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Original article

Impact of the COVID-19 pandemic on the health care of >1,000 People living with multiple sclerosis: A cross-sectional study

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ABSTRACT

Background: People with multiple sclerosis (PwMS) experienced changes in health behaviors and access to MS care due to the COVID-19 pandemic. The USA has the highest recognized number of Covid19 infections globally. The extent of the impact of COVID-19 has not been well characterized in large samples of PwMS to date. The MS patient perspective on COVID-19 would complement the physician-reported cases of MS and COVID-19 in the literature.

Methods: A cross-sectional survey of adult PwMS was performed online, using the U.S.-based patient-powered iConquerMS™ platform, in April 2020.

Results: There were 1,145 respondents (response rate: 20%). 1,019 had a diagnosis of MS and responded completely (average age: 54.2 years, range: 20–81; 79% female; 64% relapsing remitting, 22% secondary progressive, 12% primary progressive; 88% in the USA). 748 (73%) used a DMT in the last year, primarily higher-efficacy therapies: ocrelizumab ($n=238$), dimethyl fumarate ($n=85$), fingolimod ($n=80$). The most frequent comorbidities were depression (41%), hypertension (26%), and asthma (12%). Women were more worried than men about COVID-19 ($p=0.001$); non-white-identifying PwMS believed it was a greater danger to their health than white-identifying PwMS ($p=0.002$). Through the continuum of symptoms to care, 61% of PwMS ($n=617$) reported symptoms associated with COVID-19, 39% ($n=395$) knew someone exposed to COVID-19, 4% ($n=38$) were aware of a personal COVID-19 exposure, 13% ($n=128$) wanted testing for COVID-19 but could not access it, and 4% ($n=43$) were tested. Specific to their MS care, 64% ($n=650$) canceled a medical visit, 22% ($n=222$) canceled a neurologist visit, 11% ($n=112$) canceled an MRI, 21% ($n=212$) canceled a laboratory test, and 10% ($n=98$) changed their DMT in some way due to COVID19 including 65 delaying at least one dose. 37% ($n=382$) had a telehealth visit due to COVID-19. 37% of PwMS ($n=374$) experienced employment changes, most commonly working from home ($n=194$) and having work hours reduced ($n=65$) while 32 lost their jobs. Of the 7 cases who tested positive for COVID-19 (<1% of participants) (5 female; age range: 29–64 years), DMTs included dimethyl fumarate ($n=2$), ocrelizumab ($n=1$), rituximab ($n=1$), and a clinical trial drug ($n=1$).

Conclusions: A majority of people with MS reported interruptions to their MS care along the MS care pathway alongside limited access to COVID-19 testing. Postponements and delays in care were common with 10% of participants reporting a change in their DMT administration. Less than 1% of this self-referred convenience online cohort had a positive test for COVID-19 although more than half reported symptoms that are associated with COVID-19.

1. Introduction

The COVID-19 pandemic has evolved rapidly since its initial presentation in December 2019 (World Health Organization, 2020). The first U.S. case was confirmed on January 19th, 2020 (Holshue et al., 2020) with pandemic status declared on March 11th. (World Health

Organization, 2020) By mid-April, SARS-CoV-2 was detected in 185 countries, had infected at least 19 million people worldwide, and linked to >700,000 deaths. (Johns Hopkins University, 2020) Multiple sclerosis (MS) affects more than three-quarters of a million adults in the U.S.A. People with MS (PwMS) on higher efficacy disease modifying therapies (DMTs) may be at an increased risk of infection or serious

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complications due to COVID-19. Some expert groups have recommended delaying or modifying administration of DMTs for patients on alemtuzumab, cladribine, ocrelizumab, or rituximab during COVID-19. (National Multiple Sclerosis Society, 2020; Multiple Sclerosis Society, 2020; MS International Federation, 2020; MS Australia, 2020; Brownlee et al., 2020) More recent data suggest that not all cases of COVID-19 are severe, even while taking some of the high-efficacy therapies for MS (Meca-Lallana et al., 2020).

PwMS are also vulnerable to the economic, lifestyle, and social upheaval caused by COVID-19. Essential services for PwMS have been interrupted, discontinued, or transformed. A longitudinal care approach with MRIs, laboratory tests, and outpatient follow-up visits is integral to optimized MS care but became variably accessed and available during the height of the pandemic (Rae-Grant et al., 2018). There are now multiple impacts to PwMS with widespread social distancing orders, closures of outpatient clinics, joblessness, and disruptions to major public services such as public transit. Since PwMS already experienced high rates of unemployment, prior to COVID-19, new joblessness became an added risk.

Advocacy for digitalization of MS services predates COVID-19, given its foreseen benefits to PwMS, (Lavorgna et al., 2018) but impetus to implement telehealth services for PwMS has never been as profound across locations as during COVID-19. The use of tele-health can mitigate some aspects of disruptions to MS care. The extent of its uptake during COVID-19 in the USA has not been well characterized.

Given the anecdotal experiences of PwMS and their barriers to care during COVID-19, we wrote and deployed a large-scale internet-based survey to determine the real-world impact of the COVID19 pandemic on PwMS. This survey was rapidly disseminated during the early height of epidemic in the USA to specifically probe knowledge, attitudes, and practices as they intersect between MS and COVID-19. Since the USA has more COVID-19 cases than any other country worldwide, we hope that our experiences provide lessons learned by PwMS. Such lessons could be used to identify and maintain the most essential MS services, support patients psychologically with new resources, and improve future epidemic responses in the context of specialty MS care.

2. Methods

2.1. Ethical approval and procedures

The study was approved by the Partners Healthcare Inc. Human Research Committee. The non-governmental organization *Accelerated Cure Project* (ACP) received independent ethics approval. Participants were members of ACP's iConquerMS™ research network who have previously provided informed consent to participate in surveys through the network. We adopted the STROBE guidelines for conducting and reporting observational studies (von Elm et al., 2014).

