Mental health of people with multiple sclerosis during the COVID-19 outbreak: A prospective cohort and cross-sectional case-control study of the UK MS Register

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ABSTRACT

Background: People with MS (pwMS) have had higher rates of anxiety and depression than the general population before the COVID-19 pandemic, placing them at higher risk of experiencing poor psychological wellbeing during the pandemic.

Objective: To assess mental health and its social/lifestyle determinants in pwMS during the first wave of the outbreak in the UK

Methods: This is a community-based, prospective longitudinal cohort and cross-sectional case-control online questionnaire study. It includes 2,010 pwMS from the UK MS Register and 380 people without MS.

Results: The Hospital Anxiety and Depression Scale scores of pwMS for anxiety and depression during the outbreak did not change from the previous year. PwMS were more likely to have anxiety (using General Anxiety Disorder-7) and/or depression (using Patient Health Questionnaire-9) than controls during the outbreak (OR:2.14[95%CI:1.58-2.91]). PwMS felt lonelier (OR:1.37[95%CI:1.04-1.80]), reported worse social support (OR:1.90[95%CI:1.18-3.07]) and reported worsened exercise habits (OR:1.65[95%CI:1.18-2.32]) during the outbreak than controls.

Conclusion: Early in the pandemic, pwMS remained at higher risk of experiencing anxiety and depression than the general population. It is important that multidisciplinary teams improve their support for the wellbeing of pwMS, who are vulnerable to the negative effects of the pandemic on their lifestyle and social support.

INTRODUCTION

The coronavirus disease-2019 (COVID-19) pandemic transformed the lives of people in unpredictable ways and posed a risk to their mental wellbeing.[1] Early in the pandemic, the United Kingdom (UK) general population experienced higher levels of psychological distress compared to the pre-COVID-19 era.[2] Consequently, research on mental health effects of the pandemic across vulnerable groups became a multidisciplinary research priority.[3]

At the start of the outbreak, anecdotal evidence suggested considerable fear of COVID-19 amongst people with multiple sclerosis (pwMS) because of their long-term physical disabilities and the immunosuppression caused by some disease modifying therapies (DMTs). The assessment of anxiety and depression in pwMS was specifically warranted because pwMS were known to have higher pre-COVID-19 rates of anxiety and depression than the general population.[4, 5] Furthermore, similar to the general population, changes in lifestyle and social factors could influence the mental health of pwMS.[5-8]

Therefore, we aimed to assess:

(i) mental health, its lifestyle and social determinants, and its association with general health among pwMS during the outbreak and compare them to people without MS.

(ii) levels of anxiety and depression amongst pwMS before and after the outbreak.

PATIENTS AND METHODS

Study design, setting and participants

The MS-COVID-19 study is an ongoing community-based, prospective and longitudinal cohort study conducted as part of the UK MS Register (UKMSR) (clinicaltrials.gov: NCT04354519).[9] The UKMSR has been collecting patient-reported data from pwMS since 2011.[10] For the MS-COVID-19 study, we have been collecting COVID-19 related data from pwMS using online self-administered questionnaires since 17 March 2020- the beginning of the COVID-19 outbreak in the UK.

On 22 May 2020, we invited pwMS registered with the UKMSR (including pwMS who were taking part in the MS-COVID-19 study) by email to complete questionnaires about their mental health, its social and lifestyle determinants, and their general health on a one-off basis (Supplementary Material). In addition, we provided them with a link to invite people without MS ("controls") to complete these same questionnaires, adding a case-control component to the study. PwMS and controls who responded to at least one of the questionnaires were included in the study (i.e., participants of the mental health study). The study flow diagram is depicted in Figure 1.

In this paper, we report cross-sectional findings on the mental health of pwMS, its determinants, and their general health during the outbreak (22 May 2020 to 16 July 2020) and compare them to controls. We also report longitudinal findings on anxiety and depression levels of pwMS pre-COVID-19 (28 February to 01 April 2019 and 3 September to 1 October 2019) and post-COVID-19 (7 February to 12 May 2020). We report the study according to the STROBE guidelines.

Ethical approval and consent

Ethical approval for UKMSR studies was obtained from South West-Central Bristol Research Ethics Committee (16/SW/0194). The case-control study received separate ethical approval from the Departmental Ethics Committee (4913-4902). Participants provided informed consent online.

