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# COVID-19 Severity in Multiple Sclerosis

## Putting Data Into Context

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## Abstract

### Background and Objectives

It is unclear how multiple sclerosis (MS) affects the severity of COVID-19. The aim of this study is to compare COVID-19–related outcomes collected in an Italian cohort of patients with MS with the outcomes expected in the age- and sex-matched Italian population.

### Methods

Hospitalization, intensive care unit (ICU) admission, and death after COVID-19 diagnosis of 1,362 patients with MS were compared with the age- and sex-matched Italian population in a retrospective observational case-cohort study with population-based control. The observed vs the expected events were compared in the whole MS cohort and in different subgroups (higher risk: Expanded Disability Status Scale [EDSS] score > 3 or at least 1 comorbidity, lower risk: EDSS score ≤ 3 and no comorbidities) by the $\chi^2$ test, and the risk excess was quantified by risk ratios (RRs).

### Results

The risk of severe events was about twice the risk in the age- and sex-matched Italian population: RR = 2.12 for hospitalization ($p < 0.001$), RR = 2.19 for ICU admission ($p < 0.001$), and RR = 2.43 for death ($p < 0.001$). The excess of risk was confined to the higher-risk group (n = 553). In lower-risk patients (n = 809), the rate of events was close to that of the Italian age- and sex-matched population (RR = 1.12 for hospitalization, RR = 1.52 for ICU admission, and RR = 1.19 for death). In the lower-risk group, an increased hospitalization risk was detected in patients on anti-CD20 (RR = 3.03, $p = 0.005$), whereas a decrease was detected in patients on interferon (0 observed vs 4 expected events, $p = 0.04$).

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MuSC-19 Study Group coinvestigators are listed in the appendix at the end of the article.

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## Glossary

**DMT** = disease-modifying therapy; **EDSS** = Expanded Disability Status Scale; **ICU** = intensive care unit; **ISS** = Istituto Superiore di Sanità; **MS** = multiple sclerosis; **RR** = risk ratio; **RT-PCR** = reverse transcriptase-polymerase chain reaction; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2.


### Discussion

Overall, the MS cohort had a risk of severe events that is twice the risk than the age- and sex-matched Italian population. This excess of risk is mainly explained by the EDSS score and comorbidities, whereas a residual increase of hospitalization risk was observed in patients on anti-CD20 therapies and a decrease in people on interferon.


Several studies have assessed the impact of COVID-19 in patients with multiple sclerosis (MS), unanimously indicating older age, male sex, concomitant comorbidities, and higher disability as risk factors for a more severe disease course.[1-4] The possible association between immunotherapies and COVID-19 severity was also investigated, mostly indicating an increased risk for patients with MS who are on anti-CD20 therapies or who received methylprednisolone just before the COVID-19 onset[1,3,4] and suggesting a protective role of interferon.[1,4] A recent meta-analysis of all the published studies on COVID-19 in patients with MS suggested that MS did not significantly increase the mortality rate from COVID-19,[5] but the authors pointed out that these data should be interpreted with caution as patients with MS are more likely female and younger compared with the general population where age and male sex are risk factors for worse disease outcome.[5] Therefore, even if all the studies agree that data available so far are overall reassuring, excluding major safety issues,[1-4] comparisons with external control populations are lacking.

It is unclear whether and how MS biology—apart from treatments—affects the ability to cope with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. This is not trivial as immunocompetence, in an immune-mediated disease such as MS, may be reduced. Moreover, SARS-CoV-2 interacts, in a way that is still poorly understood, with the genetic background predisposing to autoimmune diseases (including MS)[6] and misdirects host immune responses toward autoimmunity as part of COVID-19 pathophysiology.[7-9] It is therefore plausible that preexisting autoimmunity may exacerbate COVID-19 severity. Therefore, to understand whether patients with MS with COVID-19 are exposed to higher risks than the healthy population, a comparison with an external cohort is needed. The aim of this study is to compare the outcomes collected in an Italian cohort of patients with MS with COVID-19 (within the MuSC-19 project) with the outcomes expected in the age- and sex-matched Italian population, using data provided by the Italian Istituto Superiore di Sanità (ISS).

## Methods

### Data Sources: MuSC-19 Study

Data of patients with MS with suspected or confirmed COVID-19 were retrospectively collected at a national level in Italy from February 24, 2020, to February 2, 2021. Details on data collection methods and inclusion criteria were previously reported.[1] Briefly, we obtained clinician-reported demographic and clinical data on patients with MS with a confirmed or suspected COVID-19 infection from 118 Italian MS centers (eAppendix 2, links.lww.com/NXG/A493). We used a common web-based electronic Case Report Form to collect the data and a unified protocol to analyze them. Demographic, MS history, COVID-19 infection, and follow-up data were collected. For this analysis we included only patients with confirmed COVID-19. To be a confirmed case the patient must have a positive reverse transcriptase-polymerase chain reaction (RT-PCR) nasopharynegal swab.

### Data Sources: Italian Population

We made a specific data request to the ISS, who is the Italian governing body responsible for COVID-19 surveillance in Italy. Data requested (reported in Table 1) were about the percentage of patients who were hospitalized, who accessed intensive care unit (ICU), or who died for each sex and age class (0–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80–89, and >90 years), among those with a positive RT-PCR during the observation period (February 24, 2020, to February 2, 2021).

### Statistical Analysis

The probability to be hospitalized, to be admitted to ICU, and to die was extracted from ISS data (Table 1) for each patient enrolled in the MuSC-19 data set, according to their age and sex. Then, the expected number of events (e.g., hospitalizations, ICU admissions, or deaths) in the MuSC-19 population and in specific subgroups of patients (detailed below) was estimated by summing up the probabilities for each patient in the group: as an example, if 2 patients have a probability to be hospitalized of 0.5, the expected number of hospitalizations in this 2-patient group is 1. The expected proportions of hospitalizations, ICU admissions, and deaths were compared with the observed proportions by a $\chi^2$ test, and the relative

**Table 1** COVID-19 Data From the Surveillance Program in Italy

| | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| **Age** | **Cases (N or n)** | **Hosp[a] (%)** | **ICU (%)** | **Death[b] (%)** | **Cases (N or n)** | **Hosp[a] (%)** | **ICU (%)** | **Death[b] (%)** |
| **0–29** | 305,174 | 2.3 | 0.1 | 0.0 | 320,343 | 1.9 | 0.1 | 0.0 |
| **30–39** | 160,677 | 3.5 | 0.2 | 0.0 | 153,394 | 3.4 | 0.3 | 0.1 |
| **40–49** | 216,028 | 3.5 | 0.2 | 0.1 | 189,326 | 6.4 | 0.8 | 0.3 |
| **50–59** | 235,272 | 5.6 | 0.5 | 0.3 | 219,320 | 11.3 | 1.9 | 1.0 |
| **60–69** | 135,201 | 11.4 | 1.7 | 1.6 | 151,381 | 20.5 | 4.6 | 4.1 |
| **70–79** | 103,496 | 22.7 | 3.2 | 6.5 | 111,032 | 34.1 | 6.7 | 1.3 |
| **80–89** | 109,071 | 29.0 | 2.5 | 15.2 | 74,091 | 43.6 | 4.6 | 26.7 |
| **>90** | 53,545 | 22.7 | 1.3 | 21.8 | 15,884 | 40.6 | 2.6 | 37.6 |
| **Unk[c]** | 58 | 0 | 0 | — | 53 | 0 | 0 | 0 |
| **Total** | 1,318,522 | | | | 1,234,824 | | | |

Abbreviation: ICU = intensive care unit.
[a] Admission at hospital.
[b] Data on deaths are relative to the January 29 report.
[c] Unknown age.

difference expressed as risk ratios (RRs). Binomial 95% CIs were calculated for the observed proportion of events.