2.2. Survey instrument

A new survey instrument to assess the knowledge, attitudes, and practices of PwMS related to COVID-19 and explore the impact on health, medical care, and daily life was designed by the authors. Baseline demographic, income, and MS disease variables were included from the iConquerMS semi-annual data collection process and confirmed where needed. The approximately 75-question instrument was piloted by the authors and MS patient advocates. The final survey included multiple choice, open-ended, and ordinal rating questions (Appendix 1).

Four themes were emphasized: (1) SARS-CoV-2 awareness, including symptoms of COVID19 and information sources; (2) experience with COVID-19, including exposed contacts, symptoms, access to testing, and worry; (3) healthcare changes, including DMT use, delays in treatment and care seeking, comfort in visiting health care centers; and (4) effects on daily life, including job changes, access to food, and

ability to exercise.

PwMS were queried on current clinical, demographic, and MS disease state variables, including duration of disease, and current DMT use. Current functional status was measured via the Patient Determined Disease Steps (PDDS) scale, a patient-reported metric of disability in MS ranging from 0 (no disability) to 8 (bedridden) (Learmonth et al., 2013). Subjective measures (i.e. worry about COVID-19) were evaluated on a 7-point scale where 1 corresponded to "low" and 7 to "high" degrees of a value.

2.3. Recruitment, distribution, enrollment

PwMS were recruited via the iConquerMS platform (<https://www.acceleratedcure.org/iconquerms>), a patient-designed and patient-governed research network based in Massachusetts that reaches adults with MS in all 50 US states as well as worldwide. PwMS who were 21 years and older and registered with the network received e-mail invitations to participate in the study on April 3, 2020 with reminders sent until April 30, 2020. At the time of survey administration, iConquerMS included 5,700 PwMS. Advertisements were made through the iConquerMS website, social media, and emails as well as web posts and emails from social influencers and partner organizations including the MS Association of America, the National Multiple Sclerosis Society, and the MS Foundation.

Surveys were filled on the iConquerMS platform in a cross-sectional design. Participants were considered to be enrolled until either 1) survey completion or 2) drop-out, defined as having an incomplete survey at the pre-specified time of analysis (May 1, 2020)

2.4. Data analysis

Quality control included removal of respondents who self-declared that they did not have MS or did not answer two or more key variables, such as both MS disease phase and age. Responses to variables of interest were displayed graphically. Variables were reported as means and ranges or medians and interquartile ranges, as appropriate. For questions with multiple-choice options, results were calculated as counts and percentages. Missing responses were assumed to be missing completely at random.

There were no pre-specified hypotheses. The survey was intended to depict the range of experiences of COVID-19 in PwMS residing predominantly in the USA. When comparisons were made *post hoc*, a *p*-value of <0.05 was considered statistically significant. All analyses were performed using R (Vienna, Austria).

3. Results

3.1. Sample determination

1,145 people responded to the survey (response rate 20%). Participants were excluded from analysis if they did not have MS (*n* = 21) or did not answer two or more key variables (*n* = 105), yielding 1,019 analyzed PwMS.

3.2. Characteristics of participants

The average age of participants was 54.2 years old (range 20–81) (Table 1). The majority identified as white (*n* = 964, 95%), female (*n* = 810, 79%), and were diagnosed with relapsing remitting MS (*n* = 653, 64%). Most participants were from the USA (*n* = 900, 88%) representing 49 of the 50 states (Fig. 1). 36 participants (4%) were from Canada, 27 (3%) from the United Kingdom, and 56 participants came from various countries globally (Appendix 2). The modal household income was 50,001–100,000 USD per year with most participants having a Bachelor's degree or above.

Nearly three-quarters of participants (*n* = 748, 73%) took a DMT for

Table 1
Demographic data of participants with multiple sclerosis (n=1019).

(n)	72	173	267	340	167
Age group (years)	20-35	35-45	45-55	55-65	> 65
Female ^a n (%)	63 (85)	141 (82)	216 (81)	274 (81)	116 (69)
Hispanic/Latino n (%)	4 (6)	11 (6)	6 (2)	14 (4)	1 (1)
Race ^b n(%):					
White	64 (89)	163 (94)	249 (93)	327 (96)	161 (96)
Black or African American	4 (6)	7 (4)	12 (7)	8 (2)	3 (2)
Other ^c	6 (8)	6 (3)	14 (5)	16 (5)	8 (5)
Employment status n (%):					
Student	6 (8)	3 (2)	0	0	1 (1)
Employed outside home	39 (54)	83 (48)	95 (36)	65 (19)	6 (4)
Employed at home	10 (14)	27 (16)	34 (13)	31 (9)	11 (7)
Homemaker	4 (6)	7 (4)	13 (5)	6 (2)	3 (2)
Unemployed looking for work	3 (4)	4 (2)	7 (3)	6 (2)	0
Unemployed not looking for work	1 (1)	5 (3)	10 (4)	7 (2)	2 (1)
Retired	0	1 (0.6)	4 (1)	36 (11)	84 (50)
Disabled	8 (12)	43 (25)	103 (39)	187 (55)	60 (36)
Prefer not to answer	1 (1)	0	1 (0.4)	2 (1)	0
Highest educational attainment ^d (n=759)	n=50 ^e	n=123	n=183	n=264	n=139
Doctoral degree	5 (10)	15 (12)	12 (7)	24 (9)	22 (16)
Master's degree	19 (38)	27 (22)	40 (22)	47 (18)	40 (29)
Bachelor's degree	10 (20)	39 (32)	70 (38)	112 (42)	43 (31)
Associate degree	4 (8)	15 (12)	19 (10)	21 (8)	11 (8)
Technical degree	3 (6)	3 (2)	9 (5)	9 (3)	3 (2)
Some college	7 (14)	18 (15)	22 (12)	40 (15)	12 (9)
High school, some or completed	1 (2)	6 (5)	11 (6)	11 (4)	8 (6)
Annual household income level ^f (USD) (n=737)	n=49	n=118	n=179	n=255	n=136
> 200,000	4 (8)	10 (8)	12 (7)	16 (6)	4 (3)
150,001 – 200,000	5 (10)	6 (5)	22 (12)	17 (7)	9 (7)
100,001 – 150,000	4 (8)	27 (23)	22 (12)	31 (12)	20 (15)
50,001 – 100,000	16 (33)	32 (27)	43 (24)	63 (25)	35 (26)
30,001 – 50,000	4 (8)	14 (12)	21 (12)	36 (14)	26 (19)
15,000 – 30,000	10 (20)	14 (12)	24 (13)	43 (17)	15 (11)
< 15,000	4 (8)	6 (5)	8 (4)	7 (3)	3 (2)
Prefer not to answer	2 (4)	9 (8)	27 (15)	42 (16)	24 (18)

