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Abstract

Background: People with MS may have unique perspectives on COVID-19 vaccines due to their condition and/or medications.

Objective: Assess perspectives and experiences with COVID-19 vaccination, and quantify variables impacting COVID-19 vaccine willingness in people with MS.

Methods: A survey captured demographics, MS characteristics, and COVID-19 infection and exposures data; opinions on COVID-19 vaccine safety, side effects, and efficacy; and experiences following vaccination. Chi-square tests and a logistic regression model were used to denote between-group differences and variables predicting vaccine willingness, respectively.

Results: Most (87.8%) of the 237 participants were willing to receive the vaccine. Fifteen percent held or delayed a DMT dose for vaccination. MS symptoms worsened in a minority (7.6% first/only dose; 14.7% second dose), and most side effects were mild (80.0%; 55.3%). Those not planning to receive the vaccine were primarily concerned with long-term safety (70.4%). Medical comorbidities (adjusted odds ratio [aOR]=5.222; p=0.04) and following infection prevention precautions (aOR=6.330; p=0.008) were associated with vaccine willingness.

Conclusion: Most individuals with MS surveyed plan to receive the COVID-19 vaccine. People with MS experience similar side effects to the general population, and few experience transient MS symptom worsening. These results can inform conversations on vaccination between providers and people with MS.

Keywords: Multiple sclerosis, COVID-19, vaccine

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Background

Multiple sclerosis (MS) is an immune-mediated demyelinating and neurodegenerative disease of the central nervous system (CNS), with an estimated prevalence in the United States of over 600,000 people.[1] MS onset tends to occur in early adulthood and often requires chronic treatment.[2] Most people with MS are treated with disease-modifying therapies (DMTs) that can limit relapses and accrual of neurologic disability.[3] The coronavirus disease 2019 (COVID-19) pandemic poses significant challenges to the long-term management of people with MS.[4,5,6] Emerging data suggest that some DMTs, in particular those with immunosuppressive properties, may negatively impact outcomes of COVID-19 in people with MS,[7] although the effect of those DMTs on risk of COVID-19 is less certain.[8,9]

Several highly efficacious vaccines have been developed against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for COVID-19, but vaccine hesitancy remains an obstacle.[10] In addition, many people with MS are understandably anxious as to how MS or their DMT impact the safety and efficacy of the COVID-19 vaccines.[11] Concern over the effect of vaccines on MS relapses persist despite research disproving the link between vaccination and MS.[12,13] Studies conducted at various timepoints during the COVID-19 pandemic suggested that 7-15% of people with MS were unwilling to get a COVID-19 vaccine.[11,14] The COVID-19

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vaccines can also cause systemic side effects, such as fever, that can transiently worsen MS symptoms.[15] COVID-19 vaccine safety in people with MS has been supported by expert organizations such as the National MS Society (NMSS) in the United States[16] and internationally.[17] Regarding vaccine efficacy, several studies have shown that some DMTs are associated with a reduced humoral immune response to existing vaccines,[18,19] and emerging data suggest that this paradigm extends to the COVID-19 vaccines.[20,21]

In this study, we first aim to evaluate the attitudes of people with MS towards the COVID-19 vaccines. We will additionally present the collective experiences of individuals within this cohort who have received at least one dose of a COVID-19 vaccine.

Methods

This is a prospective, observational, single-cohort study assessing patient-reported opinions and experiences with COVID-19 vaccines in people with MS. This project leverages data from the COVID-19 and Multiple Sclerosis survey-based registry at Washington University in St. Louis, Missouri, which was originally developed in collaboration with Cleveland Clinic and Johns Hopkins University. This study captures details from people with MS regarding their exposures to/experiences with COVID-19. This study is currently active, and over 300 participants are already enrolled. People with MS are invited to participate by verbal invitation at clinic visits, by telephone, or by messages through the electronic medical record. Participants in this study complete periodic surveys online: after completing a baseline survey, participants complete follow-up surveys every two weeks for the first three months, and monthly follow-up surveys thereafter for up to one year. Data are collected and managed using REDCap, a secure web-based software platform designed to support data capture for research studies.[22,23] Enrollment in the registry began on September 17, 2020; a section of survey questions regarding COVID-19 vaccination was added to follow-up surveys on March 24, 2021. The data were censored on May 26, 2021.

