of country coordinators reported 15 minutes or less, 45/122 (36.9%) reported 16-30 minutes, 22/122 (18.0%) reported 31-45 minutes, 28/122 (23.0%) reported 46 minutes or more, and 13/122 (10.7%) were not sure. 0/122 (0.0%) felt this duration of such appointments was “much too long”, 0/122(0.0%) felt the duration was “slightly too long”, 53/122 (43.4%) felt the duration was “just right”, 35/122 (28.7%) felt the duration was “not quite long enough”, 13/122 (10.7%) felt the duration was “not nearly long enough” and 20/122 (16.4%) were “not sure”.

Additional questions queried coordinators concerning how neurologists in their country preferred to learn about changes to diagnostic, treatment or management guidelines for MS (such as revisions to the McDonald criteria). **Table 3** reports responses to preferred communication channels and informational sources globally and by WB income category.

Sources of Data

Country coordinators could select multiple sources of evidence (**eTable2 and eTable 3**). For assessment of paraclinical testing availability and routine use, scientific publications were cited by 40/119 (33.6%), patient-derived data by 63/119 (52.9%), and advocacy or policy reports by 44/119 (37.0%). Overall, 84/119 (70.6%) reported at least one evidence-based source. Opinion-based

sources were also used by 100/119, (85.7%), with 33/119 (29.4%) relying solely on opinion and 67/119 (56.3%) combining evidence and opinion. For assessment of barriers to routine use, scientific publications were cited by 19/98 (19.4%), patient-derived data by 41/98 (41.8%), and advocacy or policy reports by 23/98 (23.5%). 52/98, 53.1% reported any evidence-based source, while 88/98, 89.8% selected opinion-based sources, with 46/98 (46.9%) relying solely on opinion.

Comparisons by World Bank Income Categories

Responses were stratified by WB income categories. Responses from LLMIC and UMIC were compared to responses from HIC. **Figure 3** and **Figure 4** report the results of comparing availability and routine use of paraclinical testing between these income categories respectively.

Availability of a CBA for AQP4-IgG testing was significantly diminished in LLMIC compared to HIC (11/20, 55.0% vs 35/40, 87.5%; p = 0.009) whereas there was no significant difference between UMIC and HIC (15/21, 71.4% vs 35/40, 87.5%; p = 0.164). Similarly, availability of a CBA for MOG-IgG testing was significantly lower in LLMIC compared to HIC (10/18, 55.6% vs 32/36, 88.9%; p = 0.012) whereas there was no significant difference between UMIC and HIC (14/21, 66.7% vs 32/36, 88.9%; p = 0.078).

Amongst countries where MRI was used routinely for MS diagnosis, an average time of 1 month or less to perform the scan and receive the results was reported by a significantly higher proportion of LLMIC than HIC (38/40, 95.0% vs 33/42, 78.6%; p = 0.049) but there was no difference between UMIC and HIC (25/32, 78.1% vs 33/42, 78.6%; p =1). The median and interquartile range for appointment duration were 30 (25) in LLMIC, 30 (40) in UMIC and 45 (30) in HIC. The average duration of the appointment in which a patient receives their MS diagnosis was significantly shorter in LLMIC compared to HIC (p= 0.016) and shorter in UMIC compared to HIC (p = 0.019). Neurologists in HIC more frequently reported that this appointment duration was too short

compared to LLMIC (24/42, 57.1% vs. 9/32, 28.1%; p = 0.018) whereas there was no difference between UMIC and HIC (15/26, 57.7% and 24/42, 57.1%; p = 1).

Discussion

In this study we evaluated access to paraclinical testing incorporated in MS diagnostic criteria in 122 countries. No single paraclinical test was available across all countries, all ten tests were available in only 41% of countries, and some reported lack of availability of all testing. Testing availability did not guarantee access for the diagnostic evaluation for MS in many regions - barriers such as cost and lack of expertise for performance and interpretation precluded use in routine care. Barriers to access were prevalent and present even in HIC. However, as might be expected, the data highlight disparities in access to paraclinical testing between LLMIC and HIC.

