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Original article

Perceptions of risk and adherence to care in MS patients during the COVID-19 pandemic: A cross-sectional study

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ABSTRACT

Background: The COVID-19 pandemic has raised concerns for increased risk of infection in patients with multiple sclerosis (MS) and disrupted their routine MS care. The aim of this study is to characterize the extent of MS patients' perceptions of risk and adherence to care during the pandemic.

Methods: A survey was emailed to patients from a large MS center in New York City during the local peak of the pandemic to assess perceptions of infection risk and adherence to MS care including appointments, laboratory studies, MRIs, and taking disease-modifying therapies (DMT).

Results: 529 patients from the MS center responded to the survey during two weeks in April 2020. Patients collectively showed concern about becoming infected with COVID-19 (88%) and perceived a higher infection risk due of having MS (70%) and taking DMTs (68%). Patients frequently postponed appointments (41%), laboratory studies (46%), and MRIs (41%). Noncompliance with DMTs was less common (13%). Decisions to alter usual recommendations for care were made by the patient more often than by the provider regarding adherence to appointments (68%), laboratory studies (70%), MRI (67%), and DMT (65%). Degree of concern for infection was associated with adherence to appointments ($p=0.020$) and laboratory studies ($p=0.016$) but not with adherence to MRI and DMTs. Thirty-five patients reported being tested for COVID-19, of whom fourteen reported a positive test.

Conclusion: Patients with MS were highly concerned about becoming infected during the local peak of the COVID-19 pandemic. Behaviors that deviated from originally recommended MS care were common and often self-initiated, but patients were overall compliant with continuing DMTs.

1. Introduction

The COVID-19 pandemic raised concerns about the risk of infection in populations with underlying health conditions. One such group are people with autoimmune conditions, many of whom take immunomodulatory therapies. (Askanase et al., 2020) Multiple Sclerosis (MS) is an autoimmune disease predominantly characterized by inflammatory activity in the central nervous system, and patients with MS frequently use disease-modifying therapies (DMT) with immunosuppressive mechanisms of action. Compared to the general population, patients with MS also have higher rates of infections and hospitalizations. (Marrie et al., 2014) Although the risk of severe COVID-19 infection in MS patients is overall low, (Louapre et al., 2020) concern for potentially

increased risk of COVID-19 infection appears to have altered patients' adherence to care through avoidance of medical facilities and healthcare workers during the pandemic.

A survey was distributed in April 2020 to patients at a large MS center in New York City (NYC) during the local peak of the pandemic where the death toll in the city surpassed 500 daily. (NYC Health, 2020) The aim of this study was to characterize the degree of concern in MS patients during the height of the pandemic and assess the prevalence of deviations to routine care for MS. In addition, associations between patient characteristics and adherence to care were investigated.

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2. Methods

An internet survey was developed using REDCap by physicians at the Corinne Goldsmith Dickinson (CGD) Center for Multiple Sclerosis at Mount Sinai in NYC. The survey collected data on perceptions of COVID-19 infection risk, adherence to routine care for MS, and demographic information. Invitations to participate in the survey by accessing a web address link were emailed to patients at the CGD Center on April 10, 2020. The survey remained accessible for two weeks until April 24, 2020, and two reminders were sent after the initial invitation to increase the response rate.

The survey was sent to all individuals from a patient contact list maintained by the CGD Center. In addition, all patients with a scheduled appointment at the CGD Center from February 2020 to the start of the data collection date were sent invitations to participate in the survey. Prior to the survey distribution, an information document on COVID-19 and MS was sent to all recipients on the contact list, and patients who visited the CGD Center were given a physical copy of the information document. Individuals below age 18 were not permitted to take the survey. Respondents who did not identify themselves as patients at the CGD Center were excluded from data analysis. Results of the survey were analyzed using SAS V9.4 statistical software. Descriptive statistics were generated for categorical variables. Chi-square tests were used to assess relationships between patient characteristics and adherence to care.

The study was determined by the Mount Sinai institutional review board to be exempt human research. Responses to the survey were anonymous and no identifier information were collected. Participants were permitted to leave any survey question unanswered.

