

Implications for Multiple Sclerosis in the Era of the Affordable Care Act: The Shifting Managed Care Landscape

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Abstract

Multiple sclerosis (MS) is a disorder of the central nervous system that is associated with disability, reduced quality of life, extensive medical and nonmedical costs, and lost productivity. Specialty medications that are crucial to effective disease management, helping to prevent debilitating episodes of relapse, account for a substantial portion of the medical expenditures associated with MS. Although these therapies are not considered cost-effective by conventional definitions, they are comparable to one another in cost-effectiveness estimates, leaving the complex task of designing cost-efficient formulary management strategies to managed care professionals. Current epidemiologic data suggest that most patients with MS are covered by some form of healthcare insurance, but plan designs and formulary restrictions may still create access barriers for some patients. The Affordable Care Act (ACA) is recent federal legislation that seeks to provide new consumer protections, improve healthcare quality and accessibility while mitigating expenditures, and increase accountability of healthcare insurance companies. The impact of the ACA on specialty pharmaceuticals is unclear at this time, but it does appear to have already begun improving healthcare coverage across the population. Managed care professionals must work within the confines of the ACA to provide better and more affordable care that targets overall cost reductions rather than just pharmacy expenses.

Am J Manag Care. 2014;20:S242-S253

For author information and disclosures, see end of text.

Multiple sclerosis (MS) is a debilitating, chronic inflammatory disorder of the central nervous system that affects approximately 570,000 individuals (0.21%) in the United States (contrary to the commonly cited estimate of 400,000), with a worldwide prevalence estimated to exceed 2.3 million people.¹⁻³ Although the MS patient population is relatively small, medications for MS was the second-ranked specialty prescription class in the United States, based on per member per year (PMPY) spend, according to the 2013 Drug Trend Report published by Express Scripts.⁴ At \$46.03 PMPY, MS ranked behind only inflammatory conditions such as rheumatic conditions and psoriasis (\$63.31 PMPY), and ahead of all types of cancer combined (\$36.34 PMPY). Together, these top 3 specialty medication classes accounted for 60.6% of all specialty medications billed through a pharmacy benefit in 2013, although it is important to note that these data did not account for medications that may have been billed through patients' medical benefit. The market share of the top 5 medications used in MS is shown in [Table 1](#).⁴ The average cost per prescription for MS medications in 2013 was \$4137.23, with a PMPY number of prescriptions of 0.011. Additionally, the top 4 MS drugs listed in [Table 1](#)⁴ accounted for 4 of the top 10 specialty medications in PMPY spend from all classes. Further, spending on MS medications is expected to increase by 12.5% in 2014, 11.7% in 2015, and 11.7% in 2016, but it should be noted that these market shifts are primarily driven by patent expiration for glatiramer in 2014, brand inflation, and the conversion to oral product alternatives.⁴ Together, these data indicate that MS is a major market driver in the United States for the use of specialty pharmacy, and that the budget impact of MS is substantial from the medication perspective. This article explores the costs of MS from a variety of perspectives, including the patient's and society's, and examines the impact of the ACA on cost and access to care.

Overview of MS Costs

There are several ways to examine the costs of MS: via the direct medical, nonmedical, and indirect costs that are

incurred, and economic analyses that offer a global perspective of the total costs from several different points of view, such as the healthcare provider, employer, and society as a whole. As in other chronic disease states, the costs of MS are driven by direct and indirect costs, and data from several studies have been compiled in **Table 2**.^{1,5-11} Some of the studies found in Table 2^{1,5-11} evaluated the direct medical costs of MS exclusively, with 4 studies demonstrating mean total medical costs per year equaling \$12,879 (SD, \$18,583 [2004 US\$]),⁵ \$18,829 (SD, \$28,973 [2010 US\$]),⁶ \$26,520 (SD, \$38,478 [2011 US\$]),⁷ and \$32,051 (SD, \$1125 [2011 US\$]).¹ The differences in these cost estimates are affected by differences in time, cost assumptions, and the wide variability observed. The cost estimates also demonstrate how dominant the costs of disease-modifying therapies (DMTs) can be, as these medications can cost tens of thousands of dollars per year. Perhaps a better perspective on cost is to compare an MS population with a non-MS population. Two studies compared direct total healthcare utilization in patients with MS versus a non-MS population, in non-matched¹ or matched fashion.⁶ In a 2014 publication, Campbell et al found that individuals within the MS population exceeded the per person annual direct costs by \$24,327 (95% CI, \$22,320-\$26,333) compared with the non-MS population.¹ In a 2010 publication, Asche et al identified a 3.5-fold increase in the rate of hospitalization (15.2% vs 4.3%; $P < .001$), a 2-fold increase in emergency department (ED) visits (25.5% vs 12.2%; $P < .001$), a 2.4-fold increase in the use of physical, occupational, or speech therapy (23.7% vs 9.9%; $P < .001$), and higher annual spending on inpatient services (\$4110 vs \$836; $P < .001$), radiology services (\$1693 vs \$259; $P < .001$), emergency care (\$432 vs \$189; $P < .001$), office visits (\$849 vs \$310; $P < .001$), and physical, occupational, or speech therapy (\$295 vs \$81; $P < .001$) for patients with MS.⁶ Fishman et al used estimates from a large health maintenance organization and documented that the mere presence of MS increased the cost per person by 297%.¹² Patients with MS also incur direct nonmedical costs that include out-of-pocket (OOP) expenses (informal care), home care, transportation costs, mobility aids, and investments in home modifications,⁸ but these costs vary widely by study, and many economic analyses do not include direct nonmedical costs because they are difficult to accurately estimate. Direct costs range from approximately 15% to 85% of total costs, with medical and nonmedical expenditures accounting for about 60% and 40% of total direct costs, respectively.^{1,5-11}

