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Disease-Modifying Therapies, Outcomes, Risk Factors and Severity of COVID-19 in Multiple Sclerosis: A MENACTRIMS Registry Based Study

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Disclosures

- I have received honoraria for lectures from Biologix, Biogen, Janssen, Hikma Pharmaceuticals, Novartis, Merck, Roche and Sanofi-Genzyme
- I have received travel grants from Novartis, Merck and Roche
- I have received research grant from Biogen

- No Conflict of Interest related to this study



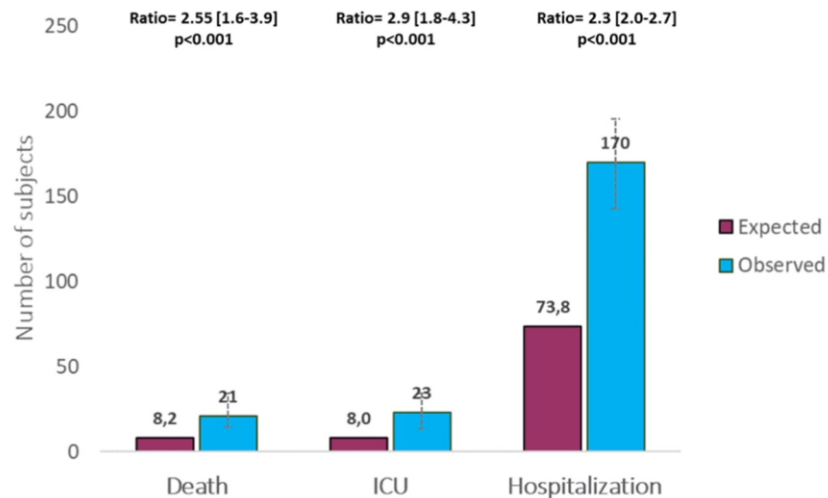
MS and COVID-19

- Multiple sclerosis (MS) patients have been considered a higher-risk population for COVID-19 due to the high prevalence of disability and disease-modifying therapy use
- On March 13, 2020, the Multiple Sclerosis International Federation issued recommendations regarding the risk of COVID-19 in patients with MS, with a specific statement regarding disease modifying therapies (DMTs), indicating that “some MS medications might increase the likelihood of developing complications from a COVID-19 infection but this risk needs to be balanced with the risks of stopping treatment.”
- Expert panels and national MS societies published editorials recommendations regarding delaying DMT initiation for those treatments with the highest presumed infectious risk or delaying the completion of a course for sequential DMTs



Data from ISS extracted on February 2, 2021

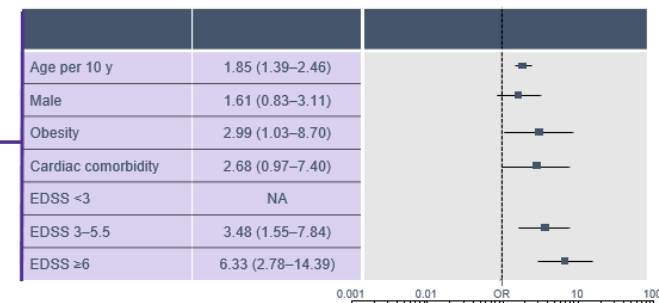
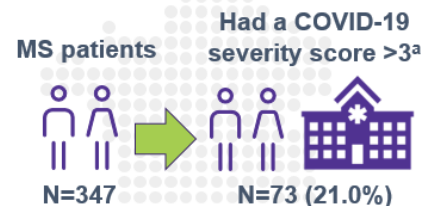
Expected death, ICU and hospitalization are calculated according to the age and sex Italian event rates



French COVISEP registry: Neurological disability, age and obesity were risk factors for severe COVID-19 infection



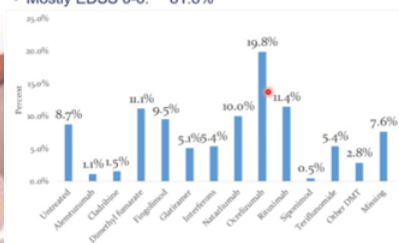
Multivariate analysis of factors influencing COVID-19 severity defined by a severity score^a of 3 or more