After the comparison of the rate of hospitalization, ICU admission, and death between the MuSC-19 cohort and the age- and sex-matched Italian population was run, we tried to explain the differences observed between patients with MS and the general population by evaluating the role of MS related risk factors, that is, Expanded Disability Status Scale (EDSS) score, comorbidities, and disease-modifying therapy (DMT) exposure, as indicated by previous literature.[1-4] We focused this additional analysis on hospitalization rates only because the number of observed ICU admissions and deaths was too low to be evaluated in separate subgroups of patients. The same results on observed and expected deaths and ICU admissions are reported in eTable 1 (links.lww.com/NXG/A492).

The specific subgroups of patients were defined according to a cutoff of EDSS score = 3 and the presence of at least 1 comorbidity. The EDSS score cutoff was chosen based also on the EDSS distribution of the MuSC-19 cohort to have 2 balanced groups. Therefore, the lower-risk group included patients with EDSS score ≤ 3 and no comorbidities, whereas the higher-risk group included patients with EDSS score > 3 or at least 1 comorbidity. DMTs were grouped, according to previous literature, as no therapy, interferon therapy, anti-CD20 therapy (rituximab or ocrelizumab), and other DMTs. A $\chi^2$ test for heterogeneity was used to compare the RR between groups.

### Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Regional Ethics Committee of Liguria (University of Genoa) (n 130/2020—DB id 10433) and at a national level by Agenzia Italiana del Farmaco. Written informed consent was obtained from all participants before starting any study procedures.

### Data Availability

MuSC-19 data that support the findings of this study are available on request from the first author (M.P.S). The data are not publicly available due to information that could compromise the privacy of research participants.

## Results

In the MuSC-19 database 1,362 patients with MS had a positive RT-PCR swab for COVID-19 over the observation period and were included in the analysis. The characteristics of the included patients are reported in Table 2. In this cohort, we observed 174 hospitalizations (12.8%), 22 ICU admissions (1.62%), and 22 deaths (1.62%) (not mutually exclusive). The expected number of hospitalizations in an age- and sex-matched cohort extracted from the Italian population was 82 (6.0%), the expected number of ICU admissions was 10 (0.73%), and the expected number of deaths was 9 (0.66%).

In Figure 1, the number of observed and expected events is reported. As compared to an age- and sex-matched cohort extracted from the Italian population, the MuSC-19 MS cohort had an excess of hospitalizations (RR = 2.12, 95% CI = 1.83–2.44, $p < 0.001$), an excess of ICU admissions (RR = 2.19, 95% CI = 1.38–3.30, $p = 0.007$), and an excess of deaths (RR = 2.43, 95% CI = 1.53–3.66, $p = 0.007$).

We tried to explain this excess of risk in 2 steps. First, we checked the MS related risk factors (EDSS score and comorbidities), by splitting the cohort in 2 risk groups, as previously described. The MS lower-risk patients were 809 (60%), and the MS higher-risk

**Table 2** Characteristics of Patients With MS

| | Overall (N = 1,362) |
|---|---|
| **Age, mean (SD)** | 44·1 (12.6) |
| **Female sex, no. (%)** | 936 (68.7) |
| **Comorbidities, no. (%)** | |
| **Hypertension, no. (%)** | 147 (10.8) |
| **Major depressive disorder, no. (%)** | 49 (3.6) |
| **Hematologic disease, no. (%)** | 38 (2.8) |
| **Diabetes, no. (%)** | 47 (3.5) |
| **Cancer, no. (%)** | 23 (1.7) |
| **Coronary heart disease, no. (%)** | 15 (1.1) |
| **MS duration, median (IQR)** | 8.9 (3.8–15.9) |
| **EDSS score, median (IQR)** | 2.0 (1.0–3.5) |
| **MS treatment, no. (%)** | |
| **Dimethyl fumarate** | 239 (17.5) |
| **Natalizumab** | 188 (13.8) |
| **Fingolimod** | 166 (12.2) |
| **Ocrelizumab** | 149 (10.9) |
| **Interferon** | 133 (9.8) |
| **Copaxone** | 101 (7.4) |
| **Teriflunomide** | 79 (5.8) |
| **Cladribine** | 27 (2.0) |
| **Rituximab** | 27 (2.0) |
| **Azathioprine** | 26 (1.9) |
| **Alemtuzumab** | 24 (1.8) |
| **Methotrexate** | 3 (0.2) |
| **Other** | 11 (0.8) |
| **None** | 189 (13.9) |

Abbreviations: EDSS = Expanded Disability Status Scale; IQR = interquartile range; MS = multiple sclerosis.

patients were 553 (40%). In the higher-risk group, 119 (22%) had both EDSS score > 3 and comorbidities, 150 (27%) had comorbidities and EDSS score ≤ 3, and 283 (51%) had EDSS score > 3 and no comorbidities. The observed vs expected number of events in these 2 groups is reported in Figure 2. The excess of risk of the MS cohort is mainly confined in the MS higher-risk group: the hospitalization RR was 2.85 (95% CI = 2.44–3.29, $p < 0.001$) in the higher MS group, whereas it was 1.12 (95% CI = 0.80–1.52, $p = 0.44$) in the lower-risk group (the 2 RRs were significantly heterogeneous, $p < 0.001$). The ICU admission RR was 2.52 (95% CI = 1.48–4.00, $p < 0.001$) in the MS higher-risk group and 1.52 (95% CI = 0.49–3.52, $p = 0.27$) in the MS lower-risk group (heterogeneity test, $p = 0.11$). Finally, the death RR was 2.71 (95% CI = 1.67–4.14, $p < 0.001$) in the MS higher-risk group and 1.19 (95% CI = 0.14–4.29, $p = 0.68$) in the MS lower-risk group (heterogeneity test, $p = 0.17$).

To try to understand the role of DMTs in explaining the small residual increase of risk in the MS lower-risk group, we split the observed and the expected hospitalization events in 4 groups: untreated patients, patients treated with interferon, patients treated with anti-CD20, and patients treated with other DMTs. In the lower-risk group (Figure 3A), the RRs were significantly heterogeneous among DMT groups ($p = 0.048$): there was no residual risk in untreated patients (RR = 1.15, 95% CI = 0.31–2.92, $p = 0.78$) nor in patients treated with other DMTs (RR = 1.09, 95% CI = 0.72–1.57, $p = 0.61$) as compared to the age- and sex-matched general population; patients with MS treated with interferon had no hospitalization (RR = 0, 95% CI = 0–3.7), whereas about 4 were expected, and the difference was statistically significant ($p = 0.042$). Patients treated with anti-CD20 had a significantly higher risk of hospitalization (RR = 3.03, 95% CI = 1.30–5.94, $p = 0.005$) than the age- and sex-matched general population, showing that the small increase of risk of patients with MS with EDSS score ≤ 3 and no comorbidities is confined to this class of patients.