■ **Table 1.** Top Medications in the MS Class, 2013⁴

2013 Medication	Percent of Market Share
Glatiramer (Copaxone)	30.6%
Interferon beta-1a (Avonex)	19.7%
Interferon beta-1a (Rebif)	12.9%
Fingolimod (Gilenya)	9.3%
Dimethyl fumarate (Tecfidera)	8.2%

MS indicates multiple sclerosis.
Reprinted with permission from Express Scripts' 2013 Drug Trend Report.

Indirect costs, which relate to lost work productivity from the employee and caregiver, early retirement, unemployment, sick time, and disability, can account for up to 60% of total costs associated with MS. These costs are primarily influenced by the extent of disability, which is covered in further detail below.⁸ Intangible costs reflect changes in quality of life (QOL) that affect activities of daily living, and may account for up to 32% of total estimated costs.⁹ Assessments of indirect and intangible costs are found more often in formal pharmacoeconomic analyses than in cost-description studies, and some authors have argued that pharmacoeconomic analyses have little value in clinical practice because prescribers choose what they believe is best for their patients rather than what is best for controlling costs or improving outcomes from a societal perspective.¹³ However, comparative information for indirect costs and QOL is also important to the individual patient, as they speak to the patient's ability to lead a relatively normal life.

Other Major Cost Drivers in MS

Disability and Lost Productivity

Many of the studies previously summarized evaluated the impact of disability and QOL on cost.^{1,8-11} Campbell et al examined the number of days in bed and found an adjusted 4.4-fold higher risk (95% CI, 2.97-6.45; $P < .05$) in the MS cohort compared with the non-MS cohort, and also noted a loss of quality-adjusted life-years (QALYs) in the MS cohort relative to the non-MS cohort (-10.04; 95% CI, -10.52 to -9.44; $P < .05$).¹ These studies have consistently demonstrated that the total costs (direct and indirect) associated with MS grow with increasing disability.^{1,8-11} The systematic review by Naci et al, published in 2010, identified total annual costs (direct and indirect, in 2008 US\$) of \$2000 to \$40,000 for Kurtzke Expanded Disability Status Scale (EDSS) scores less than 3.5, \$2000 to \$62,000 for EDSS scores of 3.5 to 6.5, and \$5000 to

■ **Table 2.** Cost Factors in MS^{1,5-11}

Cost Factor	Percent of Total	Percent of Category
Direct Costs	15%-85%	
<i>Direct Medical Costs</i>	22.4%-60%	
Inpatient (hospitalization costs)		7.8%-21.8%
Outpatient (physician visits, laboratory, physical therapy, radiology services, injections)		19.4%-43.2%
Emergency		0.1%-2.2%
Pharmacy (DMTs and other medication)		32.7%-64.8%
<i>Direct Nonmedical Costs</i>	8.0%-40.6%	
Informal care (using disposable income for costs)		77.2%
Transportation		1.0%
Investments (stair lifts, ramps, rails, wheelchairs, etc)		16.6%
Home help		5.2%
Indirect Costs	20%-60%	
Missed work productivity		2.0%-3.0%
Early retirement		67.5%-98%
Disability		17.5%
Unemployment		2.7%
Sick time		9.3%
Intangible Costs	0%-32%	
Changes in health state affecting activities of daily living		100%

DMT indicates disease-modifying therapy; MS, multiple sclerosis.

■ **Table 3.** The Impact of EDSS Score on Employment Rate and QOL in Patients With MS⁸

EDSS Score	Employment Rate (<i>P</i> not reported)	QOL Score (<i>P</i> < .001 for correlation of utility with EDSS score)
0	77%	0.91
1	77%	0.82
2	54%	0.72
3	44%	0.58
4	66%	0.62
5	29%	0.52
6	17%	0.46
6.5	14%	0.48
7	6%	0.31
8 or 9	1%	0

EDSS indicates Expanded Disability Status Scale; MS, multiple sclerosis; QOL, quality of life.
Adapted from Kobelt G, Berg J, Lindgren P, Kerrigan J, Russell N, Nixon R. *Eur J Health Econ.* 2006;7:S96-S104.