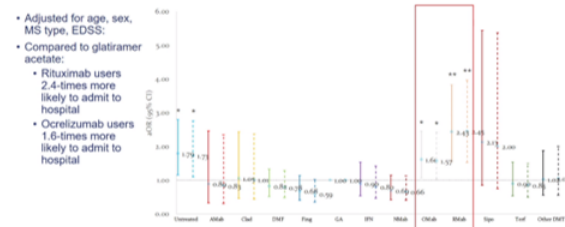
No increased risk of severe outcome associated with DMTs
MS patients with high EDSS (>3), obesity and older age were at highest risk of severe COVID-19 infection

COVID-19 and MS: MS Global Data Sharing Initiative

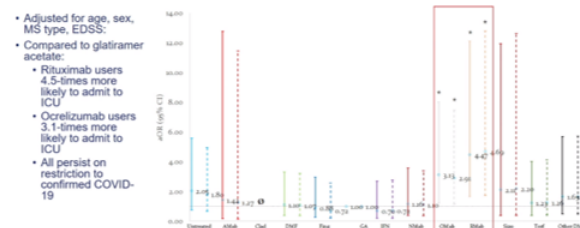
- 5,568 patients
 - 922 (16.6%) suspected COVID-19
 - 4,646 (83.4%) confirmed COVID-19
- 815 hospital admission, 208 ICU admission, 187 ventilation, 82 deaths
- 73.1% female
- Mostly 18–<50: 66.3%
- Mostly RRMS type: 84.3%
- Mostly EDSS 0–6: 81.8%



Q1a: What are associations of DMTs with COVID-19 severity vs GA? Hospital admission (815, 761 events)



Q1a: What are associations of DMTs with COVID-19 severity vs GA? ICU admission (208, 201 events)

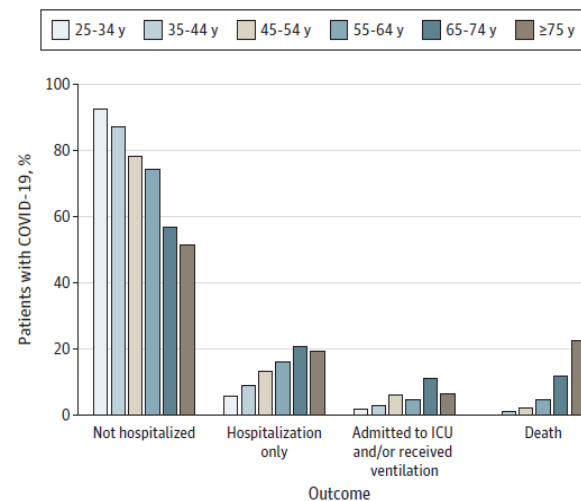


SARS-CoV-2 Infection in a North American Registry of Patients With Multiple Sclerosis

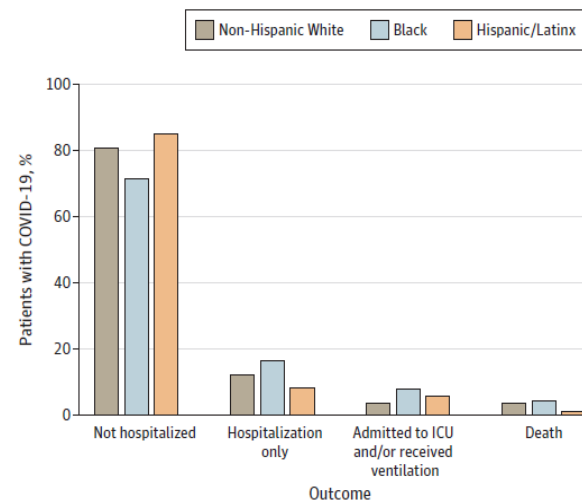
Original Investigation Research

Figure 2. COVID-19 Clinical Severity Rates by Age and Race/Ethnicity

A Clinical severity rates of COVID-19 by age



B Clinical severity rates of COVID-19 by race/ethnicity



Rationale and Objective

- Few data in our Middle East and North Africa region (MENA) identifying clinical characteristics of MS associated with worse COVID-19 outcomes
 - Small studies from Iran and GCC
- To examine outcomes and risk factors associated with COVID-19 clinical severity in a large, diverse cohort of Mediterranean patients with MS



