Self-diagnosed COVID-19 in people with multiple sclerosis: a community-based cohort of the UK MS Register

INTRODUCTION
In the early phases of the UK COVID-19 outbreak, in the absence of clear evidence about the risks for people with multiple sclerosis (pwMS) and those taking immunomodulatory disease-modifying therapies (DMT), we launched a community-based study as part of the UK MS Register (UKMSR). We intended to capture the picture of COVID-19 among pwMS and their risk of contracting the disease. Here, we report our findings from 17 March to 24 April 2020.

METHODS
The COVID-19 study (clinicaltrials.gov: NCT04354519) is a prospective observational cohort launched on 17 March 2020 as part of the UKMSR (Ethics:16/ SW/0194). PwMS completed a specific COVID-19 related survey which was combined with data held from before the pandemic where available. The primary outcome of the study is participant-reported self-diagnosis of COVID-19. Participants were asked if their diagnosis was confirmed by testing—the available test in the UK was reverse transcriptase-PCR. Participants reported if their sibling without MS, closest in age who was not living with them, had self-diagnosed COVID-19.

RESULTS
As of 24 April, out of 3910 participants, 237 (6.1% (95% CI 5.3% to 6.8%)) reported self-diagnosed COVID-19 among whom 54 (22.8% (17.5% to 28.2%)) also had a diagnosis by a healthcare professional based on symptoms and 37 (15.6% (11.2% to 20.6%)) a confirmed diagnosis by testing. Three participants reported hospitalisation due to COVID-19. No deaths were reported.

Among 1283 siblings without MS, 79 (6.2%) had reported a diagnosis of COVID-19. Adjusting for age and gender, the likelihood of contracting COVID-19 in pwMS was similar to siblings (OR 1.180 (0.888 to 1.569)).

Seven hundred and fifty-nine of 3812 participants reported that they were isolating for at least 2 weeks before symptom onset if they had COVID-19. Of these, 2 (0.3% (0% to 0.7%)) had self-diagnosed COVID-19 whereas 137 of 3053 participants not self-isolating (4.5% (3.8% to 5.2%)) had the disease (p=0.001). Among participants with confirmed COVID-19, 94.6% (86.5% to 100%) were not self-isolating which was higher than those without the disease (79.9% (78.7% to 81.3%), p=0.023). Self-isolating participants were slightly older than those not self-isolating (p=0.001). A lower proportion of participants on DMTs were self-isolating compared with those not taking DMTs (18.1% (16.4% to 20%) vs 21.5% (19.6% to 23.3%), p=0.01). Rate of self-isolation in participants taking high-efficacy DMTs was similar to those not taking DMTs and higher than those taking moderate-efficacy DMTs (21.3% vs 21.4% and 16.5%, p=0.993 and p=0.014, respectively). More participants with progressive MS (PMS) were self-isolating compared with relapsing-remitting MS (RRMS) (23.2% (21% to 25.3%) vs 17.9% (16.3% to 19.5%), p<0.001).

Using self-diagnosed and confirmed COVID-19 as outcomes, 3714 and 3618 participants were included in the regression analysis, respectively. Self-isolation predicted a lower likelihood of having self-diagnosed COVID-19 (OR 0.064 (0.016 to 0.259)) but not confirmed COVID-19.

Participants on DMTs were less likely to have self-diagnosed COVID-19 (OR 0.640 (0.428 to 0.957)), which remained significant after removing self-isolating participants (OR 0.633 (0.402 to 0.998)).

