Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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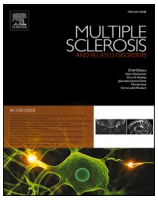

Distress and risk perception in people living with multiple sclerosis during the early phase of the COVID-19 pandemic

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ABSTRACT

Background: People living with MS during COVID-19 are experiencing the disruptions of the pandemic and concerns that their health status may place them at greater risk for worse COVID-19 outcomes.
Objective: This study sought to understand how people living with MS in the United States experienced distress and perceived their COVID-19-related risk during the first surge of the pandemic.
Methods: This was a web-based, self-report survey of people with MS who were living in the United States during the early stage of COVID-19. Primary outcomes were depression, anxiety, and positive-affect and well-being. Participants (N = 491) also provided data on demographics, MS-related factors, COVID-19 factors, and psychological coping.
Results: Psychological distress was associated with age, psychological coping strategies, and having had symptoms consistent with COVID-19, but not with MS disease-related variables and COVID-19 risk factors. Perception of COVID-19-related risk was associated with age, MS disease severity, COVID-19-related factors, and anxiety.
Conclusion: This study demonstrated that even during COVID-19, distress and risk perception are primarily driven by psychological factors, experiencing symptoms consistent with COVID-19 and age, with minimal contribution from individual differences in health status, providing an impetus for continued efforts to optimize psychological interventions for people living with MS.

1. Introduction

The emergence of the novel coronavirus disease 2019 (COVID-19) was met with heightened concern in the multiple sclerosis (MS) community given the potential increased risk posed by disease-modifying therapy-associated immunosuppression, (Giovannoni et al., 2020; Vishnevetsky and Levy, 2020; Willis and Robertson, 2020) as well as the fact that people with MS experience higher rates of comorbidities and are more likely to live in care facilities than the general population (Marrie and Horwitz, 2010; Marrie et al., 2012; National Multiple Sclerosis Society, 2020). Concerningly, many of these factors, such as being immunocompromised or immunosuppressed due to their disease modifying therapies or having comorbidities such as heart disease or obesity, map onto the Centers for Disease Control and Prevention's (CDC) initial (and subsequently revised) list of COVID-19 risk factors (Center for Disease Control and Prevention, 2020).[1]

Many people are experiencing heightened distress in the setting of COVID-19 (Holmes et al., 2020). While factors such as age or health status may shape how individuals perceive the threat of the virus, research on prior public health crises has also implicated psychological factors as central to pandemic-related distress. During the H1N1 pandemic, individuals who were less tolerant of uncertainty were more anxious (Taha et al., 2013), and individuals were likely to minimize or underestimate their personal risk until they knew somebody who had contracted the virus, at which point their perception of risk rose (Taha et al., 2013).

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[1] At the time individuals participated in this study there was no empirical research on the extent to which MS-related variables (health status and/or disease-modifying therapies) impacted COVID-19 risk. We recognize that in the months since this study was conducted, emerging empirical research has suggested that the effect of these MS-related variables is less clear. (Sormani, 2020; Parrotta et al., 2020) However, the limited information available at the time of the study – and, thus, *the context within which individuals assessed their personal situation* – was that MS-related factors, at least in terms of certain disease-modifying therapies, may place an individual at greater risk. (Giovannoni et al., 2020; Vishnevetsky and Levy, 2020; Willis and Robertson, 2020).

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A small body of literature has emerged examining distress among people living with MS during COVID-19. Three studies reassessed participants who had participated in trials prior to the pandemic to examine the extent to which distress changed over the studied interval. These studies produced mixed results, suggesting no or modest changes in anxiety or depression (Capuano et al., in press; Stojanov et al., 2020; Chiaravalloti et al., 2020). These studies had the advantage of pre-pandemic data to use as a baseline comparator, but were run on small samples (e.g., $N = 67$ (Capuano et al., in press)) with restricted characteristics (e.g., only relapsing-remitting MS (Stojanov et al., 2020) or only progressive MS (Chiaravalloti et al., 2020)) due to the inclusion criteria of the trials from which they were drawn. In addition to those distress-focused studies, a large survey study on the healthcare impact of COVID-19 for people living with MS noted that "[p]articipants believed COVID-19 presents a major danger to their health and reported being generally highly worried about the disease" (Vogel et al., 2020).

