PRACTICE CURRENT

Approach to Managing the Initial Presentation of Multiple Sclerosis

A Worldwide Practice Survey

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Abstract

Background and Objectives

Available disease-modifying therapies (DMTs) for multiple sclerosis (MS) are rapidly expanding; although escalation approaches aim to balance safety and efficacy, emerging evidence suggests superior outcomes for people with MS who are exposed to early high-efficacy therapies. We aimed to explore practice differences in prevailing management strategies for relapsing-remitting MS.

Methods

We used a worldwide electronic survey launched by the Practice Current section of *Neurology® Clinical Practice*. Questions pertained to a case of a 37-year-old woman presenting with optic neuritis. Respondents were asked to indicate their initial investigations, relapse management strategy, choice of disease-modifying therapy, and plan for follow-up imaging (contrast/noncontrast). Survey responses were stratified by key demographic variables along with 95% confidence intervals (95% CIs).

Results

We received 153 responses from 42 countries; 32.3% responders identified as MS specialists. There was a strong preference for intravenous delivery of high-dose corticosteroids (87.7%, 95% CI 80.7–92.5), and most of the responders (61.3%, 95% CI 52.6–69.4) indicated they would treat a nondisabling (mild sensory) MS relapse. When asked to select a single initial DMT, 56.6% (95% CI 47.6–65.1) selected a high-efficacy therapy (67.5% MS specialists vs 53.7% non-MS specialists). The most selected agents overall were fingolimod (14.7%), natalizumab (15.5%), and dimethyl fumarate (20.9%). Two-thirds of respondents indicated they would request contrast-enhanced surveillance MRI.

Discussion

Although there is a slight preference for initiating high-efficacy DMT at the time of initial MS diagnosis, opinions regarding the most appropriate treatment paradigm remain divided.

Introduction

Proliferation of available disease-modifying therapies for multiple sclerosis (MS) has led to a modern era of MS treatment with increased availability of and choice among high-efficacy therapies.[1] Coinciding with increased availability, several large observational studies have demonstrated that early intensive therapy improves disability outcomes,[2,3] decreases risk of progression to SPMS,[4] and increases the probability of NEDA-3 at 2 years.[5] However, existing guidelines suggest a risk stratification or escalation approach, presumably prioritizing safety

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and cost-effectiveness.[6] The rapid evolution of MS therapies and the supporting literature base may be widening practice variation, leaving MS care providers and individuals living with MS behind.

In addition to the controversy surrounding disease-modifying therapy selection, evolving diagnostic advancements have produced uncertainty about management of MS relapses, including calls for an updated optic neuritis corticosteroid treatment trial.[7] The contemporary diagnostic workup for optic neuritis has advanced to include cell-based assays for anti-aquaporin-4 and anti-MOG antibodies,[7] along with superior long-term visual outcome measures such as optical coherence tomography, patient-reported outcome measures (PROMs), and low-contrast visual acuity.[7] This, along with a paucity of other landmark studies to guide corticosteroid management of MS relapses, raises questions about how to accurately counsel patients about corticosteroid treatment, particularly those whose symptoms do not interfere with daily activities.

A third area of emerging uncertainty in MS management relates to use of gadolinium-based contrast agents (GBCAs) for surveillance neuroimaging. GBCAs have been associated with nephrogenic systemic fibrosis; although this condition is exceedingly rare (occurring in people with severe renal failure), its potentially lethal impact has raised discomfort in providers who order frequent MRI scans with GBCAs.[8] Recent autopsy studies have shown gadolinium deposition in bone and skin tissues as well as within the globus pallidus, dentate nucleus, and white matter.[9] Despite a paucity of research demonstrating adverse effects associated with gadolinium retention, anecdotally many MS care providers are shifting away from performing surveillance neuroimaging with GBCAs.

Practice Current is a worldwide electronic survey platform developed by *Neurology: Clinical Practice* to capture real-life decision making for clinical scenarios where enduring areas of uncertainty may produce practice differences. Using the Practice Current platform, we developed and launched a survey entitled "How Do You Manage the Initial Clinical Presentation of Multiple Sclerosis?" to explore (1) selection of initial disease-modifying therapy, (2) corticosteroid treatment of MS relapses, and (3) use of gadolinium-enhanced MRI for routine disease surveillance. We aimed to describe inconsistencies in the approach to these common clinical scenarios by surveying clinicians on their current MS practice; these data are needed to kindle initiatives to address practice heterogeneity in routine MS care.