In the MS higher-risk group (Figure 3B), the RRs were also significantly heterogeneous among DMTs groups ($p = 0.050$); the RR was 4.27 (95% CI = 2.91–6.18, $p < 0.001$) for patients under anti-CD20, 3.13 (95% CI = 2.40–4.04, $p < 0.001$) for untreated patients, 2.31 (95% CI = 1.74–3.04, $p < 0.001$) for patients under other DMTs, and 1.80 (95% CI = 0.66–4.42, $p = 0.50$) for patients under interferon.

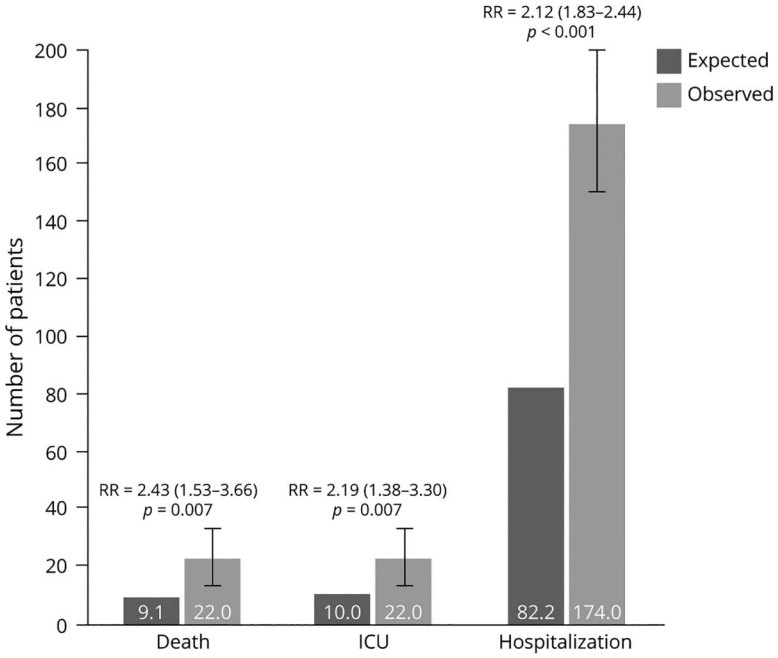
The number of deaths and ICU admissions according to DMT use in the lower- and in the higher-risk groups is reported in table e-1 (links.lww.com/NXG/A492). In the higher-risk group, the excess of death risk was mainly in the no therapy group (RR = 3.26, 95% CI = 1.77–5.37) and in the anti-CD20 group (RR = 5.40, 95% CI = 1.11–15.25), even if the low number of events does not allow to conclude for an heterogeneity of mortality risk according to the DMT group.

## Discussion

Several registries reported the COVID-19 lethality rates of MS cohorts with heterogeneous results, ranging from estimates of 1.6% in an Italian cohort and 1.7% in a French cohort[4] to estimates of 3.6% in a US cohort.[3] Explaining these differences is not straightforward and can be linked to the intrinsic limitation of registry data analyses: they are based, in fact, on a voluntary reporting by health care professionals, that may bias collected data toward more severe cases. This may cause an overestimation of clinical severity, with less effect on the internal comparisons among risk factors but challenging external comparisons.

Moreover, comparing the lethality rate of the MS cohorts with the respective national lethality rates in the general population is not meaningful without an adjustment for age and sex. The

**Figure 1** Observed Hospitalizations, ICU Admissions, and Deaths in the MuSC-19 Cohort and Age-Sex–Matched Italian Population

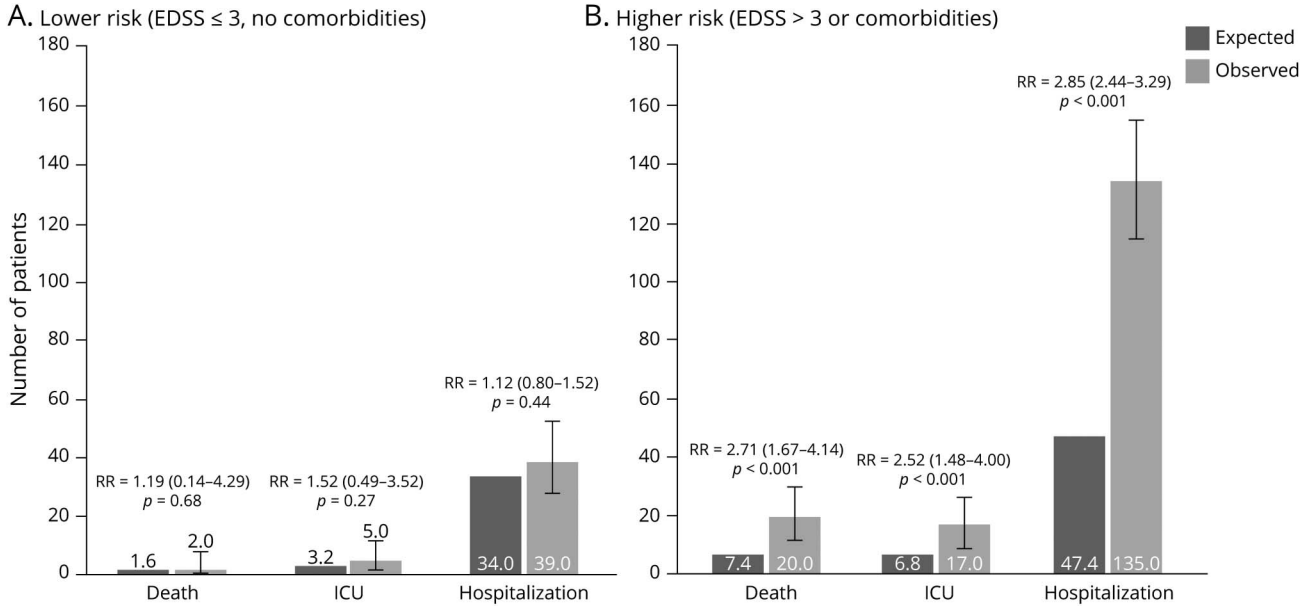



Observed hospitalizations, ICU admissions, and deaths in the MuSC-19 cohort (n = 1,362) as compared to the expected number of events in an age and matched cohort from the Italian population. ICU = intensive care unit; RR = risk ratio.

MS population is, in fact, more likely female and younger compared with the general population, and age and male sex are well known risk factors for COVID-19.