3. Results

3.1. Participant demographics

Survey invitations were sent to 2,313 email addresses from the CGD Center’s patient contact list. An additional 840 unique email addresses were obtained from all scheduled visits from February 2020 to the start of the data collection. Of the 3,153 survey invitation emails sent, 596 responses were returned, corresponding to a 18.9% response rate. Fifty-five respondents were not patients at the CGD Center, and their responses were excluded from analysis. The survey used categorical variables instead of continuous variables, so mean and median values were not reported. Participant demographics are shown in Table 1.

The majority of patients (91.8%) were diagnosed with multiple sclerosis. Other diagnoses included neuromyelitis optica (2.5%) and <1% MOG-antibody disease, encephalitis, radiologically isolated syndrome, acute disseminated encephalomyelitis, transverse myelitis, and neurosarcoidosis. The majority of patients were female (78.9%), Caucasian (71.1%), lived in the state of New York (77.8%), and currently take a DMT (87.0%). Slightly more than half were below age 50 (53.6%).

Slightly more than half (58.9%) of respondents reported receiving educational information from the CGD Center about COVID-19 either through the information document or other forms of communication such as speaking with a provider. A minority of respondents (19.7%) reported exposure to someone with suspected COVID-19 infection, and fewer (10.4%) reported exposure to someone with confirmed COVID-19 infection. Only 35 patients (6.7%) received testing for COVID-19 at the time of the survey, of whom 14 (40%) tested positive.

3.2. Perceptions of COVID-19 infection risk

Respondents were presented with 3 statements to assess perception of COVID-19 infection risk and were asked to select their level of agreement with each statement (strongly agree, agree, neutral, disagree, strongly disagree). Each statement also had an additional option for “not

Table 1
Respondent demographics.

Characteristics	No. (%)
Diagnosis	
Multiple sclerosis	472 (90.4)
Neuromyelitis optica	13 (2.5)
Clinically isolated syndrome	7 (1.3)
Other	30 (5.7)
Age	
18-29	35 (6.8)
30-39	103 (20.0)
40-49	138 (26.8)
50-59	127 (24.7)
60-69	80 (15.6)
70-79	28 (5.4)
>80	4 (0.8)
Sex	
Male	416 (78.9)
Female	111 (21.1)
Race	
Caucasian	364 (71.1)
African American	75 (15.2)
Hispanic	67 (13.1)
Asian	13 (2.5)
Other	17 (3.3)
State of residence	
New York	409 (77.8)
New Jersey	78 (14.8)
Connecticut	13 (2.5)
Other	26 (4.9)
DMT use	
Ocrelizumab	131 (25.5)
Dimethyl fumarate	91 (17.7)
Glatiramer acetate	58 (11.3)
Natalizumab	43 (8.4)
Fingolimod	30 (5.8)
Rituximab	26 (5.1)
Interferon beta-1a	24 (4.7)
Teriflunomide	14 (2.7)
Siponimod	5 (1.0)
Other	25 (4.9)
None	67 (13.0)
Suspected exposure to COVID-19	
Yes	103 (19.7)
No	420 (80.3)
Confirmed exposure to COVID-19	
Yes	55 (10.4)
No	472 (89.6)
Tested for COVID-19	
Yes	35 (6.7)
No	491 (93.3)
Test result positive for COVID-19	
Yes	14 (40.0)
No	21 (60.0)

applicable,” which was not counted in the analysis. For the statement “*I am or was concerned about becoming infected with COVID-19,*” 458 (88.1%) respondents agreed or strongly agreed. For the statement “*I am or was concerned my diagnosis of MS or related disorder alone puts me at higher risk for infection with COVID-19,*” 362 (69.9%) of respondents agreed or strongly agreed. For the statement “*I am or was concerned my medication for MS or related disorder puts me at higher risk for infection with COVID-19,*” 322 (67.5%) of respondents agreed or strongly agreed. Table 2 presents the distribution of responses for each statement on risk of COVID-19 infection.