There is a need to expand this line of research to better inform the deployment of psychological interventions. In particular, there is a need to understand the complex relationship of demographic factors, MS disease-related factors, COVID-19-related factors, and modifiable psychological factors with distress during COVID-19. Given that many of these factors are fixed and/or unmodifiable, it is particularly important to understand the role of modifiable psychological factors, such as mindfulness (Schirda et al., 2015), intolerance of uncertainty (Alschuler and Beier, 2015), optimism (Sinnakaruppan et al., 2010), loneliness (Balto et al., 2016), and resilience (Kasser and Zia, 2020), that are the core targets of empirically-supported psychological interventions that have been shown to reduce distress in people living with MS (Leavitt et al., 2019; Molton et al., 2019; Alschuler et al., 2018; Schirda et al., 2020; Turner and Knowles, 2020; Bombardier et al., 2013).

The purpose of this study was to understand how people living with MS in the United States (US) experienced distress and perceived their personal risk of COVID-19 during April and May 2020, the period during which (a) the least was known about the virus, creating the most uncertain situation; (b) the initial spike in cases, hospitalizations, and deaths occurred; and (c) the first significant public health measures were implemented. Within this context, we aimed to (1) describe the level of distress experienced by people with MS during the initial phase of the pandemic; (2) describe the extent to which people with MS perceived themselves to be at risk for contracting and/or dying from COVID-19; (3) understand the extent to which demographic, MS disease and treatment-related, COVID-19-related, psychological, and social factors are associated with distress; and (4) understand the extent to which distress is associated with a person's perception of their risk for contracting and/or dying from COVID-19.

2. Methods

2.1. Participants, recruitment, and data collection

We developed a cross-sectional online survey in April 2020 to assess how individuals were responding to the emerging COVID-19 pandemic. Participation was open to individuals ≥18 years old who could read English and were in the US at some point on or after January 20, 2020, the date of the first identified COVID-19 case in the US. We targeted part of our recruitment specifically to individuals with a self-reported MS diagnosis. Participants were invited to complete the survey through emailed newsletters disseminated by the University of Washington (UW), as well as other online sources, including social media, the study team's website, and research recruitment websites or registries (ParticipateinResearch.org and researchmatch.org). A link to the survey was also posted publicly on the National MS Society's (NMSS) COVID-19 research webpage and in their emails highlighting COVID-19 research opportunities. Our goal was to capture a convenience sample of approximately $N = 500$ to give adequate power for the planned statistical analyses (Cohen, 1992).

Data were collected 4/10/20 to 5/26/20, the period of the most restrictive public health measures to date. Participants who followed the link to the study were taken to the survey on the REDCap (Research Electronic Data Capture) platform, a secure, HIPAA-compliant, password protected web-based data platform hosted by UW (Harris et al., 2009). To prevent responses from bots, respondents had to engage with a human verification service (reCAPTCHA). The first page of the survey was an information statement that provided standard informed consent information. Participants indicated their consent by proceeding with the survey, which included the measures described below. Participants were not compensated for participation in the study. This study's procedures were approved by the UW Human Subjects Division.

2.2. Measures

2.2.1. Primary outcomes

Distress. Participants completed measures of depression (PROMIS Short Form v1.0 – Depression 6a) (Cella et al., 2007; Hays et al., 2009; Cella et al., 2010), anxiety (PROMIS Short Form v1.0 – Anxiety 6a) (Cella et al., 2007; Hays et al., 2009; Cella et al., 2010), and positive affect and well-being (Neuro-QoL Short Form v1.0 - Positive Affect and Well-Being) (Cella et al., 2011; Miller et al., 2016) as proxies for distress. PROMIS and Neuro-QoL measures use a T-score metric, with a score of 50 being normative for the general population and every 10 points indicating 1 standard deviation separation from the mean. Higher scores indicate higher levels of the construct being measured. Prior research has established that in MS samples, the mean PROMIS depression and anxiety scores were 52.3 for depression and 52.5 for anxiety (Amtmann et al., 2018). In the present study, reliability of these three measures was very high (PROMIS depression $\alpha = 0.930$, PROMIS anxiety $\alpha = 0.930$, Neuro-QoL positive affect and well-being $\alpha = 0.939$).