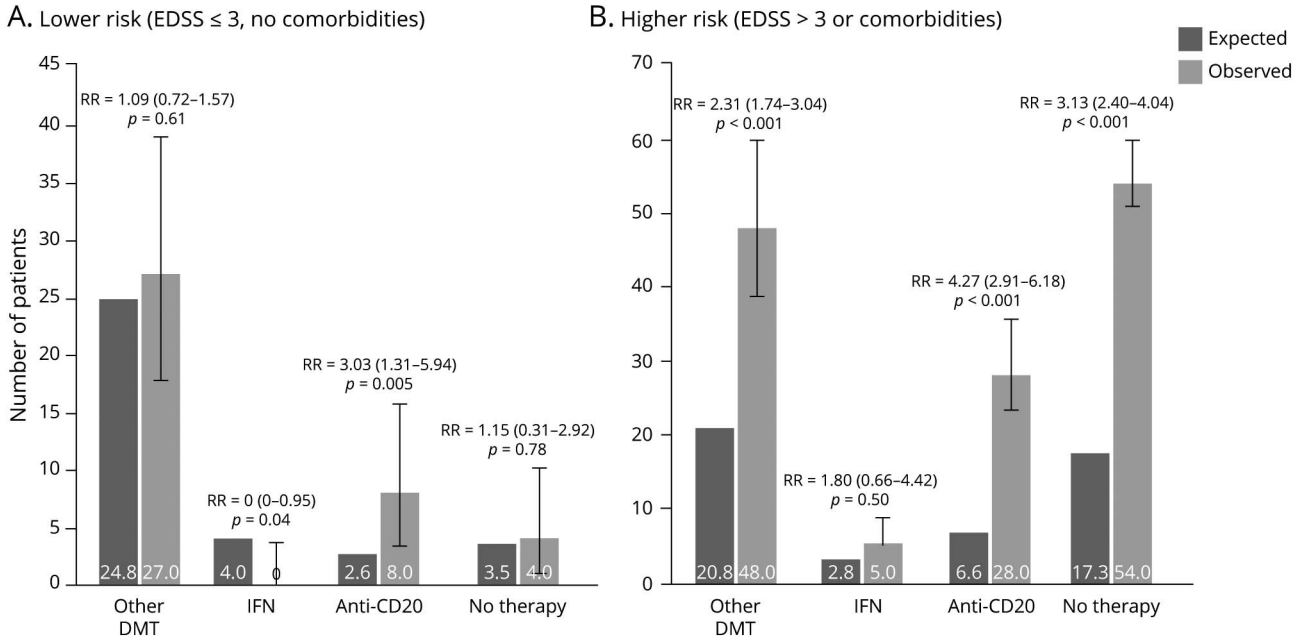
This study shows that overall, the patients with MS have a risk of developing a severe COVID-19 that is twice the risk of the age- and sex-matched Italian population. This excess of risk could be in part explained by the abovementioned bias affecting collected data toward more severe cases. However, in patients with MS with a low EDSS score (≤3) and no comorbidities, the risk of severe events is very close to the risk of the age- and sex-matched Italian population; in this lower-risk group, only patients under

**Figure 2** Observed and Expected Hospitalizations, ICU Admissions, and Deaths in Lower-Risk (A) and Higher-Risk (B) Patients




Observed hospitalizations, ICU admissions, and deaths in the lower-risk patients (A; EDSS score ≤ 3 and no comorbidities, n = 809) and in the higher-risk patients (B; EDSS score > 3 or comorbidities, n = 553) as compared to the expected number of events in the age and matched cohort from the Italian population. EDSS = Expanded Disability Status Scale; ICU = intensive care unit; RR = risk ratio.

**Figure 3** Observed and Expected Hospitalizations, ICU Admissions, and Deaths According to DMT and Lower-Risk (A) and Higher-Risk (B) Groups




Observed hospitalizations, ICU admissions, and deaths in the lower-risk patients (EDSS score ≤ 3 and no comorbidities, n = 809) and in the higher-risk patients (EDSS score > 3 or comorbidities, n = 553) according to the DMT taken as compared to the expected number of hospitalizations in the age- and sex-matched sample from the Italian population. In the interferon group, the RR = 0 because there were no observed events. DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; ICU = intensive care unit; IFN = interferon; RR = risk ratio.

anti-CD20 therapy show an increased risk of hospitalization than the age- and sex-matched Italian population. Of interest, the protective role of interferon previously suggested[1,3,4] is supported here because patients with MS taking interferon show a significantly lower number of hospitalization events than the age- and sex-atched Italian population. In patients with MS, the excess of risk of severe COVID-19 detected is confined to the group of patients with EDSS score > 3 or with additional comorbidities, were the RR ranges from 1.80 in patients treated with interferon to 4.27 in patients treated with anti-CD20.

The association with disability, and not with the disease itself, suggests that the immunologic defects determining MS do not impair the immunocompetence against SARS-CoV-2 infection. Furthermore, this result is consistent with data from the largest health analytic platforms[10] where neurologic diseases emerged as factors associated with COVID-19 severe outcome, independently of their immune-mediated pathogenesis. However, we cannot exclude that an increased attention to social distancing[11] may have counterbalanced the risk of COVID-19 linked to a dysfunctional immune system.

In conclusion, this study shows that in Italy, disability and comorbidities are determinants of an increased risk of severe COVID-19 in patients with MS. Among DMTs, a residual increase of hospitalization is associated with anti-CD20, whereas with interferon, the risk seems to be reduced. These results cannot be generalized because of possibly relevant differences in heritable and nonheritable factors affecting the response to SARS-CoV-2 in different populations.[12] However, the consistency of the results of previous studies on the impact DMTs on COVID-19 severity in MS, performed in different nations, supports the possibility that our results will be replicated also in other geographic areas and populations.


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## Disclosure

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| **Nicola De Rossi, MD** | Centro Sclerosi Multipla ASST Spedali Civili di Brescia, Montichiari, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Giampaolo Brichetto, PhD** | AISM Rehabilitation Center, Italian MS Society, Genoa, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Eleonora Cocco, MD** | Centro Sclerosi Multipla, ATS Sardegna; Dipartimento Scienze Mediche e Sanità Pubblica, Università di Cagliari | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Cinzia Scandellari, MD** | IRCCS Istituto delle Scienze Neurologiche di Bologna, UOSI Riabilitazione Sclerosi Multipla | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Paola Cavalla, MD** | MS Center, Department of Neuroscience, City of Health and Science University Hospital of Turin, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Ilaria Pesci, MD** | Centro SM UOC Neurologia, Fidenza, AUSL PR | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Antonio Zito, MD** | Multiple Sclerosis Research Center, IRCCS Mondino Foundation, Pavia | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Paolo Confalonieri, MD** | Multiple Sclerosis Centre, Neuroimmunology Department—"Carlo Besta" Neurological Institute, Milan, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Girolama Alessandra Marfia, MD** | Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Tor Vergata University, Rome, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Paola Perini, MD** | Department of Neurology Multiple Sclerosis Center, University of Padua, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Matilde Inglese, MD** | Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, Italy; IRCCS Ospedale Policlinico San Martino, Genoa, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |

Continued

## Appendix 1 *(continued)*

| Name | Location | Contribution |
|---|---|---|
| **Maria Trojano, MD** | Department of Basic Medical Sciences, Neurosciences and Sense Organs, University of Bari, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Vincenzo Brescia Morra, PhD** | Federico II University of Naples, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Gioacchino Tedeschi, MD** | Department of Advanced Medical and Surgical Sciences, University of Campania, Napoli, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Giancarlo Comi, MD** | Università Vita Salute San Raffaele, Casa di Cura Privata del Policlinico, Milan, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Mario Alberto Battaglia, MD** | Research Department, Italian Multiple Sclerosis Foundation, Genoa, Italy; Department of Life Sciences, University of Siena, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Francesco Patti, MD** | Department of Medical and Surgical Sciences and Advanced Technologies, GF Ingrassia, University of Catania; Centro Sclerosi Multipla, Policlinico Catania, University of Catania | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |
| **Marco Salvetti, MD** | Department of Neuroscience, Mental Health and Sensory Organs, Sapienza University of Rome, Italy; Unit of Neurology, IRCCS Neuromed, Pozzilli, Isernia, Italy | Drafting/revision of the manuscript for content, including medical writing for content, and major role in the acquisition of data |