\$142,000 for EDSS scores greater than 6.5, respectively.¹⁰ Kobelt et al documented a 3-fold increase in total costs for patients with an EDSS score of 4 to 6.5, and a 5.6-

fold increase in patients with EDSS scores of 7 to 9.5, relative to EDSS scores of 3.5 or less.⁸ A retrospective analysis published in 2014 found that medical and pharmacy claims both account for approximately 50% of the medical costs of MS,⁷ and data show that as disability increases, the use of DMTs decreases.⁹ For EDSS scores of 0 to 3, about 30% to 70% of patients receive DMTs; for EDSS scores of 4 to 6, about 25% to 60%; and greater than 6, about 0% to 40%.⁹ These figures demonstrate that the costs associated with increasing disability in patients with MS may be more heavily impacted by factors other than pharmacy claims for DMTs.

As disability in patients with MS increases, the contribution of indirect costs to total healthcare costs approaches or even exceeds 50%,^{8,14} in part because disability, QOL, and unemployment are closely related. One European study by Kobelt et al discovered that 77% of the patients with MS younger than 65 years with EDSS scores of 0 to 1 were employed, and that as disability and EDSS scores in persons with MS increased, both employment rates and QOL decreased (Table 3),⁸ subsequently raising indirect costs.⁸ Gupta et al examined self-reported disease severity in 536 patients with MS and compared

■ **Table 4.** Impact of Self-Reported Disease Severity on QOL and Productivity¹⁵

Parameter Evaluated	Mild Disease	Moderate Disease	Severe Disease
QOL			
Mental component summary scores	45.2 ± 12.6	43.1 ± 12.5	42.2 ± 12.5
Physical component summary scores (<i>P</i> < .001)	40.7 ± 10.8	31.2 ± 10.1 ^a	28.7 ± 9.1 ^b
Health utilities (<i>P</i> < .001)	0.67 ± 0.15	0.59 ± 0.1 ^a	0.57 ± 0.11 ^b
Absenteeism			
Work time missed	7.1 ± 16.5%	13.2 ± 24.3%	16.1 ± 25.6%
Hours of work missed	2.6 ± 7.3	5.2 ± 10.2	4.1 ± 8.3
Presenteeism			
Impairment at work	23.2 ± 27.5%	37.9 ± 27.7% ^a	56.4 ± 33.4% ^{b,c}
Hours missed due to impairment	6.9 ± 9.6	11.7 ± 10.6 ^a	15.3 ± 12.9 ^b
Work Productivity			
Overall impairment (<i>P</i> < .001)	26.2 ± 30.7%	44.8 ± 30.9% ^a	59.1 ± 34.7% ^b
Activity impairment (<i>P</i> ≤ .001)	42.6 ± 30.9%	63 ± 25.1% ^a	74.5 ± 25.4% ^{b,c}
^a <i>P</i> < .05 mild vs moderate. ^b <i>P</i> < .05 mild vs severe. ^c <i>P</i> < .05 moderate vs severe. QOL indicates quality of life. Adapted from Gupta S, Goren A, Phillips AL, Dangond F, Stewart M. <i>Mult Scler Relat Disord</i> . 2014;3:78-88.			

health utilities and work productivity when the disease was characterized as mild, moderate, or severe.¹⁵ The study found that mental component summary scores for QOL were similar across all 3 severity categories, and physical component summary scores and health utilities declined with increasing severity. Absenteeism tended to be numerically, but not statistically, higher in the moderate and severe patient groups than in those with self-reported mild MS. On the other hand, measurements of presenteeism and work productivity were both significantly impacted by increased disability, with the percent of impairment at work, hours missed due to impairment, percent of overall work productivity impairment, and percent of work productivity activity impairment all increasing with increased perceived disability severity (Table 4).¹⁵ In a retrospective evaluation of a privately insured US claims database with disability data from 17 companies, Ivanova et al matched patients with MS by age and sex to non-MS patients to examine the cost of disability and medically related absenteeism among employees with MS.¹⁶ The results of the analysis, as shown in Table 5,¹⁶ demonstrated that direct, indirect, and overall costs were higher among employees with MS, with the largest cost drivers being pharmacy-related expenses (57.2%) and disability (67%).¹⁶ Further, when compared with non-MS employees over 12 months, those with MS had higher incidences of having at least 1 disability day, medically related absenteeism day, and

work loss day, and more total disability days and work days lost, highlighting the significant costs of MS from both an employer and societal perspective.¹⁶