Methods

Survey Development

Our anonymous electronic survey was launched by the Practice Current section of *Neurology: Clinical Practice*.[10] We developed 11 original clinical questions that pertained to an evolving clinical scenario (eAppendix 1). The clinical scenario was developed by a MS specialist and trainee to simulate a commonly encountered first presentation of relapsing-remitting MS. Questions aimed to assess practice patterns in areas where there was uncertain or newly emerging supporting evidence. The survey was further refined for readability by the editors of Practice Current and informally pilot tested by the editors and survey authors. The scenario consisted of a 36-year-old woman presenting with optic neuritis who was found to have mild asymptomatic dysdiadochokinesia and a text description of brain MRI findings suggestive of MS (images not provided). Respondents were provided with a list of potential serologic, CSF, and neuroimaging investigations (cervical spine MRI, thoracic spine MRI, routine CSF studies, oligoclonal bands, systemic screening, NMOSD-IgG, MOG-IgG) and asked to select which studies they would typically perform in this scenario. They were told that the patient had left eye visual acuity of 20/70 and asked whether they would offer the patient therapy to manage this episode of demyelination. They were asked to specify which specific therapy they would offer (high-dose intravenous steroids, high-dose oral steroids, plasmapheresis, or low-dose oral steroids). They were then asked to indicate whether they would offer treatment if the patient had presented with a nondisabling (e.g., sensory) relapse. Upon being provided with information that the patient had a spinal cord lesion and positive oligoclonal bands, they were asked to specify whether they believed this patient was at risk of developing a severe course of multiple sclerosis.

Respondents were asked which disease-modifying therapy agent they would recommend. They were first given the opportunity to select all therapies they considered appropriate from a list of available disease-modifying therapies. Next, they were asked to write in a single preferred agent that they would offer in this clinical scenario. They were told that at 6-month follow-up, the patient's noncontrast brain MRI shows 2 new hyperintense supratentorial T2 lesions and asked whether they would continue, escalate, or switch to a disease-modifying therapy within the same efficacy category.

Respondents were asked how frequently they would suggest this patient be seen in follow-up by a neurologist or MS specialist (annually/every 6 months/every 3 months/other) and the suggested frequency of surveillance neuroimaging (annually/every 6 months/other). They were then asked to indicate whether they would order MRI with or without contrast.

At the end of the survey, respondents were asked to answer 8 demographic questions, including their current role (e.g., trainee/consultant/mid-level practitioner), primary work setting (outpatient or hospital-based), patient population (adults/children/both), number of years in practice, number of new MS cases they had managed in the past 12 months, and whether they were an MS specialist. Respondents were also asked to indicate the location of their practice regarding continent, country, and state (if applicable).

Participation did not require membership in the American Academy of Neurology (AAN) or subscription to AAN journals. No compensation was offered. A link to the questionnaire was available in the *Neurology*® journals' webpages, in online ads and the print version of the journals, and in the Practice Current dedicated webpage. The survey was advertised by the AAN and *Neurology* journals through social media. Individual internet protocol addresses were collected to ensure authenticity of responses. We opened the survey from July 23, 2021, to January 7, 2022, and all responses collected were included in the analysis.

Statistical Analysis

The frequency of responses for each scenario was calculated for different demographic groups, focusing on (1) subspecialty status (MS specialist vs not) and (2) location of practice (high-income country [HIC] or a low/middle-income country [LMIC]). Countries were classified according to the 2023 World Bank Country Classification. For the question which asked respondents to write in which single agent they would choose for the described patient, responses were collapsed into "high-efficacy" and "low-efficacy" categories: The high-efficacy category included alemtuzumab, cladribine, cyclophosphamide, fingolimod, natalizumab, ocrelizumab, ofatumumab, ozanimod, ponesimod, rituximab, and siponimod, and the low-efficacy category included corticosteroid, dimethyl fumarate, glatiramer acetate, interferon-beta, mycophenolate mofetil, PLEX, and teriflunomide. Multivariable analyses were precluded by low response numbers. Distributions of binary responses were estimated with binomial distribution and presented as 95% confidence intervals. All analyses were performed using R version 4.2.2.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was certified as exempt from review by the Children's National Medical Center Institutional Review Board.

Data Availability

Anonymized data will be shared on request from any qualified investigator.

Results

Demographics

We received a total of 153 responses from 42 countries. Characteristics of 128 participants who completed the demographic questionnaire are presented in Table 1. One-third of the responders identified as MS specialists, and trainees (residents and fellows) made up another third of the sample population (Table 1). One quarter of participants had seen more than 20 people with a new MS diagnosis in the past year (Table 1). Participants practicing in North America, Europe, or Asia made up most of the sample population (84.6%); one-third practiced in a LMIC (Table 1).

