

# Reasons for Hospital Admission in Individuals With Multiple Sclerosis

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## ABSTRACT

**BACKGROUND:** Health care utilization is higher in individuals with multiple sclerosis (MS) than in the general population. However, there are limited data on the reasons for their hospital admissions. Our primary objective is to analyze the reasons for the hospitalization of individuals with MS with the goal of identifying preventable causes.

**METHODS:** We conducted a retrospective analysis of a cohort of adults with a confirmed diagnosis of MS admitted to Duke University Hospital between January 2018 and January 2020. This yielded a cohort of 210 individuals. Data were analyzed using descriptive statistics.

**RESULTS:** The most common reason for admission was urinary tract infection (UTI; 10.3%). The average length of stay was 6.1 days for the individuals with MS vs 5.5 days for the general population. The 30-day readmission rates were 14.9% and 15.5%, respectively. A significant number of admitted patients were not on any disease-modifying therapy (DMT), and no difference in median age was identified between those with a DMT vs those without.

**CONCLUSIONS:** Length of stay and readmission rates were similar to those of the general population in this contemporary cohort. Given the prevalence of bladder dysfunction in MS, it is not surprising that a UTI was the most common reason for admission. Actively addressing management of and techniques for bladder dysfunction may decrease the admission rate for individuals with MS. Though we now have more treatment options for MS, many individuals with the highest health care utilization are not on a DMT. Future research is needed to identify the factors that can be addressed to support these patients and reduce preventable hospitalizations.

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**M**ultiple sclerosis (MS) is the most common autoimmune disease affecting the central nervous system, with a recent estimate of more than 850,000 people with the disease in the United States.<sup>1</sup> The majority of individuals with MS have a relapsing-remitting (RRMS) disease course characterized by inflammatory relapses. Primary progressive (PPMS) and secondary progressive MS (SPMS) are marked by gradual disability accumulation not delineated by discrete relapse and remission. The social and economic burdens of MS span from direct disability-related individual limitations to broad downstream effects, including impacts on relationships and employment.<sup>1</sup>

Prior studies have shown that people with MS are more likely to have chronic comorbid conditions that place them at risk for increased hospitalization rates and higher health care utilization following acute illness.<sup>2,3</sup> In recent years, interest in the interaction between comorbid illnesses and MS has increased as disease-modifying therapies (DMTs) have become better at preventing relapses. However, there are not a lot of current data on acute illness in MS and its impact on disability. Prior evidence from international studies shows that hospitalization of people living with MS contributes independently to disability progression.<sup>2</sup>

Here, we analyze the reasons for hospitalization of individuals with MS with the goal of identifying preventable causes of admission. Targeting preventive measures for the most common causes of admission may provide data to reduce hospitalization rates for people with MS and potentially reduce disability accrual.

## METHODS

An institutional review board exemption (Pro00109722) was obtained to retrospectively review Duke University Hospital electronic health records for adults ( $\geq 18$  years of age) who were admitted from January 1, 2018, to January 1, 2020, with the *International Classification of Diseases, Tenth Revision*, code for an MS diagnosis (G35). These records were identified using SlicerDicer.<sup>4,5</sup> A total of 268 records that fit these criteria were obtained. Scheduled admissions were excluded, as well as

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**TABLE 1.** Admission Causes for Individuals With MS Admitted to DUH 2018-2020