Risk perception. Participants were asked to indicate their perception of the percent likelihood of the following four outcomes: contracting COVID-19, being hospitalized due to COVID-19, requiring ICU care due to COVID-19, and dying from COVID-19. Answers were provided on a 0% (no risk) to 100% (guaranteed to happen) scale (Chapman and Coups, 2006).

2.2.2. Predictors

Demographics. Participants indicated their age, sex, gender, race, ethnicity, relationship status, and level of education.

MS variables. Participants reported their disease duration, disease course, and current use of disease-modifying therapies (DMTs). MS disability severity was assessed via the Patient Determined Disease Steps (PDDS) (Learmonth et al., 2013).

COVID-19 variables. Participants were asked to indicate whether they had symptoms consistent with COVID-19 (with onset since the known date of the first case in the US and not better explained by another condition), had been tested for COVID-19, and had received a positive COVID-19 test result. Participants also indicated the presence or absence of CDC-defined COVID-19 risk factors, available at the time the study survey was developed (age older than 65, blood disorders, chronic kidney disease, chronic liver, compromised immune system/immunosuppression, pregnancy, endocrine disorders, metabolic disorders, heart disease, lung disease, and neurological disorders) (Center for Disease Control and Prevention, 2020).

Psychological variables. Participants completed validated measures to assess for mindfulness (Five Facet Mindfulness Questionnaire-15 (FFMQ-15)) (Baer et al., 2008), intolerance of uncertainty (Intolerance of Uncertainty Scale - Short Form (IUS - Short Form)) (Carleton et al., 2007), optimism (Life Orientation Test-Revised (LOT-R)) (Scheier et al., 1994), loneliness (PROMIS Loneliness Fixed Form) (Hahn et al., 2010), and resilience (University of Washington Resilience Scale (UWRS)) (Amtmann et al., 2020). Each of these measures has been fully validated and demonstrates sound psychometrics (Baer et al., 2008; Carleton et al., 2007; Scheier et al., 1994; Hahn et al., 2010; Amtmann et al.,

2020). The measures of mindfulness, intolerance of uncertainty, and optimism have each also been previously used in studies of people living with MS (Molton et al., 2019; Senders et al., 2014; Calandri et al., 2017), and the resilience scale was calibrated in part on people with chronic illnesses, including MS (Amtmann et al., 2020).

2.3. Statistical analysis

Prior to testing the study hypotheses, the data were inspected for duplicates, missing data, and outlier variables. All responses were verified for validity by cross-checking participants' identifiable information (e.g., name, phone number, email address). Where duplicate responses were identified, the first complete survey response was retained. Survey completion time was reviewed in order to identify any surveys in which participants completed the questionnaire faster than a human could read, which did not result in removal of any participants. There was very little missing data, primarily limited to individuals who stopped participation without fully completing the survey. In total, we collected surveys on $N = 522$ individuals living with MS; $N = 31$ were removed due to being duplicates ($N = 7$) or not completing the survey ($N = 24$), resulting in a final sample of $N = 491$.

Preliminary analyses were then conducted to ensure that study data met the assumptions for the planned analyses, including verifying that there was no evidence for significant skew, kurtosis, or heteroscedasticity. This revealed that the vast majority of the variables were appropriate for the planned analyses, with two primary exceptions: (Giovannoni et al., 2020) consistent with samples reported in prior studies of people with MS, the sample overwhelmingly identified as white, with insufficient numbers of individuals distributed across the other racial categories to conduct meaningful analyses and (Vishnevetsky and Levy, 2020) there were very few individuals who had received a COVID-19 test or tested positive for COVID-19 during the study period. Thus, we were unable to include these variables in the study analyses.

To describe the study sample and address the first two study aims, we ran descriptive analyses yielding means and standard deviations or frequency counts with percentages, as appropriate. The third aim, examining biospsychosocial factors associated with distress, was addressed through a series of stepwise multiple regression analyses that predicted three outcomes: anxiety, depression, and positive affect and well-being. Each analysis was conducted using the same model, with the outcome predicted by participant demographics (age and gender) in the first step, MS disease-related variables (disease course and level of disability) in the second step, COVID-19 factors (CDC-defined risk factors, DMT-associated risk factors, and the presence of COVID-19 symptoms) in the third step, and psychological variables (mindfulness, intolerance of uncertainty, optimism, resilience, loneliness) in the fourth step. Similarly, the fourth aim, examining the extent to which distress was associated with risk perception, was analyzed through two more multiple regression analyses that predicted perceived risk of contracting COVID-19, and perceived risk of dying from COVID-19. In these two regressions, the first three steps were identical to that of aim three, while distress (depression, anxiety, and positive affect and well-being) was in the fourth step.