3.3. Adherence to care

Respondents were asked about adherence to components of routine care for MS including appointments, laboratory studies, MRIs, and DMTs. In addition, those who deviated from usual recommendations for care were asked to specify whether that decision was primarily theirs or their provider’s. A “not applicable” option was designed for patients who were not due for an appointment or procedure at the time of the

Table 2
Perceptions of COVID-19 infection risk.

Response	No.(%)
Concerned about COVID-19 infection	
Strongly agree	281 (54.1)
Agree	177 (34.0)
Neutral	39 (7.5)
Disagree	15 (2.9)
Strongly disagree	8 (1.5)
Concerned about MS increasing risk of COVID-19 infection	
Strongly agree	200 (38.6)
Agree	162 (31.3)
Neutral	82 (15.8)
Disagree	50 (9.7)
Strongly disagree	24 (4.6)
Concerned about DMT increasing risk of COVID-19 infection	
Strongly agree	174 (36.5)
Agree	148 (31.0)
Neutral	82 (17.2)
Disagree	47 (9.9)
Strongly disagree	26 (5.5)

survey or were not taking DMTs, and responses for this option were excluded from analysis. Respondents were asked “Did you postpone or not schedule a follow-up appointment for MS or related disorder because of the COVID-19 outbreak?” A significant number (40.8%) answered yes, of whom 68.3% made the decision to delay appointments on their own and the remainder (31.7%) were recommended to do so by their provider. The same questions were asked for laboratory studies and MRIs. Laboratory studies were postponed by 45.6% of respondents, and 40.7% of respondents postponed their MRI. Decisions to postpone laboratory studies and MRIs were made by patients 70.0% and 67.0% of the time respectively. Respondents were also asked “Did you postpone or stop taking your disease-modifying therapy for MS or related disorder as scheduled at some point because of the COVID-19 outbreak?” A minority (12.5%) stopped or postponed their DMT, of whom 65.4% made the decision on their own. Table 3 presents the distribution of responses for each question on adherence.

3.4. Associations of perception of risk and demographics with adherence to care

Higher degree of concern for COVID-19 infection was associated with postponing appointments ($p=0.020$) and laboratory studies ($p=0.016$). Concern for COVID-19 infection was not significantly associated with adherence to getting MRIs and taking DMTs. There were no significant associations between concern of MS or DMTs increasing the risk of COVID-19 infection with adherence to appointments, laboratory studies, MRIs, or DMTs. Fig. 1 shows the frequency of deviations to

Table 3
Deviations from originally recommended care for multiple sclerosis.

Response	No.(%)
Postponed appointments	
Yes, patient's decision	125 (27.9)
Yes, provider's decision	58 (12.9)
No	265 (59.2)
Postponed laboratory studies	
Yes, patient's decision	91 (31.9)
Yes, provider's decision	39 (13.7)
No	155 (54.4)
Postponed MRIs	
Yes, patient's decision	73 (27.2)
Yes, provider's decision	36 (13.4)
No	159 (59.3)
Postponed DMTs	
Yes, patient's decision	34 (8.2)
Yes, provider's decision	18 (4.3)
No	364 (87.5)

recommended care for each degree of concern about COVID-19 infection.

Respondents with younger age (<50 vs ≥ 50) were more likely to postpone appointments ($p=0.003$), where 52.1% of younger respondents postponed an appointment compared to 37.0% in older respondents. There were no associations between age and adherence to laboratory studies, MRIs, and DMTs. Women were more likely to postpone laboratory studies than males ($p=0.011$), where 49.0% of women postponed laboratory studies compared to 32.8% in men. There were no associations between sex and adherence to appointments, MRIs, and DMTs. There were no associations between race and adherence to appointments, laboratory studies, MRIs, and DMTs.

