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Optimizing Outcomes in Multiple Sclerosis Through Individualized Treatment: Managed Care Considerations

KEY TAKEAWAYS

- Multiple sclerosis (MS) is a chronic demyelinating disease with a heterogeneous presentation that can result in permanent neurologic damage and disability.^{1,3}
- Early initiation of treatment and adherence to disease-modifying therapies (DMTs) have been shown to help reduce disease relapses and disability progression which may help reduce the associated health care resource utilization and cost burdens.⁴⁻⁸
- Barriers to treatment access, such as those related to insurance and out-of-pocket (OOP) costs for patients, can impact adherence to DMTs and lead to greater health care resource utilization; social determinants of health may also impact treatment.⁹⁻¹²
- Consensus guidelines from national MS organizations highlight the importance of early treatment with a DMT to delay damage, progression, and disability. They emphasize that a DMT should be chosen based on the patient's individual needs and preferences as well as on clinical condition and disability prognosis.¹³⁻¹⁴

INTRODUCTION

MS is a chronic, neuroinflammatory disorder that affects the brain and spinal cord.^{2,15} Multiple DMTs are available in different forms to slow disease progression and slow accumulation of disability; however, there is currently no cure for MS.³ Therefore, treatment considerations include providing patients with early access to an optimal DMT to help prevent accumulation of irreversible central nervous system (CNS) damage that can lead to increased disability and progressive disease and to limit the occurrence and severity of relapses, as well as providing support to help ensure patients are able to adhere to treatment.^{2,4,13,14} Relapse and disability progression are associated with high overall health care resource utilization and substantial direct health care costs.^{7,8} Access and adherence to treatment can be hindered by insurance-related barriers (eg, high cost-sharing for patients) and social determinants of health that result in differences in access to and utilization of health care in underserved populations.^{9-11,16} This article will explore the economic impact of these barriers with the objective of increasing awareness and understanding of these factors to facilitate positive outcomes in patients with MS.

BACKGROUND: MS IS A HETEROGENEOUS DISEASE

Disease Overview and Diagnosis

MS is a chronic, immune-mediated disease characterized by disseminated lesions throughout the CNS that appear as focal areas of demyelination, inflammation, and glial reaction.^{1,17} Patients with MS may experience symptoms such as pain and fatigue, as well as signs of neurologic dysfunction that include sensory and visual disturbances, motor impairments, and cognitive deficits.² Initial presentation is heterogeneous and related to the location of the CNS lesions.¹ Patients may experience continuous progression of symptoms or have periods of reduced or absent disease activity.^{1,2} Because of this heterogeneity, patients may initially present to a wide range of medical providers (eg, general practitioners, ophthalmologists, orthopedic surgeons), although referral to a neurologist is recommended if a patient is suspected to have MS.¹

In 2013, the International Advisory Committee on Clinical Trials in MS updated their definitions of MS to include the following 4 types based on assessments of disease activity and progression:

clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS).¹⁸ A relapse in MS is an inflammatory demyelinating event in 1 or more CNS locations that occurs for at least 24 hours without a precipitating fever or infection and results in noticeable symptoms and neurologic abnormality upon clinical examination.¹⁹ The first instance of such an event is CIS.¹⁹ Patients who experience multiple attacks between periods of stable neurologic disability are diagnosed with RRMS.¹⁹ About 10% to 15% of patients experience a steady progression in neurologic disability from disease onset that typically does not feature periods of remission; this is known as PPMS.^{1,19} Some patients with RRMS develop progressive disease over time, transitioning from RRMS to SPMS.^{1,19}

Relapses are associated with CNS inflammation and damage and followed by periods of remission characterized by clinical and symptom recovery with reduced disability.² Neurologic damage eventually accumulates as recovery during remission lessens, leading to increased disability and, ultimately, progressive disease in most patients.² Therefore, immediate initiation of treatment when a diagnosis of MS is confirmed is advisable to limit irreversible CNS damage.¹⁴ Accurately diagnosing MS as early as possible is critical to supporting early initiation of effective treatments.¹