Table 1 Demographic Characteristics of Survey Participants (Available for 128 of 153)

Demographic Characteristic	n	Proportion (%)
MS specialist		
Yes	42	32.3
Number of *new* patients with MS seen in the past year		
>50	11	8.5
20–50	22	16.9
1–20	80	61.5
None	17	13.1
Provider role		
Consultant physician	77	59.2
Resident or fellow	48	36.9
Nurse practitioner or physician assistant	5	3.9
Years in training		
10 or more years	44	33.9
Less than 10 y	47	36.2
In training	39	30.0
Patient population		
Adult	104	80.0
Both adults and children	20	15.4
Children	6	4.6
Primary setting		
Hospital or inpatient	78	60.0
Outpatient	52	40.0
Continent of practice		
North America	49	38.0
Europe	42	32.6
Asia	18	14.0
South America	12	9.3
Africa	5	3.8
Australia	3	2.3
Country of practice (top 5 of 42)		
United States	39	30.2
Italy	8	6.2
Brazil	5	3.9
Germany	5	3.9
Turkey	5	3.9
Country type[a]		
High income	89	69.5
Low or middle income	39	30.5

[a] Classified by the 2023 World Bank Country Classification.

Components of Diagnostic Workup

The proportion of respondents ordering specific serologic, CSF, and neuroimaging investigations as part of their MS diagnostic workup are presented in Table 2. Most clinicians indicated that they would request cervical spine MRI in an individual with suspected MS; thoracic spine imaging was less commonly requested (Table 2). Approximately half of the respondents indicated that they would pursue routine CSF testing (60.9% of non-MS specialists (95% CI 49.85–71.0) vs 45.2% of non-MS specialists (95% CI 30.2–61.2)). Similarly, roughly half of the participants selected to send serum antibodies for NMOSD or MOGAD (Table 2).

Relapse Treatment

Nearly all participants (95.2%, 95% CI 90.0–97.9%) indicated they would treat the current patient with corticosteroids, with a strong preference for intravenous (87.7%, 95% CI 80.7–92.5%) rather than oral formulations (Figure 1). A small majority (61.3%, 95% CI 52.6–69.4) of participants indicated that they would choose to treat a nondisabling MS relapse; proportions were similar between MS specialists and non-MS specialists as well as between LMICs and HICs (Figure 1).

Selection of Initial Disease-Modifying Therapy

When participants were allowed to indicate multiple agents as appropriate initial disease-modifying therapies, the most selected agents were dimethyl fumarate (49.0%), fingolimod (41.8%), and glatiramer acetate (37.3%) (Figure 2a). When participants were allowed to recommend only 1 agent, dimethyl fumarate (20.9%), natalizumab (15.5%), and fingolimod (14.7%) were most suggested (Figure 2b). Slightly over half (56.6%, 95% CI 47.6–65.1) recommended a high-efficacy therapy as the initial agent (Figure 3). A larger proportion of MS specialists chose a high-efficacy agent for initial disease-modifying therapy compared with non-MS specialists (67.5%, 95% CI 50.8–80.9 vs 53.7%, 95% CI 42.4–64.6%) (Figure 3). Proportions of respondents choosing a high-efficacy therapy were similar between HICs (56.5%, 95% CI 45.3–67.0) and LMICs (61.1%, 95% CI 43.5–76.4) (Figure 3).

Influence of Perceived Severity on DMT Selection

In total, 59.4% (95% CI 50.9–67.5) felt that the patient was at risk of a severe MS course (Figure 3). Approximately 69.0% (95% CI 52.8–81.9) of MS specialists felt that the patient was at risk of a severe MS course, in contrast to 52.9% (95% CI 41.9–63.6) of non-MS specialists (Figure 3). The proportion of physicians indicating the patient was at risk of a severe disease course appeared lower in HICs (55.7%, 95% CI 44.7–66.1) vs LMICs (66.7%, 95% CI 49.7–80.4) (Figure 3). Initial high-efficacy therapy was selected by 41.1% (95% CI 27.9–55.8) of responders who did not think the patient was at risk of a severe MS course and 67.5% (95% CI 55.8–77.5) of responders who felt the patient was at risk of a severe MS course. After noting that the patient had 2 new lesions and a new neurologic examination finding at 1-year follow-up, 58.9% (95% CI 45.1–71.6) who initially selected a lower efficacy therapy indicated that they would escalate to a more potent disease-modifying therapy.