Causes	n (%)	Average days of stay ( $\pm$ SD)
<b>Neurologic</b>	<b>109 (41.6%)</b>	<b>6 (2.4)</b>
Neurologic deficits of nonidentifiable cause	24 (9.2%)	5.5 (2.3)
MS exacerbation	20 (7.6%)	4.3 (2.2)
Falls/ambulation difficulty/spasticity	16 (6.2%)	7.4 (6.5)
New MS diagnosis	10 (3.8%)	6.0 (5.4)
Strokes	10 (3.8%)	9 (5.1)
Seizures	9 (3.4%)	5.6 (6.5)
Cognitive decline/delirium	7 (2.7%)	5.2 (3.9)
Headache/migraines/neuropathic pain	4 (1.5%)	40 (0.8)
Dysphagia/malnutrition	3 (1.1%)	5.3 (3.1)
Neurosurgical complication	3 (1.1%)	6.0 (1.0)
Other inflammatory: AIDP/CIDP, vasculitis	3 (1.1%)	11 (4.6)
<b>Infectious</b>	<b>65 (24.8%)</b>	<b>6.9 (2.4)</b>
Urinary tract	27 (10.3%)	5.5 (1.1)
Pulmonary	15 (5.7%)	5.3 (3.0)
Skin	13 (5.0%)	10.4 (2.5)
Abdominal	10 (3.8%)	6.2 (3.8)
<b>Cardiovascular</b>	<b>16 (6.1%)</b>	<b>3.7 (1.8)</b>
STEMI/NSTEMI/angina	7 (2.7%)	3.3 (1.6)
Arrhythmia	5 (1.9%)	4.4 (2.1)
Other	4 (1.5%)	3.7 (1.8)
<b>Gastrointestinal</b>	<b>15 (5.7%)</b>	<b>5.6 (2.6)</b>
Other	10 (3.8%)	5.0 (2.2)
SBO	3 (1.1%)	5.7 (2.5)
Bleed	2 (0.8%)	8.5 (3.5)
<b>Pulmonary</b>	<b>17 (6.5%)</b>	<b>6.2 (6.1)</b>
Respiratory failure/effusion	10 (3.8%)	10.7 (18.2)
Asthma/COPD exacerbation/cough	5 (1.9%)	4.4 (3.4)
Pulmonary embolism	2 (0.8%)	6.5 (15.6)
<b>Psychiatric</b>	<b>9 (3.4%)</b>	<b>10.8 (10.6)</b>
Psychosis/delusions/hallucinations	5 (1.9%)	13.4 (14.0)
Suicide attempt/suicidal ideation	2 (0.8%)	8.0 (2.8)
Depression	1 (0.4%)	10.0 (0.0)
Conversion disorder	1 (0.4%)	4 (0.0)
Hematology/oncology	10 (3.8%)	5.6 (3.4)
Other pain	7 (2.7%)	6.7 (2.8)
Endocrine	3 (1.1%)	9.0 (4.6)
Obstetrics	3 (1.1%)	8.0 (8.7)
Renal	2 (0.8%)	5.5 (3.5)
Ophthalmologic	2 (0.8%)	5.5 (2.1)
Trauma (eg, vehicular crash)	2 (0.8%)	8.5 (2.1)
Alcohol withdrawal	2 (0.8%)	5.0 (2.8)

AIDP/CIDP, acute inflammatory demyelinating polyneuropathy/chronic inflammatory demyelinating polyneuropathy; COPD, chronic obstructive pulmonary disease; DUH, Duke University Hospital; MS, multiple sclerosis; SBO, small bowel obstruction; STEMI/NSTEMI, ST-elevation myocardial infarction/non-ST-elevation myocardial infarction. Note: Admissions and readmissions causes were analyzed together for a total of 262 causes.



# PRACTICE POINTS

Bladder dysfunction may significantly contribute to the hospitalization of individuals with multiple sclerosis.

Because many individuals with multiple sclerosis are admitted to the hospital without an identifiable cause, increasing access to outpatient care and subsequent workups may help reduce preventable admissions. ■

individuals with no confirmed diagnosis of MS at admission, for a total of 210 records. Two authors (D.P. and E.L.) reviewed the charts and abstracted the data.