MRI has been a critical tool for the diagnosis of MS since its incorporation in the 2001 criteria.[12] Yet even after more than two decades, MRI remains unavailable in 2% of LLMIC and in a further 5%, despite the availability of MRI, it is not used routinely for the diagnostic evaluation of MS. Interestingly, the study found that wait times for MRIs were lower in LLMIC countries. This likely reflects selection bias for where patients of higher socioeconomic status can receive prompt evaluation and access to testing, often through private care models outside national healthcare systems, in situations with limited MRI availability. Importantly, MRI wait times do not reflect barriers to access to clinical evaluation that prompted the MRI and this data is also likely prone to recall bias. Economic and technological barriers to radiology equity are well documented in LLMIC. Global disparities in MRI access have been recognized with a recent resolution on strengthening medical imaging capacity adopted by the World Health Assembly in May 2025 and are likely to remain a challenge requiring advocacy and investment in LLMIC [13-15] with tailored country-specific

solutions. Emerging approaches that include portable low field MRI scanners with artificial intelligence-informed interpretation[16, 17] may one day improve MRI access for the evaluation of MS in patients where barriers to conventional MRI persist.

CSF assessment has been incorporated within MS diagnostic criteria longer than MRI.[18] 2017 criteria revisions allowed CSF restricted oligoclonal bands (OCBs) to substitute for dissemination in time (DIT) to expedite diagnosis,[19] yet seven years later OCB testing remains unavailable in one third of LLMIC and is not used in routine care for diagnosis in approximately half of LLMIC. Although OCB testing was available in almost all HIC and UMIC, OCBs were not routinely used for diagnosis in approximately 20% of UMIC and 10% of HIC. Cost, lack of available expertise, and lack of awareness of the importance of OCB testing were frequently reported barriers to OCB testing. Although CSF IgG index availability and routine use was surveyed as it was an element of previous MS diagnostic criteria, this testing is no longer incorporated in the 2024 criteria. The incorporation of kappa free light chain (kFLC) testing as a substitute for OCBs in the 2024 criteria promises to improve global access to CSF testing for the evaluation of MS by reducing cost and expertise required for CSF interpretation.[20, 21] Encouragingly, almost half of participating coordinators reported kFLC testing was already available in their country, yet only 10% reported routine use of kFLC. This finding may not represent barriers to use of kFLC given that the survey was completed prior to 2024 McDonald criteria recommendations for methodological approaches to kFLC testing and its role in the MS diagnostic process.

Although VEPs have long been used to provide objective evidence of an episode of acute optic neuritis,[18] the 2024 McDonald criteria incorporate the visual pathway as a fifth topography for the fulfillment of dissemination in space (DIS) for the first time and include specific VEP and OCT thresholds for evidence of a lesion.[22] This change promises earlier diagnosis of MS in some patients.[23] Over one third of countries reported lack of awareness of the importance of OCT or VEP

testing for diagnosis of MS as a barrier to routine use. Routine use of OCT and VEP for MS diagnosis was 27% and 52% respectively. This highlights the need for future educational efforts, particularly as the survey was conducted before the expanded role of the visual system in the 2024 criteria was widely known. LLMIC reported significantly less availability of OCT and VEP compared to HIC, which may be due to both limited resources and lack of awareness of the role of these tools for diagnosis in these regions. Half of all country coordinators felt that incorporation of OCT or VEP to provide evidence for an optic nerve lesion fulfilling DIS was likely to improve speed of MS diagnosis, one fourth reported this change would improve access to diagnostic tests for MS due to affordability compared to MRI, and approximately one third felt this change could facilitate advocacy to improve access to this testing, suggesting enthusiasm for this revision to the 2024 criteria.

Laboratory testing for AQP4-IgG and MOG-IgG critically aids differentiation of neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) from MS. AQP4-IgG and MOG-IgG testing was unavailable in countries across every WB income level, although barriers to access were significantly greater in LLMIC (compared to HIC) with 28% reporting unavailability of AQP4-IgG testing and 42% unavailability of MOG-IgG testing. Of note, testing availability was explicitly defined to include the ability to send serum to a different country to complete testing. These reported barriers to AQP4-IgG and MOG-IgG testing are comparable to the results of a recent survey of sixty countries focused on global NMOSD and MOGAD care.[24] Importantly, given that up to 50% of children under 12 years of age who present with acute demyelination have MOGAD, the 2024 McDonald criteria specify that MOG-IgG testing with a CBA should be considered in all children under 12 years of age where MS is being considered.[11] In this survey, in addition to lack of access to testing as reported above, 28% of all countries reported that the results of MOG-IgG testing when available did not

provide a titer to guide diagnostic evaluation,[25] and many reported access restricted to a variety of non-CBA testing of varying sensitivity and specificity. Of note, the availability of live compared to fixed CBA was not assessed and should be considered in future surveys. Routine use of AQP4-IgG and MOG-IgG testing was quite low and while cost was an often-cited barrier, some coordinators indicated in their responses that these tests were not "used for diagnosis of MS" thus making this data challenging to interpret. MS remains a diagnosis of exclusion, and MS diagnostic criteria continue to stipulate that evaluation for a "better explanation"[26-29] than MS is an integral element of the diagnostic process - future surveys will need to consider how to better assess testing aimed at MS differential diagnosis. New approaches in LLMIC such as dried blood spot testing [30] may reduce cost and improve access to AQP4-IgG and MOG-IgG testing in the future. In the meantime, education concerning changes in 2024 focused on diagnostic approaches to pediatric MS will require concerted global efforts.