Surveillance Neuroimaging

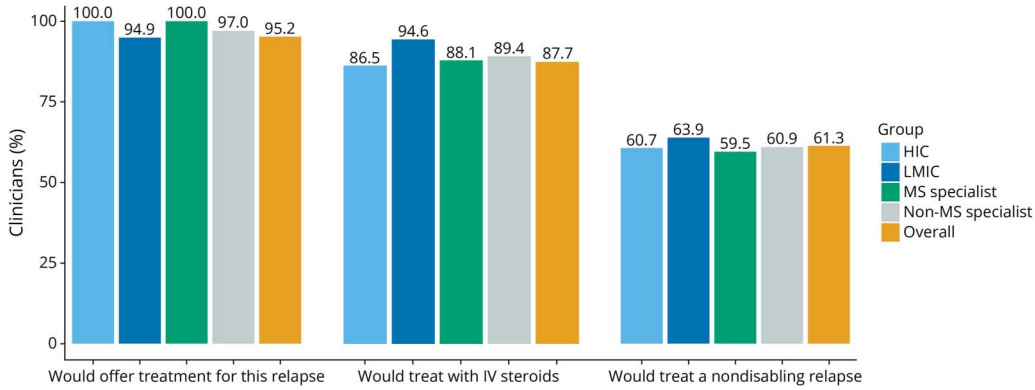
Half of the participants (48.6%, 95% CI 40.2–57.1) indicated that the patient should be seen in follow-up every 6 months, and another third (39.4%, 95% CI 31.5–48.0) suggested follow-up every 3 months. Responses were divided as to whether surveillance neuroimaging should be performed annually (49.3%, 95% CI 40.9–57.8) vs every 6 months (41.5%, 95% CI 33.4–50.1). Overall, 69.2% (95% CI 60.9–76.5) indicated that they would repeat surveillance imaging with gadolinium enhancement; 61.9% (95% CI 45.7–76.0) of MS specialists indicated a preference for

Table 2 Responses to the Question "Which of the Following Tests Would You Include as Part of Your Initial Workup for This Patient?"

	All responders (N = 153) % (95% CI)	MS specialist (N = 42) % (95% CI)	Non-MS specialist (N = 87) % (95% CI)
Cervical spine MRI	85.6 (78.8–90.6)	90.5 (76.5–96.9)	88.5 (79.4–94.1)
Thoracic spine MRI	59.5 (51.2–67.2)	66.7 (50.4–80.0)	52.3 (44.1–60.4)
Routine CSF studies[a]	52.3 (44.1–60.4)	45.2 (30.2–61.2)	60.9 (49.8–71.0)
Oligoclonal bands[b]	69.3 (61.2–76.3)	59.5 (43.3–74.0)	77.0 (66.5–85.1)
Systemic screening[c]	57.5 (49.3–65.4)	61.9 (45.7–76.0)	64.4 (53.3–74.1)
Serum NMOSD-IgG	56.9 (48.6–64.8)	54.8 (38.8–69.8)	63.2 (52.1–73.1)
Serum MOG-IgG	47.7 (39.6–55.9)	57.1 (41.1–71.9)	48.3 (37.5–59.2)

Respondents were given the option to check all that applied or select "None of the above."
MOG-IgG = serum myelin oligodendrocyte glycoprotein (MOG) IgG antibodies; NMOSD-IgG = aquaporin-4 IgG antibodies.
[a] CSF cell counts, protein, glucose, viral panel, and bacterial culture.
[b] CSF and serum.
[c] Screening serology for systemic autoimmune disease (ANA, ENA, C3, C4).

Figure 1 Clinician Preferences for Treatment of MS Relapses by Specialization and Country Type



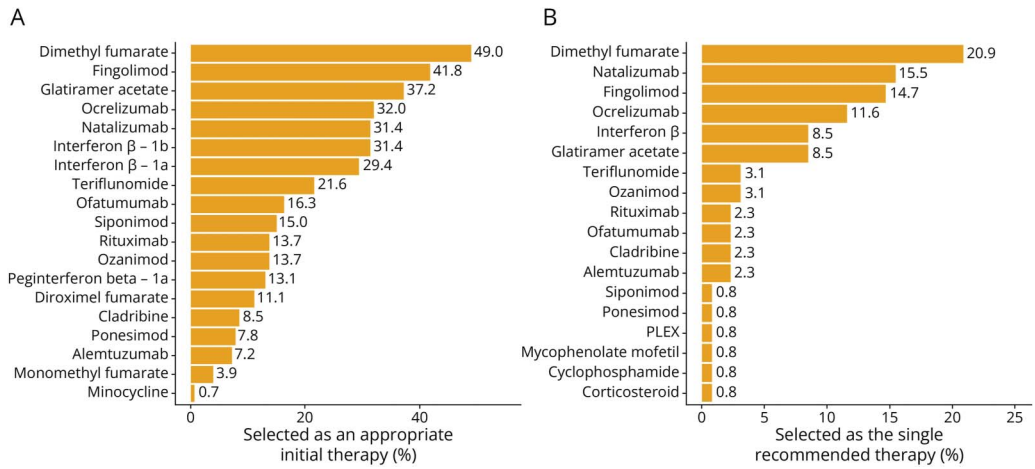
Described clinical relapse was a 3-day history of painful right eye vision loss with a corrected visual acuity of 20/70. Clinicians were able to select 1 treatment option (short course of high-dose intravenous (IV) corticosteroids, short course of high-dose oral corticosteroids, short course of low-dose oral corticosteroids, plasma exchange, IV immunoglobulin, or other). Participants were asked whether they would offer therapy for relapse management if symptoms were nondisabling (e.g., mild sensory loss). HIC = high-income country; LMIC = low/middle income country.