US Epidemiology

Between 2008 and 2010, the estimated average prevalence of MS in adults living in the United States increased by 6.3% per year, according to an analysis of private and public health insurance data sets during this time period.²⁰ In 2010, the highest prevalence of MS in both men and women was seen among those aged 55 to 64 years.²⁰ According to the most recent estimate available, nearly 1 million adults (range, 851,749-913,925) were living with MS in the United States in 2017.²⁰

In 2010, more than 70% of patients with MS in the United States were women, and evidence suggests that Black women are at higher risk than White women.^{20,21} The results of a 2013 US retrospective cohort study of data from Kaiser Permanente Southern California health plan members newly diagnosed with MS between 2008 and 2010 (N = 496) indicated that Black women had a significantly higher MS risk vs White women (risk ratio [RR], 1.59; 95% CI, 1.27-1.99), whereas Hispanic and Asian men and women had a significantly lower risk (RR, 0.42; 95% CI, 0.35-0.51) when compared with White men and women (RR, 0.20; 95% CI, 0.12-0.32; all $P \leq .0005$).²¹ In addition, Black women had more than 3 times the risk of developing MS than did Black men (95% CI, 2.07-4.81; $P < .0001$).^{21,*}

TREATMENT OF MS

DMTs are the mainstay of treatment for MS.¹³ The primary goal of treatment with DMTs is to reduce the occurrence of relapses and the formation of new CNS lesions.⁴ A full exploration of available DMTs is beyond the scope of this manuscript; however, at the time of this publication, 21 DMTs have been approved by the FDA.³

The American Academy of Neurology (AAN) notes that adherence is an important aspect of treatment and is necessary for full efficacy of DMT treatment.⁴ Adherence to a DMT can have a considerable effect on relapse activity.^{4,5,22} The results of a 2015 prospective, observational cohort study of patients with MS (N = 2966) showed that among participants who took the same DMT for 24 months (n = 2049), the proportion who did not experience relapse over that time period grew with increasing adherence (measured by medication possession ratio; $P < .0008$).²² In addition, in a 2017 retrospective study, investigators analyzed claims data from the MarketScan (Truven Health Analytics) Commercial Claims Database for the period between January 1, 2008 and September 30, 2015 for patients with MS initiating DMT treatment (N = 12,431).⁵ After controlling for sex, age at initiation of index DMT, and Charlson Comorbidity Index, when compared with those who were nonadherent, patients who were adherent to their index DMT were found to be approximately 42% less likely to experience relapse (odds ratio [OR], 0.576; 95% CI, 0.526-0.63; $P < .0001$) and had about a 52% lower risk of hospitalization and a 38% lower risk of visiting an emergency department (ED) (both $P < .0001$).^{5,†}

THE IMPORTANCE OF EARLY TREATMENT INITIATION

The Consortium of Multiple Sclerosis Centers (CMSC) recommends early initiation of treatment for MS.¹⁴ Early treatment can help minimize axonal damage—a key determinant of irreversible disability—and help minimize disease activity in the early relapsing phases, which is predictive of long-term disability.^{23,24} Early initiation of treatment after the first clinical event suggestive of MS also has been shown to reduce progression of disability in patients with MS compared with a delayed start of treatment.^{23,25}

Beginning treatment soon after disease presentation may lead to lower future disability scores, regardless of how well a patient recovers after an initial relapse.⁶ In a double-blind North American trial, patients with CIS were randomized within 27 days of symptom onset to receive 3 years of either a DMT or placebo.⁶ In a 2019 extension

*Limitations included the use of diagnostic coding data to identify incidence; thus, the classification of a patient as having MS was dependent upon clinicians' inference of demyelinating disease from symptoms and excluded misdiagnosed patients. In addition, the study population used was older at symptom onset and had more patients with progressive-onset MS vs other similar studies and included few members from Asian/Pacific Islander populations or Black or Hispanic men.²¹