This study has limitations. In the absence of evidence-based data concerning access to and routine use of paraclinical testing to aid the diagnosis of MS (**eTable2, eTable3**), data was derived from expert opinion. Future studies in these regions might further pursue evaluation of administrative or direct clinical data to verify and better characterize our findings. These data may inadequately capture regional heterogeneity that may influence access to and use of MS-related diagnostic testing diagnosis in each country, for instance coordinators and their data sources may overrepresent access in urban regions in their country. Both the diminished availability of neurologists and the lower reported prevalence of MS in LLMIC compared to HIC may also influence availability and use of paraclinical testing for MS diagnosis. Furthermore, to improve statistical power and interpretability, LMIC and LIC were combined into a single category for data analysis. However, these groups are also not homogeneous. The availability of some diagnostic tests was lower in LICs compared to LMICs (i.e. MRI 92.9% vs 100%; OCB 28.6% vs 86.2%) and

there was also considerable variation within income categories (i.e. the number of diagnostic tests available in each country ranged from 1 to 10 among LMICs and from 0 to 8 among LICs). In addition, this approach may have resulted in underestimation of disparities in LIC or overestimation of such in LMIC, particularly as fewer LIC participated in the survey (**Table 1**, **Figure** 1). Although the definition of "routine use" provided in the survey was reviewed by multiple stakeholders for clarity, incorporation of "the majority of people undergoing testing" this phrasing might have remained susceptible to varying interpretations and phrasing such as "routine use where appropriate" might have been superior. The survey did not capture details about MRI field strength, access to gadolinium enhanced scans or MRI sequences specified by past or recent MS consensus MRI guidelines.[31] As a result of implementation prior to publication of the 2024 criteria availability of new MRI diagnostic biomarkers incorporated in the 2024 criteria ("central vein sign" and "paramagnetic rim lesions")[31] were not surveyed and should be incorporated in future studies evaluating access to diagnostic paraclinical testing for MS. While not every paraclinical test surveyed is required to ensure early diagnosis of MS, despite the availability or routine use of such testing barriers to early diagnosis persist in many countries due to lack of access to neurologists[32] to initiate the diagnostic evaluation. The national or regional prevalence of neurologists with subspeciality training in MS might also influence the availability or routine use of paraclinical testing, however this data is lacking. Also of note, barriers to awareness of MS onset prior to age 18 years and its diagnosis remain of importance globally and this study did not specifically address access to paraclinical testing in the context of pediatric-onset MS.

This study highlights worldwide barriers and disparities in access to paraclinical testing that can expedite the diagnosis of MS. As evolving MS diagnostic criteria increasingly incorporate paraclinical testing, creative approaches are urgently needed to minimize their cost and develop the required expertise to administer and interpret such tests. Approaches to reduce cost will likely

be challenging, and will require country and healthcare system specific advocacy, reform, and innovation. However, lack of awareness of the importance of paraclinical testing and lack of expertise for their performance or interpretation were frequent barriers to access that may be more easily addressed (compared with cost) by leveraging educational efforts. Webinars, journal articles, and continuing education platforms were highly valued for the communication of MS guidelines. They could provide increased accessibility to UMIC and LLMIC providers and could be developed within any region, allowing for generalizability and versatility. As surveys concerning prior MS diagnostic criteria have demonstrated,[33] targeted education surrounding 2024 criteria revisions will be critical to ensure awareness of these changes and reduce barriers to implementation. These efforts must be developed with a lens toward global accessibility. Our data encouragingly report paraclinical testing newly incorporated in the 2024 criteria is already in place in many countries and enthusiasm that these changes will reduce cost and expedite diagnosis of MS. This study will provide valuable baseline data to inform future assessments of access to paraclinical testing for the diagnosis of MS and ongoing 2024 McDonald criteria implementation efforts.