## Appendix 2 Coinvestigators

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Gianmarco Abbadessa** | Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, 80138 Naples, Italy; | Site Investigator | Data collection |
| **Umberto Aguglia** | Department of medical and surgical sciences, Magna Graecia University Catanzaro | Site Investigator | Data collection |
| **Lia Allegorico** | Multiple Sclerosis Centre A. Cardarelli Hospital, Naples, Italy | Site Investigator | Data collection |
| **Beatrice Maria Allegri Rossi** | Centro SM Fidenza (PR) | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Maria Pia Amato** | Università degli Studi di Firenze, Dipartimento NEUROFARBA, Firenze - IRCCS Fondazione Don Carlo Gnocchi, Firenze | Site Investigator | Data collection |
| **Pietro Annovazzi** | Centro Sclerosi Multipla Ospedale di Gallarate, ASST della Valle Olona | Site Investigator | Data collection |
| **Carlo Antozzi** | Centro Sclerosi Multipla, U.O Neurologia IV, Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milano | Site Investigator | Data collection |
| **Lucia Appendino** | SC Neurologia1 Ospedale Maria Vittoria- Torino | Site Investigator | Data collection |
| **Sebastiano Arena** | Dipartimento Scienze Mediche e Chirurgiche e Tecnologie Avanzate, GF Ingrassia, Università di Catania; Centro Sclerosi Multipla Policlinico "G Rodolico"- San Marco, Università di Catania | Site Investigator | Data collection |
| **Viola Baione** | Department of Human Neurosciences, Sapienza, University of Rome | Site Investigator | Data collection |
| **Roberto Balgera** | MS Center, ASST Lecco | Site Investigator | Data collection |
| **Valeria Barcella** | USS Neuroimmunologia, ASST Papa Giovanni XXIII | Site Investigator | Data collection |
| **Damiano Baroncini** | Centro Sclerosi Multipla Ospedale di Gallarate, ASST della Valle Olona | Site Investigator | Data collection |
| **Caterina Barrilà** | ASST Rhodense | Site Investigator | Data collection |
| **Alessandra Bellacosa** | Centro Sclerosi Multipla, UO Neurologia, Ospedale San Giacomo, Monopoli (Bari) | Site Investigator | Data collection |
| **Gianmarco Bellucci** | Department of Neuroscience, Mental Health and Sensory Organs Sapienza University S. Andrea Hospital-site Rome | Site Investigator | Data collection |
| **Roberto Bergamaschi** | IRCCS Mondino Foundation, Pavia | Site Investigator | Data collection |
| **Valeria Bergamaschi** | AISM Rehabilitation Service Liguria | Site Investigator | Data collection |
| **Daiana Bezzini** | Department of Life Sciences, University of Siena, Siena, Italy | Site Investigator | Data collection |
| **Beatrice Biolzi** | Centro SM Fidenza (PR) | Site Investigator | Data collection |
| **Alvino Bisecco** | Centro SM, I Clinica Neurologica, AOU-Policlinico, Università della Campania "Luigi Vanvitelli" | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Simona Bonavita** | Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, 80138 Naples, Italy; | Site Investigator | Data collection |
| **Giovanna Borriello** | NCL Isituto di Neuroscienze Roma | Site Investigator | Data collection |
| **Chiara Bosa** | MS Center, Department of Neuroscience, City of Health and Science University Hospital of Turin, Turin, Italy | Site Investigator | Data collection |
| **Antonio Bosco** | Neurology Unit, Department of Medical, Surgical, and Health Sciences, Cattinara University Hospital, ASUGI, Trieste | Site Investigator | Data collection |
| **Francesca Bovis** | Department of Health Sciences, University of Genoa, Genoa, Italy. | Biostatistician | Support in statistical analysis |
| **Marco Bozzali** | Neurology II, Dept of Neuroscience, University of Turin | Site Investigator | Data collection |
| **Laura Brambilla** | Centro Sclerosi Multipla, U.O Neurologia IV, Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milano | Site Investigator | Data collection |
| **Maria Buccafusca** | Centro Sclerosi Multipla UOC Neurologia e Malattie Neuromuscolari, AOU Policlinico G. Martino Messina | Site Investigator | Data collection |
| **Elisabetta Bucciantini** | Ospedale Savigliano ASLCN1 | Site Investigator | Data collection |
| **Sebastiano Bucello** | Centro SM Ospedale Muscatello Augusta (ASP8 SR) | Site Investigator | Data collection |
| **Maria Chiara Buscarinu** | Department of Neuroscience, Mental Health and Sensory Organs Sapienza University S. Andrea Hospital-site Rome | Site Investigator | Data collection |
| **Maria Paola Cabboi** | UOC Neurologia- centro SM- AUSL- IRCCS RE | Site Investigator | Data collection |
| **Massimiliano Calabrese** | The Multiple Sclerosis Center of University Hospital of Verona Dept. of Neuroscience, Biomedicine and Movements | Site Investigator | Data collection |
| **Francesca Calabria** | UO Neurologia A-Azienda Ospedaliera Universitaria Integrata Verona | Site Investigator | Data collection |
| **Francesca Caleri** | Multiple Sclerosis Center, Department of Neurology - Franz Tappeiner Hospital Meran (BZ), Italy | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Federico Camilli** | IRCCS Istituto delle Scienze Neurologiche di Bologna, UOSI Riabilitazione Sclerosi Multipla | Site Investigator | Data collection |
| **Luisa Maria Caniatti** | Centro sclerosi Multipla azienda ospedaliera universitaria S. Anna, Ferrara | Site Investigator | Data collection |
| **Roberto Cantello** | Neurology Unit, Maggiore della Carità Hospital, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy | Site Investigator | Data collection |
| **Ruggero Capra** | Centro Sclerosi Multipla ASST Spedali Civili di Brescia, Ospedale di Montichiari | Site Investigator | Data collection |
| **Rocco Capuano** | Centro SM, I Clinica Neurologica, AOU-Policlinico, Università della Campania "Luigi Vanvitelli" | Site Investigator | Data collection |
| **Patrizia Carta** | Centro Sclerosi Multipla Ospedale di Gallarate, ASST della Valle Olona | Site Investigator | Data collection |
| **Maria Grazia Celani** | Azienda Ospedaliera di Perugia, SC di Neurofisiopatologia | Site Investigator | Data collection |
| **Maria Cellerino** | DINOGMI Universita' di Genova | Site Investigator | Data collection |
| **Raffaella Cerqua** | Clinica Neurologica Ospedali Riuniti Ancona | Site Investigator | Data collection |
| **Clara Chisari** | Dipartimento Scienze Mediche e Chirurgiche e Tecnologie Avanzate, GF Ingrassia, Università di Catania; Centro Sclerosi Multipla Policlinico "G Rodolico"-San Marco, Università di Catania | Site Investigator | Data collection |
| **Raffaella Clerici** | Centro Sclerosi Multipla U.O. Neurologia Ospedale Valduce Como | Site Investigator | Data collection |
| **Marinella Clerico** | Clinical and Biological Sciences Dept, University of Torino | Site Investigator | Data collection |
| **Gaia Cola** | Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Tor Vergata University, Rome, Italy | Site Investigator | Data collection |
| **Antonella Conte** | 1) Department of Human Neurosciences, Sapienza, University of Rome. 2) IRCCS Neuromed, Pozzilli (IS) | Site Investigator | Data collection |
| **Marta Zaffira Conti** | USS Neuroimmunologia, ASST Papa Giovanni XXIII | Site Investigator | Data collection |