3. Results

3.1. Participant demographic and descriptive data

Participants with MS who provided complete data (N = 491) are described in Table 1. In line with the majority of MS research, the study population was, on average, middle-aged ($M = 55.77 \pm 12.60$ years) and was overwhelmingly comprised of individuals who identify as women (81.3%) and white (90.4%). Participants were from 42 states and Washington, D.C., with 51.5% ($N = 253$) from Washington state and the remainder distributed in small numbers ($N \leq 15$) across the other 42 states/territories. Regarding MS (Table 2), the largest proportion of the sample reported a relapsing-remitting disease course (64.8%). The majority of the sample was on DMTs (69.9%); of these, 39.5% were on immunomodulators or immunosuppressants which, at the time of data collection, were identified by the NMSS as associated with greater risk of COVID-19 infection (National Multiple Sclerosis Society, 2020).

Table 1
Participant demographic data.

Demographic variable	Mean (SD) or N (%)	
Age	55.77 (12.60), range 22–83	
18–29	9 (1.9%)	
30–39	42 (9.5%)	
40–49	75 (15.3%)	
50–59	129 (26.3%)	
60–69	124 (25.3%)	
70–79	56 (11.4%)	
80+	6 (1.2%)	
Gender		
Woman	399 (81.3%)	
Man		85 (17.3%)
Non-binary	2 (0.4%)	
Transgender	1 (0.2%)	
Other/Prefer Not to Say/No answer	4 (0.8%)	
Race		
White	444 (90.4%)	
More than one race	20 (4.1%)	
Black/African American	13 (2.6%)	
Prefer not to say	7 (1.4%)	
Other	4 (0.8%)	
American Indian/Alaska Native	2 (0.4%)	
Asian	1 (0.2%)	
Employment		
Retired	146 (29.7%)	
Employed full-time	144 (29.3%)	
Unable to work	109 (22.2%)	
Employed part-time	34 (6.9%)	
Unemployed due to COVID-19	30 (6.1%)	
Unemployed unrelated to COVID-19	20 (4.1%)	
Student	4 (0.8%)	
No response	4 (0.8%)	
Education		
9th grade or less	1 (0.2%)	
10th–12 grade	1 (0.2%)	
High school graduate or GED	23 (4.7%)	
Vocational or Technical School	28 (5.7%)	
Some college	97 (19.8%)	
College graduate	187 (38.1%)	
Graduate or professional school	154 (31.4%)	
Marital status		
Married	279 (56.8%)	
Divorced	93 (18.9%)	
Never married	65 (13.2%)	
Widowed	21 (4.3%)	
Domestic partner	20 (4.1%)	
Legally separated	8 (1.6%)	
Not answered	3 (0.6%)	
Annulled	2 (0.4%)	

A small number of participants (16.9%) reported experiencing symptoms consistent with COVID-19, with an even smaller number undergoing COVID-19 testing (6.1%) and only one individual (0.2%) testing positive. Most of the sample reported at least one CDC-defined risk factor for COVID-19 (87.8%); the most commonly endorsed factors were neurological disorders (69.2%), compromised immune system (40.5%) and age (26.3%).

Descriptive data for the primary variables are reported in Table 3. Clinically significant levels of depressive symptoms were observed in 24.1% of the sample and anxious symptoms in 31.4%. Participants, on average, reported their perceived risk of contracting COVID-19 was 36.2%, being hospitalized was 29.1%, requiring ICU care was 25.0%, and dying from COVID-19 was 18.7%.

Table 2
Multiple sclerosis descriptive variables.