^a5 participants declined to answer. 1 participant selected “other”. ^bParticipants were asked to choose all options that applied. ^cIncluding: 18 American Indian, 4 Middle Eastern, 2 Asian, and 27 who did not answer. ^dEducation data were collected in separate surveys and available for 759 participants. ^e1 participant did not know his/her highest education level. ^fIncome data were collected in separate surveys and available for 737 participants.

MS in the past year (Table 2). Of 731 participants who reported the DMT they used, 238 (32% of 748) took ocrelizumab, 85 (11%) took dimethyl fumarate, and 80 (11%) took fingolimod. Approximately one-third of respondents reported being hospitalized due to MS in their lifetime. The most commonly reported comorbidity was depression (n=422, 41%), followed by hypertension (n=264, 26%), asthma (n=127, 12%), heart disease (n=54, 5%), and diabetes (n=53, 5%). The median PDSS was 2 in PwMS ≤ 55 years old (“moderate disability”) and 4 in PwMS > 55 years old (“late cane”).

3.3. COVID-19 exposures

Seven participants (0.7%; 5 female, 2 male; 6 white, average age: 43 years, range: 29 – 64 years; average PDDS: 1.7 points) reported testing positive for SARS-CoV-2. None were hospitalized. Two were untreated with DMTs. The others were treated with dimethyl fumarate (n=2), ocrelizumab (n=1), rituximab (n=1), and 1 was participating in a clinical trial of a DMT that was unknown by name to the participant. Five were from the U.S.A., 1 was from Canada, and 1 was from Spain. Three reported having an MS relapse in the last month. Their comorbidities included hypertension (n=3), diabetes mellitus (n=2),

lung disease (n=1), and heart disease (n=1) (Table 3).

617 participants (61%) reported experiencing at least one symptom associated with COVID-19 since February 2020. 395 participants (39%) reported knowing somebody who was exposed to COVID-19 and 38 (4%) reported being personally exposed to someone with COVID-19. Participants who knew somebody exposed to COVID-19 were younger than those who did not (average age of 52.8 years vs. 55.5 years, $p < 0.001$); this was also the case for participants who had been personally exposed to COVID-19 compared to those who had not (average age 48.8 years vs. 54.4 years, $p = 0.01$).

Participants who knew someone exposed to COVID-19 reported being significantly more worried about COVID-19 than those who did not know someone exposed (mean 4.8 vs. 4.4 points out of 7; $p = 0.002$). A higher proportion of participants who knew someone exposed to COVID-19 reported canceling neurologists' visits, MRIs, non-neurologists' medical visits, and laboratory tests compared to those who did not know someone exposed to COVID-19.

3.4. Testing access and availability

Most respondents had not been tested for COVID-19 (n=975, 96%), although two-thirds of those who had not been tested stated they did not want to be tested (651/975, 67%). By contrast, 128 participants (13%) wanted to be tested but were unable to do so, including 46 (36% of 128) who replied that the tests were unavailable and 23 (18%) who replied that their doctor did not offer the test. An additional 27 participants (21%) explained their inability to be tested in open response questions, which largely included that the participants were either self-isolating and did not want to leave their house or were asymptomatic (Table 3).

3.5. Changes to MS care due to COVID-19

98 participants (10%) reported making a change to their DMT, dose, or dosing schedule due to COVID-19; of these, the most common change was to delay at least one dose of DMT (n=65, 66% of 98). For PwMS who made DMT changes, 25 (26%) reported making the change without the input of their neurologist or physician. The most common DMT with an altered dosing regimen was ocrelizumab (n=37, 38%) (Table 4).

110 participants (11% of 1,019) reported experiencing difficulties and delays in accessing DMTs. For these participants, ocrelizumab was the most difficult to access and delayed DMT, with a total of 42 (38%) participants describing difficulties related to the drug (2 with prescription, 19 with infusion, and 21 with monitoring tests). 14 participants reported difficulties with dimethyl fumarate (5 with prescription, 9 with safety visits), and 8 reported difficulties with rituximab (1 with prescription, 5 with infusion, and 2 with monitoring visits).

PwMS reported delays and difficulties in other aspects of their care: 186 (18% of 1,019) in non-MS related medical procedures, 177 (17%) in accessing complementary and alternative medical services, and 77 (8%) in accessing non-DMT medications.

650 participants (64%) reported canceling or postponing medical visits. 222 (34% of 650) reported canceling a neurologist's visit, 112 (17%) an MRI, 499 (77%) a non-neurologist medical visit, and 212 (33%) a laboratory visit. Of these 650 participants, 138 (21% of 650) took ocrelizumab, 52 (8%) took glatiramer acetate, 50 (8%) took dimethyl fumarate, 50 (8%) took fingolimod, 39 (6%) took natalizumab, and 23 (4%) took rituximab. The proportion of female respondents who reported canceling or postponing medical visits was greater than the proportion of male respondents who reported doing so (Table 4).