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## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Christian Cordano** | UCSF, San Francisco, USA | Site Investigator | Data collection |
| **Susanna Cordera** | SC Neurologia Ausl Valle D' Aosta | Site Investigator | Data collection |
| **Francesco Corea** | Neurologia, Ospedale San Giovanni, Foligno | Site Investigator | Data collection |
| **Claudio Correale** | AISM Vicenza Rehabilitation Service | Site Investigator | Data collection |
| **Salvatore Cottone** | Centro Sclerosi Multipla U.O.C. Neurologia con Stroke Unit A.R.N.A.S Civico (Palermo) | Site Investigator | Data collection |
| **Francesco Crescenzo** | The Multiple Sclerosis Center of University Hospital of Verona Dept. of Neuroscience, Biomedicine and Movements | Site Investigator | Data collection |
| **Erica Curti** | Multiple Sclerosis Centre, Department of General Medicine, Parma University Hospital, Parma | Site Investigator | Data collection |
| **Alessandro d'Ambrosio** | Centro SM, I Clinica Neurologica, AOU-Policlinico, Università della Campania "Luigi Vanvitelli" | Site Investigator | Data collection |
| **Emanuele D'Amico** | Dipartimento Scienze Mediche e Chirurgiche e Tecnologie Avanzate, GF Ingrassia, Università di Catania; Centro Sclerosi Multipla Policlinico "G Rodolico"- San Marco, Università di Catania | Site Investigator | Data collection |
| **Maura Chiara Danni** | Clinica Neurologica Ospedali Riuniti Ancona | Site Investigator | Data collection |
| **Alessia d'Arma** | IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milano | Site Investigator | Data collection |
| **Vincenzo Dattola** | UOC Neurologia, Grande Ospedale Metropolitano "Bianchi Melacrino Morelli", Reggio di Calabria | Site Investigator | Data collection |
| **Stefano de Biase** | Neurology Unit, Ospedale dell'Angelo, Venezia-Mestre, Italy | Site Investigator | Data collection |
| **Giovanna De Luca** | MS Centre, Department of Clinical Neurology, SS. Annunziata, University Hospital, Chieti, Italy | Site Investigator | Data collection |
| **Stefania Federica De Mercanti** | Clinical and Biological Sciences Dept, University of Torino | Site Investigator | Data collection |
| **Paolo De Mitri** | Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Nicola De Stefano** | Department of Medicine, Surgery and Neuroscience, University of Siena, Italy | Site Investigator | Data collection |
| **Marco Della Cava** | AISM Padova Rehabilitation Service | Site Investigator | Data collection |
| **Mario di Napoli** | Centro Sclerosi Multipla Rieti (Rieti) | Site Investigator | Data collection |
| **Alessia Di Sapio** | Department of Neurology, Regina Montis Regalis Hospital, Mondovì (CN) | Site Investigator | Data collection |
| **Renato Docimo** | Centro Sclerosi Multipla, Presidio Ospedaliero "San Giuseppe Moscati" ASL Caserta, Aversa (CE). | Site Investigator | Data collection |
| **Anna Dutto** | Ospedale Savigliano Aslcn1 | Site Investigator | Data collection |
| **Luana Evangelista** | Demyelinating Disease Center, San Salvatore Hospital, L'Aquila | Site Investigator | Data collection |
| **Salvatore Fanara** | Department of Biomedicine, Neurosciences and Advanced Diagnsotics; University of Palermo | Site Investigator | Data collection |
| **Diana Ferraro** | Department of Biomedical, Metabolic and Neurosciences, University of Modena and Reggio Emilia, Modena, Italy | Site Investigator | Data collection |
| **Maria Teresa Ferrò** | Neuroimmunology, Center for Multiple Sclerosis, ASST, Crema, Italy | Site Investigator | Data collection |
| **Cristina Fioretti** | UO Neurologia Livorno | Site Investigator | Data collection |
| **Mario Fratta** | II Clinica Neurologica, Università della Campania Luigi Vanvitelli, Naples | Site Investigator | Data collection |
| **Jessica Frau** | Centro Sclerosi Multipla, ATS Sardegna/ Dpt Scienze Mediche e Sanità Publica, Università di Cagliari, Cagliari | Site Investigator | Data collection |
| **Marzia Fronza** | Centro Sclerosi Multipla, ATS Sardegna/ Dpt Scienze Mediche e Sanità Publica, Università di Cagliari, Cagliari | Site Investigator | Data collection |
| **Roberto Furlan** | Institute of Experimental Neurology, Division of Neuroscience, IRCCS Ospedale San Raffaele, Milano, Italy, and Italian Neuroimmunology Association-AINI | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Alberto Gajofatto** | Dipartimento di Neuroscienze, Biomedicina e Movimento, Università di Verona | Site Investigator | Data collection |
| **Antonio Gallo** | Centro SM, I Clinica Neurologica, AOU-Policlinico, Università della Campania "Luigi Vanvitelli" | Site Investigator | Data collection |
| **Paolo Gallo** | Multiple Sclerosis Centre of the Veneto Region (CeSMuV), University Hospital of Padua, Italy. | Site Investigator | Data collection |
| **Claudio Gasperini** | Dept Neurosciences, San Camillo Forlanini Hospital - Rome | Site Investigator | Data collection |
| **Anna Ghazaryan** | UO Neurologia | Site Investigator | Data collection |
| **Bruno Giometto** | Ospedale Santa Chiara, Trento. UO Neurologia (Trento) | Site Investigator | Data collection |
| **Francesca Gobbin** | Dipartimento di Neuroscienze, Biomedicina e Movimento, Università di Verona | Site Investigator | Data collection |
| **Flora Govone** | Department of Neurology, Regina Montis Regalis Hospital, Mondovì (CN) | Site Investigator | Data collection |
| **Franco Granella** | Unit of Neurosciences, Department of Medicine and Surgery, University of Parma, Parma & Multiple Sclerosis Centre, Department of General Medicine, Parma University Hospital, Parma | Site Investigator | Data collection |
| **Erica Grange** | Dept. of Rehabilitation, CRRF "Mons. Luigi Novarese", Moncrivello, Italy | Site Investigator | Data collection |
| **Maria Grazia Grasso** | IRCCS Fondazione Santa Lucia | Site Investigator | Data collection |
| **Angelica Guareschi** | Centro SM Fidenza (PR) | Site Investigator | Data collection |
| **Clara Guaschino** | Centro Sclerosi Multipla Ospedale di Gallarate, ASST della Valle Olona | Site Investigator | Data collection |
| **Simone Guerrieri** | Neurology Department, Multiple Sclerosis Center, San Raffaele Hospital, Milan | Site Investigator | Data collection |
| **Donata Guidetti** | Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy | Site Investigator | Data collection |
| **Pietro Iaffaldano** | Department of Basic Medical Sciences, Neurosciences and Sense Organs - University of Bari Aldo Moro | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Antonio Ianniello** | Centro SM S.Andrea Dip. Neuroscienze Umane Sapienza Roma | Site Investigator | Data collection |
| **Luigi Iasevoli** | IRCCS Fondazione Santa Lucia | Site Investigator | Data collection |
| **Daniele Imperiale** | SC Neurologia1 Ospedale Maria Vittoria- Torino | Site Investigator | Data collection |
| **Maria Teresa Infante** | Neurologia ASL 1 imperiese | Site Investigator | Data collection |
| **Rosa Iodice** | Department of Neuroscience, Reproductive Sciences and Odontostomatology, University Federico II of Naples, Naples, Italy | Site Investigator | Data collection |
| **Aniello Iovino** | Department of Advanced Biomedical Sciences, University Federico II, Naples, Italy | Site Investigator | Data collection |
| **Giovanna Konrad** | AISM Aosta Rehabilitation Service | Site Investigator | Data collection |
| **Doriana Landi** | Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Tor Vergata University, Rome, Italy | Site Investigator | Data collection |
| **Roberta Lanzillo** | Federico II University of Naples | Site Investigator | Data collection |
| **Caterina Lapucci** | DINOGMI Universita' di Genova | Site Investigator | Data collection |
| **Luigi Lavorgna** | Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, 80138 Naples, Italy; | Site Investigator | Data collection |
| **Maria Rita L'Episcopo** | Centro Sclerosi Multipla ospedale San Lazzaro (Alba, CN) | Site Investigator | Data collection |
| **Serena Leva** | Centro Sclerosi Multipla, Ospedale di Legnano, ASST OVEST MI, Italia | Site Investigator | Data collection |
| **Giuseppe Liberatore** | Neuromuscular and Neuroimmunology Service, IRCCS Humanitas Clinical and Research Institute, Rozzano, Milan, Italy | Site Investigator | Data collection |
| **Marianna Lo Re** | SCDO Neurologia e Centro di Riferimento Regionale Sclerosi Multipla, AOU San Luigi - Orbassano (TO) | Site Investigator | Data collection |
| **Marco Longoni** | Local Health Agency of Romagna, Maurizio Bufalini Hospital (Cesena) - Neurology Unit | Site Investigator | Data collection |
| **Leonardo Lopiano** | Neurology II, Dept of Neuroscience, University of Turin | Site Investigator | Data collection |

