

Descriptive Analysis of the Direct Medical Costs of Multiple Sclerosis in 2004 Using Administrative Claims in a Large Nationwide Database

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ABSTRACT

BACKGROUND: Multiple sclerosis (MS) is chronic and debilitating, afflicts patients in the prime of their lives, and requires costly, decades-long disease management. MS prevalence is increasing, and treatment with new drug therapies is expensive.

OBJECTIVES: The objectives of this analysis were to (1) determine the average total and component direct medical costs incurred in the treatment of MS patients in 2004, and (2) compare MS treatment costs and cost factors in 2004 with 1995.

METHODS: The data for this analysis were abstracted from the PharMetrics Integrated Patient-centric Database, which contains administrative claims data from more than 80 private and public health plans in the United States, representing more than 9.6 million unique patients in 2004. To be included in this analysis, each patient had to have at least 1 medical claim with a diagnosis of MS (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 340) in the date of service period from January 1, 2004, through December 31, 2004. Patients were segmented according to patient age and sex, comorbid conditions, payer type, and use of specific types of disease-modifying drugs (DMDs). Episode Treatment Group (ETG) software (ETG numbers 149 or 150) was used to aggregate medical claims related to MS since not all MS-related medical claims have the ICD-9-CM code 340. ETGs are commonly used to aggregate administrative claims data and to define discrete periods of care (episodes); this study used ETGs only to aggregate administrative claims. Statistical comparisons were subsequently performed using analysis of variance and chi-square analyses. The source of the data for the aggregate MS treatment costs in 1995 was the Medstat MarketScan database.

RESULTS: In calendar year 2004, a total of 13,420 patients were identified with a medical or hospital claim with ICD-9-CM code 340, a prevalence of approximately 14.0 per 10,000. The final study population was reduced to 10,099 patients (75.3%) after applying the criterion of 12 full months of available claims data. The total average annual cost for the 10,099 MS patients in 2004 was \$12,879 (standard deviation, \$18,582), 64.8% of which was attributable to the cost of prescription drugs and 61.4% to the cost of DMDs in particular, 26.2% to outpatient care, 7.8% to inpatient care, and 1.1% to emergency room visits. There was no difference in total average annual medical costs for males compared with females, but costs did differ among age categories and by insurance type and payer. A total of 5,810 patients (57.5% of the study population) reported at least 1 pharmacy claim for a DMD, and these patients had average annual costs of \$18,944 compared with \$4,662 total annual costs for MS patients who did not receive DMDs. Pharmacy costs represented 75.3% of annual medical costs for the patients who reported at least 1 pharmacy claim for a DMD but only 7.4% for patients who did not receive DMDs. A comparison of 2004 costs with 1995 costs (adjusted for 2004 based on the Consumer Price Index; CPI-U [All Urban Consumers, All Items]; 1982-84 = 100) demonstrated that total annual MS-related treatment costs increased by 35%, from \$9,515 in 1995 to \$12,879 in 2004. There was some difference in total annual MS-related treatment costs in 2004 among the 4 DMD therapy groups—\$16,928 for glatiramer, \$17,987 for IFN beta-1a (intramuscular), \$19,616 for IFN beta-1b, and \$22,557 for IFN beta-1a (subcutaneous), $P < 0.001$.

CONCLUSION: Pharmacy costs accounted for 65% of total MS-related medical costs in 2004 and 75% of total costs for the subset of MS patients

(58%) who received at least 1 DMD.

KEYWORDS: Multiple sclerosis, Benchmarking, Managed care
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Multiple sclerosis (MS) is a chronic debilitating disease characterized by inflammatory demyelination (loss of myelin) within the central nervous system (CNS).¹ Loss of myelin disrupts the nerves' ability to conduct electrical impulses to and from the brain, triggering a variety of symptoms, including fatigue, visual disturbances secondary to optic neuritis, and sensory disturbances such as paresthesias or hypoesthesia (numbness).¹ Spasticity of the limbs and bladder, impotence, fatigue, depression, and mild emotional or intellectual changes may also develop over time.¹

MS affects approximately 350,000 people in the United States, with approximately 12,000 new cases diagnosed each year.² The majority of MS cases (approximately two thirds) occur in young adults between the ages of 20 and 40, with incidence peaking between the ages of 30 and 35.³ Females are 2 to 3 times more likely to develop MS than males, and whites are more likely to develop MS than persons of Asian or African descent.³