3.5. Associations of DMT use with perception of risk and adherence to care

There was an association between patients receiving an infusion DMT including natalizumab, rituximab, or ocrelizumab as opposed to a non-infusion DMT and increased perception that their medication increased the risk for COVID-19 infection ($p=0.028$). Of patients receiving infusion DMTs, 77.2% agreed or strongly agreed with the statement regarding concern for infection with COVID-19 compared to 65.9% who used a non-infusion DMT. Patients receiving an infusion DMT were more likely to deviate from the standard treatment schedule compared to those on non-infusion DMTs ($p<0.001$), where 21.6% of patients receiving an infusion DMT postponed treatment compared with 6.2% of patients using a non-infusion DMT who were nonadherent. Patients who were not taking a DMT were more likely to postpone follow-up appointments ($p<0.001$), where 59.0% of patients not on a DMT postponed their follow up appointment while 42.2% of patients on infusion DMTs and 34.3% of patients on non-infusion DMTs postponed their appointments. There were no associations between DMT use and general concern of COVID-19 infection or adherence to laboratory studies and MRIs. Fig. 2 shows the frequency of deviations to recommended care by category of DMT use.

4. Discussion

The study results show a high degree of concern among MS patients for COVID-19 infection during the local peak of the pandemic. Deviations to recommended routines for MS care occurred through frequent postponing of appointments, laboratory studies, and MRIs. Nevertheless, noncompliance with DMTs was rare.

NYC was the largest epicenter of the COVID-19 pandemic in the United States to date. During the study period from April 10 to April 24, 2020, cases in NYC increased from 94,409 to 146,139, corresponding to an estimated prevalence between 1.1-1.7%. (NYC Health, 2020) There were appropriately high concerns of becoming infected with COVID-19 among MS patients at the CGD Center. In addition, patients believed taking DMTs increases the risk of infection with COVID-19 despite limited data suggesting DMTs do not substantially increase the risk of COVID-19 infection. (Louapre et al., 2020; Berger et al., 2020; Fan et al., 2020) Surprisingly, patients also believed the risk of COVID-19 infection was increased by having MS alone when there is no evidence nor postulated mechanisms to suggest this. Preliminary studies in Italy reported on a cohort of 232 MS patients with COVID-19 showed 222 patients had mild infection while only 10 cases were severe or critical. (Sormani, 2020) A larger observational study of 347 MS patients who developed COVID-19 infection showed a 21% hospitalization rate and 3.5% mortality rate. (Louapre et al., 2020) Prior to the present study, the CGD Center informed patients about MS and COVID-19 through the distribution of information documents sent to the same contact list used in the study. Nevertheless, the survey results identify a potential gap between provider and patient understanding of COVID-19 infection risk in MS. Closing this gap would require more evidence-based data from ongoing COVID-19 research related to MS and effective education of