All participants in the registry meeting the inclusion criteria were included in this analysis. Individual respondents were confirmed to be patients with a clinical diagnosis of MS followed at the tertiary care MS subspecialty outpatient clinic at Washington University, at which all people with MS are encouraged to get a COVID-19 vaccine when it is available to them in accordance with NMSS guidance.[16]

Patient-level variables collected in this survey study include demographics; comorbidities applicable to COVID-19 such as hypertension, COPD, diabetes, and smoking status; employment status; MS characteristics such as subtype (per neurologist assessment in the medical record), date of last relapse, and which DMT they are treated with (as well as whether any alterations in dosing regimen were made); clinical information on any COVID-19 infection/exposures, if applicable; and behavioral modifications in response to the pandemic. Participants are also asked to report subjective and objective data on COVID-19 vaccines, such as whether they have received or are planning to receive the vaccine, whether they have concerns about vaccine safety/side effects/efficacy, and, if so, what those concerns are. If they have already received a COVID-19 vaccine, participants report the vaccine date/manufacturer, whether they experienced side effects or MS symptom worsening, what those side effects were, how long they lasted, and how severe they were.

Descriptive statistics are used to report COVID-19 vaccine perspectives and experiences of study participants. For some comparative analyses, respondents are categorized, such as those taking DMTs expected to have a large impact on humoral vaccine responses (i.e., B cell depleting monoclonal antibodies, sphingosine 1-phosphate [S1P] receptor modulators),[19,24] denoted as "high-risk," vs. DMTs expected to have a low impact, denoted as "low-risk;" those with and without medical comorbidities; and those with and without prior COVID-19 infection. Between-group comparisons of dichotomous categorical outcomes are analyzed using a chi-square test; where sample sizes are small, Fisher's exact test is used instead. Between-group comparisons are presented alongside p-values to demonstrate statistical significance.

We also aimed to quantify the effects of gender, age, medical comorbidities, employment, history of COVID-19 infection, following infection prevention precautions, MS subtype, current DMT, and DMT changes on whether a participant will receive a COVID-19 vaccine. Univariate analyses are performed for each variable using a chi-square test as above. Relationships between independent variables and whether a participant will receive a COVID-19 vaccine are expressed as odds ratios and are presented alongside 95% confidence intervals and p-values. For

Table 1. Demographics.[a]

n	237
Age, years - median (IQR)	53.4 (43.7-63.0)
Female - no. (%)	188 (79.3%)
Pregnant/postpartum - no. (%)[b]	1 (0.5%)
Race/ethnicity - no. (%)	
White	224 (94.5%)
Black	10 (4.2%)
Asian	2 (0.8%)
Other	1 (0.4%)
Ethnicity - no. (%)	
Hispanic or Latino	6 (2.5%)
Comorbid medical conditions - no. (%)[c]	
0	96 (40.5%)
1	92 (38.8%)
2 or more	49 (20.7%)
MS subtype - no. (%)	
RRMS	163 (68.8%)
CIS	1 (0.4%)
SPMS	50 (21.1%)
PPMS	14 (5.9%)
Unclear	9 (3.8%)
Active disease - no. (%)[d]	40 (16.9%)
Current DMT - no. (%)[e]	
Low-risk	88 (37.1%)
High-risk	107 (45.1%)
Untreated	41 (17.3%)
Confirmed COVID infection - no. (%)[f]	34 (14.3%)
Required hospital admission/supplemental oxygen	2 (5.9%)
Disposition	
Home	2 (100%)
Skilled nursing facility/inpatient rehab	0 (0%)
COVID infection outcome	
Fully recovered	18 (52.9%)
Recovered with complications	11 (32.4%)
Improving	4 (11.8%)
Worsening	1 (2.9%)
Social behaviors - no. (%)[g]	
Social distancing (leaving home less than before pandemic)	206 (92.4%)
Wearing a mask at least some of the time	218 (97.8%)
Maintaining 6 feet of separation when out	211 (94.6%)