Because MS is chronic and disabling—and because, despite their disability, most people with MS have a normal life span⁴—MS imposes considerable cost on individuals, families, the health care system, and society. In 1998, it was estimated that the total annual economic burden of MS in the United States

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TABLE 1 Disease-Modifying Drugs for Multiple Sclerosis*

Generic Name	Abbreviation	Label Name	Date of FDA Approval
Interferon beta-1b	IFN beta-1b	Betaseron	July 1993
Interferon beta-1a (for intramuscular administration)	IFN beta-1a (IM)	Avonex	May 1996
Glatiramer acetate	Glatiramer	Copaxone	December 1996
Interferon beta-1a (for subcutaneous administration)	IFN beta-1a (SC)	Rebif	March 2002

* Disease-modifying drug (DMD) is common term used by the National Multiple Sclerosis Society, and these drugs are also known as immunomodulators or biologic agents.¹⁴

FDA=U.S. Food and Drug Administration.

TABLE 2 Sample Selection

Criteria	Number Removed	Number Remaining
Total MS patient population in 2004*	—	13,420
MS patients with full 12 months claims data	3,321	10,099 (75.3%)
MS patients who received at least 1 claim for a DMD†	4,289	5,810 (57.5% of above)
MS patients who received monotherapy with a DMD	333	5,477 (94.3% of above)

* Patients with ETGs 149 or 150 and at least 1 medical claim with an ICD-9-CM code for multiple sclerosis (340).

† DMD=disease-modifying drug, defined as use of any of the drugs listed in Table 1.

ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; MS=multiple sclerosis.

exceeded \$6.8 billion, with a lifetime cost (direct and indirect) of \$2.2 million per patient.⁵ Since MS patients are typically affected in the prime of life, most of the total costs (57%) are related to indirect costs such as lost income, equipment and alterations, and formal (paid) and informal (unpaid) care. MS is, in fact, more costly than other debilitating diseases, such as stroke or Alzheimer's disease, that generally occur later in life.⁵ Moreover, as the prevalence of MS increases, and new, more expensive drugs are launched, MS-related costs are becoming more closely scrutinized by payers in the managed care arena.

This background underscores the need for managed care professionals to understand how MS is treated and managed system-wide. However, little current information is available because much of the available research was conducted before the emergence of contemporary disease-modifying drugs (DMDs) or immunomodulators, such as the interferons and glatiramer. For example, the first of these agents (interferon beta-1b, Betaseron) was approved by the U.S. Food and Drug Administration for use in the United States in 1993, and the most recently approved product (interferon beta-1a, Rebif) entered the market in 2002 (Table 1).

This is a descriptive analysis of the results of aggregating administrative claims for more than 10,000 MS patients in 2004. The direct medical costs are reported by component cost categories and arrayed by other variables of interest that may be useful to managed care clinicians and administrators.

Methods

Source Data

Patient-level administrative claims data were obtained from the PharMetrics Integrated Patient-centric Database, a large data warehouse of administrative claims. At the time of this analysis, the database contained data from more than 80 private and public (Medicare and Medicaid) health care plans across the United States, representing more than 9.6 million unique patients in 2004. Medical and facility claims have diagnosis codes in The *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) format, and procedure codes are in Current Procedural Terminology version 4 (CPT-4) and Health Care Procedure Coding System formats. National Drug Code (NDC) numbers are used to identify drugs in pharmacy claim records from both community and mail-service pharmacies. Additional data elements from the database used in this analysis include patient characteristics such as geographic region, age and gender, insurance type (e.g., health maintenance organizations [HMOs], preferred provider organizations [PPOs]), and payer type (e.g., commercial, self-insured, Medicare risk).