On a scale of 1 (“not comfortable”) to 7 (very comfortable), participants reported discomfort with the idea of going to the hospital for emergencies (median score: 3, 1st quartile: 1, 3rd quartile: 5) and infusions (median: 2, 1st quartile: 1, 3rd quartile: 4); however, in both cases, men reported a higher mean level of comfort (emergency: 4 vs.

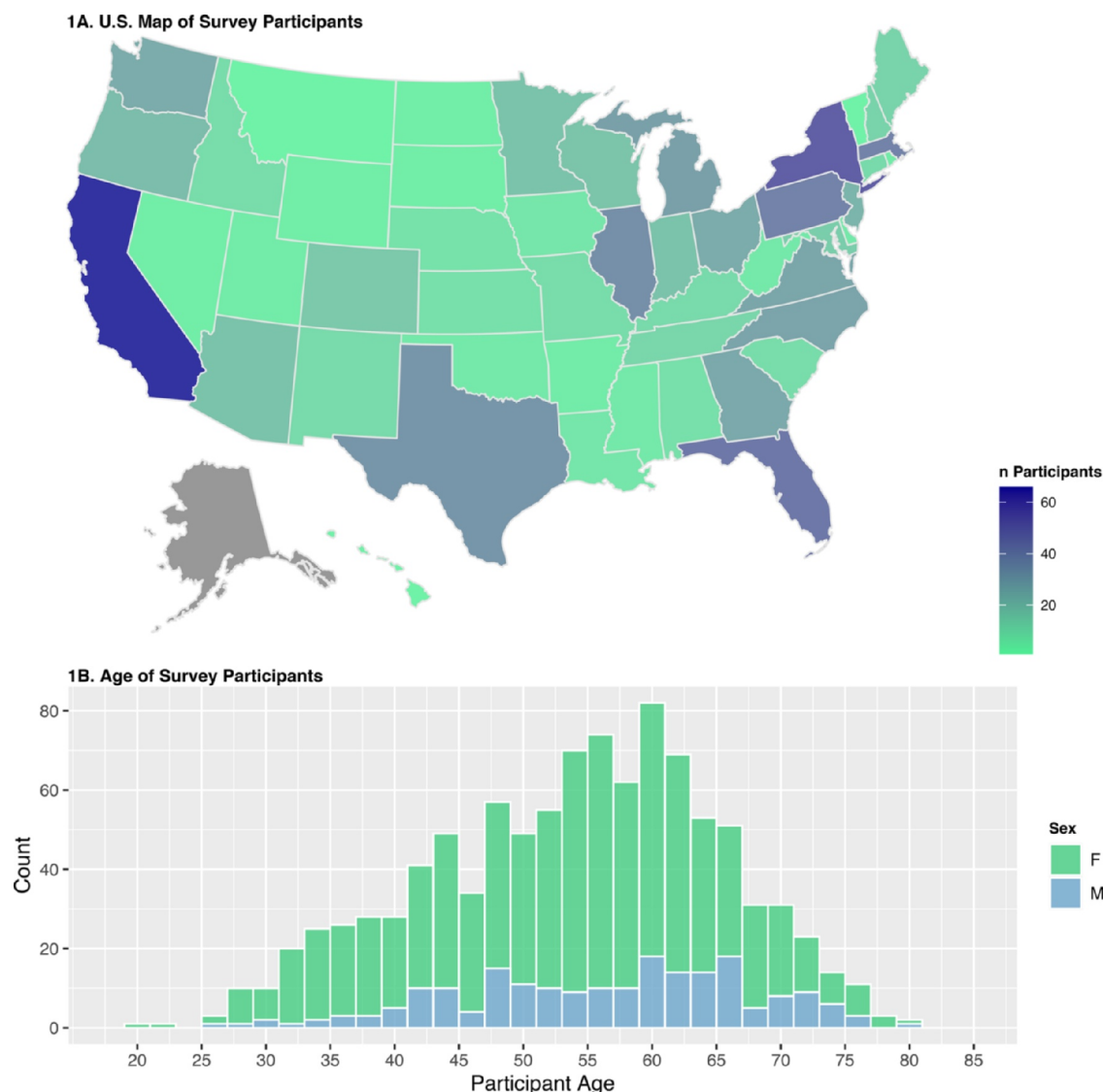


Fig. 1. Title: U.S. geographic distribution and age range of survey participants.

3.3, $p < 0.001$; infusion: 3.5 vs. 2.8, $p < 0.001$) (Fig. 2). 382 participants (37%) had telemedicine visits due to COVID-19.

3.6. COVID-19 awareness and concern

There was an overall high degree of worry about COVID-19 and belief that it presents a major danger to one's health (Fig. 2). A small number ($n = 37$, 4%) of participants reported never having heard of the virus prior to the survey. 916 participants (90%) reported that there had been a case of COVID-19 in their city/town.

Most participants recognized that fever and dry cough are symptoms of COVID-19; however, only 65% of participants correctly identified pneumonia as a possible symptom of the disease. 80% of participants recognized that issues with smell and taste are a symptom.

Participants reported receiving news about COVID-19 from a variety of sources, including TV news ($n = 729$, 73%), internet news sites like the *New York Times* ($n = 663$, 65%), and national- and state-level government websites ($n = 606$, 59%; 580, 57%; respectively). Social media sites such as Facebook, Twitter, and Reddit were less commonly used (24%, 9%, and 2%, respectively). Participants reported being confident in their knowledge of the guidelines for immunocompromised patients in the setting of COVID-19, the number of cases in their area, how to protect against COVID-19, what to do if infected, when they should be

tested, and what to do if positive. Participants reported less confidence on MS-specific guidelines in the setting of COVID-19, where to get tested, and which drugs could potentially exacerbate or ameliorate the disease (Appendix 3).

