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An Assessment of Factors Associated with High Costs Among Patients with Multiple Sclerosis (MS) Receiving Disease-Modifying Drug (DMD) Therapy

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Introduction

- Multiple sclerosis (MS), a chronic, recurrent inflammatory disease of the white and gray matter of the central nervous system (CNS), is characterized by inflammatory attacks on CNS myelin, which result in a variety of symptoms such as blurred vision, walking and coordination problems, bladder or bowel dysfunction, numbness, and cognitive impairment.[1]
- Relapsing–remitting multiple sclerosis (RRMS), which accounts for approximately 85% of MS diagnoses, is characterized by defined attacks or relapses that result in worsening of neurological function, with partial to complete recovery between attacks.[1]
- Previous studies have traditionally relied on assessing the rate of MS relapses, defined by MS-related hospitalizations or outpatient visits and steroid use. However, other markers of disease progression exist, which may be associated with higher costs and reduced quality of life.
- The ability to identify disease severity at a broader level is important to identify patient populations likely to benefit from intervention, as well as for evaluating the effectiveness and value of treatment.

Objective

- To compare patient characteristics and the frequency of diagnoses between high-cost and non-high-cost MS patients receiving disease-modifying-drugs (DMDs).

Methods

Study Design and Subjects

- Patients were identified from a retrospective database (IMS PharMetrics Plus) between January 1, 2007 and June 30, 2012 and placed into two cohorts based on all-cause total costs (excluding DMD costs). Patients with costs ≥ the 75th percentile were considered high-cost, while patients with costs < the 75th percentile were considered non-high cost. In both cohorts, subjects had ≥ 1 medical claim (at any service location) with a diagnosis for MS (ICD-9-CM code 340).
- Eligible subjects had ≥ 1 prescription for a DMD; the date of the first prescription was the index date. Included subjects had continuous eligibility (medical and pharmacy) for 1 year prior to (baseline) and 1 year following (follow-up) the index date. Subjects were also required to have ≥ 1 medical claim (at any service location) with a diagnosis for MS (ICD-9-CM code 340) during the baseline or follow-up period. Subjects were aged 18 to 63 years as of the index date.

Patient Characteristics

- **Demographic characteristics** included:
  - Age as of index (continuous and grouped; 18-34, 35-44, 45-54, 55-63 years)
  - Sex
  - Census region
- **Diagnosis and treatment characteristics** included the following:
  - Newly diagnosed with MS, defined as no diagnosis of MS during baseline period
  - Newly treated with MS, defined as no evidence of DMDs during baseline period
  - DMD adherence, defined as medication possession ratio (MPR) ≥ 0.8 during follow-up period
- The presence and count of **diagnosis codes (ie, "condition indicators")** were evaluated during the 1-year baseline period and grouped into 3 domains:
  - MS-related conditions: altered mental state, balance disorders, constipation, depression, infections, malaise and fatigue, muscle spasm, musculoskeletal, numbness, optical neuritis, rehabilitation, stiffness, urinary incontinence, pain, disability, and spirometry
  - Clinical Classification System (CCS) code categories: arthritis bone and joint, cancer, congenital abnormalities, cardiovascular system, dermatologic, drug/device complication, endocrine, eye and ear, fetal and congenital, genitourinary, gastrointestinal, gynecological, hematologic, infectious disease, injuries, intra-abdominal organ, metabolic/nutritional, obstetrical, poisoning/overdose, psychiatric, pulmonary and venous
  - Charlson-Deyo comorbidities: AIDS, any primary malignancy, congestive heart failure, chronic pulmonary disease, cerebrovascular disease, dementia, diabetes with and without chronic complications, hemiplegia or paraplegia, metastatic solid tumor, myocardial infarction, mild liver disease, moderate or severe liver disease, peptic ulcer disease, peripheral vascular disease, renal disease, and rheumatologic disease
  - Dalfampridine use, a symptomatic agent, was also evaluated

Outcomes

- Costs were defined as all-cause total costs (excluding DMD costs) based on paid amounts, and were evaluated over the 1-year follow-up period

Methods

Analysis

- **Descriptive:**
  - Baseline demographic and clinical characteristics were evaluated for patients in both cohorts
  - All descriptive analyses included mean, median, standard deviation, minimum, maximum, and interquartile ranges (IQR) for continuous measures and proportions for binary and categorical measures
  - Statistical testing was completed to test the significance of any observed differences between cost groups
  - Chi-square and Fisher tests were used for binary/categorical measures
  - Wilcoxon-Mann-Whitney tests were used for continuous measures, including costs, where a normal distribution was not assumed
- **Multivariate Analysis:**
  - Logistic regression was used to evaluate the likelihood membership of being in the high-cost cohort
  - Covariates included patient demographics, condition indicators, dalfampridine use, newly initiating DMDs, and DMD adherence
  - Four specifications were used with regards to the condition indicator covariates:
  - Counts of condition indicators only
  - Binary indicators for each condition
  - Flags for condition indicators differing by ≥ 5% between cohorts
  - Flags for condition indicators differing by ≥ 10% between cohorts

Results

Figure 1. Patient Selection Flowchart.