Variable	Mean (SD) or *N* (%)
Disease duration	16.71 (11.22)
Disease course	
Relapsing remitting	318 (64.8%)
Secondary progressive	81 (16.5%)
Primary progressive	50 (10.2%)
Unknown or no answer	37 (7.5%)
Clinically isolated syndrome	5 (1.0%)
Disease modifying therapy	
Increased risk	194 (39.5%)
Ocrelizumab	85 (17.3%)
Dimethyl fumarate	45 (9.2%)
Fingolimod	30 (6.1%)
Teriflunomide	22 (4.5%)
Alemtuzumab	9 (1.8%)
Siponimod	1 (0.2%)
Cladribine	1 (0.2%)
Diroximel fumarate	1 (0.2%)
No additional risk	129 (26.3%)
Glatiramer acetate	64 (13.0%)
Interferons	38 (7.7%)
Natalizumab	27 (5.5%)
Other/off-label	20 (4.1%)
No DMT	148 (30.1%)
Disability (PDDS)	
0	95 (19.3%)
1	95 (19.3%)
2	64 (13.0%)
3	63 (12.8%)
4	63 (12.8%)
5	37 (7.5%)
6	43 (8.8%)
7	28 (5.7%)
8	1 (0.2%)
No answer	2 (0.4%)

Table 3
Descriptive data for distress outcomes and psychological predictors.

Variable	Mean (SD) or %
Distress	
Depression	53.55 (8.83)
% above clinical severity cutoff *	24.1%
Anxiety	55.19 (9.52)
% above clinical severity cutoff *	31.4%
Positive affect and well-being	51.32 (6.90)
% below clinical severity cutoff *	4.5%
Risk perception (0% to 100%)	
Perceived risk of contracting COVID-19	36.18% (24.52)
Perceived risk of being hospitalized due to COVID-19	29.12% (24.99)
Perceived risk of requiring ICU care due to COVID-19	25.03% (25.46)
Perceived risk of dying from COVID-19	18.66% (23.33)
Psychological predictors	
Mindfulness (FFMQ)	54.09 (7.64)
Intolerance of Uncertainty (IUS)	27.73 (9.20)
Optimism (LOT-R)	15.83 (4.71)
Loneliness (PROMIS Loneliness)	55.36 (12.26)
Resilience (UWRS)	49.46 (8.90)

Note. * Clinical cutoff was calculated based on being one standard deviation from the mean in the "worse direction" (e.g., more depressed, more anxious, less positive affect; $T \geq 60$ for depression and anxiety, $T \leq 40$ for positive affect and well-being), which is consistent with studies that have analyzed the association of PROMIS scores with measures with established clinical cutoffs (Amtmann et al., 2015; Schalet et al., 2014).

3.2. Association of demographic, MS disease, COVID-19 factors, and psychological variables with distress

The overall model for depression was significant ($F(12, 374) = 34.39$, $p < 0.001$; see Table 4), accounting for 52.5% of the variance in depression scores. In step 1, younger age ($\beta = -0.25$, $p < 0.001$) was significantly associated with higher depressive symptom severity, accounting for 6.6% of the variance in depression. In step 2, worse MS disease severity was associated with higher depressive symptom severity ($\beta = 0.12$, $p < 0.05$), accounting for 1.5% of the variance. In step 3, COVID-19 factors accounted for 1.4% of the variance, but the block was not associated with depression. In step 4, less mindfulness ($\beta = -0.16$, $p < 0.01$), less tolerance of uncertainty ($\beta = 0.15$, $p < 0.01$), less optimism ($\beta = -0.11$, $p < 0.05$), more loneliness ($\beta = 0.36$, $p < 0.001$), and less resilience ($\beta = -0.13$, $p < 0.001$) were all associated with depression, accounting for an additional 43.0% of the variance.

The overall model for anxiety was significant ($F(12,375) = 24.22$, $p < 0.001$), accounting for 43.7% of the variance in anxiety scores. In step 1, younger age ($\beta = -0.25$, $p < 0.001$) was significantly associated with greater anxiety and accounted for 7.4% of the variance in anxiety severity. Step 2 (MS disease-related variables) was not statistically significantly related to the anxiety outcome. In step 3, having had COVID-19 symptoms was associated with greater anxiety ($\beta = 0.19$, $p < 0.001$) and accounted for 3.4% of the variance in anxiety severity. In step 4, less mindfulness ($\beta = -0.13$, $p < 0.05$), less tolerance of uncertainty ($\beta = 0.35$, $p < 0.001$), more loneliness ($\beta = 0.17$, $p < 0.01$), and less resilience ($\beta = -0.15$, $p < 0.01$) were all associated with worse anxiety, accounting for an additional 32.2% of the variance.