Data Collection

- We conducted a multicenter, retrospective, observational cohort study of patients with MS with confirmed or highly suspected COVID-19 diagnosis
- Conducted between March 2020 and February 2021 – Before introduction of the COVID-19 vaccine in our region
- Data collected from the MENACTRIMS registry and local COVID-19 registries
 - Expert centers part of the MENACTRIMS registry
 - Neurologists collaborating with MENACTRIMS



Inclusion Criteria

- Positive SARS-CoV-2 polymerase chain reaction
- Positive thoracic computed tomography scan without fulfilling above criteria : Ground-glass opacity
- Typical clinical presentation
 - Anosmia/ageusia or Typical COVID-19 symptoms, without fulfilling above criteria



Definition of Study Endpoints

- We collected patient demographics, current DMT use, Expanded Disability Severity Scale score (EDSS) before COVID-19, and comorbidities
- Regarding COVID-19, we collected symptoms and diagnostic data (PCR for SARS-CoV-2 or chest CT)
- The primary end point was the participant's clinical status at the most severe point of their COVID-19 course (on a 7-point ordinal scale), referred as the *COVID-19 severity score*
 - 1: the patient was not hospitalized and had no limitations on activities;
 - 2: the patient was not hospitalized and had limitation on activities;
 - 3: the patient was hospitalized and did not require supplemental oxygen;
 - 4: the patient was hospitalized and required supplemental oxygen;
 - 5: the patient was hospitalized and receiving noninvasive ventilation or high flow oxygen;
 - 6: the patient was hospitalized and receiving invasive mechanical ventilation or extracorporeal membrane oxygenation;
 - 7: death



Results: Study Population

- A total of 600 patients included



COVID-19 Diagnosis

PCR	Serological Test	CT CHEST	COVID Symptoms
Positive N=542			
Negative N=1		Positive N=1	
Not Available N=57	Positive N=27		
			Positive N=23
		Positive N=7	