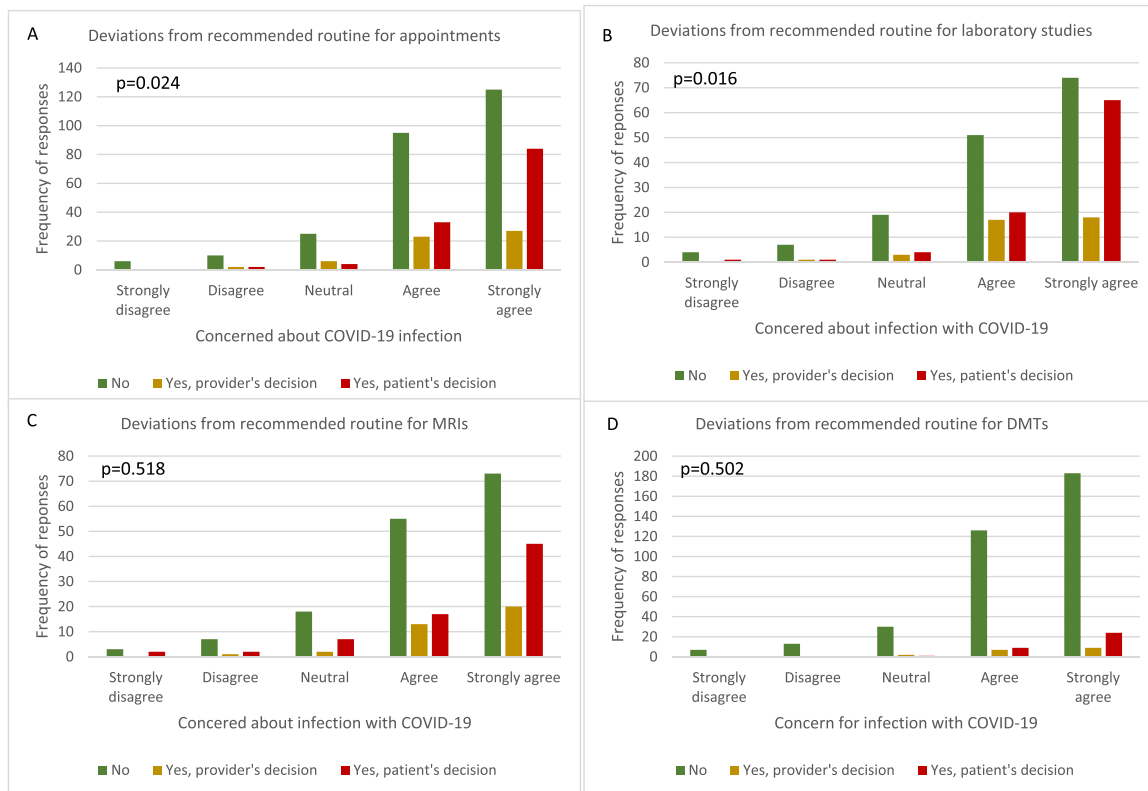


Fig. 1. Deviations from recommended to care for multiple sclerosis (MS) for each degree of concern about COVID-19 infection. Respondents were asked whether they postponed or not scheduled any components of their MS care including appointments (A), laboratory studies (B), and MRIs (C). They were also asked whether they postponed or stopped taking disease-modifying therapies (DMT) (D). Responses were further characterized by the responder’s degree of concern for COVID-19 infection. Significance values from Chi-square tests of association are shown in the respective plots.

patients.

The survey results reflected pronounced disruptions to the care of MS patients. Adherence to standard care for MS requires both clinical and radiological monitoring of disease activity as well as compliance with DMT serological monitoring for treatment-related adverse reactions. Patients at the CGD Center are routinely seen by the treating physician or nurse practitioner every 3 to 6 months depending on the stability of their disease and type of DMT prescribed. MRIs are typically obtained on an annual basis for surveillance of radiological disease activity. The COVID-19 pandemic hindered access to healthcare through fear of higher infection risk at medical facilities and restricted in-person access to healthcare. Patients often faced choices to delay their care or risk increasing exposure to infection, both with potentially detrimental consequences. At the same time, providers were tasked to implement new guidelines to the standard of care during the pandemic with limited evidence to work with. While no universal guidelines on the treatment of MS patients during the pandemic were adopted by providers at the CGD Center at the time of the study, providers often offered patients the options for telehealth appointments and to postpone labs and MRIs in those without clinical disease activity. Furthermore, providers suggested to patients extended dosing intervals for infusion therapies including 6-week intervals for natalizumab and 7-month intervals for rituximab or ocrelizumab. Overall, decisions to deviate from recommended routines for MS care were initiated by patients most of the time, but provider decisions also contributed notably. These results highlight the uncertainty and the challenges in continuing care for MS during the COVID-19 pandemic. The impact of deviating from recommended MS care during the pandemic on MS disease outcomes remains to be seen and will be difficult to measure.

There were significant associations between concern for COVID-19 infection risk and adherence to appointments and laboratory studies,

but not for adherence to MRIs and DMTs. Since most patients with MS are clinically stable at their follow-up visits and do not exhibit laboratory abnormalities, postponing appointments and laboratory studies may avoid unnecessary exposure. Despite the availability of telehealth visits for patients at the CGD Center a month prior to the study, many patients had not pursued this option. The reasons for this are unclear, but may be related to unfamiliarity with this nascent healthcare delivery method at the time of the study. The lack of association between concern for COVID-19 infection and adherence to MRIs suggests that other reasons likely contributed to decisions to postpone care such as limited availability of outpatient MRIs during the pandemic. Although there is well-established racial disparity in the impact of COVID-19, (Webb Hooper et al., 2020; Chowkwanyun and Reed, 2020) there were no associations between race and adherence to care in this study.