Demographic data (eg, age, sex, and race); length of stay; type of MS; extent of disability; admission diagnosis; DMT at time of admission; admitting service; and evaluations by physical therapy, occupational therapy, and speech therapy during admission were obtained, as were 30-day readmission rates and the associated diagnosis. Admission diagnoses were categorized by system (neurologic, cardiovascular, pulmonary, infectious, etc) and subcategorized by particular problems within those systems. A category for neurologic deficits without an identifiable cause was made to capture patients who presented with a neurologic complaint, but for whom further workup did not identify pathology or cause. Pseudorelapses were not included in this category.

Data were analyzed using descriptive statistics. Continuous variables are summarized as median, mean, and standard deviations. Categorical data are presented as percentages.

## RESULTS

### Cohort

A total of 210 individuals fulfilled the inclusion criteria. As expected from previous studies, there was a 3:1 female-to-male ratio.<sup>1</sup> The average age of our study population was similar to the national average, 54.4 years vs 51.7 years, respectively (TABLE S1).<sup>6</sup> The average years since diagnosis was 16. Of the cohort, 111 (52.4%) had RRMS, 50 (28.3%) had SPMS, 30 (14.2%) had PPMS, and 9 (4.2%) did not have a phenotype identified. Assistive devices for ambulation (ie, cane, walker, or wheelchair) were used by 131 (62.4%).

### Common Causes of Admission

Identified reasons for admission are summarized in TABLE 1. The most common systems cited were neurologic

(41.6%), followed by infectious (24.8%). The most common overall reason for admission was urinary tract infection (10.3%), followed by neurologic deficits without identifiable cause (9.2%). Of interest, as they are common issues for those with MS, gait instability and falls combined to be the third most common neurologic cause of admission (3.4%), and 6 of the 9 falls caused fractures (2.3% of admissions), including facial, femur, ankle, and greater tuberosity fractures.

### DMT Use

Approximately half of the admitted patients were not on any DMT (48.2%) (TABLE 2). The median age among the group not taking any DMT was comparable to the median age of the treated group. The median age was lower for the group taking fingolimod and natalizumab (40 years and 46 years, respectively), compared with the other treatment groups (Table 2). The most common DMTs for admitted patients were ocrelizumab and dimethyl fumarate (13.1% and 12.1%, respectively). No major trends were identified when causes of admission were compared with DMT used. Also, no differences were observed in admission due to infectious causes in patients on high-efficacy therapy vs low- to moderate-efficacy therapy. The most common causes of admission for untreated patients were MS exacerbation (15.7%), UTI (11.0%), and pulmonary infection (7.9%). The most common causes for admission in patients who were on a DMT were neurologic deficits of unclear etiology (13%), UTI (13%), and skin infection (5.8%).

### Readmission Rate

The 30-day readmission rate was 14.9%. The most common cause for readmission was pain (25.0%), followed by infectious (22.5%), cardiogenic (15.0%), and neurologic (15.0%) causes.

### Services During Hospitalization and Discharge

The neurology service was consulted in 69% (184 times) of the admitted and readmitted cases from the emergency department (ED). Of these consults from the ED, 79% were admitted to the neurology service. The average length of stay was 6.1 days. Longer lengths of stay were observed for individuals admitted to the cardiology service ( $9.1 \pm 5.0$ ; TABLE S2). No major discrepancies in ancillary evaluations from physical therapy, occupational therapy, and speech pathology services were noticed among the different services. Compared with other services, patients admitted to the cardiology service were more likely to be discharged with home health occupational therapy (37.5%; Table S2). Patients admitted to the inpatient neurology service were slightly more likely to be discharged to acute rehabilitation (6.9%) in comparison with the other services. Surgical and oncologic services more often discharged patients to skilled nursing facilities.