Table 1: Characteristics of participating countries

	Global	Low and Lower Middle Income[f]	Upper Middle Income[f]	High Income[f]
Participation coverage				
Number of countries in analysis (n)	122	43	33	45
Countries included, % of global total	55.7% (122/219)	55.8% (43/77)	61.1% (33/54)	52.9% (45/85)
Population covered, % of global	92.8%	88.9%	97.4%	94.2%
Number of countries by UN Geographic Region[a]				
Africa	28	24	4	0
Americas	20	2	12	5
Asia	36	17	10	9
Europe	36	0	7	29
Oceania	2	0	0	2
Country population[b]				
Mean (millions)	61.30	78.34	83.45	29.50
Median (millions)	17.94	28.00	17.90	8.84
Interquartile range (IQR), millions	40.11	36.78	46.94	28.44
Benchmark: all Atlas recognised countries (n=219)[bc]				
Mean (millions)	36.77	49.19	52.37	16.58
Median (millions)	6.79	14.23	5.69	2.95
Interquartile range (IQR), millions	25.22	28.03	32.86	10.30
MS prevalence per 100,000[bd]				
Countries included with prevalence data (n)	99	25	31	42
Median MS prevalence (per 100,000)	34.0	1.4	14.5	128.7
Interquartile range (IQR) MS prevalence	105.24	19.85	30.31	107.65
Neurologist density per 100,000 (population)[be]				
Countries included with neurologist data (n)	86	25	23	38
Median neurologist density (per 100,000)	1.9	0.1	1.9	5.1
Interquartile range (IQR) neurologists	4.85	0.33	3.09	4.93

Notes:

[a]Countries are grouped into regions using United Nations geographic classifications.

[b]Country populations, MS prevalence and Neurologist density vary widely within income groups. Medians and interquartile ranges are shown to describe a typical country and the spread of values, while means are included for comparison.

[c]Benchmark rows show population statistics for all 219 countries recognised by the Atlas of MS, to provide context for how participating countries compare with the global distribution.

[d]MS prevalence values are country-reported estimates (per 100,000) from the 2022 Atlas update.

[e]Neurologist density reflects nationally reported data collected in 2019-2020. Definitions likely vary by country (e.g., practising vs. all certified neurologists; occasional grouping with related specialties).

[f]Venezuela is not currently classified by the World Bank income grouping and was therefore not included in income-group comparisons. It is included in global results.

Table 2: Selected explanations for why an available paraclinical test was not used routinely for MS diagnosis

	MRI	OCT	VEPs	Other EPs	LP	OCBs	kFLC	IgG index	AQP4-IgG	MOG-IgG
Lack of awareness of importance of this test in the diagnosis of MS	1/2 (50.0%)	38/76 (50.0%)	13/41 (31.7%)	18/60 (30.0%)	3/9 (33.3%)	5/18 (27.8%)	19/47 (40.4%)	11/41 (26.8%)	13/46 (28.3%)	10/48 (20.8%)
Health professionals (lab assistants, radiographers, neurologists, ophthalmologists etc.) with specialist knowledge to perform or analyze this test not readily available	1/2 (50.0%)	33/76 (43.4%)	17/41 (41.5%)	20/60 (33.3%)	1/9 (11.1%)	8/18 (44.4%)	16/47 (34.0%)	8/41 (19.5%)	9/46 (19.6%)	9/48 (18.8%)
Concern about the accuracy or reliability of this test (due to lack of laboratory expertise, or lack of quality equipment)	0/2 (0.0%)	14/76 (18.4%)	10/41 (24.4%)	12/60 (20.0%)	3/9 (33.3%)	3/18 (16.7%)	9/47 (19.1%)	7/41 (17.1%)	5/46 (10.9%)	5/48 (10.4%)
Cost of this diagnostic test is too expensive for the government, health provider or insurance provider	1/2 (50.0%)	15/76 (19.7%)	5/41 (12.2%)	5/60 (8.3%)	1/9 (11.1%)	6/18 (33.3%)	9/47 (19.1%)	10/41 (24.4%)	14/46 (30.4%)	14/48 (29.2%)
Cost of this diagnostic test is too expensive for the people suspected as having MS (e.g. lack of health insurance, or tests not covered/fully covered by health insurance, etc.)	2/2 (100.0%)	20/76 (26.3%)	7/41 (17.1%)	8/60 (13.3%)	4/9 (44.4%)	11/18 (61.1%)	10/47 (21.3%)	15/41 (36.6%)	21/46 (45.7%)	21/48 (43.8%)
Cost barrier combined responses: (either: Cost of this diagnostic test is too expensive for the government, health provider or insurance provider OR Cost of this diagnostic test is too expensive for the people suspected as having MS	2/2 (100.0%)	29/76 (38.2%)	8/41 (19.5%)	9/60 (15.0%)	4/9 (44.4%)	12/18 (66.7%)	12/47 (25.5%)	17/41 (41.5%)	24/46 (52.2%)	24/48 (50.0%)
People are not able to travel to access this diagnostic test (e.g. live too far away, cannot afford transport costs, not physically able to travel etc.)	1/2 (50.0%)	13/76 (17.1%)	4/41 (9.8%)	3/60 (5.0%)	4/9 (44.4%)	3/18 (37.5%)	1/47 (2.1%)	4/41 (9.8%)	4/46 (8.7%)	4/48 (8.3%)
People are worried about the social stigma related to having a confirmed diagnosis of MS	0/2 (0.0%)	0/76 (0.0%)	0/41 (0.0%)	0/60 (0.0%)	0/9 (0.0%)	0/18 (0.0%)	0/47 (0.0%)	1/41 (2.4%)	0/46 (0.0%)	0/48 (0.0%)
People are scared or worried about this diagnostic procedures/test (e.g. cultural superstition/myths, concern over side effects / pain / claustrophobia)	0/2 (0.0%)	0/76 (0.0%)	0/41 (0.0%)	0/60 (0.0%)	1/9 (11.1%)	1/18 (5.6%)	0/47 (0.0%)	3/41 (7.3%)	0/46 (0.0%)	0/48 (0.0%)
This diagnostic test is not recommended in the national guidelines for MS diagnosis	0/2 (0.0%)	38/76 (50.0%)	15/41 (36.6%)	24/60 (40.0%)	1/9 (11.1%)	2/18 (11.1%)	22/47 (46.8%)	13/41 (31.7%)	9/46 (19.6%)	9/48 (18.8%)
This diagnostic test is only used for differential diagnosis e.g. ruling out other demyelinating disorders	0/2 (0.0%)	20/76 (26.3%)	16/41 (39.0%)	14/60 (23.3%)	1/9 (11.1%)	4/18 (22.2%)	9/47 (19.1%)	8/41 (19.5%)	28/46 (60.9%)	28/48 (58.3%)

