A Retrospective Analysis of Insurance Policy Impact on the Choice of Multiple Sclerosis Disease Modifying Therapies

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Background

Financial limitations and insurance restrictions are frequently cited barriers to both starting and transitioning between DMTs[1]. These factors influence the approach to selecting a DMT by both patients and providers[2].

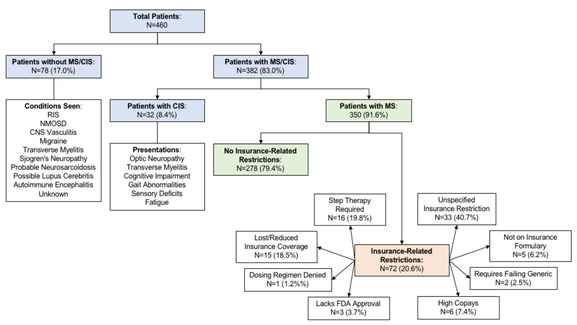
The choice of DMT for MS treatment is influenced by Individual patient and drug-specific factors[3]. Perceived severity of MS course, patient views and preferences about drug tolerably, safety, convenience, efficacy, and insurance restrictions are among the factors considered. Patient prognostic profile is also used to guide initial DMT selection including demographic, clinical, and imaging characteristics that help predict disease severity. Potential predictors of severity include male gender, early progressive disability, poor relapse recovery, high burden of disease on MRI, or frequent early attacks[4].

Access to high-efficacy DMTs is affected by health insurance coverage[3]. These DMTs are often more expensive than injectables with lower-efficacy profiles. For this reason, insurance companies have adopted step therapy approaches to MS treatment, in which patients are required to fail a cheaper DMT before pursuing a more costly, often higher efficacy, DMT. Although this approach is seen as cost-effective, there is no data to support a specific sequencing schema for MS treatment. This practice has continued largely due to the growing costs of MS treatment, irrespective of the growing number of approved DMTs. It has been reported that DMTs increase in price above the level of inflation after entering the US market[5-7]. This is contrary to other drug categories that decrease in price after entering a competitive drug market. These trends in DMT prices continue to drive healthcare costs among persons with multiple sclerosis and result in reduced adherence and access to DMTs[7].

Study Aim

This study aims to evaluate the financial limitations and insurance restrictions experienced by patients pursuing disease modifying therapy for multiple sclerosis and how the approach to choosing treatment for MS is affected.

Figure 1: Study Population Diagnoses and Insurance-related Restrictions



Methods and Materials

A retrospective chart review of patients seen in the multiple sclerosis (MS) specialty clinic at Alfred Taubman Health Care Center of Michigan Medicine between January 1st 2020 and February 29th 2020 was performed. Adult patients with a diagnosis of MS based on the McDonald Criteria were included in the study.

Medical records were accessed electronically on the medical-record software Epic. Data was collected from results of diagnostic tests, notes from health care providers and denial letters from insurance companies.

Descriptive statistics were calculated using the statistical software IBM SPSS statistics. A chi-square test was used to compare categorical data. T-tests were used to compare means and a z-score test was used to test for statistically significant differences in gender. Alpha was set at 0.05 with a significance level of p<0.05 for statistical significance testing.