Cost-Aggregating Software

The source data for this analysis were organized and grouped using Episode Treatment Group (ETG) software from Symmetry Health Data Systems, a widely used illness-classification and episode-building software application. The ETG methodology

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TABLE 3 Total Average Annual MS Cost per Patient by Region (2004)

Region	N	% of Total	Average Cost per Year (\$) [SD]	P Value*
Midwest	4,817	47.7	13,228 [19,301]	<0.001
Northeast	1,821	18.0	12,471 [13,809]	
Southcentral	650	6.4	8,418 [9,907]	
Southeast	2,099	20.8	12,912 [22,459]	
West	712	7.1	15,533 [16,990]	
Overall (all regions)	10,099	100.0	12,879 [18,583]	–

* Calculated using analysis of variance.

MS= multiple sclerosis.

matches medical claims and pharmacy claims data to specific diagnoses through a series of temporal and clinical-association algorithms. ETG-based episodes of care are longitudinal packages of disease-specific claims data and provide a consistent method for reporting health care economics spanning the entire continuum of care and for relating these measures to independent variables such as patient demographics, clinical markers, and pharmacotherapy.⁶ For purposes of this analysis, only the aggregation feature of ETGs was employed; i.e., ETGs were used to aggregate medical costs and not to define discrete episodes of care.

The ETGs used in this analysis, ETG 149 (inflammation of the CNS, with surgery) and ETG 150 (inflammation of the CNS, without surgery), are based on ICD-9-CM codes that include MS (340) and other neurological conditions such as 336 (spinal cord disease not elsewhere classified), 337 (autonomic nerve disorder), 341 (other CNS demyelination), and 344 (other paralytic syndromes). ETG-based episodes are typically built using a variety of similar ICD-9-CM codes to compensate for variations or errors in provider coding practices; however, as noted in the patient selection criteria sections of this analysis, only ETGs built upon ICD-9-CM code 340 were used in this analysis. The ETG methodology was used to identify and aggregate claims data for economic measurements and, as mentioned, captures claims that are not only directly identified by ICD-9-CM code 340 for the treatment of MS but also other, less specific ICD-9-CM codes that are associated with procedures and services identified as being specific and relevant to the treatment of MS, compensating for coding variations or errors.

Patient Selection

Patient data comprising the primary MS study population were selected from the source database for January 1, 2004, through December 31, 2004. Patients were selected on the basis of the presence of ETGs 149 or 150 and at least 1 medical claim with a diagnosis of MS (ICD-9-CM code 340). This ICD-9-CM code is

specific to ETGs 149 and 150 and is a primary marker used by the ETG software methodology to define the MS episodes for this analysis. The ETG codes were used to capture MS-related costs.

Reporting Metrics

Cost information related to use of medical and pharmacy services was captured using ETG-defined aggregation for dates of service over an interval of 365 days (representing the 2004 calendar year); thus, each patient contributed only 1 episode to the analysis. The cost fields from the administrative claims data used in this analysis are submitted charges (i.e., charges submitted by providers) and do not represent actual payer costs. The cost data were then broken down into the following categories and, where applicable, subcategories, thereby identifying the point along the patient care continuum at which MS-specific service was received:

- **Inpatient**
 - Ancillary: diagnostic or treatment-related procedures
 - Facility: room and board charges
 - Management: clinician inpatient visit
 - Surgical: surgical procedures
- **Outpatient**
 - Ancillary: diagnostic or treatment-related procedures
 - Management: office visit charges for usual care
 - Surgical: surgical procedures
- **Pharmacy.** All prescription drug claims (provided by in-office administration, community, or mail-order pharmacies) defined by an NDC code and/or a J code. J codes used in this analysis for the identification of DMDs were J1825 (injection beta-1a, 33 mcg), J1830 (injection, interferon beta-1b, 0.25 mg), and J1595 (injection, glatiramer acetate, 20 mg).
- **Emergency room.** Any medical claim containing procedure codes (CPT-4) 99281-99288 or revenue codes 450-452, 456, 459, or 981.

Cost Aggregation by Drug

Costs were also aggregated by DMD for the 3 interferons and glatiramer. Each DMD patient had to have at least 1 pharmacy claim with an NDC code for a DMD or at least 1 medical claim with a J code for a DMD in 2004. A subanalysis was also performed for patients who received only 1 DMD (i.e., monotherapy).

Statistical Analysis

Analysis of univariate means was performed using analysis of variance, and proportions were compared with chi-square testing. All statistics were generated using SPSS version 13.0 software (SPSS Inc., Chicago, IL).