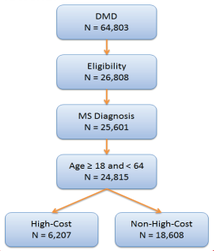

Table 1. Demographic and Treatment/Diagnosis Characteristics among Patients with MS Treated with DMDs

Characteristic	High-Cost	Non-High-Cost	p-value
N	6,207	18,608	
Age			
Mean (SD)	46.3 (9.8)	44.2 (9.9)	<0.001
Median (IQR)	47.0 (40.0 - 54.0)	45.0 (37.0 - 52.0)	
Minimum	18	18	
Maximum	63	63	
Age Group, N (%)			<0.001
18 to 34	837 (13.5%)	3,297 (17.7%)	
35 to 44	1,608 (25.9%)	5,740 (30.8%)	
45 to 54	2,340 (37.7%)	6,577 (35.3%)	
55 to 64	1,422 (22.9%)	2,994 (16.1%)	
Sex, N (%)			<0.001
Female	4,911 (79.1%)	14,146 (76.0%)	
Male	1,295 (20.9%)	4,462 (24.0%)	
Region, N (%)			<0.001
Midwest	2,001 (32.2%)	6,126 (32.9%)	
Northeast	2,125 (34.2%)	5,762 (31.0%)	
South	1,258 (20.3%)	4,206 (22.6%)	
West	823 (13.3%)	2,514 (13.5%)	
Newly diagnosed, N (%)	276 (4.4%)	1,230 (6.6%)	<0.001
Newly treated, N (%)	3,782 (60.9%)	10,800 (58.0%)	<0.001
Adherent, N (%)	3,009 (48.8%)	11,731 (63.3%)	<0.001

Data Source: IMS PharMetrics Plus (January 1, 2006 – June 30, 2013)

DMD: disease modifying therapy; IQR: Interquartile Range; MS: multiple sclerosis; SD: standard deviation

Results

- A total of 24,815 patients were identified (Figure 1)
- The threshold for high-cost status was $11,740, yielding 6,207 high-cost and 18,608 non-high cost patients
- Baseline patient characteristics for both cohorts, including demographic, diagnosis, and treatment characteristics, are shown in Table 1.
  - High-cost patients were slightly older (46.3 years vs. 44.2 years; p<0.001).
  - Females comprised the majority of both cohorts (79.1% [high-cost] and 76.0% [non-high-cost])
  - More patients were newly diagnosed and adherent to therapy in the non-high-cost cohort (6.6% vs. 4.4% and 63.3% vs. 48.8%, respectively ; both p<0.001)
  - A majority of patients in both cohorts were newly treated, with a slightly higher proportion newly treated in the high-cost cohort (60.9% vs. 58.0%, p<0.001)

Table 2. Condition Indicators among Patients with MS Treated with DMDs

Characteristic	High-Cost	Non-High-Cost	p-value
N	6,207	18,608	
MS Condition Indicator, N (%)			
Balance disorders	2,160 (34.8%)	2,713 (14.6%)	<0.001
Depression	1,850 (29.8%)	2,414 (13.0%)	<0.001
Disability	4,655 (75.0%)	8,186 (44.0%)	<0.001
Malaise and fatigue	2,199 (35.4%)	3,559 (19.1%)	<0.001
Musculoskeletal	4,943 (79.6%)	9,501 (51.1%)	<0.001
Number of MS Condition Indicators			
Mean (SD)	3.6 (2.0)	1.9 (1.6)	<0.001
Median (IQR)	3.0 (2.0 - 5.0)	2.0 (1.0 - 3.0)	
Range	0 - 13	0 - 11	
CCS Code Category, N (%)			
Arthritis, bone and joint	4,981 (80.2%)	9,637 (51.8%)	<0.001
Cardiovascular system	4,069 (65.6%)	7,565 (40.7%)	<0.001
Eye and ear	3,523 (56.8%)	7,858 (42.2%)	<0.001
Gynecological	2,983 (48.1%)	6,427 (34.5%)	<0.001
Infectious disease	4,625 (74.5%)	10,232 (55.0%)	<0.001
Number of CCS Code Groups			
Mean (SD)	7.4 (3.1)	4.3 (2.6)	<0.001
Median (IQR)	7.0 (5.0 - 9.0)	4.0 (2.0 - 6.0)	
Range	0 - 19	0 - 16	
Charlson Comorbidities, N (%)			
Any primary malignancy	445 (7.2%)	359 (1.9%)	<0.001
Chronic pulmonary disease	943 (15.2%)	1,130 (6.1%)	<0.001
Cerebrovascular disease	518 (8.3%)	492 (2.6%)	<0.001
Diabetes without CC	806 (13.0%)	950 (5.1%)	<0.001
Hemiplegia or paraplegia	303 (4.9%)	182 (1.0%)	<0.001
Rheumatologic disease	192 (3.1%)	159 (0.9%)	<0.001
Charlson Score			
Mean (SD)	0.9 (1.4)	0.2 (0.6)	<0.001
Median (IQR)	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)	
Range	0 - 12	0 - 10	
Use of dalfampridine, N (%)	244 (3.9%)	133 (0.7%)	<0.001