Data collection

The UKMSR data

The UKMSR holds demographic data (age, gender, ethnicity), clinical data (type of MS, MS disease duration from diagnosis, DMTs), web-based Expanded Disability Status Scale (webEDSS) scores,[11] and Hospital Anxiety and Depression Scale scores of registered pwMS.[12] We used the last webEDSS scores collected from 9 February 2017 to 3 August 2020 to measure physical disability in pwMS. We used HADS scores for anxiety (HADS-A) and depression (HADS-D) among pwMS to compare their anxiety and depression levels during the outbreak to the year before. We considered a HADS score ≥11 as probable caseness of anxiety or depression (referred to as *having HADS-anxiety or HADS-depression*, here).[13] HADS scores for controls were not available.

The MS-COVID-19 study data

In the MS-COVID-19 study, we asked pwMS whether they were self-isolating and whether they had symptoms suggestive of a diagnosis of COVID-19.[9] These data were not available for controls.

Mental health questionnaires

We used the General Anxiety Disorder 7-item (GAD-7) and Patient Health Questionnaire 9-question (PHQ-9) scales to assess anxiety and depression, respectively, among pwMS and controls during the outbreak.[14, 15] We used a cut-off ≥10 for probable caseness of anxiety or depression (referred to as *having anxiety or depression*, here).[13]

We used the Impact of Event Scale-Revised (IES-R) to assess symptoms of post-traumatic stress disorder (PTSD) in pwMS and controls during the outbreak.[16] We considered scores ≥33 as probable caseness of PTSD (referred to as *having PTSD*, here).[16] We considered the IES-R subscales, including avoidance, hyperarousal, and intrusion in the analysis.[16]

To measure optimism during the outbreak, we used the Revised Life Orientation Test (LOT-R) scale with higher scores indicating more optimism.[17]

Social and lifestyle determinants of mental health questionnaires

We developed a questionnaire to assess whether participants had any changes (better/worse) in their lives related to social (relationships, social support, work, feeling of loneliness) and lifestyle (exercise, diet, smoking, and alcohol intake) factors during the outbreak compared to the year before. Participants used a visual analogue scale to indicate the change, with "no change" in the middle (45-55), "better" to the right (56-100), and "worse" to the left (0-44).

General health and MS symptoms questionnaires

We asked participants to report how their general health and (only for pwMS) MS symptoms had changed during the outbreak compared to the year before. We developed a similar questionnaire as described above.

Statistical analysis

Data were analysed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA; 2017) and R (R Core Team, 2019).

Cross-sectional analysis

Continuous variables were assessed for normality of distribution by visual inspection of data. Data were analysed using the Mann-Whitney U test and presented as median (interquartile range [IQR]) when not normally distributed and using the t-test and presented as mean (standard deviation [SD]) when normally distributed. The Mann-Whitney U test was also used for assessing ordinal variables. To assess the association between categorical variables, the Chi-square test was used (Fischer's exact test when expected count ≤5).

For comparisons between pwMS and controls, multivariable logistic regression analysis was used-binomial or multinomial, based on the dependent variable. To ascertain the association between mental health variables or having had COVID-19 and changes in general health or MS symptoms, multivariable multinomial logistic regression analysis was used. In each regression analysis, no change in the outcome was set as the reference value.

Directed Acyclic Graphs (DAGs) were built to determine potential confounding factors for individual regression analyses (Supplementary Material).[18] A separate DAG was used for each exposure and outcome analysis model.[18] We chose this approach to avoid introducing bias by controlling for colliders and mediators in the regression analyses models which is a common issue in psychological research.[19] Confounding factors controlled for in each analysis have been stated in the results, and where not mentioned, adjustments for age, gender, and ethnicity were made. Listwise deletion was implemented for missing data. The number of cases included in each regression analysis has been indicated where there was missing data. The results of the regression analyses are presented as odds ratio (OR) and 95% confidence intervals (95%CI).

Longitudinal analysis

The HADS scores of pwMS before and during the outbreak were compared using the Mann Whitney U test (paired). The proportion of pwMS with HADS-anxiety or HADS-depression before and during the outbreak were compared using the McNemar's test.

RESULTS

Participants

A total of 2,010 pwMS and 380 controls were included in the study (Figure 1). Characteristics of pwMS (participants and non-participants from the total UKMSR population) and controls are presented in Table 1. A total of 2,226 pwMS on the UKMSR had provided a HADS score both during and before the outbreak (1,165 were participants of the mental health study).