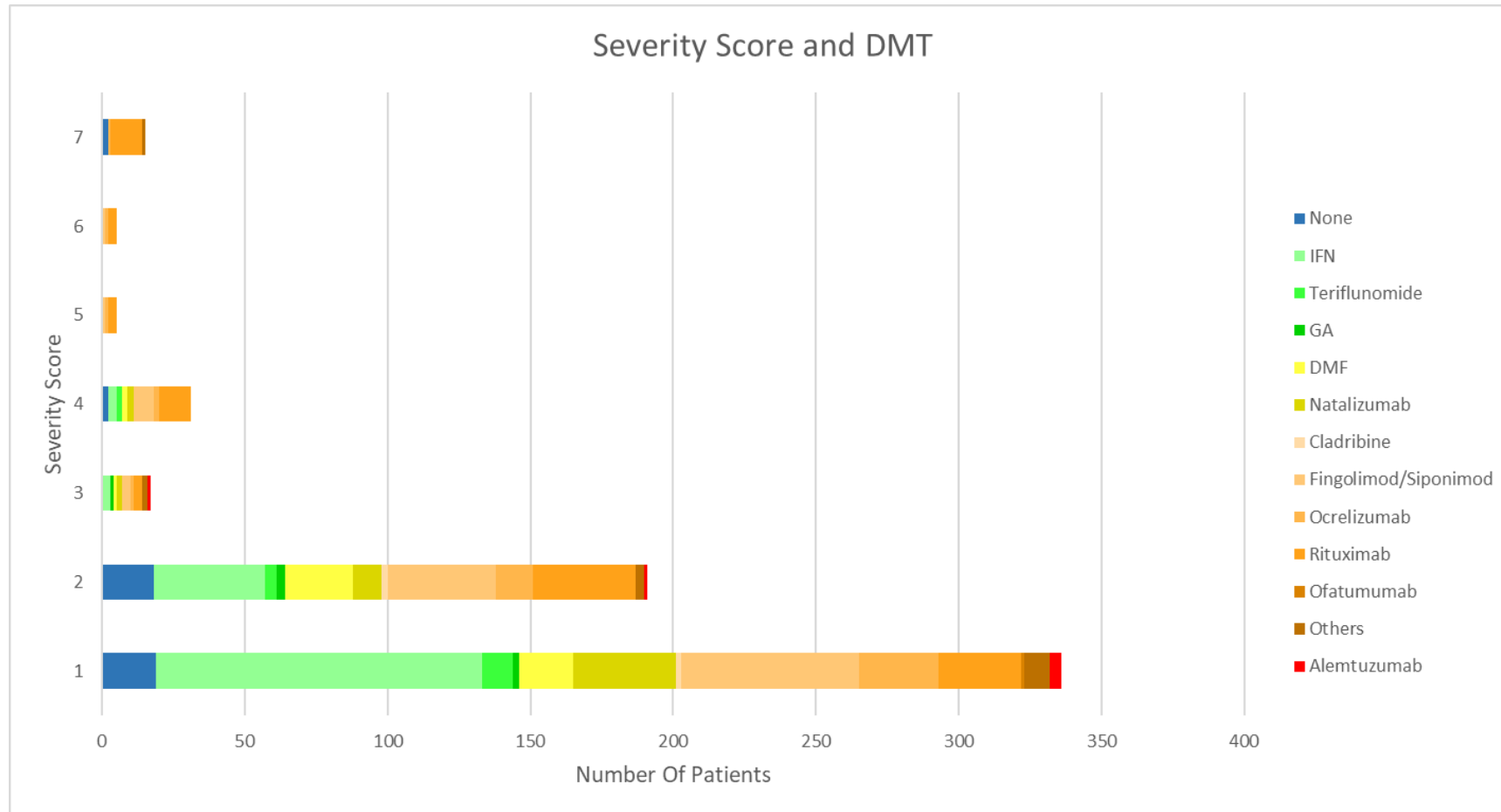
Baseline and Clinical Characteristics

Characteristics	N	%
No. of patients with MS	600	
Demographics		
Age, mean (SD) in years	36.4 (10.16)	
Gender		
Male	186	31.0
Female	414	69.0
Current Smoker	121	20.2
Former Smoker	27	4.5
Disease Course		
Clinically isolated syndrome (CIS)	13	2.2
Relmitting-relapsing MS (RRMS)	495	82.5
Secondary progressive MS (SPMS)	66	11.0
Primary progressive MS (PPMS)	26	4.3
Disease Duration in years		
Mean (SD)	8.3	(6.6)
Median (Range)	7.0	(0 – 45)
Expanded Disability Severity Scale Score		
Median (Range)	2.0	(0.0 – 9.0)
Used Steroids in the last month	16	2.7
Disease-modifying therapies		
None	41	6.8
IFN	159	26.5
Terifunomide	17	2.8
DMF	46	7.7
Cladribine	4	.7
Fingolimod/Siponimod	112	18.7
Natalizumab	50	8.3
Ocrelizumab	47	7.8
Rituximab	96	16.0
Ofatumumab	1	.2
Alemtuzumab	6	1.0
GA	6	1.0
Others	15	2.5

Comorbid Condition		
Obesity	77	12.8
HTN	41	6.8
CVD	41	6.8
DM	17	2.8
Thyroid Disease	12	2
Chronic Lung Disease	5	0.8
Anemia	4	0.7
Active Malignancy	3	0.5
Malignancy Remission	2	0.3
Renal Disease	1	0.2
Liver Disease	1	0.2
DMT was withheld	107	19.4
Covid-19 symptoms		
Fever	318	53.0
Cough	226	37.7
Anosmia	203	33.8
Fatigue	179	29.8
Sore Throat	136	22.7
Pain	124	20.7
Dyspnea	85	14.2
Runny Nose	78	13
Headache	66	11
Diarrhea	31	5.2
Nausea/Vomiting	6	1.0
Other Symptoms	11	1.8