Comorbidities

In addition to the disability and lost productivity, the various comorbidities associated with MS may significantly impact the burden and cost of the disease.^{5,7} Table 6^{5,7} compiles data from 2 economic models published in 2004 and 2011 that summarized the prevalence of several common comorbidities found in patients with MS, the mean medical costs (expense of treatment), and charges (what the patient or insurance is billed for treatment).^{5,7} Conditions frequently associated with elevated medical costs over a hypothetical baseline state where none of the conditions were present in MS were abnormality of gait, ataxia, optic neuritis, spasms, urinary incontinence, and voice disturbance.^{5,7} Unfortunately, treating these comorbid conditions not only leads to additional medical costs, but also additional medication. Polypharmacy may increase the likelihood of adverse effects from medications and the risk of negative impact on fatigue, perceived cognition, and cognitive performance.¹⁷ Thelen et al assessed the effects of polypharmacy (vs lack of polypharmacy), having adjusted for clinical factors such as demographics and comorbid diseases in patients with MS, on the Modified Fatigue Impact Scale (12.04 ± 3.82 vs 8.79 ± 3.62; *P* = .011), the Prospective and Retrospective

Table 5. A 12-Month Comparison Between Employees With and Employees Without MS¹⁶

Parameter	With MS	Without MS	P
Mean direct medical cost	\$15,277 ± \$19,521	\$3948 ± \$24,122	<.0001
Mean indirect medical costs	\$5769 ± \$14,075	\$1417 ± \$3931	<.0001
Total costs	\$21,046 ± \$26,003	\$5365 ± \$25,836	<.0001
Incidence of ≥1 disability day	21.4%	5.2%	<.005
Incidence of ≥1 medically related absenteeism day	88.5%	84%	<.005
Incidence of ≥1 lost work day	97.5%	85%	<.005
Number of disability days	29.8 ± 77.5	4.5 ± 29.6	<.005
Number of medically related absenteeism days	7.9 ± 12.7	4.3 ± 6.9	<.005
Number of work days lost	37.7 ± 76.1	8.8 ± 30.7	<.005

MS indicates multiple sclerosis.

Adapted from Ivanova JI, Birnbaum HG, Sanuels S, Davis M, Phillips AL, Meletiche D. *Pharmacoeconomics*. 2009;27:681-691.

Table 6. Prevalence and Medical Costs of Comorbidities^{5,7}

Condition	Prevalence (%)	Mean Medical Cost to Patient (2004 US\$)	Mean Medical Charge to Patient (2011 US\$)
Baseline state of MS	100%	\$12,879	\$26,520
Abnormality of gait	7.4%-7.5%	\$20,871	\$48,361
Ataxia	2.2%-3.1%	\$16,168	\$48,605
Burning, numbness, tingling sensations	9.8%-17.2%	\$12,504	\$33,648
Convulsions	0%-3.5%	\$15,664	Not identified
Depression	7.9%-19.8%	\$13,928	\$42,831
Fecal incontinence	0%-0.4%	\$18,964	Not identified
Fibromyalgia/myalgia and myositis	2.5%-7.4%	\$11,478	\$38,319
Malaise and fatigue	14.1%-21.6%	\$14,604	\$39,948
Optic neuritis	0.2%-0.4%	\$39,247	\$82,134
Spasms	2.6%-3.3%	\$20,376	\$48,337
Trigeminal neuralgia	0.9%	\$12,467	\$38,165
Urinary incontinence	2.1%-5.5%	\$16,898	\$47,885
Voice disturbances	0.1%-1.6%	\$16,463	\$44,973

MS indicates multiple sclerosis.

Memory Questionnaire (46.12 ± 9.95 vs 39.02 ± 9.04 ; $P = .003$), and the Processing Speed Difficulties Scale (41.54 ± 13.52 vs 32.89 ± 10.83 ; $P = .043$), and found worsened fatigue and cognitive problems in the MS patients with polypharmacy; these factors would be expected to have a negative influence on patient QOL, although it was not specifically studied.¹⁷ Another study by Forbes et al did examine the impact of fatigue, pain, urinary incontinence, bowel disorders, depression, pressure ulcers, sexual dysfunction, and employment problems on the QOL of individuals with MS, and found in a cross-sectional postal survey that 74% of patients with MS

had at least 4 of the listed problems, and the extent and severity of these problems increased with the level of perceived disease severity ($P < .001$).¹⁸ Further, fatigue, pain, employment, depression, and relationship problems had a significant negative impact ($P < .001$ for each analysis) on the 36-item Short Form Health Survey, independent of MS disease impact, and depression, pain, and fatigue were found to be interdependent.¹⁸