Anxiety, depression, and PTSD

Mental health characteristics of pwMS and controls are presented in Table 2.

PwMS were more likely to have anxiety and/or depression during the outbreak than controls (n=1,982; OR 2.14, 95%CI 1.57-2.91). The likelihood of having PTSD in pwMS during the outbreak was not different from controls (n=1,996; OR 1.13, 95%CI 0.84-1.52).

The HADS scores of pwMS during the outbreak had not significantly changed from their last score the year before (Table 3).

Having had COVID-19 was not associated with having anxiety and/or depression during the outbreak (after the infection, if present) (OR 1.43, 95%CI 0.75-2.74) (n=1,128; adjusted for age, gender, ethnicity, webEDSS, self-isolation, taking DMTs, and HADS-anxiety and/or HADS-depression before the outbreak). HADS-anxiety and/or HADS-depression before the outbreak did not predict self-reporting COVID-19 among pwMS (OR 1.04, 95%CI 0.73-1.48) (n=2,655; adjusted for age, gender, webEDSS, and taking DMTs).

General health and MS symptoms

A total of 1,829 pwMS and 274 controls responded to the change in general health question, and 1,829 pwMS responded to the change in MS symptoms question (Table 4).

PwMS were more likely than controls to report a decline in their general health during the outbreak compared to before (OR 1.95, 95%CI 1.43-2.65). In a *post hoc* analysis, we compared this outcome (decline in general health) between pwMS and controls separately within two groups: 1) participants *with* anxiety and/or depression, and 2) participants *without* anxiety or depression. Among participants *without* anxiety or depression (n=1,263), the findings were similar: pwMS had a higher likelihood of a decline in general health than controls (OR 1.79, 95%CI 1.16-2.76). However, among participants *with* anxiety or depression (n=673), there was no difference between pwMS and controls in reporting a decline in general health (OR 1.51, 95%CI 0.86-2.65).

Among only pwMS, the general health of participants with anxiety and/or depression during the outbreak was more likely to deteriorate than those without anxiety or depression (OR 3.59, 95%CI 2.71-4.76) (n=1,398; adjusted for age, webEDSS, self-diagnosed COVID-19, LOT-R, and changes in loneliness).

PwMS with COVID-19 were more likely to report deterioration in their general health than those without COVID-19 (OR 1.99, 95%CI 1.07-3.69) (n=1,055; adjusted for age, gender, ethnicity, webEDSS, taking DMTs, self-isolation, and changes in HADS-A and HADS-D from before the outbreak).

PwMS with anxiety and/or depression during the outbreak were more likely to report worsening of their MS symptoms compared to those without anxiety or depression (OR 5.23, 95%CI 4.16-6.57) (n=1,611; adjusted for taking DMTs, MS type, COVID-19, and LOT-R).

Having had COVID-19 predicted a higher likelihood of MS symptoms worsening (OR 1.97, 95%CI 1.06-3.67) (n=1,052; adjusted for age, gender, ethnicity, webEDSS, taking DMTs, self-isolation, and changes in HADS-A and HADS-D from before the outbreak).

Social and lifestyle determinants of mental health during the outbreak

Changes in social and lifestyle factors of pwMS and controls during the outbreak are presented in Table 5.

PwMS were more likely to feel lonelier than controls (OR 1.36, 95%CI 1.04-1.80). Among pwMS *with* anxiety and/or depression during the outbreak, 73.3% (n=442) reported feeling lonelier as opposed to 31.5% (n=340) of those *without* anxiety or depression (p<0.001). The findings were similar among pwMS with and without HADS-anxiety and/or HADS-depression before the outbreak (60.5% [n=214] vs 37.2% [n=336] felt lonelier, p<0.001).

PwMS were more likely to experience worsening of their social support than controls (OR 1.90, 95%CI 1.18-3.07). A larger proportion of pwMS with anxiety and/or depression during the outbreak reported worsening of their social support than those without anxiety or depression (23.9% [n=144] vs 9.5% [n=103], p<0.001)- similar to those with and without HADS-anxiety and/or HADS-depression before the outbreak (24% [n=85] vs 11% [n=99], p<0.001). The likelihood of experiencing worse relationships during the outbreak among pwMS was not significantly different from controls (OR 1.35, 95%CI 0.93-1.96), but pwMS were less likely to report having better relationships compared to before the outbreak (OR 0.65, 95%CI 0.48-0.88).