†Limitations included the nature of administrative claims data wherein it could not be determined whether a DMT was used as prescribed. Furthermore, coding errors could have affected the identification of MS cases and DMT indexing. In addition, the cohort only included commercially insured patients, and the study did not collect data regarding clinical characteristics such as MS subtype, disability status, duration of disease, or other factors that may influence adherence or outcomes.⁵

study, all patients were offered up to 7 years of treatment with the DMT.⁶ After 10 years, 127 patients were stratified by recovery after initial relapse based on improvement in Expanded Disability Status Scale (EDSS) score.⁶ Patients with poor recovery who received immediate DMT treatment were as likely to remain at a minimal disability level 1 year after the beginning of their recovery as were those with good recovery who had delayed DMT treatment initiation.⁶

Some DMTs may lower the risk of disease progression more effectively than do others in patients with certain MS types.²⁶ In 2019, the MSBase Study Group published an analysis of data from an international cohort of 1555 patients with RRMS who initiated DMT treatment between 1988 and 2011.²⁶ Patients initially treated with agents showing higher efficacy (based on the results of clinical trials²⁷⁻²⁹) had a significantly lower risk of developing SPMS over a median of 5.8 years (interquartile range [IQR], 4.7-8.0 years) than did those treated with DMTs considered to be of lower efficacy (HR, 0.66; 95% CI, 0.44-0.99; $P = .046$).²⁶ Notably, even patients treated with lower-efficacy DMTs had a significantly lower risk of progression to SPMS over a median follow-up of 7.6 years (IQR, 5.8-9.6 years) versus patients who received no treatment (HR, 0.71; 95% CI, 0.61-0.81; $P < .001$).^{26,*}

COST BURDEN OF RELAPSE AND DISEASE PROGRESSION

The high cost and health care resource utilization associated with relapse and increased disability in MS highlight the importance of access to treatment early in the disease course.^{7,8}

Frequent relapses can have substantial economic effects, as demonstrated by the results of a 2021 retrospective, observational analysis of claims data from 2012 to 2018 from the MarketScan Commercial Claims and Encounters Database and the Medicare Supplemental and Coordination of Benefits database of adult patients with newly diagnosed MS.⁷ Of 8775 patients, those who experienced at least 1 relapse had significantly higher all-cause costs (mean difference, \$24,995; 95% CI, \$22,461-\$27,529; $P < .0001$) and MS-related costs

(mean difference, \$23,791; 95% CI, \$22,057-\$25,885; $P < .0001$) than did those who did not experience a relapse.^{7†}

Furthermore, a 2016 study of data from a 2013 to 2014 cross-sectional survey of neurologists treating US patients with MS showed that relapse and higher disability were associated with increased health care resource utilization and costs.⁸ The survey included both physician-reported data on clinical information and patient-reported data on health-related quality of life and impact of MS on employment and work productivity.⁸ For the previous 12 months, patients who experienced relapse had higher estimated average costs (+\$3693; 95% CI, \$1314-\$6072) associated with more frequent hospitalizations (incident rate ratio [IRR], 7.1; 95% CI, 3.3-15.5) and higher estimated average costs (+\$464; 95% CI, \$232-\$696) associated with higher health care resource utilization as measured by consultations with certain medical providers, including neurologists (IRR, 1.2; 95% CI, 1.1-1.4), primary care physicians (IRR, 1.5; 95% CI, 1.1-2.0), ED doctors (IRR, 15.6; 95% CI, 2.2-109.9), ophthalmologists (IRR, 4.3; 95% CI, 2.0-8.9), gastroenterologists (IRR, 7.0; 95% CI, 1.2-41.4), and psychiatrists (IRR, 2.8; 95% CI, 1.0-7.7) when compared with patients who experienced no relapse (all $P < .05$).⁸ In addition, patients with high disability scores (EDSS score > 5) had higher average costs (+\$10,883) associated with more frequent hospitalizations (IRR, 3.3; 95% CI, 1.6-6.8) as well as higher average costs (+\$730) associated with higher health care resource utilization as measured by consultations with neurologists (IRR, 1.4; 95% CI, 1.2-1.6), MS nurses (IRR, 44.4; 95% CI, 8.0-248.2), physiotherapists (IRR, 9.9; 95% CI, 3.2-30.7), urologists (IRR, 7.2; 95% CI, 2.2-23.6), and other providers versus patients with EDSS scores of less than 3 (all $P < .05$) over the same time period.^{8,*}