The overall model for affect was significant ($F(12, 373) = 29.05$, $p < 0.001$), accounting for 48.3% of the variance in Positive Affect and Well-Being scores. In step 1, older age ($\beta = 0.18$, $p < 0.001$) was significantly associated with more positive affect and well-being and accounted for 3.8% of the variance in affect. In step 2, MS disease-related variables were associated with anxiety. No individual predictors were statistically significantly associated with the outcome, but the variables together accounted for 1.9% of the variance. In step 3, COVID-19 factors were not associated with anxiety. In step 4, more mindfulness ($\beta = 0.13$, $p < 0.05$), more optimism ($\beta = 0.21$, $p < 0.001$), less loneliness ($\beta = -0.32$, $p < 0.001$), and greater resilience ($\beta = 0.15$, $p < 0.01$) were all associated with higher positive affect and well-being, accounting for an additional 40.9% of the variance.

3.3. Association of demographic, MS disease, COVID-19 factors, and distress variables with risk perception

Parallel regression analyses were run for perceived risk of contracting COVID-19 and perceived risk of dying from COVID-19 (Table 5). For perceived risk of contracting COVID-19, the overall model was significant ($F(10, 461) = 9.862$, $p < 0.001$), accounting for 17.6% of the variance in perceived risk. In step 1, younger age ($\beta = -0.29$, $p < 0.001$) was significantly associated with a higher perceived risk of contracting COVID-19 and accounted for 9.0% of the variance. The second step (MS-disease related variables) was not statistically significantly associated with risk perception. In step 3, having more CDC-defined COVID-19 risk factors ($\beta = 0.10$, $p < 0.05$) and having had symptoms consistent with COVID-19 ($\beta = 0.21$, $p < 0.001$) was associated with perceiving greater risk of contracting COVID-19 and accounted for 5.2% of the variance. In step 4, higher anxiety was associated with perceiving greater risk of contracting COVID-19 ($\beta = 0.21$, $p < 0.001$), accounting for 2.6% of the variance.

For perceived risk of dying from COVID-19, the overall model was significant ($F(10, 458) = 4.683$, $p < 0.01$), accounting for 9.3% of the variance in perceived risk. Step 1 (demographic variables) was not statistically significantly associated with risk perception. In step 2, higher MS disability severity was associated with a higher perception of risk of dying of COVID-19 ($\beta = 0.15$, $p < 0.01$), accounting for 1.6% of the variance in risk perception. In step 3, having more CDC-defined COVID-19 risk factors ($\beta = 0.13$, $p < 0.01$) was associated with perceiving greater risk of dying of COVID-19 and accounted for 1.7% of the variance. In step 4, greater anxiety ($\beta = 0.25$, $p < 0.001$) and less positive affect and well-being ($\beta = -0.12$, $p < 0.05$) were associated with perceiving greater risk of dying of COVID-19, accounting for 6.0%

Table 4
Association of demographic, MS disease, COVID-19 risk factor, and psychological variables with distress.

	Depression				Anxiety				Affect			
	B	*t*	$R^2\Delta$	$F(R^2\Delta)$	*B*	*t*	$R^2\Delta$	$F(R^2\Delta)$	*B*	*T*	$R^2\Delta$	$F(R^2\Delta)$
Overall model	$F(12, 374) = 34.39^{***}$				$F(12, 375) = 24.22^{***}$				$F(12, 373) = 29.05^{***}$			
Step 1			0.066	13.47***			0.074	15.35***			0.037	7.42**
Age	−0.25	−4.927***			−0.25	−5.123***			0.18	3.492***		
Gender	0.05	1.062			0.08	1.527			−0.06	−1.227		
Step 2			0.015	3.11*			0.007	1.42			0.019	3.83*
MS disease course	−0.02	−0.314			0.07	1.144			0.07	1.187		
Patient-Determined Disease Steps	0.12	2.107*			0.09	1.608			−0.10	−1.754		
Step 3			0.014	2.00			0.034	4.80**			0.018	2.40
DMT risk	−0.00	−0.074			0.03	0.517			0.08	1.587		
COVID-19 risk factors	−0.02	−0.310			−0.02	−0.353			0.08	1.640		
COVID-19 symptoms	0.12	2.433*			0.19	3.760***			−0.08	−1.480		
Step 4			0.430	67.62***			0.322	42.92***			0.409	59.04***
Mindfulness	−0.16	−3.233**			−0.13	−2.383*			0.13	2.497*		
Intolerance of uncertainty	0.15	3.222**			0.35	7.027***			−0.08	−1.584		
Optimism	−0.11	−2.174*			0.03	0.645			0.21	4.048***		
Loneliness	0.36	8.296***			0.17	3.487**			−0.32	−7.115***		
Resilience	−0.13	−2.728**			−0.15	−2.857**			0.15	2.877**		