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## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Lorena Lorefice** | Centro Sclerosi Multipla, ATS Sardegna/ Dpt Scienze Mediche e Sanità Publica, Università di Cagliari, Cagliari | Site Investigator | Data collection |
| **Matteo Lucchini** | Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore | Site Investigator | Data collection |
| **Giacomo Lus** | II Clinica Neurologica, Università della Campania Luigi Vanvitelli, Naples | Site Investigator | Data collection |
| **Davide Maimone** | Centro SM - UOC Neurologia - ARNAS Garibaldi - Catania | Site Investigator | Data collection |
| **Maria Malentacchi** | SCDO Neurologia e Centro di Riferimento Regionale Sclerosi Multipla, AOU San Luigi - Orbassano (TO) | Site Investigator | Data collection |
| **Giulia Mallucci** | IRCCS Mondino Foundation, Pavia | Site Investigator | Data collection |
| **Simona Malucchi** | SCDO Neurologia e Centro di Riferimento Regionale Sclerosi Multipla, AOU San Luigi - Orbassano (TO) | Site Investigator | Data collection |
| **Chiara Rosa Mancinelli** | Centro Sclerosi Multipla ASST Spedali Civili di Brescia, Ospedale di Montichiari | Site Investigator | Data collection |
| **Luca Mancinelli** | Local Health Agency of Romagna, Maurizio Bufalini Hospital (Cesena) - Neurology Unit | Site Investigator | Data collection |
| **Paolo Manganotti** | Neurology Unit, Department of Medical, Surgical, and Health Sciences, Cattinara University Hospital, ASUGI, Trieste | Site Investigator | Data collection |
| **Giorgia Teresa Maniscalco** | Multiple Sclerosis Centre "A. Cardarelli Hospital", Naples, Italy | Site Investigator | Data collection |
| | Neurological Clinic and Stroke Unit "A. Cardarelli Hospital", Naples, Italy; | Site Investigator | Data collection |
| **Vittorio Mantero** | MS Center, ASST Lecco | Site Investigator | Data collection |
| **Sabrina Marangoni** | Ospedale Santa Chiara, Trento. UO Neurologia (Trento) | Site Investigator | Data collection |
| **Damiano Marastoni** | The Multiple Sclerosis Center of University Hospital of Verona Dept. of Neuroscience, Biomedicine and Movements | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Fabiana Marinelli** | Ospedale Fabrizio Spaziani Frosinone | Site Investigator | Data collection |
| | Asl Frosinone | Site Investigator | Data collection |
| **Alessandro Marti** | UOC Neurologia- centro SM Reggio Emilia- AUSL-IRCSS RE | Site Investigator | Data collection |
| **Filippo Martinelli Boneschi** | 1. IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy. Via Francesco Sforza 35, 20122 | Site Investigator | Data collection |
| | 2. Dino Ferrari Center, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy. Via Francesco Sforza 35, 20122 | Site Investigator | Data collection |
| **Federco Masserano Zoli** | AISM Padova Rehabilitation Service | Site Investigator | Data collection |
| **Francesca Matta** | Centro SM - UOC Neurologia - ARNAS Garibaldi - Catania | Site Investigator | Data collection |
| **Laura Mendozzi** | IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milano | Site Investigator | Data collection |
| **Giuseppe Meucci** | UO Neurologia Livorno | Site Investigator | Data collection |
| **Silvia Miante** | Multiple Sclerosis Centre of the Veneto Region (CeSMuV), University Hospital of Padua, Italy. | Site Investigator | Data collection |
| **Giuseppina Miele** | Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, 80138 Naples, Italy; | Site Investigator | Data collection |
| **Eva Milano** | SC Neurologia1 Ospedale Maria Vittoria- Torino | Site Investigator | Data collection |
| **Massimiliano Mirabella** | Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore | Site Investigator | Data collection |
| **Rosanna Missione** | II Clinica Neurologica, Università della Campania Luigi Vanvitelli, Naples | Site Investigator | Data collection |
| **Marcello Moccia** | Federico II University of Naples | Site Investigator | Data collection |
| **Lucia Moiola** | Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy | Site Investigator | Data collection |
| **Sara Montepietra** | Responsabile del Centro Sclerosi Multipla - Reggio Emilia- UOC Neurologia-AUSL-IRCSS RE | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Margherita MontiBragadin** | AISM Rehabilitation Service Liguria | Site Investigator | Data collection |
| **Federico Montini** | Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy | Site Investigator | Data collection |
| **Roberta Motta** | AISM Rehabilitation Service Liguria | Site Investigator | Data collection |
| **Raffaele Nardone** | 1. Paracelsus Medical University, Department of Neurology, Salisburgo, AU | Site Investigator | Data collection |
| | 2. Department of Neurology - Franz Tappeiner Hospital Meran (BZ), Italy | Site Investigator | Data collection |
| **Carolina Gabri Nicoletti** | Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Tor Vergata University, Rome, Italy | Site Investigator | Data collection |
| **Eduardo Nobile-Orazio** | 1)Neuromuscular and Neuroimmunology Service, IRCCS Humanitas Clinical and Research Institute, Rozzano, Milan, Italy | Site Investigator | Data collection |
| | 2)Department of Medical Biotechnology and Translational Medicine, Milan University, Milan, | Site Investigator | Data collection |
| | Italy | Site Investigator | Data collection |
| **Agostino Nozzolillo** | Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy | Site Investigator | Data collection |
| **Marco Onofrj** | Department of Neurosciences, Imaging and Clinical Sciences, University G. d'Annunzio of Chieti-Pescara, Chieti, Italy | Site Investigator | Data collection |
| **Riccardo Orlandi** | Dipartimento di Neuroscienze, Biomedicina e Movimento, Università di Verona | Site Investigator | Data collection |
| **Anna Palmieri** | UO Neurologia, Treviso | Site Investigator | Data collection |
| **Damiano Paolicelli** | Department of Basic Medical Sciences, Neurosciences and Sense Organs - University of Bari Aldo Moro | Site Investigator | Data collection |
| **Livia Pasquali** | Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy | Site Investigator | Data collection |
| **Luisa Pastò** | Azienda Ospedaliero Universitaria Careggi, Firenze | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Elisabetta Pedrazzoli** | AISM Padova Rehabilitation Service | Site Investigator | Data collection |
| **Maria Petracca** | Federico II University of Naples | Site Investigator | Data collection |
| **Alfredo Petrone** | Ospedale Annunziata (Cosenza) | Site Investigator | Data collection |
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| **Marta Ponzano** | Department of Health Sciences, University of Genoa, Genoa, Italy. | Biostatistician | Support in statistical analysis |
| **Emilio Portaccio** | Università degli Studi di Firenze, Dipartimento NEUROFARBA, Firenze | Site Investigator | Data collection |
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| **Carlo Pozzilli** | Centro SM S.Andrea Dip.Neuroscienze Umane Sapienza Roma | Site Investigator | Data collection |
| **Luca Prosperini** | Dept Neurosciences, San Camillo Forlanini Hospital - Rome | Site Investigator | Data collection |
| **Alessandra Protti** | ASST GOM NIGUARDA, DIPARTIMENTO NEUROSCIENZE | Site Investigator | Data collection |
| **Paolo Ragonese** | Department of Biomedicine, Neurosciences and Advanced Diagnsotics; University of Palermo | Site Investigator | Data collection |
| **Sarah Rasia** | Centro Sclerosi Multipla ASST Spedali Civili di Brescia, Ospedale di Montichiari | Site Investigator | Data collection |