enhanced MRI imaging relative to 70.1% (95% CI 59.2–79.2) of non-MS specialists (Figure 3). A larger proportion of clinicians practicing in LMICs preferred enhanced MRI imaging for surveillance relative to HICs (LMICs = 82.1% (95% CI 65.9–91.9); HICs = 60.1% (95% CI 49.7–70.7)) (Figure 3).

Discussion

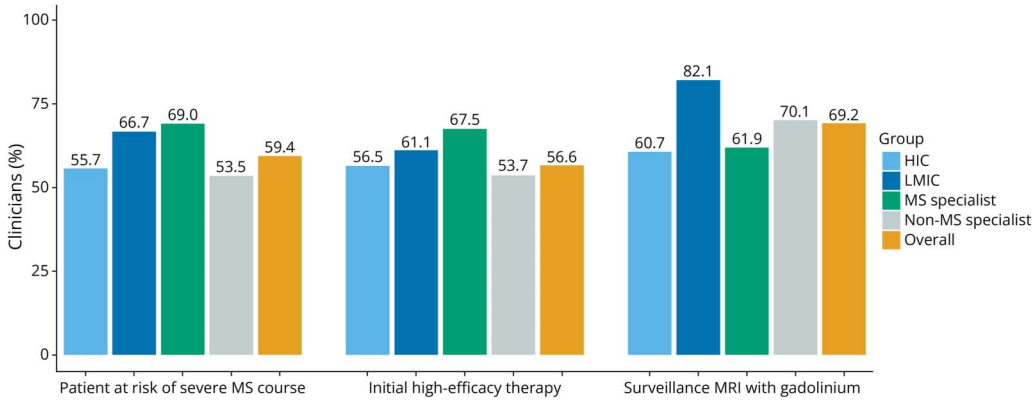
Our 42-country survey highlights overarching polarity in the use of high-efficacy MS therapies as well as emerging gaps in MS management between specialists and non-specialists; approximately half of the respondents preferred to start an individual with a new MS diagnosis on a high-efficacy therapy (67.5% of MS specialists vs 52.4% of nonspecialists). This may in part reflect guidance from Canadian MS Working Group Recommendations[11] and American Academy of Neurology Practice Guidelines[12] (published in 2020 and 2018, respectively), which favor a risk stratification approach to DMT selection. However, even among respondents who felt our illustrative patient was at risk of severe MS, only two-thirds selected high-efficacy therapy for initial treatment. Since publication of these guidelines, numerous observational studies have demonstrated advantages of early intensive therapy.[2,3,13] The ongoing randomized parallel trial DELIVER-MS (Determining the Effectiveness of earLy Intensive Versus Escalation Approaches for RRMS) is expected to complete in 2026 and hopefully will further inform treatment decisions and guideline development.[14] Although the proportion of respondents selecting initial high-efficacy therapy was similar between HICs and LMICs, it is conceivable that availability of high-efficacy agents in the

Figure 2 Overall Clinician Preferences for Initial Disease-Modifying Therapy Given a Described Clinical Scenario



(A) Respondents were provided a list of available disease-modifying therapies and asked to select the most appropriate initial disease-modifying therapies, assuming no risk of pregnancy (multiple responses allowed). (B) They were asked to write in the single agent that they would recommend. HIC = high-income country; LMIC = low/middle-income country.