DMT use also influenced patients’ perceptions of risk and adherence to care. Patients who were on infusion DMTs were more concerned that their medication increased the risk of COVID-19 infection, and they were also more likely to deviate from the standard schedule of receiving their infusions than those on other DMTs that can be self-administered. These findings likely result from concern of visiting an infusion center where the risk of exposure to the virus is higher than staying at home. Nevertheless, adherence to DMTs was overall high even for patients strongly concerned about COVID-19 infection, suggesting the perceived need to remain on treatment. On the other hand, patients who were not on DMTs were highly likely to postpone their follow-up appointments. In this group of patients who most likely do not have clinical disease activity and were not exposed to potential side effects of DMT use, the decision to forgo a follow-up appointment was much less likely to incur health detriments.

Several limitations were present in this study. Data from a single center limits generalizability to other centers with different practices in

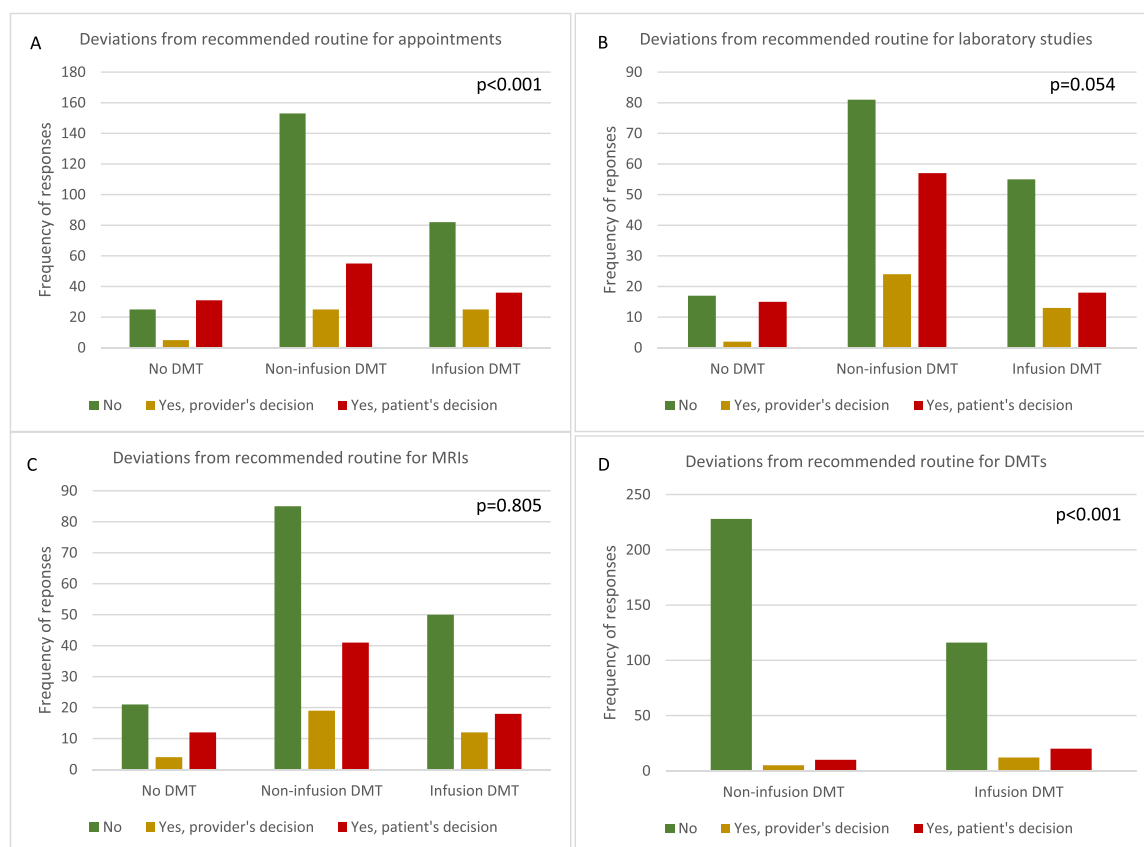


Fig. 2. Deviations from recommended to care for multiple sclerosis (MS) for categories of disease-modifying therapies (DMT). Respondents were asked whether they postponed or not scheduled any components of their MS care including appointments (A), laboratory studies (B), and MRIs (C). They were also asked whether they postponed or stopped taking DMT (D). Responses were further characterized by the category of DMT used. Significance values from Chi-square tests of association are shown in the respective plots.

MS care and in locations with different prevalence of COVID-19 infection. The timing of the study could also alter the results as patients may have responded differently earlier or later in the pandemic when the threat of infection may be lower. The study design was also subject to recall bias and selection bias. Lastly, response rate to the survey was low despite two reminder emails to complete the survey. This may have affected the results, but the direction of the potential biases is indeterminate.

The COVID-19 pandemic has undoubtedly disrupted care for patients with MS, forcing them and their providers to make difficult decisions that deviate from established routines of care to lower the risk of infection. Patients were not only highly concerned about becoming infected with COVID-19, but also assumed that MS or DMT use subject them to higher infection risk. Further research will guide the MS community towards better understanding of the risk of MS and DMTs in COVID-19 infection as well as the impact of postponing MS care during the pandemic on MS disease outcomes.