In a study published in 2014, Franklin et al took the unique approach of examining the frequency and economic impact of cardiac conditions in patients with MS who were hospitalized.¹⁹ The goal of the study

was to determine the prevalence of patients in whom fingolimod would be contraindicated due to the presence of various cardiovascular conditions. Comorbid cardiovascular conditions were fairly common among the 136,542 patients with MS (9.2%); heart failure (59.4%), myocardial infarction (17.2%), and occlusion of cerebral arteries (12.4%) were the most common comorbidities. These cardiovascular comorbidities are an important cost driver, because the mean adjusted cost per hospital discharge was higher in MS patients that had them than in MS patients with no cardiac conditions (\$17,623 vs \$11,663; $P < .0001$).¹⁹

Relapse

The pattern of disease relapse depends on the subtype of MS (ie, relapsing-remitting multiple sclerosis [RRMS], primary-progressive MS, secondary-progressive MS, and progressive-relapsing MS) and the appropriateness of treatment.^{20,21} The costs of managing an episode of MS relapse (in 2002 US\$) was estimated at \$12,870 for high-intensity management, with hospital care comprising 71% of that cost. High-intensity management involved physician care, followed by emergency and hospital inpatient care, and post discharge follow-up. In addition, it should be noted that 36% of patients with MS required subacute care, rehabilitation, or home care. The typical costs of a mild or moderate episode were estimated to be \$243 and \$1847, respectively.²² Earlier initiation of appropriate treatment, particularly in patients with RRMS, reduces the frequency of relapse and hospitalizations, and further delays the onset of disability.²³⁻²⁶

Treatment Costs and Adherence

Essential treatment parameters, such as which medication to use, when it should be used, and for how long, are important factors that influence the overall cost of MS. It is important to consider that the PMPY cost estimates alluded to in the 2013 Drug Trend Report apply across the entire insured population, not just those with MS; this means that MS is a significant cost driver in specialty pharmacy and healthcare in general.⁴ Numerous pharmacoeconomic studies²⁷⁻³⁰ and a recent comprehensive review³¹ have failed to show a cost benefit per QALY for the treatment of MS by conventional standards (<\$100,000 per QALY), and there is little evidence to differentiate MS therapies.²⁷⁻³¹ Of course, these cost estimates are sensitive to the price of the agents, duration of treatment, and whether or not the patient actually takes the medication.³²⁻³⁵

A US administrative healthcare claims study by Margolis et al, published in 2011, revealed that between 2001 and 2007, 59.7% of patients with a new diagnosis of MS were not treated with DMTs during a 35.7-month average follow-up.³⁶ It is unclear whether this was due to primary noncompliance or prescription abandonment by the patient (perhaps caused by an unwillingness to be treated or financial issues), or lack of a prescription from the clinician due to inadequate knowledge or the subtype of MS, since some types do not clearly respond to biologic agents. Further, among the 40.3% of patients who did initiate a DMT, only 72.3% remained on therapy, with discontinuation occurring at an average of 17.6 ± 14.6 months after initiation. Also, 16.5% of treated patients with MS had treatment gaps exceeding 60 days.³⁶ The nonadherence rate to MS treatment is similar to the rate reported in the 2013 Drug Trend Report, which identified a 26.8% nonadherence rate among patients with MS.⁴ A recent systematic review of adherence issues, published in 2013, noted several challenges that affected treatment adherence in patients with MS.³⁵ In pooled analyses, once-weekly intramuscular interferon beta-1a had higher adherence rates (69.4%) than every-other-day subcutaneous (SC) interferon beta-1b (63.8%), 3-times-weekly SC interferon beta-1b (58.4%), or glatiramer acetate administered daily (56.8%), indicating the potential impact of the treatment schedule on adherence. Higher OOP co-payments and coinsurance were also factors noted to reduce adherence among patients with MS.³⁵ The risk of relapse or disease progression was higher among patients with lower rates of adherence; those with medication possession ratios (MPRs) of at least 85% had fewer relapses than those with lower MPRs (relative risk [RR], 0.89; 95% CI, 0.81-0.97; $P < .05$); however, adherence could be improved by interventional programs and disease therapy management programs.³⁵ Other studies^{37,38} have further explored the reasons for nonadherence and identified forgetting to take the injection (50%) and other injection-related reasons (32%), such as longer durations of treatment and concerns about the efficacy, safety, tolerability/adverse effects, and burden of treatment as factors. It should be noted that in these studies, less disability progression and better QOL were reported in the patients who were more adherent.^{37,38}

There are minimal data that link adherence to economics in MS.^{35,39,40} Steinberg et al noted a relationship between adherence and relapse, and documented the fact that for individuals who were adherent (MPR $\geq 85\%$) in the prior year, both ED visits (RR, 0.78; 95% CI, 0.61-0.99)

