Comparison of Healthcare Utilization Among Managed Medicaid Individuals Diagnosed with Multiple Sclerosis Treated with Emergent vs. Established Disease Modifying Therapy in the US

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Background

- The efficacy and safety of established disease modifying therapies (DMTs) (i.e., interferon beta-1a, interferon beta-1b, interferon beta, glatiramer acetate, fingolimod, mitoxantrone, and natalizumab) and emergent DMTs (i.e., alemtuzumab, teriflunomide, dimethyl fumarate, and peginterferon beta-1a) for management of multiple sclerosis (MS) has been well studied[1–4]
- Randomized controlled trials suggest that emergent DMTs may have several distinct advantages relative to established DMTs, including better clinical outcomes (lower relapse rates/exacerbations) and reduced healthcare utilization[3]
- However, there is limited real-world evidence comparing clinical response and outcomes in users of established and emergent DMTs
- To address this gap, we evaluated rates of MS-related hospitalizations, ER visits, outpatient visits and inpatient and outpatient relapse events in a large managed Medicaid population of treatment-naïve patients with MS who initiated treatment with an established or emergent DMT

Objective

To compare MS related healthcare use within 1 year of initiating emergent and established DMTs among Managed Medicaid patients diagnosed with MS in the US

Methods

Data Source

Member-level data extracted from a large nationally representative and statistically de-identified administrative claims database was used for this study

- The Inovalon MORE^2 Registry® includes longitudinal patient-level data for more than 250 million individual health plan members from a broad range of sources across all payer types (commercial, ACA exchange, Medicare Advantage, Medicare Fee-for-Service, and managed Medicaid), geographic regions (capturing virtually all US counties), healthcare settings (inpatient, office-based, and outpatient services), and provider specialties

Study Population

Members were included in the study if they satisfied each of the following criteria:

- 1. Were enrolled in a Managed Medicaid health plan; 2. ≥18 years of age at the time of the index prescription; 3. The index prescription was defined as a prescription fill for an established or emergent DMT between May 2013 and June 2016, without a fill for that same DMT in the previous 6 months; 4. Had a new prescription fill for an established or emergent DMT between May 2013 and June 2016; 5. Had ≥ 2 outpatient claims occurring ≥ 30 days apart or ≥ 1 inpatient claim with a diagnosis of MS (ICD-9 340 or ICD-10 G35) within the 6 months prior to treatment initiation; and 6. Were continuously enrolled in the Managed Medicaid health plan with pharmacy and medical coverage for at least 6 months before and 1 year after initiation of therapy
- Members who were prescribed polytherapy of DMTs were excluded from the analysis

Study Outcomes

3 types of healthcare resource use (HRU) were examined during the 12-month follow-up period:

1. Number of MS-related hospitalizations – defined as the number of inpatient stays with either a primary or secondary diagnosis of MS
2. Number of outpatient relapse events – defined as a medical claim for an outpatient visit with either primary or secondary diagnoses of MS in combination with a pharmacy or medical claim for corticosteroids within 7 days of the outpatient visit
3. Number of inpatient relapse events – defined as a medical claim for an inpatient stay with a principal diagnosis of MS

Statistical Analysis

- Regression models were used to estimate the association between the use of established vs. emergent DMTs and the number of relapse events or MS-related hospitalizations
- All models adjusted for age, gender, Charlson index, and geographic region
  - Poisson regression models were fit initially to determine whether the outcomes were significant
  - Zero-inflated regression models were fit to account for distributions with a high mass at zero
  - Likelihood ratio tests were used to determine if data were over dispersed
  - HPC tests were used to compare Poisson and negative binomial regressions results to zero-inflated Poisson and zero-inflated negative binomial regression results[5]

Results

Table 1: Patient Characteristics by DMT Type

	Established DMTs		Emergent DMTs		P-Value
	N	%	N	%	
Total	5,483	78.5	1,498	21.5	<0.001
Age					
Mean (SD)	40.7 (11.4)	40.7 (11.4)	40.8 (11.1)	40.8 (11.1)	0.750
Gender					
Female	4,393	80.1	1,180	78.8	0.249
Region					
Northeast	1,286	23.5	259	17.3	<0.0001
Midwest	667	12.2	205	13.7	
South	2,496	45.5	640	42.7	
West	1,000	18.2	280	18.7	
US Territories	34	0.6	14	0.9	
Unknown	0	0	100	6.7	
CCI Score					
Mean (SD)	0.5 (1.2)	0.5 (1.2)	0.4 (1.2)	0.4 (1.2)	0.684
Comorbidities					
Cerebrovascular Disease	239	15.95	71	4.74	0.5261
Chronic Pulmonary Disease	545	9.94	135	9.01	0.2832
Congestive Heart Failure	70	1.28	19	1.27	0.9797
Diabetes with Chronic Complications	94	1.71	25	1.67	0.904
Diabetes without Chronic Complications	399	7.28	92	6.14	0.1277
Malignancy	22	1.47	23	1.54	0.7053
Mild Liver Disease	31	0.57	11	0.73	0.4537
Myocardial Infarction	42	0.77	17	1.13	0.167
Peptic Ulcer Disease	29	0.53	8	0.53	0.9806
Peripheral Vascular Disease	79	1.44	24	1.6	0.6463
Renal Disease	67	1.22	17	1.13	0.7841
Rheumatologic Disease	67	1.22	21	1.4	0.5802
Baseline Healthcare Utilization (within 6-months prior to index date)					
ER Visits	3,523	16.01	1,070	17.73	0.0014
Outpatient Visits	11,329	51.47	3,335	55.25	<0.0001
Hospitalizations	1,947	8.85	549	8.85	0.5465
Baseline Relapses (within 6-months prior to index date)					
0	13,124	59.63	3,853	63.83	<0.0001
1	1,641	7.46	407	6.74	
2	1,368	6.22	316	5.24	
3+	5,877	26.70	1,460	24.19	