3.7. Personal and lifestyle effects of COVID-19

374 participants (37% of 1,019) reported that they had experienced employment changes as a result of COVID-19. The most common change was now working from home ($n = 196$, 52% of 374), although 65 reported that their hours had been reduced, and 33 reported losing their job. A higher proportion of women of all ages reported losing their jobs compared to men (4% vs. 2%, $p = 0.39$) (Appendix 4).

COVID-19 was overall thought not to have a major negative impact on diet, exercise, or personal finances; however, women reported a significantly more negative impact of the virus on their diet than did men (scores from 1 ("no negative impact") to 7 ("significant negative impact"), F: 3.1 vs. M: 2.6, $p = 0.0013$). Participants believed COVID-19 presents a major danger to their health and reported being generally highly worried about the disease. Men reported being less worried about COVID-19 than women (average worry: 4.2 vs. 4.7, $p = 0.001$) (Fig. 2). Non-white respondents reported believing that COVID-19 presents a significantly greater danger to their health than white

Table 2Clinical data and medical history ($n=1019$ People with multiple sclerosis), stratified by age.

	<=55 years	>55 years
<i>n</i> (%)	512 (50%)	507 (50%)
CIS	10 (2)	8 (2)
RRMS	408 (80)	245 (48)
SPMS	66 (13)	155 (31)
PPMS	26 (5)	92 (18)
Unknown to participant	2 (0.4)	7 (1)
Patient-determined disease step (PDSS) score, median (1 st quartile, 3 rd quartile)	2 (0, 4)	4 (2, 5)
Taken DMT within past year		
Yes	417 (81)	331 (65)
No	88 (17)	166 (33)
Don't know	7 (1)	10 (2)
DMTs ^a :		
Glatiramer acetate	35 (7)	48 (9)
Interferon beta-1	21 (4)	23 (5)
Peginterferon beta-1a	3 (0.6)	4 (0.8)
Fingolimod	58 (11)	23 (5)
Siponimod	3 (0.6)	5 (1)
Dimethyl fumarate	52 (10)	35 (7)
Diroximel fumarate	0	3 (0.6)
Teriflunomide	20 (4)	25 (5)
Cladribine	6 (1)	4 (0.8)
Natalizumab	44 (9)	23 (5)
Rituximab	21 (4)	17 (3)
Ocrelizumab	134 (26)	104 (21)
Alemtuzumab	7 (1)	0
Other ^b	5 (1)	5 (0.9)
MS relapse in last month		
Yes	46 (9)	34 (7)
No	415 (81)	440 (87)
Don't Know	51 (10)	33 (7)
Hospitalized due to MS in 2019		
Yes	24 (5)	13 (3)
No	156 (30)	136 (27)
Don't know	3 (0.6)	0
Ever hospitalized due to MS		
Yes	183 (36)	149 (29)
No	322 (63)	350 (69)
Don't Know	7 (1)	8 (2)
Needed steroids in the last month		
Yes	27 (5)	26 (5)
No	480 (94)	475 (94)
Don't Know	5 (1)	6 (1)
In-person neurologist visit in last 6 months		
Yes	396 (77)	374 (74)
No	109 (21)	131 (26)
Don't Know	7 (1)	2 (0.4)
Medical history/comorbidities:		
Asthma	6 (1)	29 (6)
Cancer (current)	229 (45)	193 (38)
Depression	18 (4)	35 (7)
Diabetes	11 (2)	43 (8)
Heart disease	81 (16)	183 (36)
Hypertension	14 (3)	28 (6)
Lung disease	41 (8)	23 (5)
Smoke cigarettes	12	12
Avg. cigarettes/day		

^a104 participants <=55 years of age did not have DMT data available. 184 participants >55 years of age did not have DMT data available. ^bIncludes ibudilast, mycophenolate mofetil and cyclophosphamide.

respondents (median 6.1 vs. 5.4, $p=0.0015$).

376 participants (37%; PDDS: 3.4) reported engaging in a full self-quarantine (i.e. staying at home at all times). Participants who engaged in self-quarantine were older than those who did not (average age: 56.3 years vs. 53 years, $p<0.001$). Participants who self-quarantined reported that COVID-19 was having a significantly more negative impact on their personal finances, exercise, and diet than those who were not self-quarantining (finances: 3.2 vs. 2.8, $p=0.005$; exercise: 3.8 vs. 3.3, $p=0.006$; diet: 3.2 vs. 2.9, $p=0.007$).

Table 3

COVID-19 exposures and test access.

Participant sex	Male	Female
Age group (years)	<=55 >55	<=55 >55
<i>n</i> Participants (% of 1,019)	87 (9) 116 (11)	420 (41) 390 (38)
Know someone exposed to SARS-CoV-2:	39 (45) 33 (28)	177 (42) 142 (36)
- Yes	36 (41) 65 (56)	184 (44) 205 (53)
- No	12 (14) 18 (16)	59 (14) 43 (11)
- Unsure		
Personally exposed to someone with COVID-19:	3 (3) 2 (2)	23 (5) 10 (3)
- Yes	56 (64) 78 (67)	271 (65) 263 (67)
- No	28 (32) 36 (31)	126 (30) 117 (30)
- Unsure		
Have you had symptoms that are associated with COVID-19?	54 (62) 59 (51)	286 (68) 215 (55)
- Yes	33 (38) 57 (49)	134 (32) 175 (45)
- No		
Have you been tested for COVID-19?	3 (3) 3 (3)	22 (5) 14 (4)
- Yes	84 (97) 112 (97)	398 (95) 376 (96)
- No	0 1 (0.9)	0 0
- Unsure		
If tested, result:	1 (1) 1 (0.9)	4 (1) 1 (0.3)
- Positive	2 (2) 1 (0.9)	15 (4) 10 (3)
- Negative	0 0	3 (0.7) 3 (0.8)
- Results not returned		
If no, did you want to be tested for COVID-19:	16 (18) 14 (12)	47 (11) 51 (13)
- Yes	54 (62) 78 (67)	284 (68) 232 (59)
- No	20 (23) 20 (17)	67 (16) 93 (24)
- Unsure		
If unable to be tested, why:		
Unsure of location	4 (5) 2 (2)	6 (1) 6 (2)
Worried about catching a disease	0 0	1 (0.2) 1 (0.3)
Doctor did not offer/recommend testing	2 (2) 3 (3)	11 (3) 7 (2)
Test unavailable	5 (6) 5 (4)	12 (3) 24 (6)
Unsure/Don't know	1 (1) 1 (0.9)	7 (2) 3 (0.8)
Other ^a	4 (5) 3 (3)	10 (2) 10 (3)