[a]Percentages given reflect proportion responding to question.
[b]Currently pregnant or had given birth in the past 6 weeks at time of baseline survey.
[c]Including BMI >30, current smoker, chronic lung disease, heart disease, stroke, diabetes, hypertension, chronic liver disease, chronic kidney disease, cancer, history of organ transplant, HIV, and other systemic inflammatory disease.
[d]Defined as at least one relapse in the 12 months preceding the baseline survey or during the survey period.
[e]Low-risk DMT defined as interferons, glatiramer acetate, teriflunomide, fumarates. High-risk DMT defined as S1P receptor modulators, B cell depleting agents, cladribine, natalizumab, alemtuzumab.[7,19]
[f]Defined as positive COVID-19 test at any point.
[g]At time of baseline survey.

multivariable analyses, a logistic regression model was developed and is also presented to assess these relationships. All tested variables are included in the model using forced entry. These relationships are expressed as adjusted odds ratios, and are also shown alongside 95% confidence intervals and p-values.

Results

Approximately 1700 patients were invited to participate in the study via direct messaging in the electronic medical record, phone calls, and/or written fliers in clinic in which 311 responded (≈18% response rate, though it is unknown how many recipients of the electronic invitation actually accessed it). Quality control checks confirmed respondents were followed at our center with a diagnosis of MS. Of the baseline survey respondents, 237 (76.2%) had responded to a follow-up survey including questions on COVID-19 vaccination, comprising this study's overall sample. More than half of these participants had completed a follow-up survey at 8 months following their initial baseline survey (interquartile range [IQR]: Month 5 – Month 8).

Study sample demographics are presented in Table 1. This cohort had an average age of 53.4 years), was predominantly female (79.3%), and was predominantly white (94.5%). All subtypes of MS were represented, and 16.9% had active disease (at least one relapse in the 12 months preceding the baseline survey or at any point during the survey period). There was a high incidence of confirmed COVID-19 infection in the study cohort (14.3%), though few required inpatient admission, and more than half (52.9%) fully recovered. More than 90% of respondents followed general infection prevention precautions at the time of their baseline survey response, including social distancing (92.4%), wearing a mask at least some of the time (97.8%), and maintaining 6 feet of separation when out (94.6%).

Within this sample of people with MS, the vast majority (87.8%) either received or were planning to receive a COVID-19 vaccine (Table 2); only 8.0% were not planning to receive a COVID-19 vaccine, and the remainder (4.2%) were unsure. Compared to those who received or were planning to receive the vaccine, those who were not planning to receive or were unsure about receiving the vaccine were significantly less likely to be worried about being at greater risk of catching COVID-19 (58.2% received/planning to receive vs. 31.0% not planning/unsure; p=0.004) or suffering more complications from COVID-19 infection (73.7% vs. 31.0%; p<0.001). Conversely, those who were not planning to receive the vaccine were more worried about MS worsening than COVID-19 (50.0% vs. 69.0%; p=0.03), and more wary of vaccine safety/side effects (34.1% vs. 93.1%; p<0.001). The primary concern among those not planning to receive the vaccine was its long-term safety (38.0% vs. 70.4%; p=0.004). Concerns about vaccine efficacy due to a participant's DMT were more common in those who received or were planning to receive the vaccine (37.8% vs. 20.7%; p=0.001).

Of those who had already received a COVID-19 vaccine (Table 3), the majority received mRNA vaccines (57.7% Pfizer-BioNTech, 34.6% Moderna), and of those, more than 90% had completed the two-dose series. 15.0% held or delayed a dose of their DMT for vaccination, the majority of whom were on high efficacy drugs (41.7% ocrelizumab, 16.7% natalizumab). Some participants felt that their MS symptoms worsened after their first/only (7.6%) or second (14.7%) doses. Side effects from the injections were common (76.1% first/only dose, 82.7% second dose) but short-lived, with a median of 2 days duration following either dose. Most side effects were mild (80.0% first/only dose, 55.3% second dose); side effects preventing participants from performing their usual activities were uncommon (1.3% first/only dose, 17.7% second dose).