The exercise habits of pwMS were more likely to become worse than controls (OR 1.65, 95%CI 1.18-2.32). Among pwMS, HADS-anxiety and/or HADS-depression before the outbreak was associated with worsening of exercise during the outbreak (OR 1.38, 95%CI 1.03-1.86). A higher webEDSS score among pwMS was not significantly associated with worsening of exercise (OR 1.03, 95%CI 0.96-1.11), but predicted a lower likelihood of having better exercise during the outbreak than before (OR 0.77, 95%CI 0.71-0.84) (n=1,541; adjusted for age, gender, taking DMTs, and MS type). Controls were more likely to have improved their diet than pwMS during the outbreak (1.64, 95%CI 1.16-2.32).

PwMS were not significantly different from controls in terms of having undergone a change in their work (OR 0.80, 95%CI 0.59-1.08). A higher webEDSS score predicted a lower likelihood of undergoing a change in work among pwMS (OR 0.86, 95%CI 0.80-0.92) (n=1,541; adjusted for age,

gender, MS type, and taking DMTs). Among participants whose work had changed, pwMS were more likely to report being more stressed by this change than controls (OR 2.40, 95%CI 1.12-5.18). PwMS with and without anxiety and/or depression during the outbreak were not significantly different in feeling more stressed due to a change in work (OR 1.29, 95%CI 0.64-2.60). The absence of anxiety and depression among pwMS, however, was associated with a higher likelihood of feeling less stressed due to a change in work (OR 3.64, 95%CI 1.95-6.80) (n=347; adjusted for changes in support, relationships, and income).

Compared to controls, pwMS were more likely to experience a reduction in their income during the outbreak (OR 1.41, 95%CI 1.04-1.90). Among participants who underwent a change in work, there was no significant difference between pwMS and controls in having a reduction (OR 1.09, 95%CI 0.63-1.88) or increase in income (OR 0.89, 95%CI 0.39-2.06).

DISCUSSION

Our findings add to the evidence that pwMS are more likely to experience anxiety and depression than the general population.[4, 5] This study on a large national population of pwMS covers the first lockdown in the UK, which started on 23 March 2020 and was eased on 4 July 2020. We did not find a significant change in the levels of anxiety and depression among pwMS during this period compared to the year before, which is consistent with the results of other studies.[20-22] Taken together, these findings suggest that the differences we, and others,[22, 23] have found in anxiety and depression between pwMS and those without MS during the outbreak were most likely due to MS-related factors rather than the outbreak at the early phases of the pandemic. Studies of the general population have shown that levels of psychological distress have increased during the pandemic and people with higher risk of COVID-19, young adults, women, and populations with pre-existing mental or physical health conditions have fared even worse.[2, 24] Given that pwMS meet one or more of these conditions, we have considered why their anxiety and depression levels have not changed in line with general population surveys. One reason could be because pwMS are resilient,[20] or because support systems were already in place for pwMS and these were agilely mobilised to address the concerns of this population quickly when the pandemic started (e.g., the local branches of the UK MS Society, which

has peer-support groups and had a helpline that was available for pwMS);[25] more than 85% of pwMS in our study reported that the social support they received before the outbreak had improved or had not changed during the outbreak. We do not know whether the pandemic will have a more profound effect on pwMS in the future. Studies should continue to monitor the mental wellbeing of pwMS throughout the pandemic and thereafter.

Poor mental health has a negative impact on the quality of life, and physical and cognitive function of pwMS.[26] The study found that anxiety and depression have a substantial negative effect on the general health of pwMS and their MS symptoms, which can be greater than the impact of COVID-19. This points to a need for MS services to provide continued targeted multidisciplinary psychological support for this population.

We found that many pwMS were feeling lonelier during the outbreak than before and they were more likely to feel this way if they had anxiety or depression. PwMS were slightly more likely than people without MS to feel lonelier during the outbreak. The observations that loneliness is linked with poor health-related outcomes and depression,[27-29] along with our findings, point to a need to address loneliness among pwMS during periods of lockdown. Interventions for homebound older adults, that improve social connectedness and reduce depressive symptoms and disability,[30] could be adapted for pwMS.

Many pwMS did not experience any changes in their social support, relationships, work, or income after the outbreak, suggesting that the response of the MS community to the unforeseen transformations at the early stages of the pandemic was effective. The lockdown also had potential benefits to pwMS which have been pointed out by other authors.[20] However, when there was a change in these social factors, pwMS were affected more adversely than those without MS.