BARRIERS TO TREATMENT ACCESS

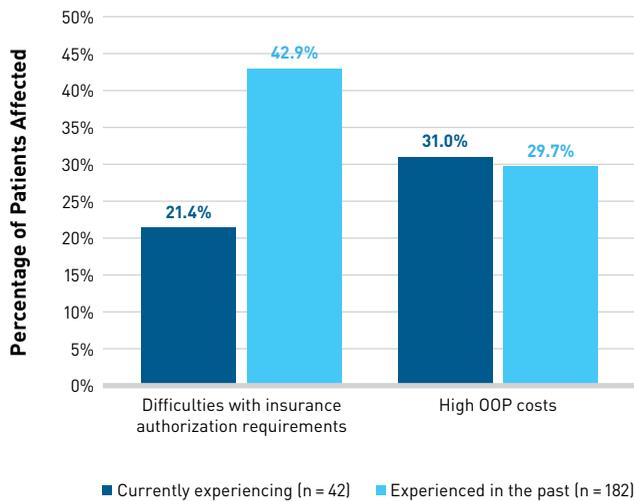
Barriers to treatment access in patients with MS include those related to insurance (eg, high OOP costs, increased cost-sharing, prior authorization requirements) and aspects of social determinants of health.^{9-11,16}

*Limitations included the observational design of the study, as the analysis was unable to distinguish between prevention of and delay of progression to SPMS. In addition, assessment of disability relied on total EDSS score, which may have captured SPMS less accurately and sensitively than would the most restrictive definition of the disease. Differing baseline demographics between treatment cohorts led to different follow-up durations for matched untreated cohorts. Incomplete reporting prevented the inclusion of non-MS-related mortality risk. Finally, risks associated with individual DMTs were not assessed.²⁶

†Relapse was defined as severe (MS as the primary diagnosis, resulting in hospitalization) or mild/moderate (MS as the primary diagnosis in an outpatient or ED visit followed by corticosteroid medication use within 7 days). Limitations included potential inaccuracies or omissions in MS classification, covariates, or outcomes; definition of relapse severity by treatment setting (which may not reflect the true clinical severity); potential for unknown confounders; and lack of adjustment of costs for inflation.⁷

‡Limitations included the cross-sectional survey-based design, which allowed for discovery of associations but not causal relationships. In addition, because physician survey data was collected at the time of consultation, data from patients who were not receiving treatment or requiring physician consultation at that time were not captured, which may have affected the generalizability of results to the US population with MS. Finally, patient-level cost data were not used. Costs were derived from a number of sources, such as the Annual Physician Fee Schedule Payment 2015 database for physician costs and the US Department of Veterans Affairs National Acquisition Center cost database for medication costs.⁸

Figure. Survey Results: Percentage of Patients With MS Who Experienced Current or Past Difficulties Accessing a DMT^{11,a,b}



DMT, disease-modifying therapy; MS, multiple sclerosis; OOP, out-of-pocket costs.

^aSource is a 2018 analysis of survey data from 2016 for US-based adults who self-reported having relapsing-remitting MS through a web-based health data-sharing social network. A total of 507 individuals completed the survey; of 386 individuals in the validated sample, 233 individuals shared that they were either currently experiencing an issue related to DMT access or had difficulty accessing a DMT in the past. The results presented in this figure are based on those 233 individuals.¹¹

^bLimitations included that the patient population on PatientsLikeMe may not have reflected the general population of patients with MS and that patient reports of access difficulties may have been subject to errors in recall and reconstruction of events. Further research is needed to evaluate the long-term effects of barriers to DMT access on patient outcomes.¹¹

High OOP costs can affect treatment access, as evidenced by a 2018 study of patients with MS identified in the MarketScan Commercial Claims Database between 2006 and 2009 showing that patients were less likely to use a DMT when annual OOP payments exceeded \$442.35.⁹ Lower OOP costs did not affect DMT use.⁹ In addition, among patients with annual OOP costs higher than \$890, a \$100 increase was associated with a significant reduction in DMT adherence (decrease of 2 days; $P < .05$).^{9,*}