Results

Population Characteristics

The MS population in this analysis consisted of 10,099 patients (Table 2). This was a national-level sample, with nearly half

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(48%) of the patients from the Midwest, and a total of 40% from the Northeast and Southeast (Table 3). These percentages do not reflect the prevalence of MS in those regions but only the composition of the database. With respect to line of business, the analyzed patient population was primarily derived from commercial insurance plans (89%) and from HMOs and PPOs (49% and 33%, respectively) (Table 4).

The average age of a patient with MS was 47 years (standard deviation [SD], 11.2 years); nearly 63% of patients were between the ages of 36 and 55 years. Female patients outnumbered male patients by more than 3 to 1 (Table 5). Of the concurrent conditions (selected conditions of interest) in the MS population in this study, the most commonly reported in medical claims were malaise and fatigue (ICD-9-CM codes 780.7, 780.71, or 780.79, in 21.6% of patients), depression (ETGs 95 or 96 [which are based on ICD-9-CM codes 296, 298, 300, 301, 309, 311 and 313], reported in 19.8% of patients), and burning/numbness/tingling sensations (ICD-9-CM code 782.0, reported in 17.2% of patients). Reported less frequently were some of the more severe complications of the disease, such as ataxia (ICD-9-CM code 781.3, reported in 3.1% of patients) and optic neuritis (ICD-9-CM code 341.0, reported in 0.4% of patients) (Table 6).

Annual Costs

The total cost for the average MS patient in calendar year 2004 (representing total direct MS costs over the 365-day period for inpatient, outpatient, emergency room, and pharmacy services) was \$12,879 (Table 7). Average outpatient costs were \$3,380 per patient (26% of total costs), attributable to 14.5 outpatient services (units of use), which included 4.4 physician office visits (outpatient management) and 10 diagnostic procedures (Table 7). Per patient, approximately 8.8 MS-specific prescriptions including DMDs were dispensed during the year 2004, representing \$8,351 in costs (64.8% of total annual costs) (Table 7).

There were significant differences in total annual costs for all demographic subgroups, except for gender. Region, line of business, payer, and patient age were associated with statistically significant variation ($P < 0.001$). There was no significant difference in total annual costs by gender ($P = 0.396$) (Tables 3, 4, and 5).

Average annual costs per patient were often significantly higher when certain conditions were present (compared with episodes that reported no evidence of those conditions). When aggregated by clinical condition, patients with medical claims with 1 or more diagnosis codes for abnormality of gait had average costs of \$20,871, and patients with diagnosis codes for spasms had average costs of \$20,376, both about 60% higher than the cost of the average MS episode (\$12,879) (Table 6).

Annual Costs by DMD

Use of a single drug in the interferon class was observed in 36.0% of MS patients (combined $n = 3,640$) with sole use of IFN beta-1a (intramuscular [IM]) the most frequent ($n = 2,023$,

TABLE 4 Total Average Annual MS Cost by Insurance Type and Payer (2004)

Insurance Type	N	% of Total	Average Annual Cost (\$) [SD]	P Value*
Health maintenance organization	4,941	48.9	12,110 [22,622]	<0.001
Indemnity plan	657	6.5	13,011 [12,532]	
Point of service	958	9.5	14,409 [13,290]	
Preferred provider organization	3,377	33.4	13,656 [13,973]	
Payer				
Commercial plan	8,982	88.9	13,152 [19,015]	<0.001
Medicaid	190	1.9	10,117 [12,173]	
Medicare cost	63	0.6	11,568 [12,276]	
Medicare risk	253	2.5	8,410 [12,431]	
Self-insured	476	4.7	11,877 [17,265]	

* Calculated using analysis of variance.
MS = multiple sclerosis.

TABLE 5 Total Average Annual MS Cost by Patient Age and Sex (2004)

Average Age		Mean	Standard Deviation		
		47.1	4.7		
Age (Years)	N	% of Total	Average Annual Cost (\$) [SD]	P Value*	
0-17	74	0.7	4,464 [7,893]	<0.001	
18-25	257	2.5	15,675 [54,044]		
26-35	1,249	12.4	12,645 [14,295]		
36-45	2,684	26.6	13,130 [12,543]		
46-55	3,651	36.2	13,525 [21,051]		
56-64	1,744	17.3	12,060 [13,850]		
≥65	440	4.4	9,677 [14,416]		
Gender					
Female	7,749	76.7	12,792 [16,249]	0.396	
Male	2,350	23.3	13,164 [24,768]		

* Calculated using analysis of variance.
MS = multiple sclerosis.