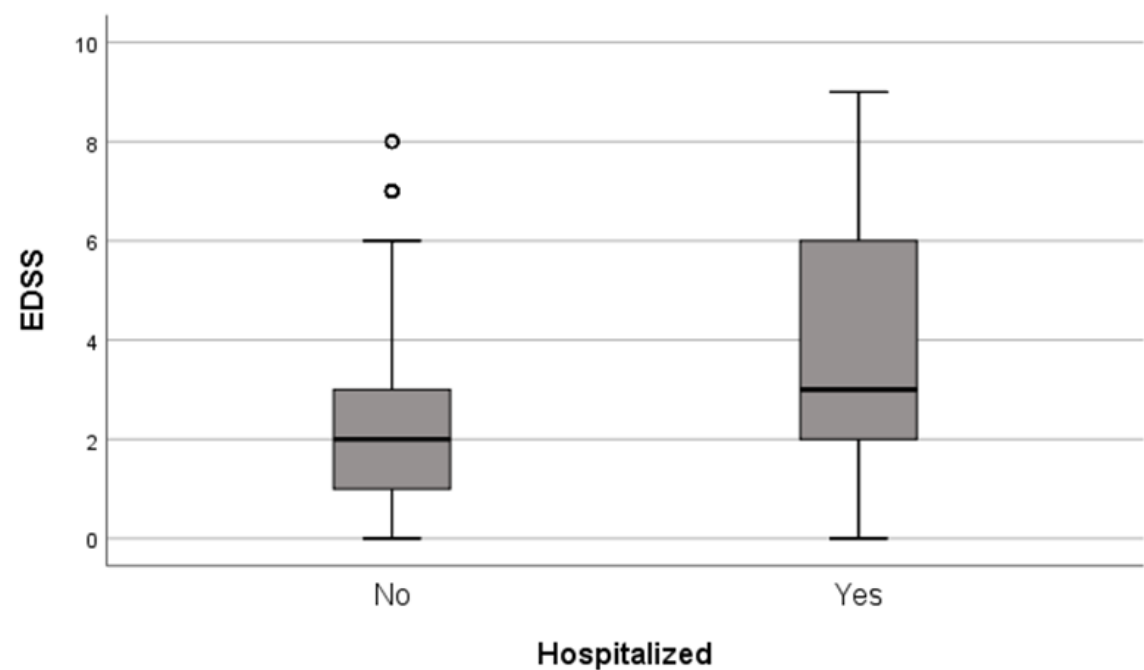
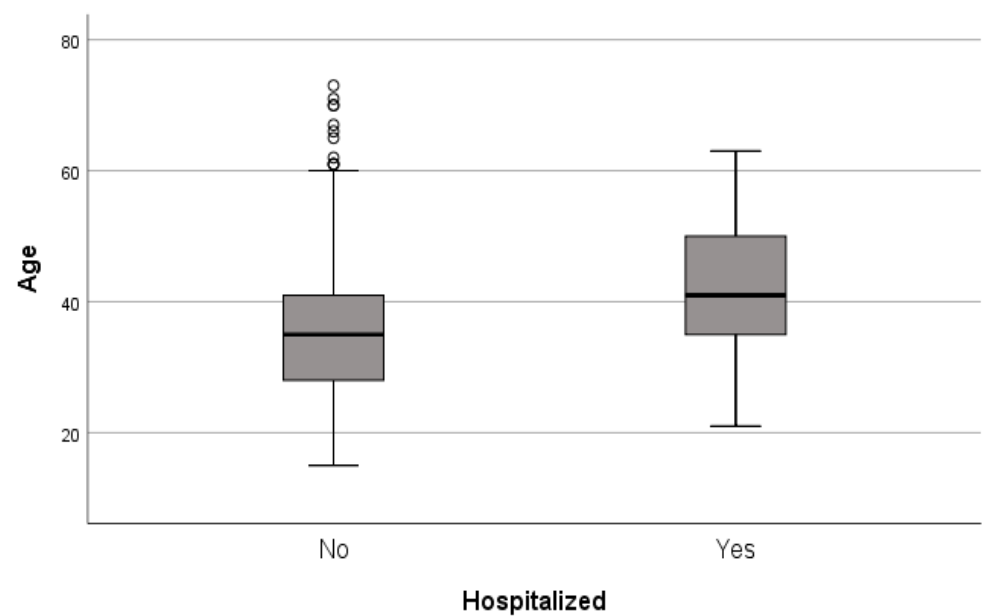