Additionally, a 2018 quasi-experimental study of Medicare beneficiary claims data from 2007 to 2010 showed that when compared with disease-matched Medicare Part D beneficiaries who were eligible for low-income subsidies (LIS) and had minimal cost-sharing, a higher proportion of LIS-ineligible Medicare Part D beneficiaries who were transitioned from cost-sharing of 5% to at least 25% had a 30-day gap in Part D specialty drug use upon transitioning.¹⁰ In the subgroup of patients with MS, the proportion of LIS-ineligible patients with a 30-day gap in use of DMT increased by 11% (from 27.2% to 38.2%) after transitioning to higher cost-sharing, whereas it increased by just 0.9% among patients with MS on LIS.¹⁰ Authors noted that the minimal cost-sharing increase in the LIS group (copayment range, \$0-\$6.30) could still present a substantial burden in this low-income population; furthermore, the burden of high cost-sharing in LIS-ineligible patients may have been underestimated, as the analysis could not account for medication cost assistance through charities and nonprofit foundations in patients otherwise unable to afford their medication.^{10,†}

A 2018 mixed-methods study that included US residents with MS who were members of PatientsLikeMe—a real-time data-sharing and research platform of patient communities for various health conditions—contained a survey portion answered by 386 patients with physician-diagnosed RRMS.¹¹ In all, 60.4% of individuals in the validated sample reported past (188 patients [48.7%]) or current (45 patients [11.7%]) difficulty with accessing a DMT.¹¹ As shown in the **Figure**, the most commonly reported reasons for having difficulties with DMT access were insurance authorization requirements (current issue, 9 of 42 patients [21.4%]; past issue, 78 of 182 patients [42.9%]) and high OOP costs (current issue, 13 of 42 patients [31.0%]; past issue, 54 of 182 patients [29.7%]).¹¹ Additionally, 41.2% (68 of 165) of individuals who reported a past issue with DMT access reported going without their medication until they were able to access their prescribed DMT, and self-reported DMT adherence was significantly lower when experiencing an access barrier (mean, 8.97 [standard deviation (SD), 2.47]) than was self-reported typical DMT adherence (mean, 9.61 [SD, 1.0]; $t_{101} = 2.48$; $P = .02$).¹¹ Of 45 patients who reported a barrier to DMT access, 22 patients (49%) with a current issue reported 1 or more disease relapses when experiencing the barrier, and 56 individuals (29.8%) reported 1 or more disease relapses when experiencing an access issue in the past.^{11,‡}

^{*}Limitations included the limited sample size from the MarketScan database. Due to the study's correlational nature, a causal relationship could not be definitively established between DMT use, adherence, and cost-sharing. In addition, the study period was restricted to before 2010, when manufacturers began to issue coupons to offset copayments that were not recorded in claims records, which could have resulted in overestimation of willingness-to-pay among patients. Also the relatively low share of enrollees in consumer-driven or high-deductible health plans may have limited generalizability to populations with higher shares of these health plans.⁹

[†]Additional limitations included the inability to identify patients receiving other types of medication assistance. Therefore, copayment assistance would have contributed to an underestimation of the effects of high cost-sharing in the non-LIS group. Furthermore, utilization may have been reduced initially, given that the effect of cost-sharing at a given refill decision point is not isolated from the effect of anticipated cost-sharing during the next coverage phase for Medicare Part D.¹⁰

[‡]Limitations included that the patient population on PatientsLikeMe may not have reflected the general population of patients with MS, and the patient reports of access difficulties may have been subject to errors in recall and reconstruction of events. Further research is needed to evaluate the long-term effects of barriers to DMT access on patient outcomes.¹¹