Univariate odds ratios and adjusted odds ratios from the logistic regression model are presented in Table 4. Low numbers of minority respondents and those who had changed their DMT dosing/frequency precluded these variables from inclusion in the model; all patients in these categories received or planned to receive a COVID-19 vaccine. After adjusting for the other variables listed in Table 4, having 2 or more medical comorbidities predisposing to worse COVID-19 outcomes was associated with 5.2-fold greater odds of receiving a vaccine (adjusted odds ratio [aOR]=5.2; p=0.04; 95% confidence interval [CI]: 1.1 to 25.7). With the same adjustments, following recommended infection prevention precautions was associated with 6.3-fold greater odds of receiving a COVID-19 vaccine (aOR=6.3; p=0.008; 95% CI: 1.6 to 24.9). Having untreated MS was associated with significantly lower adjusted odds of receiving a vaccine (aOR=0.1; p=0.003; 95% CI: 0.0 to 0.4). Female sex (aOR=3.4; p=0.06; 95% CI: 1.0 to 11.6) and a progressive MS subtype (aOR=5.3; p=0.05; 95% CI: 1.0 to 29.0) trended towards a higher likelihood of getting a vaccine,

Table 2. Attitudes towards COVID-19 and vaccination.[a]

n	237			
Received/planning to receive COVID-19 vaccine - no. (%)	208 (87.8%)			
Not planning to receive COVID-19 vaccine - no. (%)	19 (8.0%)			
Unsure about receiving COVID-19 vaccine - no. (%)	10 (4.2%)			
	Total	*Received/planning to receive vaccine*	*Not planning to receive vaccine*[b]	*p-value*
n	237	208	29	
Worried about being at greater risk of COVID-19 due to MS and/or DMT - no. (%)	130 (57.5%)	121 (58.2%)	9 (31.0%)	0.004
Worried about having more complications from COVID-19 due to MS and/or DMT - no. (%)	155 (68.6%)	146 (73.7%)	9 (31.0%)	<0.001
Switched/stopped DMTs specifically to prevent COVID-19 - no. (%)	5 (2.1%)	4 (1.9%)	1 (3.4%)	0.765
More worried about MS worsening than risk of COVID-19 - no. (%)	119 (52.7%)	99 (50.0%)	20 (69.0%)	0.034
No concerns about COVID-19 vaccine safety/side effects - no. (%)	139 (58.6%)	137 (65.9%)	2 (6.9%)	<0.001
Concerns about COVID-19 vaccine safety/side effects… - no. (%)[c]	98 (41.4%)	71 (34.1%)	27 (93.1%)	<0.001
because I have MS	46 (46.9%)	34 (47.9%)	12 (44.4%)	0.760
because of my DMT	32 (32.7%)	26 (36.6%)	6 (22.2%)	0.174
about short-term side effects	31 (31.6%)	25 (35.2%)	6 (22.2%)	0.217
about long-term safety	46 (46.9%)	27 (38.0%)	19 (70.4%)	0.004
about a possible allergy to vaccine or its components	6 (6.1%)	3 (4.2%)	3 (11.1%)	0.342
other concerns	7 (7.1%)	2 (2.8%)	5 (18.5%)	0.016
Concerns about COVID-19 vaccine effectiveness because of DMT - no. (%)[d]	74 (37.4%)	68 (37.8%)	6 (20.7%)	0.001

[a]Percentages given reflect proportion responding to question.
[b]Includes those not planning to receive vaccine or unsure about receiving vaccine.
[c]Participants able to give more than one answer; percentages may not add to 100%.
[d]Among those currently on a disease-modifying therapy.

but were not statistically significant in the final adjusted model.

Discussion

In this observational survey of people with MS, we found that the vast majority of respondents have received or are planning to receive the COVID-19 vaccine. More people with MS in our survey were concerned about being at a greater risk for COVID-19 due to MS/DMT than safety and side effects of the vaccine. Transient worsening of MS symptoms was more common after the second dose (for two-dose vaccines), but was only reported by 15% of participants. As in the general population, side effects to the vaccine were relatively common, but the majority were mild and short-lived. Participants who were concerned about being at higher risk for COVID-19 (either due to other comorbidities or being on a DMT) and those who followed infection prevention precautions at the time of the baseline survey were more willing to get the vaccine. Less than 40% of participants were concerned about vaccine effectiveness because of their DMT, though many of the survey responses were recorded before recent publications on the impact of DMTs and other immunosuppressant medications on COVID-19 vaccine efficacy.[20,21]