Abbreviations: MRI = magnetic resonance imaging, OCT = optical coherence tomography, VEPs = visual evoked potentials, Other Eps = other evoked potentials, LP = lumbar puncture, OCBs = oligoclonal bands, kFLC = kappa free light chains, IgG index = intrathecal immunoglobulin G index, AQP4-IgG = aquaporin-4 immunoglobulin G, MOG-IgG = myelin oligodendrocyte glycoprotein, immunoglobulin G

Table 3: Neurologist preferences for communications about MS guideline updates

	Global	Low and Lower Middle Income (LLMIC)	Upper Middle Income (UMIC)	High Income (HIC)
Preferred Communication Channels				
Attending conferences (national, regional or global)	105/122 (86.1%)	35/43 (81.4%)	29/33 (87.9%)	41/45 (91.1%)
Webinars	58/122 (47.5%)	28/43 (65.1%)	12/33 (36.4%)	18/45 (40.0%)
Journals - multiple sclerosis specific: e.g. MS Journal (MSJ), MS And related Disorders, (MSARD)	53/122 (43.4%)	10/43 (23.3%)	19/33 (57.6%)	23/45 (51.1%)
Journals - general neurology: e.g. Lancet Neurology, Neurology	37/122 (30.3%)	13/43 (30.2%)	6/33 (18.2%)	17/45 (37.8%)
Journals - other	2/122 (1.6%)	0/43 (0.0%)	0/33 (0.0%)	2/45 (4.4%)
Combined responses: Any Journals - MS specific, General Neurology or other types	71/122 (58.2%)	19/43 (44.2%)	19/33 (57.6%)	32/45 (71.1%)
Specialist training/education/Continuing Professional Development (CPD)/Continuing Medical Education (CME)	47/122 (38.5%)	19/43 (44.2%)	10/33 (30.3%)	17/45 (37.8%)
Electronic newsletters, blogs or email communication	11/122 (9.0%)	5/43 (11.6%)	6/33 (18.2%)	0/45 (0.0%)
Newsletters – print format	2/122 (1.6%)	1/43 (2.3%)	1/33 (3.0%)	0/45 (0.0%)
Combined responses: Any printed or electronic newsletters, blogs or email communications	13/122 (10.7%)	6/43 (14.0%)	7/33 (21.2%)	0/45 (0.0%)
Research social networks and sharing platforms	8/122 (6.6%)	2/43 (4.7%)	5/33 (15.2%)	1/45 (2.2%)
Social media (X/Twitter, LinkedIn, YouTube or other)	6/122 (4.9%)	4/43 (9.3%)	1/33 (3.0%)	1/45 (2.2%)
Word of mouth	5/122 (4.1%)	2/43 (4.7%)	1/33 (3.0%)	3/45 (6.7%)
Preferred Information Sources				
TRIMS (Treatments and Research in MS) conferences or communications	91/122 (74.6%)	24/43 (56%)	26/33 (78.8%)	40/45 (88.9%)
National Neurology Professional Organizations	64/122 (52.5%)	15/43 (35%)	15/33 (45.5%)	34/45 (75.6%)
Regional Neurology Professional Organizations	42/122 (34.4%)	16/43 (37%)	15/33 (45.5%)	10/45 (22.2%)
World Federation of Neurology	29/122 (23.8%)	14/43 (33%)	12/33 (36.4%)	2/45 (4.4%)
Healthcare professionals, researchers or decision makers	42/122 (34.4%)	17/43 (40%)	6/33 (18.2%)	19/45 (42.2%)
Continuing Professional Development/Medical Education providers/Learning Platforms	31/122 (25.4%)	12/43 (28%)	9/33 (27.3%)	10/45 (22.2%)
MS organizations	25/122 (20.5%)	9/43 (21%)	7/33 (21.2%)	9/45 (20.0%)
Patients	1/122 (0.8%)	1/43 (2%)	0/33 (0.0%)	0/45 (0.0%)