Figure 3 Clinician Responses Stratified by Neurology Specialization (MS or Non-MS) and Income Level of Practicing Country



Respondents were asked to indicate whether they felt the described patient to be at a high risk of developing severe course of MS. Write-in responses for which single disease-modifying therapy that clinicians would select for the described patient were classified into high efficacy (alemtuzumab, cladribine, cyclophosphamide, fingolimod, natalizumab, ocrelizumab, ofatumumab, ozanimod, ponesimod, rituximab, siponimod) and low efficacy (other). Clinicians were asked to indicate what type of follow-up imaging they would like for the patient (contrast or non-contrast). HIC = high-income country; LMIC = low/middle income country.

respondent's region of practice may have influenced responses. However, even HICs encounter restrictions when prescribing disease-modifying therapies; for instance, the European Medicines Agency restricts the use of certain high-efficacy therapies to individuals with disabling relapses.[15] Another explanation is that high aversion to ambiguity and low tolerance to uncertainty produces therapeutic inertia, defined as the lack of treatment initiation or escalation when there is evidence of disease activity; prior research has suggested nearly 70% of physicians caring for individuals with MS are subject to this.[16]

Over half (58.9%) of the clinicians who initially selected a lower efficacy therapy indicated that they would escalate to a more potent disease-modifying therapy given a new neurologic examination finding and 2 new MRI brain lesions. However, as a re-baseline MRI and physical examination was not provided, it is possible that those who chose not to escalate therapy concluded that these findings occurred before onset of therapeutic efficacy. In the absence of a re-baseline MRI, this approach is reasonable, given delayed time to therapeutic effect with low-efficacy disease-modifying therapies.[17]

Approximately half of the respondents indicated that they would perform serum antibody testing for NMOSD or MOGAD. Although respondents electing to send serum antibodies were likely motivated to rule out diagnoses requiring a different therapeutic approach, those not sending serum antibodies likely recognized the case description as typical for MS (a 36-year-old patient with mild unilateral retrobulbar optic neuritis and antecedent periventricular lesions). It is important to note that 2023 International MOGAD Panel criteria emphasize that MOG-IgG testing is *not* recommended for screening of all patients with CNS inflammatory demyelination and caution against universal screening of all adults with optic neuritis.[18] These specific recommendations align with the 2018 MOG Encephalomyelitis International Recommendations[19] and the 2020 Canadian MS Working Group Recommendations.[11]

The overwhelming majority (87.7%) of respondents indicated a preference for intravenous (rather than oral) high-dose corticosteroids when managing a disabling MS relapse. This is surprising given that 2 meta-analyses have found oral corticosteroids to be noninferior to intravenous corticosteroids,[20,21] and a 2018 single-blind randomized trial demonstrated equivalence of oral and intravenous corticosteroids for acute optic neuritis treatment at 6 months of follow-up.[22] Oral corticosteroids offer the advantage of convenience, as well as decreased cost to patients and health care systems; persistence of provider preference for intravenous corticosteroids requires exploration. Potential hypotheses for the enduring use of intravenous corticosteroids despite biological equivalence include ease of delivery for otherwise hospitalized patients, ensured compliance, and perceptions that adverse effects are decreased with intravenous delivery.

The notion that receiving corticosteroids for acute MS relapses serves only to hasten short-term recovery without affecting long-term outcomes is a long-standing dictum in MS care. Despite this, our survey showed that 61.3% of MS care providers would elect to treat a nondisabling MS relapse. This may reflect discomfort with the existing evidence base; the 1992 Optic Neuritis Treatment Trial (ONTT) is the pivotal study which reported that high-dose corticosteroid treatment does not influence long-term disability.[23] However, application of this trial to patients with MS is somewhat speculative—the ONTT only included 158 patients with clinically definite MS in the high-dose corticosteroid treatment group at 5-year follow-up.[24] More importantly, the ONTT only evaluated one type of relapse (optic neuritis), a

neuroanatomical location which only accounts for 20% of MS relapses,[25] and is not the primary driver of MS-related disability accumulation.[26] More research is needed to understand the long-term outcomes of treating other relapse types, particularly spinal cord lesions. Notably, a recent MSBase study demonstrated that early nondisabling relapses are associated with a heightened risk of disability accumulation—providing additional support for the hypothesis that corticosteroid treatment of all MS relapses influences long-term outcomes for individuals with MS.[15]

A preference for radiologic surveillance with contrast-enhanced MRI was indicated by three quarters of respondents (69.2%); a relatively larger proportion of non-MS specialists preferred enhanced neuroimaging (72.6% vs 63.4%). The 2021 Magnetic Resonance Imaging in Multiple Sclerosis-Consortium of Multiple Sclerosis Centres-North American Imaging in Multiple Sclerosis Cooperative Consensus Recommendations suggest performing surveillance MS imaging with contrast enhancement for patients with diffuse and confluent chronic multiple sclerosis lesions and for re-baselining if MRI imaging was not performed appropriately after starting disease-modifying therapy or it has been over 1 year since the last MRI scan.[27] These recommendations reflect that nonenhanced imaging can be used for PML surveillance and adequately detects new or enlarging T2 lesions in individuals with mild-moderate lesion burden.[28] This notion is supported by a recent retrospective MRI study which demonstrated that 92.1% of enhancing lesions corresponded to a new or enlarging T2 lesion and that GBCA administration modified the classification of MS as active in only 1.2% of patients.[29] Unfortunately, our survey design did not allow respondents to indicate varying preference for enhanced vs nonenhanced imaging in different clinical settings; this is an important question that could be addressed with future research.