Reports

and inpatient admissions were lower (RR, 0.79; 95% CI, 0.65-0.98) relative to those who were less adherent, indicating that nonadherence was linked to increased healthcare resource utilization.³⁹ Tan et al published a more formalized cost analysis in 2011.⁴⁰ Compared with patients who were less adherent, those with an MPR of at least 80% had fewer MS-related inpatient visits (odds ratio [OR], 0.63; 95% CI, 0.47-0.83) and MS relapses (OR, 0.71, 95% CI, 0.59-0.85), but there were no significant changes in ED visits (OR, 0.8; 95% CI, 0.6-1.07). Overall, the adherent group of patients with MS incurred less medical costs that were adjusted for demographic and geographic factors over a 12-month period (\$3380; 95% CI, \$3046-\$3750 vs \$4348; 95% CI, \$3828-\$4940; $P = .003$).⁴⁰

Current strategies that may improve adherence in patients with MS include reducing patient OOP expenses (increased costs have been shown to increase the risk of prescription abandonment),⁴¹ optimizing treatment and medication dosing schedules, conducting motivational interviews with patients, and providing medication therapy management services. Further, it is important to educate patients on the disease, its clinical course, management strategies, the impact of treatment, available treatment options, drug administration, the importance of adherence, and common adverse events. Also, soliciting input from patients to engage them, providing support networks that are both clinical and nonclinical, considering oral treatment options when injections create real or perceived challenges for patients, and addressing and managing symptoms are all important practices for promoting adherence.^{42,43}

The ACA

The costs of MS, the burden of disease, and the barriers to successful treatment of this challenging patient population are formidable. Access to care is one such obstacle and a critical issue, as it represents the first major step in the management of patients with MS.³⁶ In terms of delivering appropriate treatments to patients with MS in the United States, a prescription must be written before it can be filled at a pharmacy. Unfortunately, patients with MS represent a particularly vulnerable population for access to care. In a population survey by Minden et al, 81.9% of patients with MS had disabilities that affected activity and/or lifestyle, which can negatively impact their access to care.⁴⁴ Patients who are older and live in rural areas or live a greater distance from a medical center are less likely to receive the specialty care needed.⁴⁵

Studies have shown that having access to a neurologist is a major factor in patients starting or persisting on a DMT regimen.⁴⁶⁻⁴⁸ According to Iezzoni, the presence of a disability has been linked to reduced QOL and substandard care, as the US healthcare system has not been “structured to care effectively for people with disabilities.”⁴⁹

The ACA^{50,51} is legislation designed to provide improved access to affordable healthcare by driving a number of changes at the employer, state, and federal level.^{52,53} More specifically, as shown in **Table 7**,^{50,51} the ACA was designed to achieve the goals of providing new consumer protections, improving the quality of healthcare at a lower cost, increasing access to affordable care, and increasing the accountability of healthcare insurance companies.^{50,51} It is important to realize that many of these goals remain unproved in terms of whether they can be achieved. Assuming they can be delivered, a number of changes are of particular note for patients with MS, including: (1) prohibiting insurance companies from denying coverage based on preexisting condition(s); (2) eliminating annual and lifetime benefit limits; (3) establishing consumer assistance programs in states; (4) offering Medicare donut hole relief and prescription drug discounts; (5) making healthcare more affordable; (6) establishing the Health Insurance Marketplace; (7) providing healthcare access to uninsured Americans with preexisting conditions; (8) expanding coverage to early retirees; (9) rebuilding the primary care network; (10) allowing states to cover more individuals with Medicaid and increasing Medicaid eligibility and access; (11) increasing access to services in the home and in the community; and (12) bringing down overall healthcare premiums.^{50,51} Other notable changes with the ACA include standards for accessible medical equipment and standards against discrimination of those with disabilities.⁴⁹

It is estimated that 20 million Americans have gained health insurance coverage as of May 1, 2014, and the percentage of US adults lacking coverage has fallen from 18% in the third quarter of 2013 to 13.4% in May 2014. Other projections, according to Blumenthal et al, anticipate that the number of uninsured individuals in the United States will decline by 12 million in 2014 and 26 million in 2017.⁵³ While there have been some delays, controversy, and opposition, it does seem that the main goals of the ACA are gradually being met, with substantially improved access to insurance coverage.^{53,54} According to the National MS Society, approximately