^a Participants answered this question with open responses. Responses included patients not wanting to leave the house and not exhibiting enough symptoms to qualify for a test.

4. Discussion

Considerable attention has been paid to the impact of COVID-19 among those with the disease; however, the widespread implications of COVID-19, including the measures taken by society and health systems have also profoundly affected people living with chronic diseases. Particularly in April 2020, it was unclear which forms and doses of immunosuppression confer added risks to PwMS on both becoming infected with SARS-CoV-2 and having a worse prognosis if infected. Although less than 1 percent of our participants had COVID-19, the high impact of COVID-19 on health behaviors, MS care access, alterations in DMT use, and impact on work are notable. Our study occurred at the first height of the COVID-19 pandemic in the USA (April 2020). During these weeks, particularly in the Northeastern part of the USA, non-COVID-19 health care services shut down, including reduced in-person access to clinics, laboratories, MRI suites, and primary care offices. In several locations, hospitals were overwhelmed by the need to care for COVID-19 patients, and MS physicians and nurses were re-deployed to work outside of their usual practices. In many cases, practices shut down and/or moved all care to telemedicine. In cases where services remained in place, self-limited withdrawal from health services occurred due to worry, anxiety, and fear by PwMS. Taken together, even these weeks of disruption to care may have impacts to PwMS for many months to come in the form of changing immunosuppressive drug doses, deferred or avoided laboratory monitoring of existing treatment, and limited access to health providers.

Notably, women reported a significantly more negative impact from

Table 4
Health behavior changes due to COVID-19.

Participant sex	Male		Female	
Age group (years)	< =55	>55	< =55	> 55
n Participants (% of 1,019)	87 (9)	116 (11)	420 (41)	390 (38)
Last reported date of DMT was >30 days prior to survey ^a n(%)	20 (23)	53 (74)	125 (30)	163 (42)
For those who have not taken DMT in last 30 days, which DMT ^b :				
- Glatiramer acetate	0	1 (1)	2 (0.5)	1 (0.3)
- Interferon beta-1	0	2 (2)	0	3 (0.8)
- Peginterferon beta-1a	0	1 (1)	3 (0.7)	1 (0.3)
- Fingolimod	3 (3)	1 (1)	1 (0.2)	1 (0.3)
- Siponimod	0	0	0	1 (0.3)
- Dimethyl fumarate	2 (2)	0	2 (0.5)	2 (0.5)
- Teriflunomide	0	0	0	2 (0.5)
- Natalizumab	4 (5)	0	18 (4)	16 (4)
- Alemtuzumab	1 (1)	0	6 (1)	0
Changes as a result of COVID-19 ^c :				
- Delayed 1+ dose of DMT	7 (8)	6 (5)	20 (5)	32 (8)
- Delayed starting a DMT	3 (3)	1 (1)	6 (1)	7 (2)
- Stopped taking DMT	1 (1)	2 (2)	5 (1)	5 (1)
- Changed DMT	0	0	3 (0.7)	2 (0.5)
- No changes	68 (78)	62 (53)	300 (71)	215 (55)
Healthcare provider input into DMT decision:				
- Patient decision	2 (2)	1 (1)	9 (2)	13 (3)
- Mutual decision	6 (7)	8 (7)	10 (2)	19 (5)
- Healthcare provider made decision	3 (3)	0	14 (3)	13 (3)
Which DMT have you stopped or changed:				
- Fingolimod	1 (1)	0	0	0
- Siponimod	0	0	0	1 (0.3)
- Dimethyl fumarate	0	0	3 (0.7)	1 (0.3)
- Teriflunomide	0	0	1 (0.2)	2 (0.5)
- Rituximab	0	0	0	1 (0.3)
- Ocrelizumab	0	2 (2)	2 (0.5)	1 (0.3)
Which DMT have you delayed starting ^c :				
- Glatiramer acetate	0	0	0	2 (0.5)
- Interferon beta-1	0	0	1 (0.2)	0
- Fingolimod	0	0	1 (0.2)	0
- Siponimod	1 (1)	0	1 (0.2)	1 (0.3)
- Dimethyl fumarate	0	0	0	1 (0.3)
- Dimethyl fumarate	0	0	1 (0.2)	1 (0.3)
- Diroximel fumarate	0	0	1 (0.2)	0
- Teriflunomide	0	1 (1)	2 (0.5)	1 (0.3)
- Cladribine	0	0	1 (0.2)	0
- Natalizumab	0	0	1 (0.2)	0
- Ocrelizumab	2 (2)	2 (2)	3 (0.7)	8 (2)
- Alemtuzumab	0	0	1 (0.2)	1 (0.3)
- Other ^d	0	1 (1)	0	1 (0.3)
For which DMT have you delayed at least one dose due to COVID-19?				
- Glatiramer acetate	0	0	0	1 (0.3)
- Interferon beta-1	0	0	0	1 (0.3)
- Fingolimod	0	1 (1)	4 (1)	3 (0.8)
- Siponimod	0	0	0	2 (0.5)
- Dimethyl fumarate	0	0	1 (0.2)	1 (0.3)
- Teriflunomide	0	0	0	1 (0.3)
- Cladribine	2 (2)	1 (1)	4 (1)	5 (1)
- Natalizumab	1 (1)	1 (1)	1 (0.2)	1 (0.3)
- Rituximab	4 (5)	3 (3)	9 (2)	17 (4)
- Ocrelizumab	0	0	1 ^e (0.2)	0
- Other				
Experienced difficulties or delays due to COVID-19 ^c :				
- Getting DMT prescription filled	0	0	11 (3)	8 (2)
- Getting infusion of a DMT	1 (1)	4 (3)	23 (5)	14 (4)
- Getting monitoring/safety tests performed for DMT	7 (8)	3 (3)	37 (9)	12 (3)
- Accessing medications other than DMTs	6 (7)	4 (3)	47 (11)	19 (5)
- Obtaining medical equipment	0	3 (3)	10 (2)	4 (1)
- Having medical procedures performed	15 (17)	25 (22)	74 (18)	71 (18)
- Accessing complementary/alternative services	10 (11)	13 (11)	96 (23)	57 (15)
	4 (5)	4 (3)	24 (6)	16 (4)