## DISCUSSION

Our study aimed to evaluate the reasons for admission in patients with MS at Duke University Hospital in Durham, North Carolina. This study had similar results to what has been reported in the Portuguese and Finnish populations, where UTIs were the most

**TABLE 2.** Disease-Modifying Therapies in Admitted Individuals

Disease-modifying therapy	n (%) (N = 196) <sup>a</sup>	Age range (years)	Average age, years (± SD)	Median age (years)
No therapy	95 (48.5%)	23-85	57.54 (16.2)	61
Ocrelizumab	26 (13.2%)	27-69	51.85 (12.6)	55
Dimethyl fumarate	24 (12.2%)	31-74	55.26 (15.3)	57
Interferon beta (1a/1b)	10 (5.1%)	32-76	53.75 (13.8)	54
Natalizumab	9 (4.6%)	26-73	48.00 (15.5)	46
Glatiramer acetate	9 (4.6%)	48-71	56.10 (13.4)	60
Fingolimod	7 (3.6%)	27-63	44 (12.1)	40
Teriflunomide	7 (3.6%)	47-79	60 (11.5)	56
Rituximab	4 (2.0%)	50-65	54.7 (8.0)	54
Alemtuzumab	3 (1.6%)	39-48	44.67 (4.9)	47
Methotrexate	1 (0.5%)	N/Ab	82 (N/A)	82
Daclizumab	1 (0.5%)	N/Ab	27 (N/A)	27

<sup>a</sup>From 210 total, 10 individuals were eliminated from the study due to a new diagnosis of multiple sclerosis (ie, treatment naive); 2 were eliminated from the study for unknown disease-modifying therapy; and 2 switched therapies between admissions, leading to a total of 196 in this cohort.

<sup>b</sup>As only 1 individual was on methotrexate and 1 on daclizumab, age range and standard deviation do not apply.

common cause for admission.<sup>5,7,8</sup> Bladder dysfunction is common among individuals with MS and is likely to contribute to this presentation. Other potentially contributing factors include physical limitations, the use of immunosuppressive agents, and age. Developing better management of and techniques for bladder dysfunction may decrease the admission rate for individuals with MS.

The second most common reason for admission was neurologic complaint without an identifiable cause. Interestingly, 70% of this group had a documented progressive course of disease, either SPMS or PPMS, which potentially indicates smoldering progression as the cause for ED presentation.

Although MS hospitalization rates have declined dramatically over the past 25 years, they remain higher than in the general population.<sup>9</sup> One possible reason is that there may be a lower hospital admission threshold for individuals with MS. As a result, any neurologic symptom in a person with MS may be considered a reason for admission, despite a lack of clear etiology. A potential strategy to reduce unnecessary admissions would be for outpatient providers to be more proactive in performing workups and to improve access to urgent outpatient appointments.

Almost half (48.5%) of the admitted patients in our cohort were not on any DMT. That is almost 3 times more than what was seen in the outpatient Duke MS Center, where data from the center's database show 16.7% of patients were not on a DMT. One could think this is due to a tendency to discontinue DMTs as patients with MS age<sup>10</sup>; however, the median age among the group with no DMT was comparable to the median age of the groups with DMT. Though we now have more treatment options for MS, our study results suggest that the individuals with MS with the highest health care utilization are those who are untreated.

Untreated MS may lead to more hospitalizations because of symptom complications of and/or accumulated disability.<sup>9</sup> Additionally, the untreated group may include

patients with chronic progressive forms of MS that are less likely to respond to therapy. The most common DMTs in the admitted patients were ocrelizumab and dimethyl fumarate (13.2% and 12.2%, respectively). Ocrelizumab is the only DMT approved for PPMS and RRMS that does not carry a significant risk of progressive multifocal leukoencephalopathy,<sup>11,12</sup> potentially explaining why it is the most prescribed among this group. It is still, however, part of a group of B cell-depleting immunosuppressive medications that carry a higher infection risk than other available high-efficacy therapies. The median ages of patients taking natalizumab and fingolimod were lower (46 and 40 years, respectively) than those on other DMTs. This may be explained by the fact that fingolimod is preferentially prescribed to younger patients, given that the risk of bradycardia increases with age.<sup>13</sup>