Table 1: Characteristics of Multiple Sclerosis Study Population

Categories	Total MS (n = 350)	No Insurance-related Restrictions Group (n = 278)	Insurance-related Restrictions Group (n = 72)	Significance Testing
Gender (n, %)				
Female	254 (72.6%)	208 (74.8%)	46 (63.9%)	Z= 1.8528 P= .06432
Race (n, %)				Chi Square statistic=0.116
White	295 (84.3%)	234 (84.2%)	61 (84.7%)	P=.733
Black	30 (8.6%)	23 (8.3%)	7 (9.7%)	
Other/Unknown	25 (7.1%)	21 (7.5%)	4 (5.6%)	
Ethnicity (n,%)				Chi Square statistic=1.533
Non-Hispanic	333 (95.1%)	265 (95.3%)	68 (94.4%)	P=.216
Hispanic	6 (1.7%)	6 (2.2)	0 (0%)	
Unknown	11 (3.1%)	7 (2.5%)	4 (5.6%)	
Mean Age (years)	49.36 (min 18, Max 79) Sd 12.728,	50.45 (Min 18, Max 79) Sd 12.755	45.17 (Min 26, Max 74) Sd 11.796	P=.002
Mean Age at Diagnosis (years)	39.10 (min 12, Max 71) Sd 11.947	39.70 (min 16, Max 71) Sd 12.080	37.14 (Min 12, Max 70) Sd 11.451	P=.269
Insurance Type (n, %)				
Private	203 (58.0%)	169 (60.8%)	34 (47.2%)	Chi Square statistic=4.005
Public	145 (41.4%)	108 (38.8%)	37 (51.4%)	P=.045
None	2 (0.6%)	1 (0.4%)	1 (1.4%)	
Marital Status (n,%)				
Single	197 (22.3%)	54 (19.4%)	24 (33.3%)	Chi Square statistic=6.235
Married	167 (47.7%)	139 (50.0%)	28 (38.9%)	P=.013
Divorced	18 (5.1%)	13 (4.7%)	5 (6.9%)	
Legally Separated	3 (0.9%)	1 (0.4%)	2 (2.8%)	
Widow	8 (2.3%)	4 (1.4%)	4 (5.6%)	
Unknown	76 (21.7%)	67 (24.1%)	9 (12.5%)	
Clinical Course (n,%)				
Relapsing Remitting	287 (82.0%)	220 (79.2%)	67 (93.1%)	Chi Square statistic =
Primary Progressive	22 (6.3%)	20 (7.2%)	2 (2.8%)	7.938
Secondary Progressive	41 (11.7%)	38 (13.6%)	3 (4.2%)	P=.094
Mean time from diagnosis to start of DMT (months)	4.73 Sd 9.106	4.86 Sd 10.022	4.37 Sd 6.058	P=0.6726
On DMT (n, %)	265 (75.7%)	207 (74.5%)	58 (80.6%)	P=0.863
Mean number of DMTs	2.01 (Min 0, Max 9), Sd 1.498,	2.01 (min 0, Max 9) Sd 1.571	2.04 (Min 0, Max 5) Sd 1.192	

Results

460 patients were evaluated in the study of which 350 (76.1%) carried a diagnosis of MS. Of these patients, 72 (20.6%) were unable to start or continue their desired DMT, as agreed upon by the provider and patient, at some point during their treatment course due to financial limitations related to their insurance coverage. The most common limitation was a required step therapy approach to treatment, followed by lost or reduced insurance coverage, and high copays among others. DMTs found to be difficult to access financially were glatiramer acetate (17.7%), dimethyl fumarate (17.7%), ocrelizumab (15.2%), beta-interferon-1a (12.7%), natalizumab (11.4%), teriflunomide (7.6%), rituximab (6.3%), fingolimod (6.3%), beta-interferon-1b (2.5%) and alemtuzumab (2.5%). Tecfidera and beta-interferon-1a were the DMTs most likely to be discontinued secondary to high copays. Ocrelizumab was the most likely DMT to be rejected by insurance due to a required step therapy approach to treatment, followed by dimethyl fumarate, natalizumab, fingolimod, alemtuzumab, and teriflunomide. Patients experienced most of these insurance difficulties at the initiation of treatment with DMTs (65.8%). Due to lack of insurance coverage, 46 (12.1%) patients were off DMT at some point during their MS.