Figure 1. Countries participating in the survey, by World Bank income group.
Participating countries are color-coded according to World Bank income classification: high-income countries (blue), upper-middle-income countries (orange), low and lower-middle- income countries (green), and unclassified (purple). Countries not participating in the survey are shown in grey.

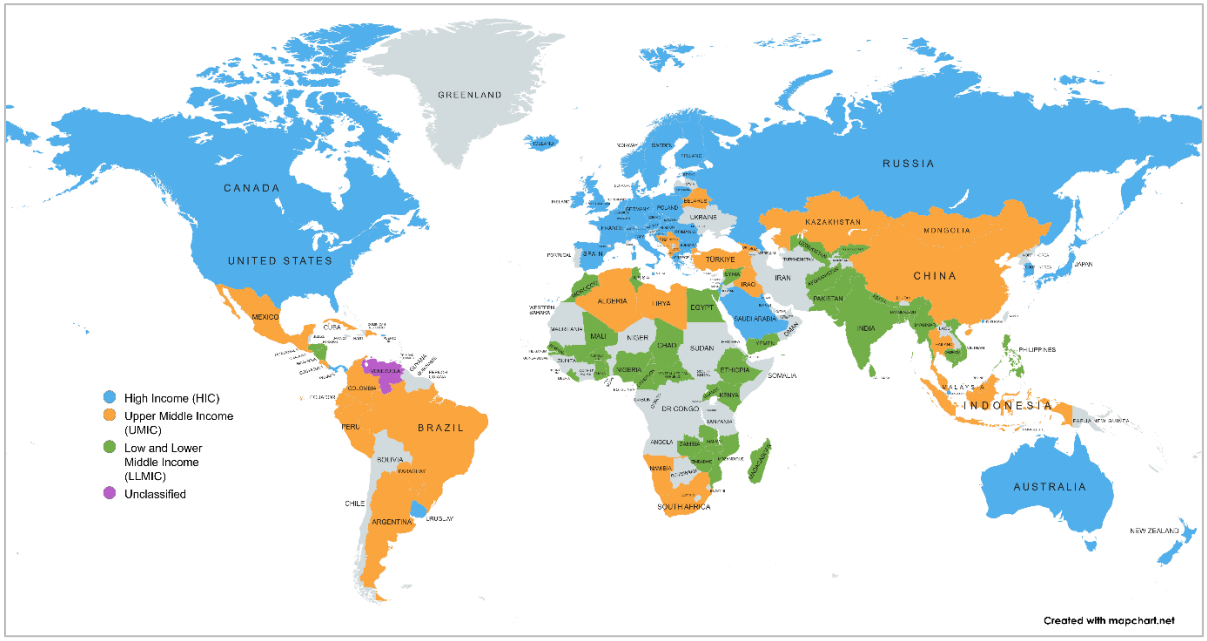


Figure 2. Availability and routine use of paraclinical tests for MS diagnosis reported by participating countries.
For each test, black circles indicate the proportion of countries reporting the test as available, while grey circles indicate the proportion reporting the test as used routinely. Differences between availability and routine use highlight gaps between access and implementation across paraclinical modalities.