Based on a search of the literature, there are no studies in MS that explore further the effect of prior authorization requirements on medication adherence and clinical outcomes. Investigators on a 2014 disease-blind, systematic literature review of 93 studies (year range, 1993-2013) analyzed the impact of formulary restrictions (eg, prior authorization requirements, step therapy, cost-sharing, preferred drug lists, quantity limits) on patient outcomes. A total of 262 patient outcomes were included in these studies and the results showed that such restrictions were negatively associated with medication adherence. Of 120 medication adherence outcomes stratified by direction of association, 68.3% were negative, and only 3.3% were positive.³⁰

Guidelines from the AAN recommend that a DMT be continued indefinitely unless the patient continues to experience clinical relapses or progression, adverse events (AEs) or complications related to the DMT, difficulties with adherence, or a preference for an alternative mode of administration.⁴ However, switching of DMTs for nonmedical reasons (eg, insurance-related changes) can lead to increased burden on patients and physicians that may affect health outcomes.^{31,32} The results of a 2012 study of a survey of a random sample of patients from 1 of 3 family practices in northeastern Ohio showed that respondents (N = 428) who reported 1 or more insurance-related prescription-filling problems (n = 100) encountered an average of approximately 3 resultant problems, with 41% of patients experiencing adverse medical outcomes, 68% reporting decreased satisfaction with the health care system, and 83% reporting problems that burdened the physician practice.³¹ Medication categories with the most problems related to formulary changes or restrictions were neurologic/psychiatric and cardiac/hypertension/lipid medications.^{31*}

The results of a 2020 online survey of 1010 physicians based in the United States who received a nonmedical switch request for at least 1 patient in the past year, the majority (84.3%) of respondents agreed with statements that nonmedical switching diverted patient communication time away from other important clinical issues.³² More than half of respondents agreed that nonmedical switching put them in a situation of conflict between patient needs and fiscal responsibilities of the practice (69.8%) and undermined patient trust

in the physician's capabilities (56.1%).³² In addition, 49.5% to 59.6% of physicians agreed with statements that nonmedical switching was associated with a decrease in patient adherence to prescription medication and increases in AEs, OOP costs, abandonment of treatment, and medical errors.^{32,†}

Impact of Social Determinants of Health

Social determinants of health (including access to and quality of health care and education, social and community context, economic stability, and the neighborhood and built environment) may create substantial barriers that affect treatment and outcomes in patients with neurologic conditions, including MS.^{12,16,33}

A 2017 analysis of a nationally representative sample of patients with a self-reported neurologic condition from the 2006 to 2013 Medical Expenditure Panel Survey (MEPS) showed that Black participants (OR 0.72; 95% CI, 0.64-0.81) and Hispanic participants (OR, 0.61; 95% CI, 0.54-0.69) were significantly less likely to visit an outpatient neurologist than were White participants after controlling for age, sex, activity limitation, self-reported health status, health insurance coverage, family income, education, and geographic region.¹² Additionally, Black participants were more likely to present to the ED (mean encounters per 100 individuals with a known neurologic condition, 12.55; 95% CI, 10.52-14.58) than were White participants (mean, 7.70; 95% CI, 6.91-8.68) and had more hospital stays and higher per capita expenditures related to hospitalizations than White participants.¹² The authors noted that multiple factors likely contribute to discrepancies in neurology health care among racial and ethnic groups, including mistrust or misunderstanding of the health care system, differences in cultural beliefs about aging and illness, and fewer social and medical resources to facilitate diagnosis of disease and make informed decisions about treatment.^{12,‡}

Disparities in sociodemographic and clinical characteristics were also shown in a 2020 exploratory analysis of data from the North American Registry for Care and Research in Multiple Sclerosis that included 722 patients (age, 18-50 years) with MS who were enrolled between December 2016 and May 2020 across 24 sites from the United States and Canada.¹⁶ The proportion of patients with an EDSS score

*Limitations included a modest response rate (36%), with slightly younger nonrespondents than respondents. Therefore, study results may have underestimated the frequency of insurance-related problems (which tend to be more common among younger patients). Recall bias also may have been a factor, because respondents were asked to recall events that occurred over the past year. The sample size was slightly underpowered (N = 428; N = 480 was calculated as the number needed for sufficient power), and the practices only included 1 geographic region, although it did include urban, suburban, and semirural practices.³¹