Note. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 5
Association of demographic, MS disease, COVID-19 risk factor, and distress variables with risk perception.

	Perceived risk of contracting COVID-19				Perceived risk of dying from COVID-19			
	B	*t*	$R^2\Delta$	$F(R^2\Delta)$	*B*	*t*	$R^2\Delta$	$F(R^2\Delta)$
Overall model	$F(10,461) = 9.862^{***}$				$F(10,458) = 4.683^{***}$			
Step 1			0.090	23.117***			0.000	0.004
Age	−0.29	−6.564***			−0.04	−0.084		
Gender	0.05	1.154			0.00	0.007		
Step 2			0.009	2.286			0.016	3.729*
MS disease course	−0.04	−0.591			0.07	1.225		
Patient-Determined Disease Steps	−0.11	−2.115*			0.15	2.729**		
Step 3			0.052	9.445***			0.017	2.672*
DMT risk	0.03	0.557			0.02	0.341		
COVID-19 risk factors	0.10	2.315*			0.13	2.789**		
COVID-19 symptoms	0.21	4.684***			0.01	0.262		
Step 4			0.026	4.811**			0.060	10.116***
Depression	−0.05	−0.770			−0.12	−1.591		
Anxiety	0.21	3.533***			0.25	3.983***		
Affect and Well-being	0.04	0.639			−0.12	−2.012*		

Note. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

of the variance.

4. Discussion

COVID-19 is posing a once-in-a-generation public health challenge. At the time this study was conducted – a period that included the first surge of cases, hospitalizations, and deaths, and the most significant public health measures in the US – people with MS were living with not only the disruptions of the pandemic, but also the possibility that their health status and MS treatment may place them at greater risk for worse COVID-19 outcomes.

Rates of distress in this study were aligned with the other studies published on distress in the MS population during COVID-19. (Capuano et al., in press; Stojanov et al., 2020; Chiaravalloti et al., 2020) Both depression and anxiety were elevated above the rates observed in the general population, but only marginally above typical levels for the MS population relative to prior studies. (Amtmann et al., 2018) Anxiety was slightly more elevated and more prevalent than depression in our participants. Both were associated with being younger, less mindful, more intolerant of uncertainty, less optimistic, lonelier, and less resilient. While having more COVID-19 risk factors were not associated with greater distress, it is notable that having had symptoms consistent with COVID-19 that could not be explained by another medical condition was associated with greater distress. It is undoubtedly the case that having COVID-19 symptoms increases distress because it makes the threat more apparent or real. Moreover, given the high level of concern about COVID-19 that was reported in another large survey of people living with MS (Vogel et al., 2020) and the admission that fears of the severity and contagiousness of COVID-19 is the most common COVID-19 associated stressor in a general population sample (Park et al., 2020), it may be the case that individuals are primed to experience increased distress when evidence of the threat is more apparent. Many of the other factors that were found to be associated with distress are also potentially influenced directly or indirectly by the pandemic. For example, younger participants were more distressed; they may be the age group most likely managing the demands of both work (e.g., working remotely, being laid off or furloughed) and family obligations (e.g., lack of childcare) and may experience more disruptions or stressors. The added challenge of COVID-19 also likely impacts the psychological domains implicated in the study's analyses. In parallel to findings in the general population (Killgore et al., 2020), COVID-19 has increased social isolation and, not surprisingly, we observed a relationship between loneliness and distress. It is also possible that the restrictions and economic, social, and physical challenges imposed by the pandemic may interfere with the ability to remain mindful, cope with uncertainty, or remain optimistic, each of which was also associated with distress.