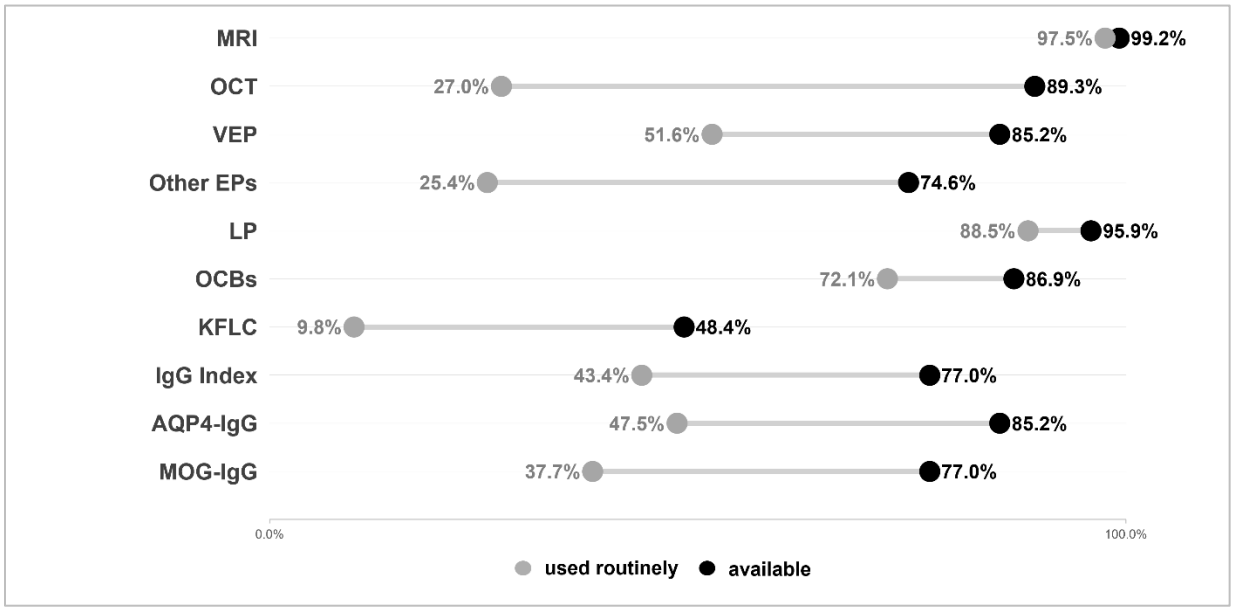


Figure 3. Availability of paraclinical testing for the diagnostic evaluation of multiple sclerosis, by World Bank income category.

Panels show the proportion of countries reporting availability of ten paraclinical tests, grouped as: (A) MRI and lumbar puncture (B) optical coherence tomography (OCT) and visual evoked potentials (VEP), and other evoked potentials; (C) CSF-testing : IgG index, oligoclonal bands (OCBs, kappa free light chains (kFLC); and (D) antibody testing (AQP4-IgG and MOG-IgG). Bars indicate low and lower-middle-income countries (LLMIC), upper-middle-income countries (UMIC), and high-income countries (HIC). Brackets denote pairwise comparisons between World Bank income groups using Fisher's exact test; corresponding p-values are shown.