This descriptive and exploratory study is subject to several limitations. Our population was self-selected from the readership of AAN journals, websites, and media channels and may not be representative of worldwide practice patterns. It is important to recognize that the small sample of MS specialists in our study were self-identified and that responses from this group should not be considered an expert consensus. Unfortunately, the descriptive nature of our study and small sample size precluded multivariable analysis, and as a result, we cannot evaluate geographic trends or effect modification by clinical practice demographics. Although our results suggest several differences between groups (i.e., MS specialists and non-MS specialists), our wide confidence intervals imply low precision, and we cannot be sure that these differences truly exist. Nonetheless, the primary intention of this study (to spark a narrative highlighting MS practice variability and areas of evidence scarcity) is appropriately addressed with the current design and sample population.

Although our survey demonstrated a slight preference for high-efficacy DMT at the time of initial MS diagnosis, opinions regarding the most appropriate treatment paradigm remain divided. Our study revealed polarized opinions regarding corticosteroid treatment of nondisabling MS relapses and use of GBCAs for routine surveillance neuroimaging. More research is needed in these areas to guide clinician decision making. There is a clear need for updated MS clinical practice guidelines, and we call on national and international MS organizations to rise to this task, aiming specifically to provide recommendations to guide selection of initial DMT, relapse management, and use of GBCAs for surveillance neuroimaging.

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Aravind Ganesh, MD, PhD	Department of Clinical Neurosciences; Hotchkiss Brain Institute, University of Calgary, Canada	Major role in the acquisition of data; study concept or design
Luca Bartolini, MD, FAAN, FAES	Hasbro Children's Hospital, Brown University, Providence, RI	Major role in the acquisition of data; study concept or design
Tomas Kalincik, MD, PhD	Neuroimmunology Centre, Department of Neurology, Royal Melbourne Hospital; Clinical Outcomes Research Unit, Department of Medicine, University of Melbourne, Australia	Major role in the acquisition of data; study concept or design; analysis or interpretation of data