Table 2: Disease Modifying Therapies with insurance-related restrictions experienced by study population

Disease Modifying Therapy (Route of administration)	Total Occurrences N = 81	Insurance-Related Restrictions	
Glatiramer Acetate (Injectable)	14 (17.3%)	• Required Failing Generic prior to starting brand name • Lost/Reduced Insurance Coverage • Not on insurance formulary • Dosing Regimen Denied • High Copays • Lacks FDA approval for MS Subtype, CIS or use in pregnancy • Unspecified Insurance Limitation	N=2 (14.3%) N=2 (14.3%) N=2 (14.3%) N=1 (7.1%) N=1 (7.1%) N=1 (7.1%) N=5 (35.8%)
Dimethyl fumarate (Oral)	14 (17.3%)	• Lost/Reduced Insurance Coverage • Step Therapy Required • High Copays • Not on insurance formulary • Unspecified Insurance Limitation	N=4 (28.6%) N=4 (28.6%) N=2 (14.3%) N=1 (7.1%) N=3 (21.4%)
Ocrelizumab (Infusion)	13 (16.0%)	• Step Therapy Required • Unspecified Insurance Limitation	N=5 (38.5%) N=8 (61.5%)
Beta-Interferon-1a (Injectable)	10 (12.3%)	• Lost/Reduced Insurance Coverage • High Copays • Not on insurance formulary • Unspecified Insurance Limitation	N=4 (40%) N=2 (20%) N=1 (10%) N=3 (30%)
Natalizumab (Infusion)	9 (11.1%)	• Step Therapy Required • Lacks FDA approval for MS Subtype, CIS or use in pregnancy • Lost/Reduced Insurance Coverage • Unspecified Insurance Limitation	N=3 (33.3%) N=1 (11.1%) N=1 (11.1%) N=4 (44.5%)
Teriflunomide (Oral)	6 (7.4%)	• Lost/Reduced Insurance Coverage • Step Therapy Required • Unspecified Insurance Limitation	N=1 (16.7%) N=1 (16.7%) N=4 (66.6%)
Fingolimod (Oral)	6 (7.4%)	• Step Therapy Required • Lost/Reduced Insurance Coverage • Unspecified Insurance Limitation	N=2 (33.3%) N=2 (33.3%) N=2 (33.3%)
Rituximab (Infusion)	5 (6.2%)	• Lost/Reduced Insurance Coverage • Lacks FDA approval for MS Subtype, CIS or use in pregnancy • Unspecified Insurance Limitation	N=1 (20%) N=1 (20%) N=3 (60%)
Alemtuzamab (Infusion)	2 (2.5%)	• Step Therapy Required • Unspecified Insurance Limitation	N=1 (50%) N=1 (50%)
Beta-Interferon-1b (Injectable)	2 (2.5%)	• Not on insurance formulary • High Copays	N=1 (50%) N=1 (50%)

Discussion

In this study of 350 patients with multiple sclerosis, we found that although the majority benefited from health insurance (99.4%), approximately 1 in 5 experienced difficulty accessing disease modifying therapies due to insurance limitations. We also found that the financial burdens resulting from these insurance restrictions reduced the ability of patients with MS to adhere to therapy with 63.9% (46/72) of these patients (12.1% of the total MS population) unable to continue on a DMT at some point during their MS course. This data suggests a gap between health insurance needs and current coverage.

Inability to continue on disease modifying therapies for MS due to high copays has been reported previously and continues to serve as a barrier to access. Of the 72 patients experiencing financial difficulties, 7.6% (n=6) were unable to continue on their current DMT because their copays were too high, with subjective reports of up to $3000 a month in copay requirements.

This study found that patients who experienced insurance restrictions while pursuing DMTs for MS were more likely to benefit from public insurance in the form of Medicare and Medicaid compared to MS patients who did not experience insurance restrictions.

The high prices of DMTs has forced patients and providers to abandon shared decision making based on patient preferences and clinical data for adherence to step therapy requirements enforced by insurance companies. At least 16 of our patients reported an inability to access their desired DMT due to step therapy requirements.

Insurance policies should eliminate step therapy programs to further increase access to DMTs for patients with MS, while further research is needed to identify the patients that would most benefit from low-efficacy vs intermediate efficacy vs high efficacy DMTs.