■ **Table 7. Affordable Care Act Summary**^{50,51}

Category/Description	Implementation Year
New Consumer Protections	
Putting information for consumers online	2010
Prohibiting denial of coverage of children based on preexisting conditions	2010
Prohibiting insurance companies from rescinding coverage	2010
Eliminating lifetime limits on insurance coverage	2010
Regulating annual limits on insurance coverage	2010
Appealing insurance company decisions	2010
Establishing consumer assistance programs in states	2010
Prohibiting discrimination due to gender or preexisting conditions	2014
Elimination of annual limits on insurance coverage	2014
Ensuring coverage for individuals participating in clinical trials	2014
Improving Quality and Lowering Costs	
Providing small business health insurance tax credits	2010
Offering relief for 4 million seniors who hit the Medicare prescription drug donut hole	Pre-2010
Providing free preventive care (no co-payment on certain services)	2010
Preventing disease and illness (funding public health programs)	2010
Cracking down on healthcare fraud	Pre-2010
Offering prescription drug discounts (seniors who hit the coverage gap of Medicare Part D get a 50% discount on brand name medications; gap closes in 2020)	2011
Providing free preventive care for seniors	2011
Improving healthcare quality and efficiency (established Center for Medicare & Medicaid Innovation)	2011
Improving care for seniors after they leave the hospital (Community-based Care Transitions Program)	2011
Introducing new innovations to bring down costs (Independent Payment Advisory Board begins operations)	2011
Linking payment to quality outcomes (value-based purchasing)	2012
Encouraging integrated health systems (incentives to develop accountable care organizations)	2012
Reducing paperwork and administrative costs (adoption of electronic health records and standardized billing procedures)	2012
Understanding and fighting health disparity	2012
Improving preventive health coverage (funding to state Medicaid programs to provide preventive care at little or no cost)	2013
Expanding authority to bundle payments (steps to streamline payment and eliminate fragmented billing)	2013
Making care more affordable (tax credits to afford insurance)	2014
Establishing the Health Insurance Marketplace	2014
Increasing the small business tax credits	2014
Paying physicians based on value, not volume	2015
Increasing Access to Affordable Care	
Providing access to insurance for uninsured Americans with preexisting conditions	2010
Extending coverage for young adults	2010
Expanding coverage for early retirees	2010
Rebuilding the primary care workforce	2010
Holding insurance companies accountable for unreasonable rate hikes	2010
Allowing states to cover more people with Medicaid	2010
Increasing payments for rural healthcare providers	2010
Strengthening community health centers	2010
Increasing access to services in the home and in the community	2011
Providing new, voluntary options for long-term care insurance	2012
Increasing Medicaid payments for primary care doctors	2013
Open enrollment in the Health Insurance Marketplace begins	2013
Increasing access to Medicaid	2014
Promoting individual responsibility	2014
Holding Insurance Companies Accountable	
Bringing down healthcare premiums (requirement to spend at least 80% of premiums on healthcare or else provide a rebate to customers)	2011
Addressing overpayments to big insurance companies and strengthening Medicare Advantage	2011

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25% to 30% of patients with MS are on Medicare, but less is known about Medicaid, since those programs are run by individual states.⁵⁵ Evidence from the Sonya Slifka MS population study, collected in the early 2000s, found that among 2000 study patients, 3.8% did not have insurance, which was estimated to represent 7000 total uninsured in the US MS population. In that study, 24.4% had Medicare and 5% had Medicaid, while 75.5% had some type of private insurance. Despite the high rate of insurance coverage, 17.5% of insured participants reported that their prescription plan paid nothing toward prescription coverage, and 9.4% found it difficult to obtain a referral to a specialist.⁴⁷ These data suggest that even though there may be a high baseline insurance coverage rate among patients with MS in the United States, access and coverage continue to be barriers to optimal care, thereby highlighting the fact that the ACA could aid many of these patients.

What remains unclear, however, is the role of the ACA in specialty pharmacy medications, which are currently a major driver of total direct medical expenditures in MS.⁴⁻¹⁰ Trends leading up to healthcare reform have demonstrated that drug expenditures are growing faster than any other healthcare service category, with a 9.2% (\$14.9 billion) overall increase between 2005 and 2009. From 2005 to 2009, drugs for MS accounted for \$4.7 billion of total expenditures, the number of prescriptions for MS increased 27%, and the expenditure per fill nearly tripled.⁵⁶ The need to effectively manage the ever-increasing drug coverage costs, and the struggle to avoid shifting excess costs to patients in the era of the ACA, has reintroduced debate regarding the need for cost-effectiveness analysis in the United States.⁵⁷

Lessons From Managed Care

The costs associated with MS are clearly extensive. Managed care professionals are key players working with clinicians to examine the available efficacy, safety, and cost-effectiveness data and assess potential treatment barriers. Their efforts can help deliver cost-effective care that may keep patients with MS relatively healthy with an acceptable QOL and allow them to maintain productivity in society.

In recent years, much of the direct medical expenses of MS have transitioned to the pharmacy. One study compared medical and pharmacy costs between 1995 and 2004, and noted a 42% decline in medical claims and a 388% increase in pharmacy claims, with a resultant 35% increase in total annual costs over that time period, high-

lighting the impact of high-cost specialty pharmaceuticals on the total cost of care for MS.^{55,57} A health plan study by Gleason et al found that the rate of specialty drug use was 71.8% among members with MS, with a \$36,901 annual cost of care among all members with MS and \$41,760 among members with MS taking specialty medications. Specialty drugs accounted for 50% or more of total annual costs for patients with MS in the health plan, and annual spending increased 4.4% to 18% from 2008 to 2010.⁵⁸ While this increase in cost is concerning from a population-based perspective, it is also concerning to the patient. A survey published in 2014 of patients with MS regarding their healthcare worry identified the inability to pay for healthcare services as their greatest concern.⁵⁹ It is important to remove potential barriers, avoid primary noncompliance or prescription abandonment, and promote treatment adherence to further reduce the risk of hospitalization, patient disability, and lost productivity and to improve QOL.^{35,37,38} It must be considered that more specialized care, such as that provided by an MS specialist, may result in increased resource utilization and cost. Managed care professionals should be prepared to evaluate the benefits and long-term costs of various treatment scenarios.⁴⁶⁻⁴⁸