Table 2: Regression Model Estimates on the Association Between the Use of DMTs (Established DMTs as Reference Group) and Outcomes (Number of Relapse Events or MS-Related Hospitalizations)

Outcome Measures	Relative Risk (RR)	95% Confidence Interval (CI)	P-Value
Outpatient Relapse Events			
Poisson	0.84	0.81–0.89	< 0.001
Zero-Inflated Poisson	0.85	0.76–0.95	0.004
Negative Binomial	0.89	0.86–0.93	0.004
Zero-Inflated Negative Binomial	0.87	0.80–0.96	0.006
Inpatient Relapse Events			
Poisson*	0.79	0.61–1.00	0.055
Zero-Inflated Poisson*	0.79	0.61–1.00	0.055
Negative Binomial	NA	NA	NA
Zero-Inflated Negative Binomial	NA	NA	NA
MS-Related Hospitalizations			
Poisson	0.59	0.53–0.65	< 0.001
Zero-Inflated Poisson	0.63	0.50–0.81	< 0.001
Negative Binomial	0.71	0.64–0.80	< 0.001
Zero-Inflated Negative Binomial	0.74	0.55–0.99	0.048

*Poisson and zero-inflated Poisson regression model results have identical coefficient estimates and standard errors to the 5th decimal place.

Figure 1:
Distribution of MS-Related Hospitalizations by Generation of DMT

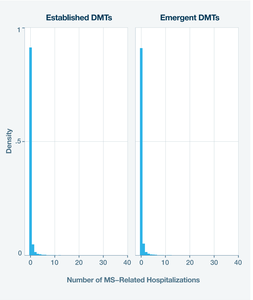


Figure 2:
Average Predicted Probabilities for the Number of MS-Related Hospitalizations by Model Type

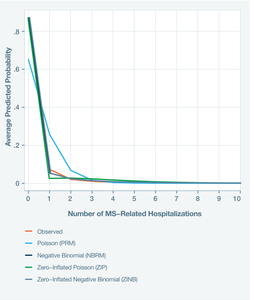
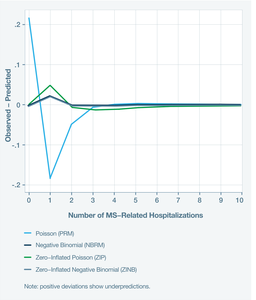


Figure 3:
Deviation of Predicted Probabilities of the Number of MS-Related Hospitalizations by Model Type



Key Findings

- In this retrospective analysis of managed Medicaid health plan members with MS, 1 in 5 patients initiated treatment with an emergent DMT
- Of those, 79.8% were female, 50.4% were ages 40-64 years, and had a mean CCI score of 0.5 (see Table 1)
- Prior to initiating treatment this Medicaid population was not well controlled with approximately 25% of patients having at least 3 relapses in the baseline period
- Emergent DMT users were found to have fewer MS-related hospitalizations compared to established DMT users within one year of initiating therapy (RR = 0.74, 95% confidence interval (CI): 0.80-0.96) and fewer outpatient relapses (RR = 0.87, CI: 0.55-0.99) (see Table 2)
- All outcomes had a high mass at zero and were over dispersed; HPC tests indicated zero-inflated negative binomial models were the preferred models for all outcomes in which estimates could be obtained, but alternative models performed well (see Figures 1-3)

Discussion

- Emergent DMTs were used in 20% of Medicaid patients that initiated treatment during the study period
- Using advanced regression modeling techniques to account for rarity of events and overdispersion of data, the relative risk for MS-related hospitalizations and outpatient relapse events were significantly lower for users of emergent DMTs vs. established DMTs
- Relative risk for inpatient relapse events were non-differential by treatment group
- This study suggests that emergent DMTs are associated with lower rates of MS-related hospitalizations and outpatient relapse events within 1 year of initiating therapy

References

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