<table>
<thead>
<tr>
<th>DMT</th>
<th>Total (n=3907), n (%)</th>
<th>Self-diagnosed COVID-19 (n=236), n (%)</th>
<th>Confirmed COVID-19 (n=37), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>2088 (53.4)</td>
<td>116 (49.2)</td>
<td>11 (29.7)</td>
</tr>
<tr>
<td>Beta-interferons*</td>
<td>232 (5.9)</td>
<td>11 (4.7)</td>
<td>1 (2.7)</td>
</tr>
<tr>
<td>Glatiramer acetate*</td>
<td>196 (5)</td>
<td>18 (7.6)</td>
<td>3 (8.1)</td>
</tr>
<tr>
<td>Dimethyl fumarate*</td>
<td>446 (11.4)</td>
<td>32 (13.6)</td>
<td>7 (18.9)</td>
</tr>
<tr>
<td>Teriflunomide*</td>
<td>93 (2.4)</td>
<td>2 (0.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fingolimod*</td>
<td>235 (6)</td>
<td>15 (6.4)</td>
<td>4 (10.8)</td>
</tr>
<tr>
<td>Siponimod</td>
<td>3 (0.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ocrelizumab†</td>
<td>193 (4.9)</td>
<td>14 (5.9)</td>
<td>4 (10.8)</td>
</tr>
<tr>
<td>Natalizumab†</td>
<td>231 (5.9)</td>
<td>19 (8.1)</td>
<td>5 (13.5)</td>
</tr>
<tr>
<td>Cladribine†</td>
<td>73 (1.9)</td>
<td>2 (0.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Alemtuzumab†</td>
<td>93 (2.4)</td>
<td>5 (2.1)</td>
<td>2 (5.4)</td>
</tr>
<tr>
<td>HSCT†</td>
<td>2 (0.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mitoxantrone†</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Others†</td>
<td>16 (0.4)</td>
<td>2 (0.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (0.2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Defined as moderate-efficacy DMTs.
†Defined as high-efficacy DMTs.
Including rituximab, ofatumumab, ublituximab, vedolizumab, ponesimod, azathioprine, mycophenolate mofetil and methotrexate.
HSCT, hematopoietic stem cell transplantation.
reduced the likelihood of self-diagnosed COVID-19 compared with no DMTs (OR 0.540 (0.311 to 0.938)) but not compared with moderate-efficacy DMTs. There was no significant association between taking DMTs and confirmed COVID-19. It was not possible to do a formal statistical test for the association between individual DMTs and COVID-19 due to small numbers (table 1).

Younger age was associated with increased likelihood of having self-diagnosed (OR 1.043 (1.022 to 1.064)) and confirmed (OR 1.048 (1.009 to 1.087)) COVID-19.

Participants with PMS were less likely to have self-diagnosed (OR 0.429 (0.241 to 0.763)) or confirmed (OR 0.119 (0.015 to 0.967)) COVID-19 compared with those with RRMS, but this effect disappeared after excluding participants who were self-isolating.

Including webEDSS (n=2808) and physical MSIS-29v2 (n=3192) as additional predictors in the analysis showed no significant association with the likelihood of contracting COVID-19.

The gender distribution was similar between participants with and without COVID-19. More participants with self-diagnosed COVID-19 reported themselves having any ethnicity other than white compared with those without the disease (6.9% (3.9% to 10.1%) vs 3.8% (3.2% to 4.4%), p=0.019). Gender and ethnicity did not affect the likelihood of having COVID-19.

**DISCUSSION**

We report initial findings of an ongoing community-based COVID-19 study in a large UK-wide population of pwMS which coincided with the peak of the COVID-19 outbreak in the UK. We show that pwMS taking immunomodulatory treatments do not have an increased risk of contracting COVID-19. We did not find individual DMTs to be noticeably over-represented among pwMS with COVID-19.

The incidence of COVID-19 in our population of pwMS was not higher than that of the general population, and pwMS were not at a higher risk of having COVID-19 compared with their siblings without MS. The low hospitalisation rate in our population is possibly due to its patient-reported nature where hospitalised pwMS would fail to respond to the surveys.

The observation that self-isolating pwMS had a lower risk of COVID-19 was not unexpected. We found older pwMS and those with PMS were less likely to have COVID-19. This could be because they were self-isolating more. Similar to previous reports, we found evidence that pwMS with any ethnicity other than white had a higher chance of contracting COVID-19, but larger numbers are required to confirm this.

When this study launched, there was no accurate or accessible test to diagnose COVID-19. Therefore, we decided to set a diagnosis of COVID-19 made by participants, based on their symptoms, as the primary outcome of the study. This approach has also been adopted in other large-scale studies and is in line with the UK government policy not to seek medical advice for mild symptoms of COVID-19. 4,5

In conclusion, during a period with strict precautions in place to prevent the spread of COVID-19, pwMS and those taking DMTs are not at an increased risk of contracting the disease.
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