Distribution of Clinical Severity for COVID-19 according to DMTs



p-value for figure above is $<.001$ using the Pearson Chi-square $X^2=143.86$ $df=72$

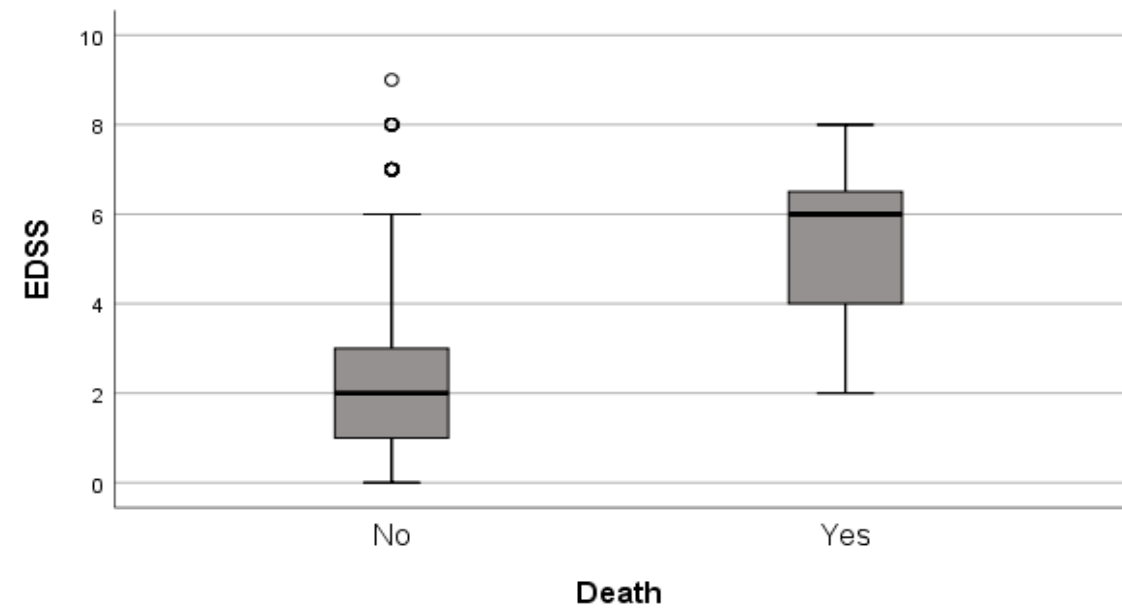
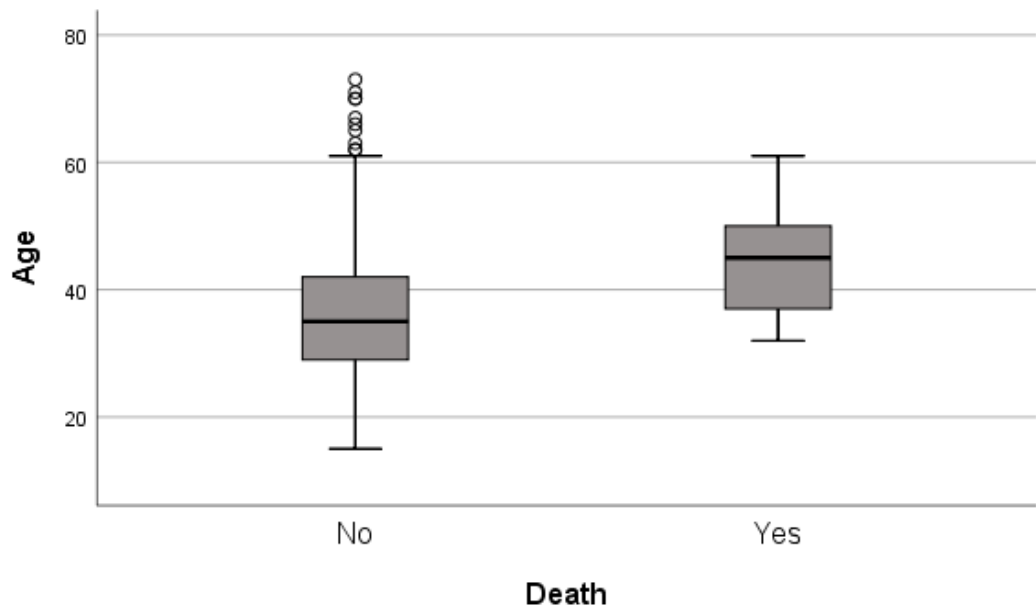
Characteristics of Patients Not Hospitalized for COVID-19 and Patients Who Were Hospitalized