The restrictions imposed by the pandemic limited the physical activity of pwMS and did not provide them the opportunity to develop better diets compared to people without MS. Therefore, pwMS appear to be more susceptible to the adverse effects of the outbreak on lifestyle. These are important

aspects for clinicians to assess and address in routine encounters because improving lifestyle factors (such as exercise) can improve the mental and physical health of pwMS.[31, 32]

Our results confirm that anxiety and depression in pwMS are not specific to the COVID-19 era: they have remained high before and during the pandemic. Social and lifestyle factors have an undeniable role in mental health,[5-8] but these factors changed in different directions among our study population of pwMS (for example, some felt lonelier while others received better social support during the outbreak) which could have resulted in the stable anxiety and depression levels observed among pwMS.

It is not uncommon for mental health conditions to go undetected.[33] There is scope for effective management of anxiety and depression in pwMS, and modifications in lifestyle and social factors may provide additional benefits to their health-related quality of life.[34, 35] Therefore, it is vital that clinicians routinely screen for mental health problems, particularly in this COVID-19 era, and refer pwMS to appropriate wellbeing or mental health services for further assessment and support. It is also important that the MS community is aware of their specific vulnerabilities, so that they can take steps to proactively seek support.

Limitations of the study

We cannot precisely calculate our response rate (in pwMS and controls) as we do not know how many people received the study emails. This is a common limitation in studies that recruit participants through registries or social media.[24] We tried to increase our recruitment by advertising the study and sending reminder emails.[36] Nevertheless, we have studied a large national population of pwMS- the largest among current COVID-19 and mental health studies among pwMS.

The mental health study MS sample had slightly lower levels of anxiety than non-participants from the UKMSR and, therefore, their response to the pandemic could have been different. Nevertheless, our findings are in keeping with the results of similar studies.[20-22]

Different cut-offs have been recommended to identify caseness of anxiety and depression using HADS.[37] Here, we used *a priori* cut-off based on a validation study in MS.[13]

Failure to find a difference between HADS scores before and during the outbreak might be influenced by seasonal effects on experiencing anxiety and depression symptoms. Changes in HADS score could not be tested for each season in 2019 and 2020 separately because of small sample sizes.

The UKMSR was not collecting data on social and lifestyle determinants of mental health (as assessed in this study) before the COVID-19 outbreak. Therefore, we were unable to directly compare these factors during and before the outbreak. We tried to overcome this problem by asking participants about *changes* in these factors during the COVID-19 outbreak compared to before.

We asked pwMS to invite people without MS ("controls") to the study who could be their friends and relatives, sharing similar social networks or living in similar neighbourhoods with similar socioeconomic status. This can be a strength in that the controls and pwMS are similar but could also lessen the actual difference between their mental health status. However, the proportion of controls who had anxiety and/or depression in our study (27.1%) is comparable to findings among the UK general population during the same period (27.3%).[2]

We included self-reported COVID-19 instead of confirmed cases since the sample size for the latter was small. However, pwMS with anxiety and/or depression did not tend to report having had COVID-19 any more than pwMS without anxiety or depression.

We could not study the association between ethnicity and mental health because the number of people from ethnic backgrounds other than White ethnicity in the UKMSR was small.

Declaration of Conflicting Interests

All authors have completed the Unified Competing Interest Form which is available on request from the corresponding author.

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Authors contributions

RdN, RH, NE, and RN conceived the idea of the study. RdN, RH, AG, RMM, KTD, NE, and RN were involved in the design and execution of the study including data collection. Data were collected through the UK MS Register with support from RMM, KTD, and DVF. AG carried out pooling of the data with support from RMM. AG performed the data analysis with support from GRL. The manuscript was drafted by AG and RdN, revised by RM, RH, NE, RN, and GRL, with intellectual contributions from all authors.

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Table 1. Demographic and clinical characteristics of participants and non-participants (from the total UKMSR population) of the MS and COVID-19 mental health study.