Vaccine hesitancy threatens the progress that has been made in combating the COVID-19 pandemic in the United States. Vaccine willingness questions in this study were answered on follow-up surveys administered between March and May of 2021. It is encouraging to see that 87.8% of participants in this study are willing to receive one of these vaccines. Other studies of COVID-19 vaccine willingness in people with MS suggested rates of vaccine willingness of 66.0% (conducted April 2020 to May 2020)[14] and 70.1% (conducted December 2020 to January 2021).[11] Though the exact questions and populations differed amongst these studies, the suggested positive trajectory of vaccine acceptance over time may reflect greater COVID-19 concern following the winter 2020 pandemic spike in the United States, FDA emergency use authorization of the vaccines, recommendations from professional bodies such as the NMSS (first published in January 2021), and/or increasing societal familiarity with the vaccines over time. These studies collectively show that people with MS are largely willing to receive the vaccine, perhaps reflecting concerns over their COVID-19 risk given their diagnosis, DMT, and/or comorbidities. Indeed, more than half of participants in this study are concerned about the interactions between COVID-19, MS, and their DMT. These interactions are complex: factors associated with MS, such as subtype and disability status, may affect an individual's risk of suffering a worse outcome from COVID-19,[7,25,26] and may also influence decision-making on DMTs, some of which may also affect these risks.[27] Harboring these concerns also appears to be significantly associated with COVID-19 vaccine willingness in our study.

Reported concerns regarding COVID-19 vaccination and MS suggest an important and ongoing role for improved patient education. Vaccine safety has been the predominant concern in prior studies of COVID-19 vaccine perspectives amongst people with MS,[11] and substantial minorities of participants in this study report concerns over vaccine safety and/or side effects, despite agreement amongst professional organizations that COVID-19 vaccines are safe for people with MS and safe to use with DMTs.[16,17] Systemic side effects such as pain at the injection site, fatigue, headaches, and myalgias following COVID-19 vaccination are relatively common in this cohort and are similar to those observed in the general population, including in terms of duration and severity.[28,29] Furthermore, only 15% of participants experienced transient worsening of their MS symptoms following vaccination, which should reassure people who have concerns about how the COVID-19 vaccine may exacerbate their symptoms. Messaging targeting those remaining unvaccinated should focus on vaccine safety, and the short duration of predominantly mild side effects observed in this study may additionally lessen the degree of perceived vaccination risk amongst this group.

Some DMTs can diminish humoral immune responses to COVID-19 vaccination,[20] which may leave some vaccinated individuals under-protected or unprotected against COVID-19. However, in this study, fewer participants expressed concern that their DMT could reduce the vaccine's effectiveness than the number taking a high-risk DMT. Of the 58 participants taking a B cell depleting therapy (ocrelizumab, ofatumumab, or rituximab), 10 (17.2%) reported an adjustment in their dosing regimen (e.g., holding or delaying an infusion or injection). Though there is a mechanistic rationale for holding a B cell depleting agent to allow B cells to repopulate prior to vaccination, clinical evidence to support this strategy is lacking,[20] and future studies evaluating both humoral and cellular immune responses in people with MS on varying degrees of B cell

Table 3. Experiences with COVID-19 vaccination.

Manufacturer - no. (%)		
Pfizer-BioNTech	120 (57.7%)	
Received both doses	113 (95.0%)	
Days between doses - mean (SD)	21.5 (3.7)	
Moderna	72 (34.6%)	
Received both doses	65 (90.3%)	
Days between doses - mean (SD)	29.5 (3.7)	
Johnson & Johnson	9 (4.3%)	
Unsure/no response	7 (3.7%)	
Held/delayed DMT dose for the vaccine - no. (%)[a]	24 (15.0%)	
Interferons	10 (41.7%)	
Ocrelizumab	10 (41.7%)	
Natalizumab	4 (16.7%)	
	After first dose[b]	*After second dose*
MS symptom worsening after vaccination - no. (%)	15 (7.6%)	26 (14.7%)
No vaccine side effects - no. (%)	48 (23.9%)	31 (17.3%)
Vaccine side effects - no. (%)	153 (76.1%)	148 (82.7%)
Pain in the arm at injection site	144 (71.6%)	119 (66.5%)
Swelling in the arm at injection site	19 (9.5%)	20 (11.2%)
Fever	9 (4.5%)	33 (18.4%)
Chills	11 (5.5%)	39 (21.8%)
Tiredness	60 (29.9%)	87 (48.6%)
Headache	38 (18.9%)	65 (36.3%)
Muscle aches	27 (13.4%)	57 (31.8%)
Lightheadedness	4 (2.0%)	17 (9.5%)
Rash	2 (1.0%)	3 (1.7%)
Nausea/vomiting	3 (1.5%)	15 (8.4%)
Diarrhea	0 (0%)	4 (2.2%)
Swollen or sore lymph nodes	3 (1.5%)	4 (2.2%)
Allergic reaction	0 (0%)	0 (0%)
Other	6 (3.0%)	12 (6.7%)
Duration of side effects, days - median (IQR)	2 (1-3)	2 (1-3)
Severity of side effects - no. (%)		
Mild (not interfering with daily activities)	120 (80.0%)	78 (55.3%)
Moderate (interfering with daily activities)	28 (18.7%)	38 (27.0%)
Severe (unable to perform usual activities or missed work)	2 (1.3%)	25 (17.7%)