6. Data availability

Anonymized data will be shared by request from any qualified investigator.

7. Funding

None

8. Disclosures

YZ and ES reports no disclosures. GC has participated on data-

monitoring and safety-monitoring boards for Avestis Pharmaceuticals, Biolinerx, Brainstorm Cell Therapeutics, CSL Behring, Galmed Pharmaceuticals, Horizon Pharmaceuticals, Hisun Pharmaceuticals, Mapi Pharmaceuticals, Merck, Merck/Pfizer, Opko Biologics, Neurim, Novartis, Ophazyme, Sanofi-Aventis, Reata Pharmaceuticals, Receptos/Celgene, Teva pharmaceuticals, Vivus, NHLBI (Protocol Review Committee), NICHD (OPRU oversight committee); participated in consulting or advisory boards for Biogen, Click Therapeutics, Genzyme, Genentech, Gilgamesh Pharmaceuticals, GW Pharmaceuticals, Klein-Buendel Incorporated, Medimmune, Medday, Novartis, Osmotica Pharmaceuticals, Perception Neurosciences, Recursion Pharmaceuticals, Roche, Somahlution, TG Therapeutics; is employed by the University of Alabama at Birmingham and President of Pythagoras, Inc. a private consulting company located in Birmingham AL. SK reports consulting or advisory work with Biogen, EMD Serono, Genentech, Genzyme, Mallinckrodt, MedDay, Novartis, Teva, and TG Therapeutics, non-promotional speaking with Biogen, EMD Serono, Genentech, and Novartis, and grant and research support from Biogen and Novartis. AEM reports consulting for AbbVie, Health Services, (Caremark), Adamas, Biogen Idec, Bristol Myers Squibb/Celgene, Corrona, EMD Serono, Mallinckrodt, Mapi-Pharma, Novartis, Roche/Genentech, non-promotional speaking with Biogen Idec, EMD Serono, Alexion, Genentech, and has received research support from Genzyme/Sanofi, Mallinckrodt, Novartis, Roche /Genentech, MedDay.

CRediT authorship contribution statement

Yinan Zhang: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing - original draft, Writing - review & editing. **Erin Staker:** Data curation, Writing - original

draft, Writing - review & editing. **Gary Cutter:** Formal analysis, Writing - review & editing. **Stephen Krieger:** Conceptualization, Writing - review & editing. **Aaron E Miller:** Conceptualization, Writing - review & editing, Supervision.

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