	Participants [a]		Non-participants [a]
	People with MS n =2,010	Controls n =380	People with MS n =17,003
Age, median (IQR), years	56 (48 – 63) n =2,006	49 (37 – 61) [d] n =340	53 (44 – 62) [d] n = 14,993
Women, n (%)	1,488 (74.3)	248 (73.6)	11,089 (74.0)
White ethnicity, n (%)	1,942 (81.8)	329 (97.1)	13,240 (96)
Smoker [b], n (%)	160 (8.7)	20 (7.2)	409 (23.8) [d]
Alcohol intake [b], n (%)	1,141 (62.4)	216 (77.7) [d]	NA
MS-related factors			
RRMS: PMS, n	1,114: 781	NA	7,031: 4,475
MS disease duration, median (IQR), years	12 (6 – 20) n =1,975	NA	12 (7 – 20) n = 13,094
Taking DMTs, n (%)	862 (42.9)	NA	2,034 (51.1) [d]
webEDSS, median (IQR)	5.5 (3 – 6.5) n =1,679	NA	5.5 (3 – 6.5) n = 5,628
HADS-A score [b], median (IQR)	6 (3 – 9) n =1,350	NA	7 (3 – 10) [d] n =1,553
with anxiety [b, c], n (%)	251 (18.6)	NA	369 (23.8) [e]
HADS-D score [b], median (IQR)	6 (3 – 10) n =1,350	NA	6 (3 – 10) n =1,553
with depression [b, c], n (%)	282 (20.9)	NA	328 (21.1)
With anxiety and/or depression [b, c], n (%)	385 (28.5)	NA	496 (31.9)

Abbreviations: COVID-19 = Coronavirus Disease 2019; HADS = Hospital Anxiety and Depression Scale (HADS-A for anxiety and HADS-D for depression); MS = Multiple Sclerosis; RRMS = Relapsing-Remitting MS; PMS = Progressive MS (includes primary and secondary progressive types of MS); DMTs = Disease-Modifying Therapies; NA = Not Applicable or Not Available; UKMSR = United Kingdom MS Register; webEDSS = web-based Expanded Disability Status Scale

[a] Participants with missing data have been excluded from the analysis for each variable separately.

[b] Before the COVID-19 outbreak.

[c] HADS score ≥11 was considered as probable caseness of anxiety or depression

[d] p-value compared to people with MS (participants) <0.001

Table 2. Mental health characteristics of participants of the MS-COVID-19 mental health study during the COVID-19 outbreak.

	People with MS	Controls	p-value
GAD-7, median (IQR)	4 (1 − 8) n =1,714	4 (1 − 7) n =269	0.81
With anxiety [a], n (%)	334 (19.5)	45 (16.7)	0.29
PHQ-9, median (IQR)	6 (3 − 12) n =1,751	5 (2 − 9) n =269	0.002
With depression [a], n (%)	573 (32.7)	64 (23.8)	0.003
With anxiety and/or depression [a], n (%)	632 (36.8) n =1,781	73 (27.1) n =269	0.002
IES-R, median (IQR)	16 (6 − 32) n =1,696	20 (10 − 33) n =306	0.01
With symptoms of PTSD [a], n (%)	398 (23.5)	77 (25.2)	0.52
IES-R subscales, median (IQR)			
Avoidance (scored 0-32)	7 (2 − 13) n =1,790	8 (4 − 13) n =307	0.06
Hyperarousal (scored 0-24)	4 (1 − 8) n =1,797	4.5 (1 − 9) n =306	0.06
Intrusion (scored 0-32)	5 (1 − 11) n =1,797	7 (3 − 12) n =307	0.001
LOT-R, median (IQR; scored 0-24)	12 (10 − 13) n =1,770	14 (10 − 18) n =296	<0.001

Abbreviations: COVID-19 = Coronavirus Disease 2019; MS = Multiple Sclerosis; GAD-7 = General Anxiety Disorder 7-item; PHQ-9 = Patient Health Questionnaire 9-questions; IES-R = Impact of Event Scale-Revised; PTSD = Post-Traumatic Stress Disorder; LOT-R = Revised Life Orientation Test

[a] GAD-7 ≥10 (scored 0-21), PHQ-9 ≥10 (scored 0-27), and IES-R ≥33 (scored 0-88) is regarded as experiencing symptoms indicative of a probable case of anxiety, depression, and PTSD, respectively.