The cohort's length of stay and readmission rates were similar to those of the general population (6.1 vs 5.5 days of stay, and 14.9% vs 15.5% readmission rates, respectively).<sup>14,15</sup> Prior studies' results have shown a longer length of stay for those with MS.<sup>16</sup> The shorter lengths of stay seen in our study may be due to greater availability of DMTs in recent years decreasing baseline disability.<sup>17</sup> The longest lengths of stay were observed for patients admitted to the cardiology service (9.1 ± 5.0). This may be explained by the fact that the degree of recovery is impacted by the area of the comorbidity.<sup>6</sup>

Limitations of this study include being retrospective and the short analysis period (2 years) at a single institution.

## CONCLUSIONS

Our study evaluated the most common reasons for hospital admissions among MS patients from a single-center cohort, identifying UTIs as the leading cause, potentially due to bladder dysfunction associated with MS. It also highlighted

that nearly half of the admitted patients were not on DMTs, suggesting that untreated MS may contribute to increased hospitalizations. Improving access to outpatient care and subsequent workups may help reduce preventable admissions.

Future studies could focus on evaluating admissions at multiple hospitals across the US, comparing different time periods as well as those admitted patients vs nonadmitted patients. Additional research is needed to identify the factors that can be addressed to support individuals with MS and reduce preventable hospitalizations.

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**TABLE S1.** Disease-Modifying Therapies in Admitted Individuals

	N (%)	Average age, years (± SD)	Median age, years	Female, n (%)
All	210	54.4 (15.6)	57	157 (74.8%)
<b>Race/ethnicity</b>				
White	109 (52.7%)	59.4 (15.4)	63	76 (69.7%)
Black	91 (43.9%)	49.3 (14.0)	46	74 (81.3%)
Hispanic	5 (2.4%)	39.2 (11.5)	37	3 (60.0%)
Native American	2 (1.0%)	57.5 (19.1)	58	2 (100%)

Note: Race/ethnicity was not indicated by 3 individuals.

**TABLE S2.** Snapshot of Therapies Accessed (A) and Discharge Location (B) by Service**A.**

	PT n (%)	OT n (%)	ST n (%)	Average days of stay (± SD)
Cardiology	8.0 (53.3)	8.0 (53.3)	3.0 (20.0)	9.1 (5.0)
Intensive care	9.0 (64.3)	8.0 (57.1)	7.0 (50.0)	5.4 (2.2)
Internal medicine	62.0 (64.6)	51.0 (53.1)	29.0 (30.2)	5.9 (3.4)
Neurology	58.0 (63.0)	47.0 (51.1)	23.0 (25.0)	6.0 (5.3)
Obstetrics	3.0 (50.0)	2.0 (33.3)	0.0 (0.0)	6.0 (3.5)
Oncology	7.0 (53.8)	6.0 (46.2)	2.0 (15.4)	5.0 (3.5)
Psychiatry	2.0 (100.0)	2.0 (100.0)	0.0 (0.0)	6.5 (3.5)
Surgery	17.0 (58.6)	17.0 (58.6)	11.0 (37.9)	6.7 (4.5)

OT, occupational therapy; PT, physical therapy; ST, speech therapy.

**B.**

	Cardiology	ICU	IM	Neuro	OB	Oncology	Psych	Surgery
Home	12.5%	33.3%	33.9%	15.5%	0	14.3%	0	11.8%
Home health OT	37.5%	11.1%	16.0%	27.6%	0	28.6%	50.0%	23.5%
Outpatient PT	25.0%	27.8%	9.7%	24.1%	100%	0	50.0%	17.7%
Acute rehabilitation	0	0	6.5%	6.9%	0	0	0	0
Skilled nursing facility	25.0%	27.8%	33.9%	25.9%	0	57.1%	0	47.0%

ICU, intensive care unit; IM internal medicine; Neuro, neurology; OB, obstetrics; OT, occupational therapy; Psych, psychology; PT, physical therapy.