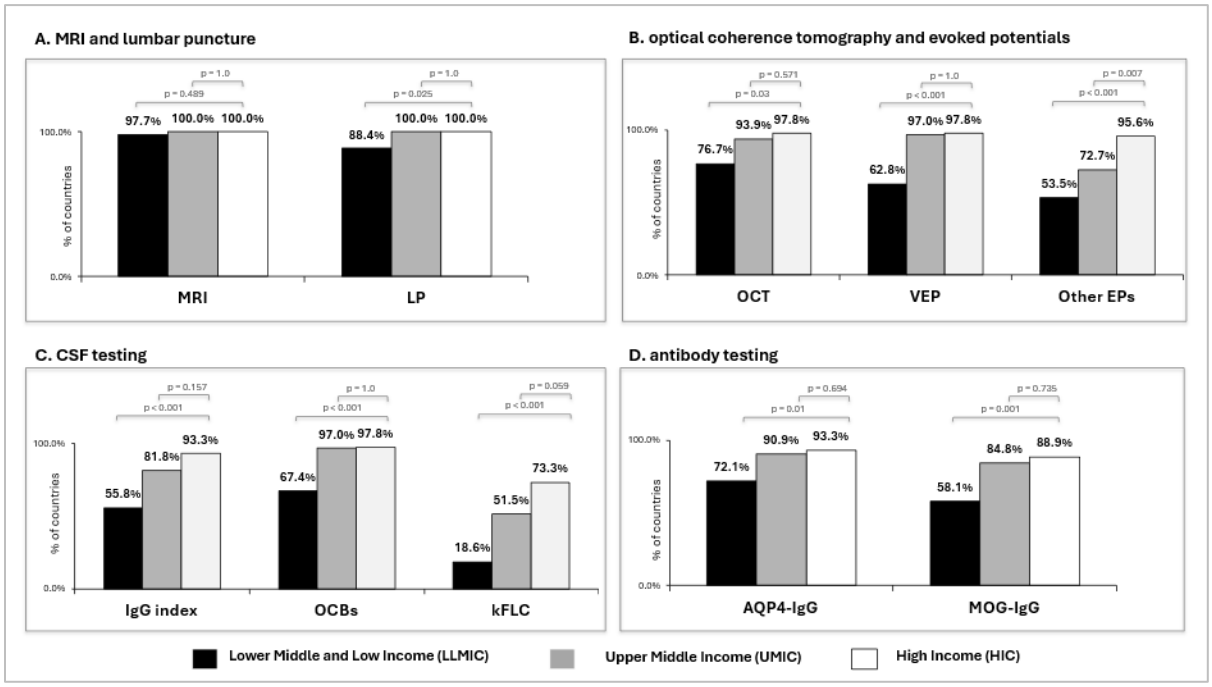
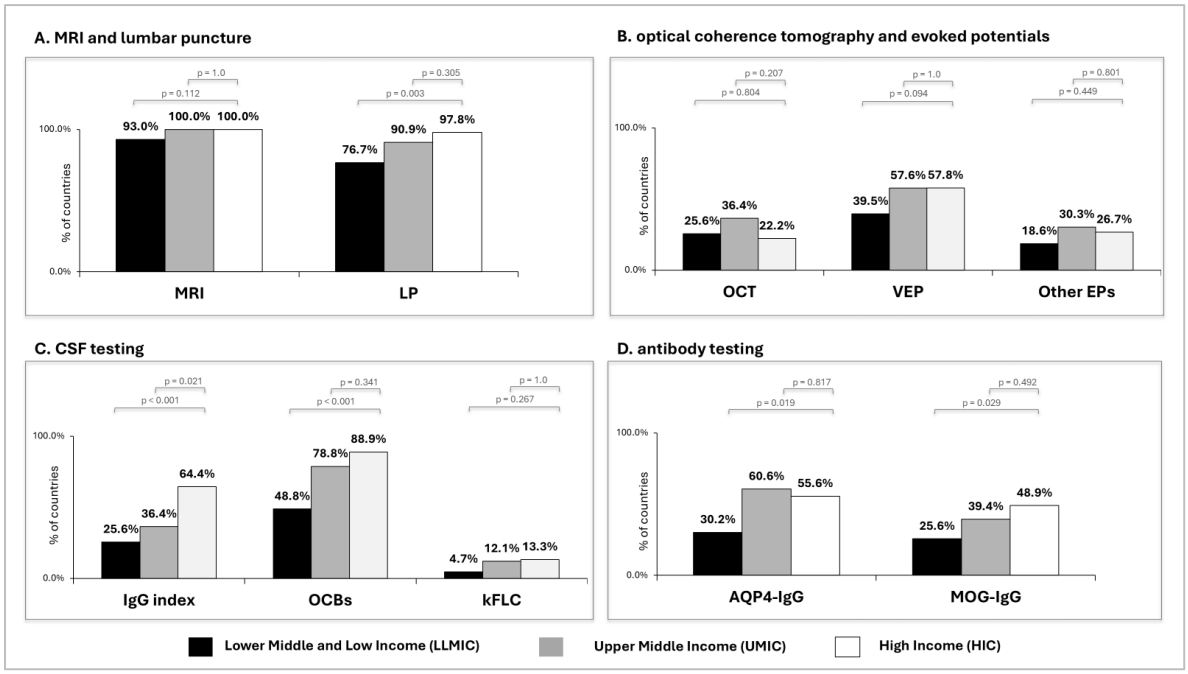


Figure 4. Routine use of paraclinical testing for the diagnostic evaluation of multiple sclerosis by World Bank income category.

Panels show the proportion of countries reporting routine use of ten paraclinical tests, grouped as: (A) MRI and lumbar puncture (B) optical coherence tomography (OCT) and visual evoked potentials (VEP), and other evoked potentials; (C) CSF-testing : IgG index, oligoclonal bands (OCBs, kappa free light chains (kFLC); and (D) antibody testing (AQP4-IgG and MOG-IgG). Bars indicate low and lower-middle-income countries (LLMIC), upper-middle-income countries (UMIC), and high-income countries (HIC). Brackets denote pairwise comparisons between World Bank income groups using Fisher's exact test; corresponding p-values are shown.



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