Table 4 (continued)

Participant sex	Male		Female	
- Accessing complementary/alternative products				
- None	57 (66)	78 (67)	234 (56)	244 (63)
Changes to healthcare due to COVID-19:				
- Postponed or canceled a neurologist visit	16 (18)	23 (20)	94 (22)	86 (22)
- Postponed or canceled MRIs	10 (11)	9 (8)	59 (14)	33 (8)
- Postponed or canceled other medical visits	32 (37)	60 (52)	190 (45)	216 (55)
- Postponed or canceled laboratory/blood tests	12 (14)	20 (17)	92 (22)	86 (22)
- None	43 (49)	49 (42)	157 (37)	121 (31)
Had telehealth visits as a result of COVID-19:				
- Yes	33 (38)	45 (39)	169 (40)	132 (34)
- No	54 (62)	70 (60)	249 (59)	255 (65)
- Unsure	0	1 (1)	2 (0.5)	3 (0.8)

^aOnly participants who reported taking a DMT in the last year were asked this question. Participants who took cladribine, ocrelizumab, or rituximab were excluded from this analysis. ^b98 participants < =55 years old did not have DMT data. 180 participants >55 years old did not have DMT data. ^cOnly participants who reported taking a DMT in the last year were asked this question. Participants chose multiple answers if they were appropriate. ^d1 ozanimod, 1 unknown and 1 undecided. ^eParticipant is in a clinical trial, drug unknown to participant.

COVID-19 than men across multiple self-reported domains. This occurred with both higher levels of worry and less comfort related to COVID-19, as well as changes in health seeking behaviors, including cancellations and postponements of medical visits. The gendered effects of viral epidemics have been explored in COVID-19. For instance, school closures may place a greater burden on women, due to gendered expectations surrounding childcare (Wenham et al., 2020; Secretary-General, 2020).

By April 2020, 10% of respondents reported making a change to their DMT administration, most commonly ocrelizumab. A quarter of these participants made the decision without the input of their neurologist. Although it is plausible that high efficacy therapies confer risk of worse outcomes in COVID-19, (Wijnands et al., 2018 Oct; Grebenciucova and Pruitt, 2017; Luna et al., 2020) not all data demonstrate as negative of a prognosis as first may have been feared (Meca-Lallana et al., 2020; Hsu et al., 2020; Mathies et al., 2020; Zhu et al., 2020; Novi et al., 2020). Some authors have posited that immunosuppression is protective due to the inflammatory nature of the SARS-CoV2 infection.

In April 2020, the USA experienced an unemployment level that has not been experienced since the Great Depression of the 1930s with a 14% unemployment rate in April 2020 (U.S. Bureau of Labor Statistics, 2020). PwMS are vulnerable to joblessness in general (Kobelt et al., 2017) and competitive work environments may especially disadvantage people with chronic conditions, disability, and fear of social interactions. Although most of our respondents did not self-quarantine, those who did reported higher financial worry.

This study reflects the step-wise pathway by which PwMS experience symptoms that are associated with COVID-19 symptoms but then drop off of the continuum of care to get testing to confirm or refute the actual COVID-19 diagnosis. In this setting, postponement and delays in MS treatment can be quantified and categorized by surveillance imaging, laboratory studies, prescriptions, infusions, and health care visits. Lessons for future MS care in the setting of interruptions to care include needs to inform patients on (i) where care can be safely received, (ii) which facilities remain available and accessible, (iii) where to receive testing for COVID-19, (iv) when telemedical services can be used in replacement for in-person visits, (v) when and how to communicate concerns about DMTs without self-discontinuation, and (vi) advocacy