21.0% of all MS patients), followed by glatiramer ($n = 1,837$, 20.2%), IFN beta 1-b ($n = 952$, 8.6%), and IFN beta-1a (subcutaneous [SC]) ($n = 665$, 6.7%) (Table 8). Among the patient groups analyzed, the group treated with IFN beta-1a (SC) was slightly younger (average of about 44 years old), but the absolute difference among the 4 DMDs was small (Table 9).

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TABLE 6 Total Average Annual MS Cost by Presence of Selected Comorbid Conditions (2004)

Condition	N	% of Total	Average Annual Cost (\$ [SD])	P Value*
Abnormality of gait (781.2)	744	7.4	20,871 [37,948]	<0.001
Ataxia (781.3)	311	3.1	16,168 [19,317]	0.002
Burning, numbness, tingling sensations (782.0)	1,738	17.2	12,504 [14,913]	0.356
Convulsions (780.3)*	349	3.5	15,664 [20,381]	0.004
Depression (ETGs 95 or 96)	2,001	19.8	13,928 [14,757]	0.005
Fecal incontinence (787.6)	40	0.4	18,694 [14,101]	0.047
Fibromyalgia/myalgia and myositis (729.1)	744	7.4	11,478 [12,574]	0.033
Malaise and fatigue (780.7*)	2,177	21.6	14,604 [17,630]	<0.001
Optic neuritis (341.0)	37	0.4	39,247 [138,557]	<0.001
Spasms (781.0)	333	3.3	20,376 [26,652]	<0.001
Trigeminal neuralgia (350.1)	92	0.9	12,467 [17,494]	0.831
Urinary incontinence (788.3*)	558	5.5	16,898 [19,118]	<0.001
Voice disturbances (784.4*, 784.5)	165	1.6	16,463 [25,537]	0.012

* The prevalence of selected conditions was based on the presence of listed ETGs or 1 or more ICD-9-CM codes present on medical claims any time during the study period.

† Calculated using analysis of variance.

MS= multiple sclerosis.

TABLE 7 MS Component Costs—Overall Population (2004)

Service Category	Units of Use* per Year	Costs per Year (\$)
	Mean [SD]	Mean (% of Total) [SD]
Inpatient ancillary	0.80 [5.76]	543 (4.2) [4,592]
Inpatient facility	0.06 [0.48]	414 (3.2) [8,716]
Inpatient management	0.24 [1.85]	39 (0.3) [277]
Inpatient surgical	0.01 [0.15]	7 (<0.1) [165]
Inpatient total	1.11 [7.36]	1,004 (7.8) [10,866]
Outpatient ancillary	9.96 [18.77]	2,777 (21.6) [5,108]
Outpatient management	4.36 [8.23]	546 (4.2) [1,171]
Outpatient surgical	0.15 [0.71]	57 (0.4) [368]
Outpatient total	14.47 [22.47]	3,380 (26.2) [5,527]
Emergency room	0.64 [3.61]	145 (1.1) [9,212]
Pharmacy	8.79 [10.4]	8,351 (64.8) [13,513]
Disease-modifying drugs	5.29 [6.37]	7,901 (61.4) [13,336]
Total annual costs	—	12,879 (100.0) [18,583]

* Units of use refers to the number of claims submitted that fall under each service category or subcategory.

MS= multiple sclerosis.

There was no difference in the ratio of females to males, about 75% to 79% for the 4 DMDs. There were small differences in the rates of selected conditions of interest among patients who received the 4 DMDs, including abnormality of gait ($P < 0.001$); ataxia ($P = 0.004$); burning, numbness, and tingling sensations ($P < 0.001$); depression ($P < 0.001$) and malaise and fatigue ($P = 0.002$); and fibromyalgia, myalgia, and myositis ($P = 0.015$) (Table 10).

