

**Project Title:** A Retrospective Analysis of Insurance Policy Impact on the Choice of Multiple Sclerosis Disease Modifying therapies

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**Summary:** The treatment of multiple sclerosis (MS) has evolved rapidly since the approval of interferon beta yet access to disease modifying therapy (DMT) remains a significant challenge<sup>1,2</sup>. Financial limitations and insurance restrictions are frequently cited barriers to both starting and transitioning between DMTs<sup>3</sup>. These factors influence the approach to selecting a DMT by both patients and providers<sup>4</sup>.

The choice of DMT for MS treatment is influenced by Individual patient and drug-specific factors<sup>5</sup>. 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<sup>6</sup>.

The desired DMT chosen by the patient and provider through shared decision-making fits into one of two treatment paradigms for initial DMT treatment, starting with low efficacy therapy or starting with high efficacy therapy. Providers vary in their approach, although most agree that patients with highly active disease or unfavorable prognosis should start high-efficacy disease modifying therapy for MS<sup>7,8</sup>. A limited number of randomized controlled trials and observational studies have suggested that the majority of infusion DMTs, including ocrelizumab and natalizumab, have the highest efficacy, followed by oral DMTs, such as fingolimod, with intermediate efficacy and the lowest efficacy is seen in the injectables of which interferon beta and glatiramer acetate are the most common.<sup>6,9-11</sup> A caveat to this is the recent approval of the injectable Ofatumumab who was found to be associated with lower annualized relapse rates compared to the oral agent teriflunomide<sup>9</sup>.

Access to high-efficacy DMTs is affected by health insurance coverage<sup>3</sup>. 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<sup>12-14</sup>. 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<sup>14</sup>.

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.

**Methodology:** A retrospective chart review of patients seen in the MS specialty clinic at Alfred Taubman Health Care Center of Michigan Medicine between January 1<sup>st</sup>, 2020 and February 29<sup>th</sup>, 2020 was performed. Medical records were assessed for insurance challenges experienced by patients with MS during initiation and transition between DMTs.

**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 course.

### **Conclusion:**

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<sup>1,3</sup>. 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. Although high copays are not unique to MS therapies, the economics of MS treatment differs from that of most other drug categories in that price inflation and lack of price transparency in a monopolistic competitive market has fostered rapidly increasing DMT prices despite the continued addition of new DMTs<sup>19</sup>. Regulatory structures are lacking and should be put in place to further control the rising prices of MS therapies.

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. This is unexpected given that Medicaid patients are required to receive the lowest drug prices available through the Medicaid Drug

Rebate Program. However, this association may be due to the inability of patients benefiting from government-funded health care to have access to patient assistant programs because of federal antikickback laws<sup>19</sup>. Medicaid, like private insurers, also enforce restrictive insurance policies regarding MS therapies with 2 examples found in this study in which patients had to switch from brand name glatiramer acetate to generic after switching from private insurance to Medicaid.

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. These requirements did not take into account the presumed MS severity or prognostic factors of the patient for which studies have shown that patients with severe prognostic profiles should initiate high efficacy DMT to reduce the number or clinical and/or radiographic activity. Step Therapy assumes a one size fits all approach to MS treatment with low efficacy DMTs as first line and oral or infusion therapies as second/third line with no evidence to support this practice. 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.

### **Reflection/Impact Statement:**

I stumbled upon this research question during my elective time in the neuroimmunology/multiple sclerosis (MS) clinic. I remember a great amount of what I learned about MS treatment and diagnosis yet what I remember most is that feeling in my gut when a patient couldn't afford to be on disease modifying therapy. That feeling is indescribable; one that lingers and has only fully resolved by working on this study. My hope is that others who did not before realize the financial limitations and barriers to MS treatment will open their hearts and help do their part in helping change the system that allows this to occur. Although there have been studies after studies analyzing the effects of insurance and drug costs for MS treatment, this study may serve as the last drop that spilled the cup. If so, hundreds of thousands of MS patients struggling to pursue their desired MS treatment may have a chance to do so.

This study has changed my life in some ways. I've realized through this study that this is the type of research I most enjoy; helping to elucidate disparities and barriers to neurologic care. I hope this study serves as the start of a career in health systems research and that it informs future studies.

To students starting their Capstone for Impact project, if I could leave you with a bit of advice. Follow your passion for it will guide you towards your future and inevitably change lives.