[a]Among those currently on a disease-modifying therapy.
[b]First dose of mRNA vaccine, or single dose of other vaccines.

depleting therapy, both in terms of duration from last infusion and total time on drug, are sorely needed.[21] Several respondents also made adjustments in their dosing regimen of interferons, which should not impact the response to COVID-19 vaccination;[19] this may reflect personal patient concerns over getting multiple injections or "stacking" of flu-like side effects from both their DMT and the COVID-19 vaccine. Decisions on whether to hold or delay a DMT dose should be made by an experienced physician, should be individualized, and should take into consideration the individual's clinical characteristics as well as their risk of COVID-19 infection. Outstanding questions on the effects of DMTs on COVID-19 vaccine efficacy provide another opportunity for patient education and counseling on the importance of continuing to follow standard infection prevention precautions, even after vaccination, especially if treated with a cell-depleting medication such as ocrelizumab, ofatumumab, or alemtuzumab, or an S1P receptor modulator (fingolimod, siponimod, ozanimod, ponesimod).[21]

Table 4. Univariate and adjusted odds ratios for receiving or planning to receive COVID-19 vaccine.

	Univariate OR	*95% CI*	*P-value*	*Adjusted OR*	*95% CI*	*P-value*
Sex						
Male	†			†		
Female	3.262	1.437-7.407	0.005	3.355	0.975-11.551	0.055
Age						
Under 60 years old	†			†		
60+ years old	2.162	0.843-5.545	0.109	1.261	0.324-4.905	0.737
Medical comorbidities[a]						
0	†			†		
1	1.138	0.496-2.611	0.760	2.205	0.706-6.880	0.173
2 or more	2.618	0.715-9.588	0.146	5.222	1.061-25.693	0.042
Employment						
Standard risk employment	†			†		
High risk employment[b]	0.726	0.238-2.211	0.573	0.703	0.175-2.828	0.620
Loss of employment during pandemic	1.517	0.277-8.310	0.631	0.803	0.121-5.316	0.820
Not employed prior to/during pandemic	2.933	0.951-9.050	0.061	0.939	0.237-3.720	0.929
Confirmed COVID-19 infection[c]						
No	†			†		
Yes	0.778	0.275-2.201	0.636	0.875	0.204-3.744	0.857
Following infection prevention precautions[d]						
No	†			†		
Yes	12.545	4.782-32.914	<0.001	6.330	1.610-24.894	0.008
MS subtype						
Relapsing MS (CIS, RRMS)	†			†		
Progressive MS (SPMS, PPMS)	3.831	1.117-13.139	0.033	5.338	0.983-28.994	0.052
Current DMT						
Low-risk	†			†		
High-risk	1.396	0.541-3.604	0.491	0.706	0.201-2.481	0.587
Untreated	0.456	0.169-1.227	0.120	0.096	0.021-0.444	0.003
Stopped/switched DMT during pandemic						
No	†			†		

(continued)

Table 4. Continued.