	Hospitalized			
	Yes	No	p-value	
Age (Median, Range)	41.4 (21 – 61)	35.0 (15 – 73)	<.001	Mann Whitney U
EDSS (Median, Range)	3.0 (0 – 9)	2.0 (0 – 8)	<.001	Mann Whitney U



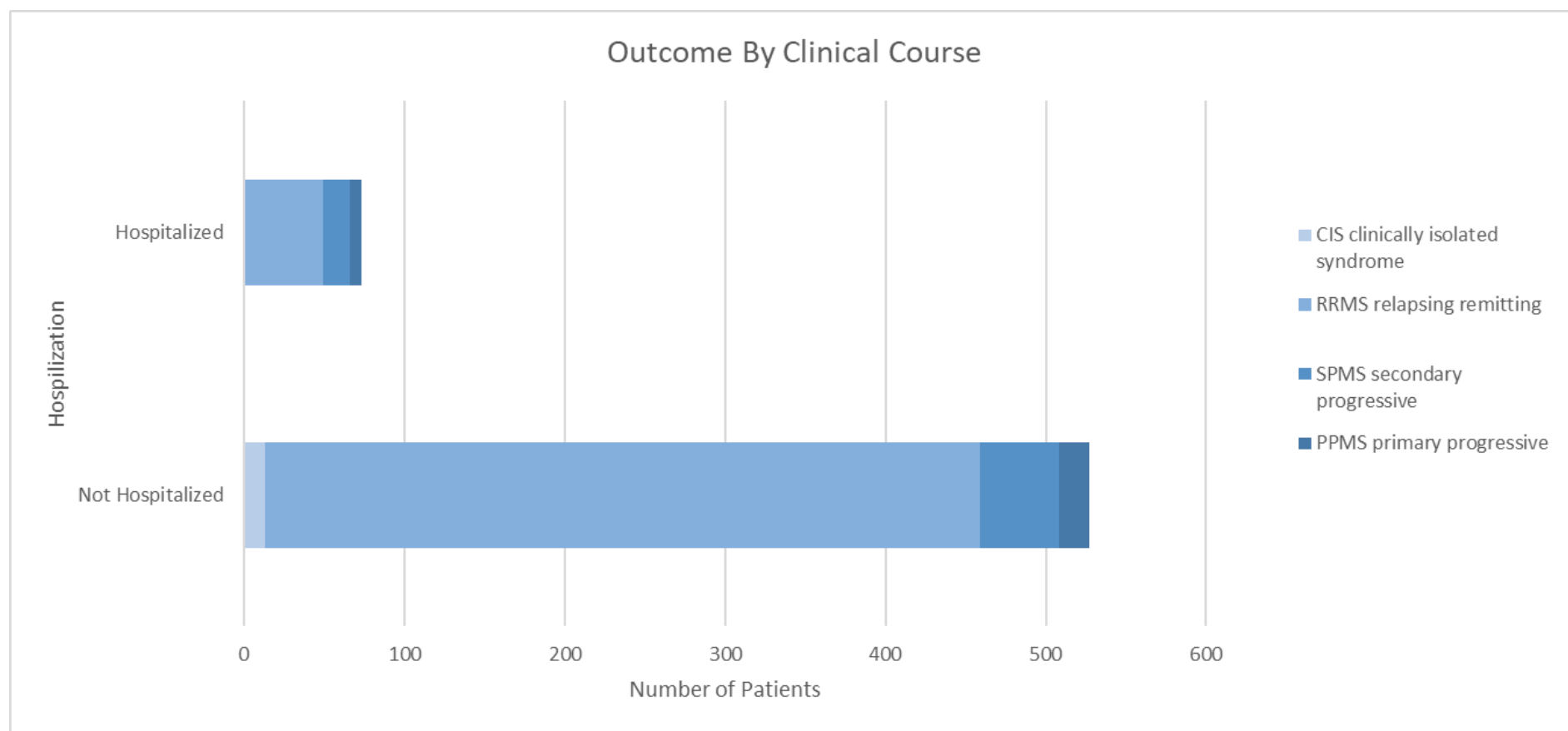
Characteristics of Patients Who Died of COVID-19 (n=15)