	During the outbreak vs anytime the year before			During the outbreak vs same period the year before		
Table 3. HADS-A and HADS-D scores (scored 0-21) of people with MS during the COVID-19 outbreak and the year before the outbreak.						
	Before [a]	During [b]	p	Before [c]	During [b]	p
Registered with the UKMSR	n =2,226			n =336		
HADS-A, median (IQR)	6 (3 – 10)	6 (3 – 10)	0.87	7 (3 – 10)	7 (3 – 10)	0.91
with anxiety [d], n (%)	463 (20.8)	470 (21.1)	0.72	77 (22.9)	81 (24.1)	0.69
HADS-D, median (IQR)	6 (3 – 10)	7 (3 – 10)	0.23	7 (4 – 10)	7 (4 – 10)	0.68
with depression [d], n (%)	470 (21.1)	475 (21.3)	0.81	79 (23.5)	69 (20.5)	0.20
With anxiety and/or depression [d], n (%)	660 (29.6)	658 (29.6)	0.96	110 (32.7)	106 (31.5)	0.72
Participants of the mental health study	n =1,165			n =114		
HADS-A, mean (SD)	6 (3 – 9)	6 (3 – 9)	0.49	6 (2 – 9)	6 (3 – 9)	0.63
with anxiety [d], n (%)	207 (17.8)	214 (18.4)	0.61	17 (14.9)	23 (20.2)	0.24
HADS-D, mean (SD)	6 (3 – 10)	6 (3 – 10)	0.63	7 (3.75 – 10)	7 (4 – 10)	0.89
with depression [d], n (%)	235 (20.2)	246 (21.1)	0.39	23 (20.2)	22 (19.3)	1
With anxiety and/or depression [d], n (%)	317 (27.2)	324 (27.8)	0.65	30 (26.3)	31 (27.2)	1

Abbreviations: COVID-19 = Coronavirus Disease 2019; HADS = Hospital Anxiety and Depression Scale; MS = Multiple Sclerosis; HADS-A = HADS for anxiety; HADS-D = HADS for depression; UKMSR = United Kingdom MS Register

[a] Most recent response from 28 February to 1 April 2019 or 3 September to 1 October 2019

[b] Most recent response from 7 February to 12 May 2020

[c] Most recent response from 28 February to 1 April 2019

[d] HADS score ≥11 was considered as probable casesness of anxiety or depression.

Table 4. Changes in general health and MS symptoms during the COVID-19 outbreak compared to before the outbreak.			
	People with MS n (%)	Controls n (%)	p-value [a]
Changes in General Health			
No change	863 (47.2)	142 (51.8)	<0.001
Worse	754 (40.7)	74 (27)	
Better	221 (12.1)	58 (21.2)	
Changes in MS Symptoms			
No change	979 (53.5)	NA	NA
Worse	758 (41.4)	NA	
Better	92 (5)	NA	
Abbreviations: COVID-19 = Coronavirus Disease 2019; MS = Multiple Sclerosis			
[a] Chi-square test			

Table 5. Changes in social and lifestyle determinants of mental health during the COVID-19 outbreak compared to before the outbreak.			
	People with MS n (%)	Controls n (%)	p-value [a]
Change in Relationships			
The same	1,042 (57)	133 (48.7)	<0.001
Worse	393 (21.5)	45 (16.5)	
Better	394 (21.5)	95 (34.8)	
Change in Social Support			
The same	821 (44.9)	122 (44.5)	0.01
Worse	265 (14.5)	23 (8.4)	
Better	743 (40.6)	129 (47.1)	
Change in Loneliness			
The same	857 (46.9)	138 (50.5)	0.51
Feeling lonelier	843 (46.1)	118 (43.2)	
Feeling less Lonely	129 (7.1)	17 (6.2)	

Change in Work			
Yes	372 (20.3)	81 (29.5)	0.001
No	1,457 (79.7)	194 (70.5)	
Change in Income			
The same	1,087 (59.4)	164 (59.9)	
Less	582 (31.8)	84 (30.7)	0.88
More	160 (8.7)	26 (9.5)	
Change in Exercise			
The same	538 (29.4)	81 (29.6)	
Worse	766 (41.9)	80 (29.2)	<0.001
Better	525 (28.7)	113 (41.2)	
Change in Diet			
The same	750 (41)	82 (30)	
Worse	704 (38.5)	108 (39.6)	<0.001
Better	375 (20.5)	80 (30.4)	
Change in Smoking			
The same	55 (34.4)	9 (45)	
More	30 (18.8)	2 (10)	0.54 [b]
Less	75 (46.9)	9 (45)	
Change in Alcohol Intake			
The same	550 (48.2)	78 (36.4)	
More	244 (21.4)	29 (13.6)	<0.001
Less	347 (30.4)	107 (50)	

Abbreviations: COVID-19 = Coronavirus Disease 2019; MS = Multiple Sclerosis

[a] Chi-square test

[b] Fischer's exact test