†Limitations included the self-reported response format, which may have promoted social desirability bias, in which questions are answered in a way that respondents perceive to be viewed positively by others. Additionally, the nonresponse bias and the sampling ratio (60% primary care, 40% specialist care) may have affected generalizability of the results. The study did not focus on specific therapeutic indications (ie, opinions on nonmedical switching may vary by medication type). Furthermore, the survey used adaptive questioning, limited the number of questions in each domain, and did not offer the ability for respondents to explain their response; the 5- and 7-point Likert scales were also collapsed to improve interpretability of results (which may have removed some information).³²

‡Limitations included that MEPS excluded individuals living in institutionalized settings (eg, nursing homes and prisons), MEPS' diagnostic coding limitations prevented a thorough assessment of disparities in care for some diagnoses, patient reports of visits were subject to recall bias, and the limited sample size prevented analysis of smaller racial and ethnic groups (eg, Asian, Pacific Islander, American Indian populations).¹²

of 4.0 or greater who were Black was approximately twice as large as the proportion of such patients who were White (15 of 74 [20%] vs 57 of 587 [9.7%], respectively).¹⁶ Hispanic patients were less likely to use DMTs than were non-Hispanic patients (65 of 152 [43%] vs 305 of 494 [62%]), with Black-Hispanic patients being least likely to use DMTs (5 of 19 [26%]).^{16,*}

EARLY INITIATION AND ADHERENCE ARE KEY TO OPTIMAL TREATMENT

Consensus recommendations from MS organizations and societies affirm the importance of initiating DMT treatment as soon as MS is clinically diagnosed to help reduce disease activity and delay CNS damage, disease progression, and disability.^{13,14}

A consensus statement from the National Multiple Sclerosis Society emphasizes that medication access should not be limited based upon a patient's age or clinical condition.³⁴ The CMSC recommends initiation of a DMT that is optimal for each individual's needs and preferences, clinical condition, and disability prognosis, and it discourages a strict stepwise approach from a perceived lower efficacy to higher efficacy treatment.¹⁴ The CMSC notes that patients dissatisfied with their current DMT are more likely to be nonadherent or to discontinue use, so consideration of patient preferences is recommended; however, there are limited data on how to transition to another therapy.¹⁴ The AAN recommends considering medication switching when patients experience break-through disease activity or intolerable AEs or when patients have low adherence to their current DMT.⁴ Notably, the AAN guidelines on starting, switching, or stopping DMTs are largely based on outcomes data from patients enrolled in clinical trials; these individuals may not be representative of the highly heterogeneous, real-world population of patients with MS.⁴

CONCLUSIONS: IMPORTANCE OF INDIVIDUALIZED TREATMENT

Although the number of available DMTs for patients with MS has increased substantially in recent years, there are considerable obstacles to implementation of best treatment practices in the United States.³ Insurance barriers (eg, medication authorization issues, high OOP patient costs) can affect DMT access and might result in lower treatment adherence, both of which could potentially lead to clinical relapse or disease progression.^{9-11,26,30} Payers should consider that MS relapses and increased MS-related disability scores are associated with increased economic burden in the form of higher medical costs and expanded health care resource use.^{7,8} They should also take into account that patients with MS who are also members of underserved populations demonstrate lower DMT use and higher disability scores than do their White counterparts.¹⁶ Furthermore, patients with neurologic conditions including MS who also are members of underserved populations have been shown to be less

likely to visit neurologists, but they may experience higher rates of hospitalization and ED admittance.¹²

To help optimize patient outcomes, MS organizations and societies, such as the Multiple Sclerosis Coalition and the National Multiple Sclerosis Society, recommend that patients be given access to the full range of FDA-approved agents regardless of disability level, relapse frequency, age, sex, or ethnicity.^{13,34}

Patients should be prescribed an appropriate DMT based upon their clinical condition and preferences and only switch medications for medically appropriate reasons; treatment should not be withheld while coverage is being determined, because this can increase the risk of permanent CNS damage.^{13,14,34} ●

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