	Univariate			*Adjusted*		
	OR	*95% CI*	*P-value*	*OR*	*95% CI*	*P-value*
Yes	1.039	0.372-2.900	0.942	0.977	0.271-3.527	0.972

[a]Including BMI >30, current smoker, chronic lung disease, heart disease, stroke, diabetes, hypertension, chronic liver disease, chronic kidney disease, cancer, history of organ transplant, HIV, and other systemic inflammatory disease.
[b]Defined as active healthcare worker (e.g. nurse, technician, physician, hospital worker), active first-line responder (e.g. police, firefighter, paramedic), active essential worker (e.g. grocery store), or active worker in shelter or prison.
[c]Defined as positive COVID-19 test at any point.
[d]Defined as social distancing (leaving home less than before the pandemic), wearing a mask at least some of the time, and maintaining 6 feet of separation when out.
[†]Referrant.

Numerous interrelated variables play a role in one's decision on whether to receive the COVID-19 vaccine. In this cohort, both following infection prevention precautions and having medical comorbidities are associated with a willingness to get the vaccine, which suggests a cohort that is more likely to follow health authority guidelines and medical advice, and that understands the importance of protective measures and their own degree of risk. Conversely, and potentially reflecting history of adverse responses or skepticism of medical advice, being untreated is associated with not receiving the vaccine, even after adjusting for age (those who are elderly may be less likely to be on a DMT, but trended towards receiving the vaccine in the univariate analysis) and other variables. Gender trended towards being a significant predictor of vaccine willingness in the adjusted model, consistent with the general population in the United States.[30] Prior studies have similarly shown race to be a significant predictor of COVID-19 vaccine willingness in the general population,[30,31,32] but low numbers of minority respondents prevented their inclusion in this regression model. It is notable that minority respondents (10 Black, 2 Asian, and 1 other) all received or plan to receive the COVID-19 vaccine.

This study is not without limitations. Survey response bias may have influenced multiple variables, including willingness to vaccinate, the proportions of participants with a prior confirmed COVID-19 infection (e.g., may be more invested in contributing to research on this subject), those with favorable outcomes from those infections (e.g., those with a poor outcome who otherwise would have participated may not be capable of doing so), and demographics (as this sample skews older). The relatively low response rate limits the generalizability of the study. Respondents to the electronic survey invitation may have skewed more technologically savvy or more engaged in their care. These data were collected from patients followed at a single center in St. Louis, Missouri that sees few, if any, uninsured or state-sponsored insured patients, which may skew unmeasured variables such as socioeconomic status and also limit the external validity of the study. Disability data were also not collected in this study, which may be associated with the dependent variable (vaccine willingness) as well as several independent variables (risk of COVID-19,[7] age, DMT, employment). Future studies should dig deeper into why patients chose to hold or change their DMT for the COVID-19 vaccine and compare COVID-19 vaccine willingness to willingness to receive other childhood or travel-related vaccines.

Conclusions

Most people with MS who responded to our survey, notably those who consider themselves at high risk for COVID-19, were willing to receive a vaccine. Vaccine side effects in people with MS were similar to the general population, and only a minority experienced transient worsening of their MS symptoms. While more work is being done to understand vaccine effectiveness in people with MS, respondents were less concerned about effectiveness and only a few adjusted their DMT schedule. This study provides reassuring and encouraging data on the COVID-19 vaccine in people with MS and can help inform conversations between healthcare providers and people with MS on this topic.

Declaration of Competing Interests

J.R.C. reports consulting fees from EMD Serono and Genentech, and grant funding from the National Multiple Sclerosis Society, all outside the submitted work. D.C.P. reports no competing interests. B.P.M. reports consulting fees from Biogen and stock in

Pfizer, and has received grant funding from Genentech, all outside the submitted work. K.C.F. reports no competing interests. J.A.C. reports personal compensation for consulting for Biogen, Bristol-Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an Editor of *Multiple Sclerosis Journal.* E.M.M. reports serving as PI or site PI for studies sponsored by Biogen and Genentech, and receiving free medication for a clinical trial, of which she is PI, from Teva, as well as royalties for editorial duties from UpToDate. R.T.N. reports consulting fees for Banner Life Sciences, Biogen, Bristol Myers Squibb, Genentech, Genzyme, Janssen, GW Therapeutics, Horizon Therapeutics, Lundbeck, NervGen, TG Therapeutics, Third Rock Ventures, and Viela Bio, all outside the submitted work. S.C. reports grant funding from Biogen (partially supporting this work), and consulting and/or speaking fees from Biogen, Genentech, Genzyme and Novartis, all outside the submitted work.

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