References

1. Tintore M, Vidal-Jordana A, Sastre-Garriga J. Treatment of multiple sclerosis—success from bench to bedside. *Nat Rev Neurol.* 2019;15(1):53-58. doi:10.1038/s41582-018-0082-z
2. Harding K, Williams O, Willis M, et al. Clinical outcomes of escalation vs early intensive disease-modifying therapy in patients with multiple sclerosis. *JAMA Neurol.* 2019;76(5):536-541. doi:10.1001/jamaneurol.2018.4905
3. He A, Merkel B, Brown JWL, et al. Timing of high-efficacy therapy for multiple sclerosis: a retrospective observational cohort study. *Lancet Neurol.* 2020;19(4):307-316. doi:10.1016/S1474-4422(20)30067-3
4. Brown JWL, Coles A, Horakova D, et al. Association of initial disease-modifying therapy with later conversion to secondary progressive multiple sclerosis. *JAMA.* 2019;321(2):175-187. doi:10.1001/jama.2018.20588
5. Alonso R, Casas M, Lazaro L, et al. Achieving no evidence of disease activity-3 in highly active multiple sclerosis patients treated with cladribine and monoclonal antibodies. *Mult Scler J Exp Transl Clin.* 2023;9(1):20552173231154712. doi:10.1177/20552173231154712
6. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology.* 2002;58(2):169-178. doi:10.1212/wnl.58.2.169
7. Petzold A, Braithwaite T, van Oosten BW, et al. Case for a new corticosteroid treatment trial in optic neuritis: review of updated evidence. *J Neurol Neurosurg Psychiatry.* 2020;91(1):9-14. doi:10.1136/jnnp-2019-321653
8. Woolen SA, Shankar PR, Gagnier JJ, MacEachern MP, Singer L, Davenport MS. Risk of nephrogenic systemic fibrosis in patients with stage 4 or 5 chronic kidney disease receiving a group II gadolinium-based contrast agent: a systematic review and meta-analysis. *JAMA Intern Med.* 2020;180(2):223-230. doi:10.1001/jamainternmed.2019.5284
9. Kobayashi M, Levendovszky SR, Hippe DS, et al. Comparison of human tissue gadolinium retention and elimination between gadoteridol and gadobenate. *Radiology.* 2021;300(3):559-569. doi:10.1148/radiol.2021204320
10. Neurology Clinical Practice Practice Current page. Accessed August 2, 2024. https://www.neurology.org/practice-current
11. Freedman MS, Devonshire V, Duquette P, et al. Treatment optimization in multiple sclerosis: Canadian MS Working Group recommendations. *Can J Neurol Sci.* 2020;47(4):437-455. doi:10.1017/cjn.2020.66
12. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology.* 2018;90(17):777-788. doi:10.1212/WNL.0000000000005347
13. Amato MP, Fonderico M, Portaccio E, et al. Disease-modifying drugs can reduce disability progression in relapsing multiple sclerosis. *Brain.* 2020;143(10):3013-3024. doi:10.1093/brain/awaa251
14. Ontaneda D, Tallantyre EC, Raza PC, et al. Determining the effectiveness of early intensive versus escalation approaches for the treatment of relapsing-remitting multiple sclerosis: the DELIVER-MS study protocol. *Contemp Clin Trials.* 2020;95:106009. doi:10.1016/j.cct.2020.106009
15. Daruwalla C, Shaygannejad V, Ozakbas S, et al. Early non-disabling relapses are important predictors of disability accumulation in people with relapsing-remitting multiple sclerosis. *Mult Scler.* 2023;29(7):875-883. doi:10.1177/13524585231151951
16. Saposnik G, Sempere AP, Prefasi D, et al. Decision-making in multiple sclerosis: the role of aversion to ambiguity for therapeutic inertia among neurologists (DIScUTIR MS). *Front Neurol.* 2017;8:65. doi:10.3389/fneur.2017.00065
17. Roos I, Leray E, Frascoli F, et al. Delay from treatment start to full effect of immunotherapies for multiple sclerosis. *Brain.* 2020;143(9):2742-2756. doi:10.1093/brain/awaa231
18. Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: international MOGAD Panel proposed criteria. *Lancet Neurol.* 2023;22(3):268-282. doi:10.1016/S1474-4422(22)00431-8
19. Jarius S, Paul F, Aktas O, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. *J Neuroinflammation.* 2018;15(1):134. doi:10.1186/s12974-018-1144-2
20. Burton JM, O'Connor PW, Hohol M, Beyene J. Oral versus intravenous steroids for treatment of relapses in multiple sclerosis. *Cochrane Database Syst Rev.* 2012;12:CD006921. doi:10.1002/14651858.CD006921
21. Liu S, Liu X, Chen S, Xiao Y, Zhuang W. Oral versus intravenous methylprednisolone for the treatment of multiple sclerosis relapses: a meta-analysis of randomized controlled trials. *PLoS ONE.* 2017;12(11):e0188644. doi:10.1371/journal.pone.0188644
22. Morrow SA, Fraser JA, Day C, et al. Effect of treating acute optic neuritis with bioequivalent oral vs intravenous corticosteroids: a randomized clinical trial. *JAMA Neurol.* 2018;75(6):690-696. doi:10.1001/jamaneurol.2018.0024
23. Beck RW, Cleary PA. Optic neuritis treatment trial: one-year follow-up results. *Arch Ophthalmol.* 1993;111(6):773-775. doi:10.1001/archopht.1993.01090060061023
24. Optic Neuritis Study Group. The 5-year risk of MS after optic neuritis: experience of the optic neuritis treatment trial. *Neurology.* 1997;49(5):1404-1413. doi:10.1212/wnl.49.5.1404
25. Kalincik T, Buzzard K, Jokubaitis V, et al. Risk of relapse phenotype recurrence in multiple sclerosis. *Mult Scler.* 2014;20(11):1511-1522. doi:10.1177/1352458514528762
26. Stewart T, Spelman T, Havrdova E, et al. Contribution of different relapse phenotypes to disability in multiple sclerosis. *Mult Scler.* 2017;23(2):266-276. doi:10.1177/1352458516643392
27. Wattjes MP, Ciccarelli O, Reich DS, et al. 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. *Lancet Neurol.* 2021;20(8):653-670. doi:10.1016/S1474-4422(21)00095-8
28. Rovira À, Wattjes MP. Gadolinium should always be used to assess disease activity in MS—No. *Mult Scler.* 2020;26(7):767-769. doi:10.1177/1352458520914819
29. Gentili L, Capuano R, Gaetani L, et al. Impact of post-contrast MRI in the definition of active multiple sclerosis. *J Neurol Sci.* 2022;440:120338. doi:10.1016/j.jns.2022.120338

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