Total average annual MS-related treatment costs appeared to be slightly lower (about 6%) for the patient group treated with glatiramer (\$16,928) compared with IFN beta-1a (IM) (\$17,987), about 14% lower compared with IFN beta-1b (\$19,616), and 25% less than the group treated with IFM beta-1a (SC) (\$22,557) (Table 11). The glatiramer group had the lowest number of pharmacy claims for the DMD (average 8.14), and the IFN beta-1a (IM) group had the highest number of DMD claims (average 10.41).

Discussion

MS disease treatment costs are affected by both clinical and nonclinical factors. The nonclinical factors include patient demographics, region of the country, type of insurance, and payer type. This study provides a description of the distribution of direct costs related to MS treatment within U.S. managed care organizations and indemnity health insurance plans. On average, the total annual cost in 2004 for MS-related medical care was

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TABLE 8 Utilization of Disease-Modifying Drugs in MS Patients (2004)

	IFN Beta-1a (IM)		IFN Beta-1a (SC)		IFN Beta-1b		Glatiramer	
	N	%*	N	%	N	%	N	%
Patients with any DMD use	2,238	22.2	850	8.4	1,032	10.2	2,038	20.2
Patients with DMD monotherapy†	2,023	21.0	665	6.7	952	8.6	1,837	18.2

* % = the ratio of DMD (disease-modifying drug) use in the total sample of 10,099 MS patients.

† Monotherapy refers to the sole use of the DMD listed in the column heading during the study year, with no evidence of other DMDs.

IFN = interferon; IM = intramuscular; SC = subcutaneous.

TABLE 9 Average Patient Age and Sex by Specific Disease-Modifying Drug (2004)

	IFN Beta-1a (IM)		IFN Beta-1a (SC)		IFN Beta-1b		Glatiramer		P Value
	N	% of Total	N	% of Total	N	% of Total	N	% of Total	
Average age	46.7		43.7		47.4		45.6		<0.001*
Gender									
Female	1,548	76.5	498	74.9	729	76.6	1,453	79.1	0.089†
Male	475	23.5	167	25.1	223	23.4	384	20.9	

* Calculated using analysis of variance.

† Calculated using chi-square analysis.

IFN = interferon.

\$12,879 per patient/episode, with 64.8% of the total charges attributable to prescription drugs. A comparison of these data with research performed before the emergence of DMDs indicates that, over time, the cost structure for treating MS has changed notably. In particular, in a 1995 analysis of 6,412 MS patients from a privately insured population Pope et al. reported annual costs per patient (in 1995 dollars) of \$7,677—equivalent to \$9,515 in 2004 dollars—with 18% attributable to prescription drugs.⁷ The analysis by Pope et al. used allowed charge data (i.e., net health plan cost plus member cost share) rather than the provider-submitted charges used in the present analysis, thereby understating the cost basis data for 1994-1995. With this caveat, the comparison reflects that 2004 pharmacy costs were higher and constituted a higher percentage of the total annual costs. Yet, 2004 costs for medical services were—after adjusting for inflation—actually lower than those reported in the 1995 study: \$4,529 in 2004 compared with \$7,802 in 1995 (Table 12). This trend may be related to the effectiveness of DMD therapy in managing MS severity and reducing functional disability, which has been correlated with lower costs.^{8,9}

With respect to the clinical factors that affect MS costs, research has shown that indirect as well as direct costs increase exponentially as disability progresses.⁹ On the standard measure of progressive disability known as the Expanded Disability Status Scale, moderate limitations increased costs by factors of 1.15 to 3.43, and losing the ability to walk without aid or a wheelchair increased costs by 3.86 to 7.46 times the cost of patients with mild disabilities.⁹ Exacerbations of MS symptoms,

referred to as relapses, also substantially increase the cost of medical care.¹⁰ Although the limitations of this analysis preclude links between clinical severity and costs, we have observed how the presence of certain concurrent conditions related to the progression of MS,¹¹ used as surrogates of disease severity, can influence costs. In the present study, the medical claim diagnoses associated with higher costs include abnormality of gait, optic neuritis, and spasms.

The present study was limited to direct medical costs in 2004. Kobelt et al. estimated that direct medical and nonmedical costs represented 53% of the total cost of MS.⁸ Almost half of the total societal cost of MS is attributable to production losses (37%) and informal care (10%). In their cross-sectional postal survey, Kobelt et al. also found considerable interpatient variability in disease severity and 29% of MS patients reporting a relapse in the past 3 months.