Managed care organizations and health plans must balance the impact of various standard cost-containment strategies on access to medications and MS outcomes. Commonly used strategies include: (1) prior authorizations to evaluate the appropriateness of medication use; (2) formulary/preferred first-line agents; (3) use of online "step edits" to automate clinical management; (4) case/therapy management when patient compliance is of particular importance or concern; (5) cost-effectiveness analysis; (6) benefit designs with cost sharing by the beneficiary; and (7) risk evaluation and management programs (eg, risk evaluation and mitigation strategies).⁶⁰ Provider plans should recognize that patient OOP expenses have been linked to prescription abandonment,⁴¹ and that it is possible to control the costs to the patient. According to the 2013 Drug Trend Report, from 2012 to 2013, the member share of total costs declined 1.3% for traditional medication and 0.2% for specialty medication; however, the average member co-payment decreased \$0.68 for traditional medication and increased \$3.89 for specialty medication.⁴ As noted earlier, this increase in cost sharing has the potential for unintended consequences, with Gleason et al indicating that OOP expenses of more than \$200 for MS medications dramatically increased prescription abandonment rate: abandonment was 5.7% for \$0

to \$100 OOP, 5.3% for \$101 to \$150 OOP, 10.6% for \$151 to \$200 OOP, and 25.8% to 28.5% for over \$200 OOP ($P < .001$ vs \$0-\$100 OOP).⁴¹ A systematic review of the literature, published in 2014 by Happe et al, that examined directional impact of managed care formulary management activities on medication adherence, healthcare utilization, and clinical and economic outcomes identified that cost sharing was the most common type of formulary restriction (60.2%), followed by prior authorization (21.5%).⁶¹ Formulary management strategies were associated with a negative outcome on medication adherence in 68.3% of studies; although medication costs decreased in restrictive formularies, economic outcomes, including total costs (beyond medication costs), were gauged as neutral (37.3%), positive (33.9%), or negative (28.8%), with healthcare utilization having no association in over 50% of outcomes assessed. It is important to note that restrictive formularies may negatively impact medication adherence and have little, if any, effect on total medical costs and healthcare resource utilization.⁶¹

Summary

Managed care professionals play a major role in working with other healthcare providers and clinicians to ensure the highest quality and effective care to patients with MS at an affordable price. While the long-term impact of the ACA on specialty pharmacy, which encompass the bulk of DMTs used in the management of MS, remains unclear, managed care organizations can begin to evaluate and improve their strategies for managing access to specialty treatments for these challenging patients. Medications for MS represent a significant portion of the US specialty market, and it appears that this trend is very likely to continue. Recent guidance (released in 2012) on MS formulary and treatment decision making is available from a consensus panel of US managed care pharmacists and physicians.⁶² Recommendations include guidance on initiation of therapy, use of first-line platform therapies such as glatiramer acetate or an interferon beta agent based on formulary availability, and procedures to switch to alternative agents in the event of patient or provider preference, which may stem from a variety of factors such as adverse events, adherence, treatment failure, and needle phobia.^{62,63} If patients are switched to another therapy, they should be monitored closely for adherence and effectiveness.⁶⁴ Managed care professionals must also stay abreast of current pharmacotherapeutic trends, such as the use of oral agents, and work toward balancing access to care with the need to

manage costs, since treatment adherence and efficacy may be enhanced in certain situations.⁶⁴ Lastly, in the era of the ACA, managed care professionals are pivotal advocates for increasing patient education, reducing economic barriers, providing case management services, and implementing the scope of the healthcare legislation to better the lives of patients with MS, their caregivers, and society as a whole.

Author affiliation: Monmouth Medical Center, Long Branch, NJ (ASM); Gary Owens Associates, Ocean View, DE (GMO).

Funding source: This activity is supported by educational grants from Biogen Idec and Teva Pharmaceuticals.

Author disclosure: Dr Owens reports serving as a consultant for and speaking on behalf of Biogen Idec, Genzyme, and Sanofi. Dr Mathis reports no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this supplement.

Authorship information: Concept and design (ASM, GMO); acquisition of data (ASM); analysis and interpretation of data (ASM); drafting of the manuscript (ASM, GMO); critical revision of the manuscript for important intellectual content (ASM, GMO); and administrative, technical, or logistic support (ASM).

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