Interestingly, the models for perceived risk of contracting and/or dying from COVID-19 demonstrated less parallelism than the distress models. In both models, anxiety was a strong predictor of risk perception, which is not surprising, as one byproduct of heightened anxiety is a greater sensitivity to threatening health information both during pandemics (Taha et al., 2013) and while living with MS (Janssens et al., 2004), including a higher perceived risk of negative outcomes. However, the two models differed significantly in the contribution of MS disease-related and COVID-19-related factors to risk perception. In the case of perceived risk of contracting COVID-19, having had symptoms consistent with COVID-19 that could not be explained by another medical condition as the strongest predictor of risk perception. As referenced previously, this finding is consistent with research from other pandemics that suggests that the increased presence of the virus in an individual's world (such as when it is contracted by someone an individual knows (Taha et al., 2013)) is associated with higher risk perception. In contrast, in the model for perceived risk of dying of COVID-19, participants appeared to focus on their health status, as their MS disease severity and presence of COVID-19 risk factors emerged as predictors. This may be indicative of the fact that a high percentage of people living with MS indicate a good understanding of the risks and dangers associated with COVID-19 (Vogel et al., 2020). The extent to which the risk perception reported in this study is accurate or distorted is impossible to determine due to limitations in the COVID-19 testing availability in the US at the time of the study.

Regardless of the extent to which distress is different from the pre-COVID-19 era, the levels of distress observed in this population are concerning, particularly due to their association with quality of life, disability, and adherence (Turner et al., 2016). While distress was not strongly associated with MS or COVID-19-related risk factors, it was guided most notably by coping, such that those who coped in a healthier or adaptive manner experienced less distress. This serves as an important reminder to providers to assess for distress in their patient populations and make appropriate referrals to optimize the ways in which patients deploy coping strategies. It appears likely that this can be addressed through existing evidence-based psychotherapies, such as mindfulness or acceptance-based approaches to target mindfulness and intolerance of uncertainty, social engagement targeted through cognitive-behavioral therapy to reduce loneliness, and positive psychology interventions that facilitate resilience and optimism (Leavitt et al., 2019; Molton et al., 2019; Alschuler et al., 2018; Schirda et al., 2020; Turner and Knowles, 2020; Bombardier et al., 2013). The rapid implementation and increased insurance coverage of telehealth interventions as a result of the pandemic (Chen et al., 2020) may facilitate access to these treatments in the MS population. Thus, there is promise for these existing interventions to be useful in the present circumstance, with the important caveat that they must be adapted to the current context (e.g., life during COVID-19). Further research is needed to demonstrate that these existing interventions can be tailored appropriately and are effective for this purpose.

This study has limitations. First, data were collected on a convenience sample. Descriptive data were notable for participants being healthier and less disabled than the MS population at large, suggesting that the sample does not fully represent the MS population. Geographic distribution included an overrepresentation of individuals from Washington state, as we had greater access to potential participants due to our research program existing in that region. Second, data were collected via self-report which, while appropriate for measuring these constructs, represents participants' perceptions. In this context, it is important to note that the presence of a physician-confirmed MS diagnosis was self-reported and was not independently verified. Third, the results need to be interpreted in context: the study was conducted in an early phase of the pandemic and how people experience and understand COVID-19 continues to evolve.

In summary, the COVID-19 pandemic has served as a unique threat to the health and well-being of the world's population, with extra concern for the impact on vulnerable populations. This includes people with MS who live with more comorbidities and worse health status than the general population. Approximately half of this study's participants experience clinically significant levels of depression and/or anxiety, and their distress is impacted primarily by their use of modifiable coping strategies. As the pandemic continues, the associated need to address the impact on mental health, distress, and well-being continues to grow. Further research is needed on the adaptation and implementation of empirically supported approaches for improving on this distress.

Author contributions

Kevin Alschuler: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Roles/Writing - original draft, review & editing. **Michelle Roberts:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Roles/Writing - original draft, review & editing. **Tracy Herring:** Conceptualization; Investigation; Methodology; Roles/Writing - original draft, review & editing. **Dawn Ehde:** Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Resources; Roles/Writing - original draft, review & editing.

Declaration of Conflicting Interest

The Authors declare that there are no conflicts of interest.

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