Data Source: IMS PharMetrics Plus (January 1, 2006 – June 30, 2013)

CC: chronic complications; CCS: clinical classifications system; IQR: inter-quartile range; MS: multiple sclerosis; DMD: disease-modifying drug; SD: standard deviation;

- Selected condition indicators for both cohorts are shown in Table 2.
  - The percentage of patients with each condition indicator was statistically significantly higher in the high-cost cohort (p<0.05)
  - Musculoskeletal was the most common MS-related condition, present in 79.6% and 51.1% of high-cost and non-high-cost patients, respectively
  - Arthritis bone and joint and infectious disease were the two most common CCS code groups in both cohorts
  - Chronic pulmonary disease was the most Charlson comorbidity, present in 15.2% and 6.1% of high-cost and non-high-cost patients

Results

Table 3. Logistic Regression Predicting Membership in the High-Cost Cohort (counts of conditions)

Covariate	OR Estimate	Lower 95% CI	Upper 95% CI	p-value
Female (vs. Male)	0.949	0.875	1.03	0.2119
Age group (vs. 18 to 34)				
35 to 44	1.028	0.924	1.144	0.6117
45 to 54	1.098	0.99	1.217	0.0758
55 to 64	1.135	1.01	1.275	0.033
Region (vs. Northeast)				
Midwest	0.995	0.917	1.079	0.8977
South	0.759	0.691	0.833	<.0001
West	0.949	0.851	1.058	0.3436
Adherent (vs. Non-Adherent)	0.57	0.533	0.61	<.0001
Newly Treated (vs. Previously Treated)	0.898	0.837	0.963	0.0026
Use of dalfampridine (vs. No Use)	5.879	4.605	7.507	<.0001
MS Condition Indicators (vs. None)				
1 to 4	2.238	1.971	2.541	<.0001
≥5	5.801	4.99	6.743	<.0001
CCS Code Groups (vs. ≤ 2)				
3 to 7	2.809	2.466	3.2	<.0001
≥8	8.922	7.722	10.307	<.0001
Charlson Score (vs. 0)				
1	1.542	1.413	1.682	<.0001
≥2	3.004	2.707	3.332	<.0001

Data Source: IMS PharMetrics Plus (January 1, 2006 – June 30, 2013)

CCS: clinical classifications software; CI: confidence interval; DMT: disease modifying therapy; OR: odds ratio

Note: high-cost determined based on all-cause total costs excluding DMTs in the follow up year ≥ the 75th percentile; adherence defined as medication possession ratio ≥ 0.8

C statistic = 0.800; Percent Concordant = 79.8%; Percent Discordant = 19.8%; Percent Tied = 0.4%

- Predictors of Being High-Cost
  - Age and sex were not consistently predictive of being high-cost
  - High counts of conditions within each domain (eg, ≥5 MS-related conditions: odds ratio [OR]: 5.801; p<0.0001) and selected individual conditions (eg, disability: OR: 1.809; p<0.0001) were associated with significantly higher likelihood of being high-cost
  - Dalfampridine use was also significantly associated with being high-cost (OR: 5.744–6.062 across specifications; p<0.0001)
  - Conversely, higher DMD adherence and newly initiating DMDs were associated with a lower likelihood of being high-cost (OR: 0.570–0.594 and 0.850–0.898 across specifications, respectively; all p<0.01)
  - Factors predictive of being high-cost from the specification with counts of conditions indicators are shown in Table 3

Conclusions

Higher counts of condition indicators, and the presence of individual MS and CCS condition indicators significantly predicted the likelihood of being a high-cost patient, while higher adherence and being new to DMD therapy significantly predicted being a non-high-cost patient

References

- 1. Menzin J et al. J Manag Care Pharm 2013;19(1 Suppl A):S24–40.

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Disclosures

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- Amy Phillips and Julie Locklear are employees of EMD Serono, Inc.

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