Table 3: Disease Modifying Therapies at initiation of DMT use and throughout disease course

Disease Modifying Therapy	Total MS Group (n = 350)	First DMT No Insurance-related Restrictions Group[1] (n = 278)	All DMTs No Insurance-related Restrictions Group[1] (n = 278)	First DMT Insurance-related Restrictions Group[2] (n = 72)	All DMTs Insurance-related Restrictions Group[2] (n = 72)
Injectable					
Glatiramer acetate (Copaxone,Glatopa)	171 (48.9%)	93 (33.5%)	135 (48.6%)	30 (41.7%)	36 (50%)
Interferon beta-1a (Avonex, Rebif)	142 (40.6%)	70 (25.2%)	112 (40.3%)	20 (27.8%)	30 (41.7%)
Interferon beta-1b (Betaseron)	22 (6.3%)	15 (5.4%)	20 (7.2%)	1 (1.4%)	2 (2.8%)
Peginterferon beta-1a (Plegridy)	3 (0.9%)	1 (0.4%)	3 (1.1)	0 (0%)	0 (0%)
Oral					
Dimethyl fumarate (Tecfidera)	92 (26.3%)	19 (6.8%)	68 (24.5%)	5 (6.9%)	24 (33.3%)
Fingolimod (Gilenya)	43 (12.3%)	7 (2.5%)	33 (11.9%)	1 (1.4%)	10 (13.9%)
Teriflunomide (Aubagio)	28 (8%)	5 (1.8%)	22 (7.9%)	3 (4.2%)	6 (8.3%)
Siponimod (Mayzent)	4 (%)	1 (0.4%)	4 (1.1)	0 (0%)	0 (0%)
Methotrexate	2 (0.6%)	0 (0%)	1 (0.4%)	0 (0%)	1 (1.4%)
Diroximel fumarate (Vumerity)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
Azathioprine (Imuran)	1 (0.3%)	1 (0.4%)	1 (0.4%)	0 (0%)	0 (0%)
Infusion					
Ocrelizumab (Ocrevus)	86 (24.6%)	20 (7.2%)	70 (25.2%)	2 (2.8%)	16 (22.2%)
Natalizumab (Tysabri)	55 (15.7%)	5 (1.8%)	45 (16.2%)	3 (4.2%)	10 (13.9%)
Rituximab (Rituxin)	26 (7.4%)	4 (1.4%)	19 (6.8%)	4 (5.6%)	7 (9.7%)
Cyclophosphamide (Cytoxane)	7 (2.0%)	1 (0.4%)	6 (2.1%)	1 (1.4%)	1 (1.4%)
Mitoxantrone (Novantrone)	7 (2.0%)	1 (0.4%)	5 (1.8%)	0 (0%)	2 (2.8%)
Alemtuzamab (Lemtrada)	4 (1.1%)	0 (0%)	3 (1.1)	0 (0%)	1 (1.4%)
Belimumab (Benlysta)	1 (0.3%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)

Conclusions

- One in five patients with MS were found to experience difficulty accessing DMTs secondary to insurance restrictions, and 12.1% of the MS population were off DMT completely at some point during their MS course.
- Step therapy as a required approach to treatment was the most common barrier to desired DMT treatment.
- Financial barriers to DMT use secondary to insurance restrictions experienced by patients with MS should be further elucidated and alleviated by both insurance and drug companies.

Limitations

The results of this study should be analyzed within the context of the following limitations.

- Patients who experienced insurance restrictions while pursuing disease modifying therapies for MS were identified via notes from health care providers and insurance denial letters scanned into their medical records. Given that some insurance denial letters may not have been incorporated into a patient's medical record or a health care provider may have excluded financial barriers to access to disease modifying therapies, this study may have underestimated the number of patients who experienced insurance restrictions in their pursuit of MS treatment.
- Given that only 150 of the 350 MS patients evaluated in this study received all of their MS treatment at Michigan Medicine, the remaining 200 patients may have experienced financial difficulties accessing disease modifying therapies that were not reported in their medical record prior to transferring their care, further underestimating the true impact of financial barriers on access to disease modifying therapies.
- Further, the use of free or discounted drug programs that help mitigate out-of-pocket drug expenses was infrequently reported in patient medical records and may have underestimated the number of patients experiencing financial difficulties.
- These limitations along with the retrospective study design may have resulted in misclassification bias.

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