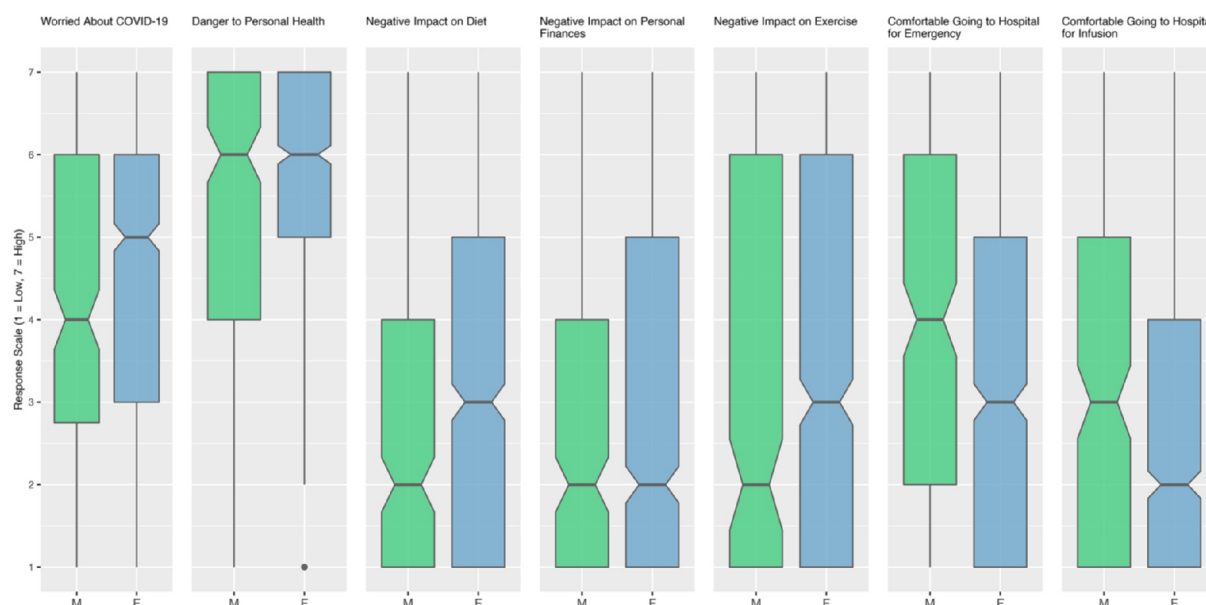


Fig 2. Title: Participant subjective measures of impact of the COVID-19 pandemic. Caption: M = male, F = female. Participants were evaluated via a 7-point scale where 1 = low and 7 = high; e.g. 1 would = “low impact” or “low comfort”, dependent on the question asked.

for innovations in care including home-based infusions and tests. Beyond these clinical needs, the use of an established platform that serves PwMS and centralizes data collection, prior to pandemics, are highly useful for understanding the scope of unanticipated events in the MS community. Although our study represents a convenience cohort, high numbers of PwMS are unlikely to be surveyed in real time without the presence of existing infrastructure.

Digitalization of MS services, through teleneurology and remote evaluation of MS patients is an important way forwards to address both ongoing disease management as well as neurorehabilitation.

Pre-visit surveys to patients including modified scales for self-assessment and patient-reported outcome measures may empower PwMS and streamline patient-physician encounters (Kobelt et al., 2017). Digital triage of PwMS who would most benefit from in-person visits based on standardized questionnaires could be rapidly and widely deployed (Moccia et al., 2020). One group has proposed the SAFE protocol based on the Italian experience during COVID-19. This includes standardizing protocols for Screening [for COVID-19 associated symptoms], Access [to MS care], Face [coverings] and E-health [options for MS] (Bunonomo et al., 2020). A “massive investment” for dedicated resources and human and technological services has been called for in the case of neurorehabilitation in particular, even while recognizing that remote evaluations have clear limitations (Leocani et al., 2020). Since our study's respondents required computer and internet access to complete the survey, it is presumed that these same PwMS are capable of participating in tele-neurology services. According to the U.S. Federal Communications Commission, however, more than 19 million Americans, 14.5 million of whom reside in rural areas, still lack broadband internet access in 2020 (Federal Communications Commission, 2020). Our study respondents thus reflect a group of PwMS with at least some access to technologies and internet services and would not reflect the most disadvantaged populations in the USA who still lack this access.

Our study had several notable strengths. We depict the situation of a large number of PwMS from all U.S. states except Alaska and across different stages of disease, ages, and socioeconomic backgrounds. Our respondents answered the survey at the early peak of the COVID-19 pandemic in the USA. We therefore present data collected in real-time during the pandemic and its response. We present comprehensive data on the MS history, disability level, and economic situation. We included

survey questions that sought direct information and allowed free text responses. Our survey also queried participants if they had COVID-19, whether they had experienced symptoms typical of COVID-19, and if they had not been tested but wanted to be. These remain salient public policy issues in the controversial U.S. response to Covid19. Finally, the iConquerMS platform allows for longitudinal follow up in practices and attitudes as they change over time, creating a foundation for measurement of future health behavior changes, expectations, and opinions.

Our study also had several limitations. This is not a population-based sample and is subject to several forms of bias. Participation is likely biased towards more informed PwMS who are cognizant of current research into the disease and favors wealthier patients with access to a computer and time available to answer an unpaid survey. Survey respondents were mostly white and on average age in the mid-50s, limiting the generalizability of our findings to minority populations, the youngest PwMS, and non-English speakers. For respondents who participated fully, we rely on the self-report with regards to factual details, such as DMT use and MS subtype. We did not independently verify the diagnosis of MS or the phase of MS through independent medical records or MRI review. PwMS who are very ill from COVID-19 are obviously less likely to reply to online surveys, biasing our results towards overall healthier respondents.

Finally, the COVID-19 epidemic is evolving, with new information emerging constantly. We provide a snapshot in time of a longer-term and complex situation for PwMS with the goal to capture a notable moment at the cross-roads of U.S. health care and the public health response to a global pandemic.

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CRediT authorship contribution statement

Andre C. Vogel: Conceptualization, Formal analysis, Visualization, Data curation, Writing - original draft, Writing - review & editing. **Hollie Schmidt:** Conceptualization, Methodology, Data curation, Writing - review & editing. **Sara Loud:** Funding acquisition, Project administration. **Robert McBurney:** Resources, Methodology, Project administration. **Farrah J. Mateen:** Conceptualization, Funding acquisition, Writing - original draft, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors have nothing to report.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.msard.2020.102512](https://doi.org/10.1016/j.msard.2020.102512).

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