	Death			
	Yes	No	p-value	
Age (median, Range)	45 (32 – 61)	35 (15 – 73)	.002	Mann Whitney U
EDSS	6 (2 – 8)	2 (0 – 9)	<.001	Mann Whitney U



Outcome By Clinical Course



p-value for figure above is <.001 using the Pearson Chi-square $X^2=20.889$ $df=3$



Risk Factors of Severe COVID-19

Univariate and Multivariate Analysis

Univariate Analysis

	Severity Score ≥ 3		
	OR	95%CI	P-value
Age per 10y	1.67	1.327-2.101	<.001
Male	1.771	1.074-2.922	0.025
Obesity	2.596	1.429-4.717	0.006
CVD comorbidity	2.939	1.403-6.158	0.004
HTN comorbidity	2.939	1.403-6.158	0.004
DM comorbidity	2.292	0.727-7.228	0.157
Smoking	0.985	0.526--1.843	0.962
EDSS score <3 ref			
EDSS score 3-5.5	3.732	2.05-6.793	<.001
EDSS score ≥ 6	5.667	2.923-10.988	<.001

Multivariate Analysis

	Severity Score ≥ 3		
	OR	95%CI	P-value
Age per 10y	1.474	(1.102 - 1.971)	0.009
Male	2.132	(1.178 - 3.858)	0.012
Obesity	2.787	(1.336 - 5.812)	0.006
DMT (IFN/GA ref)			
Teriflunomide	4.413	(0.729 - 26.723)	0.106
DMF	2.676	(0.574 - 12.482)	0.210
Fingolimod/Siponimod	2.536	(0.804 - 7.998)	0.112
Natalizumab	2.485	(0.599 - 10.317)	0.210
Ocrelizumab	4.599	(1.193 - 17.722)	0.027
Rituximab	14.077	(4.797 - 41.309)	<.001
Others	8.76	(1.742 - 44.045)	0.008
None	3.288	(0.515 - 21.003)	0.208

Conclusion

- This is the largest registry-based cohort study in our region
- Results consistent with those described in similar international studies
- In patients with MS, we identified age, sex, disability, obesity, progressive MS as independent risk factors for severe COVID-19
- There was an association found between exposure to anti-CD20 DMTs and COVID-19 severity
 - No increased risk of severe outcome associated with all other DMTs, which should reinforce the recommendation of not stopping current DMTs and not delaying treatment initiation
- Knowledge of these risk factors may help improve the clinical management of MS patients with COVID-19 infection



Disease-Modifying Therapies, Outcomes, Risk Factors and Severity of COVID-19 in Multiple Sclerosis: A MENACTRIMS Registry Based Study

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