Using administrative claims data for approximately 9.6 million patients covered by public payers (Medicare or Medicaid) and private health plans, we found a prevalence of 14.0 patients per 10,000. This is considerably lower than the prevalence of 24 per 10,000 found by Pope et al. in the privately insured population in 1994 and 1995, of 36 per 10,000 in the Medicare population (1996 and 1997), and of 71 per 10,000 in the disabled subpopulation of Medicaid recipients in 6 states (1991-1996).⁷

In the present study, use of the 4 DMDs was associated with different total MS-related treatment costs. This descriptive analysis cannot be used to ascertain the reasons for the variance in total treatment costs, which could be explained by the effect

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TABLE 10 Prevalence* of Selected Conditions by Disease-Modifying Drug Therapy (2004)

Condition	IFN Beta-1a (IM)		IFN Beta-1a (SC)		IFN Beta-1b		Glatiramer		P Value
	N	% of Total	N	% of Total	N	% of Total	N	% of Total	
Abnormality of gait (781.2)	100	4.9	57	8.6	96	10.1	126	6.9	<0.001
Ataxia (781.3)	49	2.4	28	4.2	30	3.2	41	2.2	0.035
Burning, numbness, tingling sensations (782.0)	244	12.1	132	19.8	90	9.5	272	14.8	<0.001
Convulsions (780.3*)	35	1.7	22	3.3	22	2.3	48	2.6	0.083
Depression (ETGs 95 or 96)	344	17.0	132	19.8	174	18.3	423	23.0	<0.001
Fecal incontinence (787.6)	5	0.2	0	0	6	0.6	8	0.4	0.137
Fibromyalgia/myalgia and myositis (729.1)	104	5.1	42	6.3	52	5.5	97	5.3	0.701
Malaise and fatigue (780.7*)	357	17.6	154	23.2	172	18.1	354	19.3	0.015
Optic neuritis (341.0)	3	0.1	3	0.5	1	0.1	6	0.3	0.350
Spasms (781.0)	47	2.3	19	2.9	34	3.6	49	2.7	0.275
Trigeminal neuralgia (350.1)	16	0.8	4	0.6	3	0.3	19	1.0	0.209
Urinary incontinence (788.3*)	88	4.3	38	5.7	44	4.6	76	4.1	0.394
Voice disturbances (784.4*, 784.5)	19	0.9	8	1.2	16	1.7	15	0.8	0.175

* The prevalence of selected conditions was based on the presence of listed ETGs or 1 or more ICD-9-CM codes present on medical claims any time during the study period.

IFN=interferon; IM=intramuscular; SC=subcutaneous.

of disease severity. The United Kingdom's National Institute for Health and Clinical Excellence (NICE) released an unfavorable evaluation of available DMDs in 2002,¹² but these agents are commonly used for treating MS in the United States. A 5th DMD, natalizumab (Tysabri), was withdrawn from the U.S. market in February 2005 because of an association between that drug and the development of progressive multifocal leukoencephalopathy. However, natalizumab was reintroduced to the U.S. market in June 2006, evidence of the demand and need for alternative therapies for MS, particularly for those patients with relapsing MS.

There are gaps in information about MS-related health care costs. Our results were similar to those of a 2002 study designed to measure cost-effectiveness among the DMDs, including slightly lower costs associated with use of glatiramer compared with use of interferons.¹³ However, at the time of the 2002 analysis, only 2 of the 3 interferons were available: interferon beta-1a (IM) and interferon beta-1b.

Limitations

Foremost among the limitations of this study is the method of data aggregation and follow-up for MS patients. For example, drug utilization was quite different among the 4 DMDs, an average of 10.4 DMD pharmacy claims for IFN beta-1a (IM) versus 8.7 each for IFN beta-1a (SC) and IFN beta-1b, and 8.1 for glatiramer in calendar year 2004. Second, administrative claims data do not include clinical information, such as laboratory

values, or other measures, such as disease severity, and this study could not aggregate data by MS disease type (e.g., primary progressive vs. relapsing-remitting or secondary progressive disease). There is large variation in the cost measures in the present study, as evidenced from the large standard deviation values.

Third, this is a descriptive analysis that cannot inform about cause-and-effect relationships. While we were curious about the aggregate costs by DMD, it is not possible to determine how economic outcomes are related to clinical status or the effect of patient severity on economic outcomes in this study. Fourth, the cost data in the present study were provider-submitted charges, which may, because of variable reimbursement rates, overstate actual payer costs.

Fifth, this study relied on third-party software (i.e., the ETGs) to aggregate administrative claims data since MS-related medical claims may not have the specific 340 ICD-9-CM diagnosis code for MS. This method has 2 implications. First, while MS-related costs aggregated in this manner may identify the direct medical costs to treat MS, they may not accurately reflect the actual costs of MS or the total cost burden that an MS patient places on the health care system. Second, using a commercially available and widely used tool such as ETGs enables others to perform an analysis similar to this study in their own environments and to use the data from the present study for comparison. On the other hand, the ETG software is

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TABLE 11 Average Total Annual MS Cost by Disease-Modifying Drug Utilization (2004)

Service Category	IFN Beta-1a (IM) [N=2,023]		IFN Beta-1a (SC) [N=665]		IFN Beta-1b [N=952]		Glatiramer [N=1,837]		P Value†
	Mean (\$) [SD]	% of Total	Mean (\$) [SD]	% of Total	Mean (\$) [SD]	% of Total	Mean (\$) [SD]	% of Total	
Inpatient	744 [7,297]	4.1	1,204 [6,811]	5.3	2,015 [27,818]	10.3	948 [6,075]	5.6	0.094
Outpatient	2,834 [52]	15.8	5,157 [6,722]	22.9	3,234 [4,838]	16.5	3,154 [4,797]	18.6	<0.001
Emergency room	91 [6]	0.5	265 [1,527]	1.2	91 [532]	0.5	116 [732]	0.7	<0.001
Pharmacy	14,318 [73]	79.6	15,930 [9,258]	70.6	14,276 [6,345]	72.8	2,710 [7,319]	16.0	<0.001
Total charges	17,987 [11,714]	100.0	22,557 [12,566]	100.0	19,616 [29,651]	100.0	16,928 [10,780]	100.0	<0.001
DMD claims	10.41 [7.50]	NA	8.67 [5.36]	NA	8.68 [4.24]	NA	8.14 [4.61]	NA	<0.001
DMD costs*	13,860 [7,066]	77.1	15,278 [8,890]	67.7	13,690 [6,092]	69.8	12,190 [6,979]	72.0	<0.001
All other pharmacy costs	457 [1,759]	2.5	653 [2,172]	2.9	586 [1,724]	3.0	520 [1,766]	3.1	0.065

* Refers to only the disease-modifying drug named in the respective column heading.

† Calculated using analysis of variance.

IFN=interferon; IM=intramuscular; MS= multiple sclerosis; NA=not applicable; SC=subcutaneous.

TABLE 12 Comparison of MS Costs for 1995 and 2004

Study Year	Cost Component (\$)		
	Medical	Pharmacy	Total Annual Costs
1995	6,329	1,348	7,677
Adjusted 1995*	7,802	1,713	9,515
2004	4,529	8,351	12,879
% change (from adjusted 1995 to 2004)	-42%	388%	35%

* Adjusted for inflation using the U.S. Consumer Price Index.

MS= multiple sclerosis.

not free, and other methods to group administrative claims data may produce different results.

Conclusions

Pharmacy costs represented 65% of total MS-related treatment costs in 2004, and 57.5% of all MS patients received at least 1 DMD. For the patients who used DMDs, pharmacy costs represented an average 75% of total MS-related medical care costs. While there were differences in the total MS-related treatment costs among the 4 DMDs, the reasons for these differences could not be ascertained in the present study.

What is already known about this subject

- Multiple sclerosis is a chronic and debilitating medical condition with a growing patient population that requires long-term treatment. The economic burden imposed by MS is substantial, consisting of direct and indirect costs. The indirect costs are, by definition, largely outside the control of managed care, but managed care can influence the direct costs of treating MS.

What this study adds

- This study promotes better understanding of the factors that influence direct costs. This study presents direct medical claims data that managed care decision makers can use as benchmarks to evaluate their own cost and utilization data.

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