Continued

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Sabrina Realmuto** | Centro Sclerosi Multipla, UOC di Neurologia e Stroke Unit, AOOR Villa Sofia-Cervello Palermo | Site Investigator | Data collection |
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| **Eleonora Rigoni** | IRCCS Mondino Foundation, Pavia | Site Investigator | Data collection |
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| **Calogero Marcello Romano** | Centro Sclerosi Multipla, UOC di Neurologia e Stroke Unit, AOOR Villa Sofia-Cervello Palermo | Site Investigator | Data collection |
| **Marco Ronzoni** | ASST Rhodense | Site Investigator | Data collection |
| **Marco Rovaris** | IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milano | Site Investigator | Data collection |
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| **Elvira Sbragia** | DINOGMI Universita' di Genova | Site Investigator | Data collection |
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| **Valentina Schillaci** | MS Center, Department of Neuroscience, City of Health and Science University Hospital of Turin, Turin, Italy | Site Investigator | Data collection |
| **Maria Sessa** | UOC Neurologia, USS Neuroimmunologia, ASST Papa Giovanni XXIII | Site Investigator | Data collection |
| **Caterina Sgarito** | AISM Como Rehabilitation Service | Site Investigator | Data collection |
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| **Elisabetta Signoriello** | II Clinica Neurologica, Università della Campania Luigi Vanvitelli, Naples | Site Investigator | Data collection |
| **Leonardo Sinisi** | NEUROLOGY UNIT AND MS CENTER, ASL NAPOLI 1 CENTRO, NAPLES, ITALY | Site Investigator | Data collection |
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| **Claudio Solaro** | Dept. of Rehabilitation, CRRF "Mons. Luigi Novarese", Moncrivello, Italy | Site Investigator | Data collection |
| **Stefano Sotgiu** | Dipartimento di Scienze Mediche, Chirurgiche e Sperimentali - Università di Sassari | Site Investigator | Data collection |
| **Maddalena Sparaco** | Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, 80138 Naples, Italy; | Site Investigator | Data collection |
| **Maria Laura Stromillo** | Department of Medicine, Surgery and Neuroscience, University of Siena, Italy | Site Investigator | Data collection |
| **Silvia Strumia** | MS center, Neurology Unit, Morgagni-Pierantoni Hospital, Forlì | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Emanuela Laura Susani** | ASST GOM NIGUARDA, DIPARTIMENTO NEUROSCIENZE | Site Investigator | Data collection |
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| **Francesco Teatini** | Multiple Sclerosis Outpt.Clinic, Clinical Neurology and Stroke Unit Dep., Central Country Hospital, Bolzano, Italy | Site Investigator | Data collection |
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| **Valentina Torri Clerici** | Centro Sclerosi Multipla, U.O Neurologia IV, Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milano | Site Investigator | Data collection |
| **Carla Tortorella** | Dept Neurosciences, San Camillo Forlanini Hospital - Rome | Site Investigator | Data collection |
| **Simona Toscano** | Dipartimento Scienze Mediche e Chirurgiche e Tecnologie Avanzate, GF Ingrassia, Università di Catania; Centro Sclerosi Multipla Policlinico "G Rodolico"- San Marco, Università di Catania | Site Investigator | Data collection |
| **Rocco Totaro** | Demyelinating Disease Center, San Salvatore Hospital, L'Aquila | Site Investigator | Data collection |
| **Maria Trotta** | Ospedale Annunziata (Cosenza) | Site Investigator | Data collection |
| **Gabriella Turano** | Department of Neurology, Regina Montis Regalis Hospital, Mondovì (CN) | Site Investigator | Data collection |
| **Monica Ulivelli** | Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy | Site Investigator | Data collection |

## Appendix 2 *(continued)*

| Name | Location | Role | Contribution |
|---|---|---|---|
| **Manzo Valentino** | Neurological Clinic and Stroke Unit "A. Cardarelli Hospital", Naples, Italy; | Site Investigator | Data collection |
| **Giovanna Vaula** | Neurology II, AOU Città della Salute e della Scienza -Turin | Site Investigator | Data collection |
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| **Marco Vercellino** | MS Center, Department of Neuroscience, City of Health and Science University Hospital of Turin, Turin, Italy | Site Investigator | Data collection |
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| **Marika Vianello** | UO Neurologia, Treviso | Site Investigator | Data collection |
| **Eleonora Virgilio** | Neurology Unit, Maggiore della Carità Hospital, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy | Site Investigator | Data collection |
| **Francesca Vitetta** | Neurology Unit, Ospedale Civile, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy | Site Investigator | Data collection |
| **Stefano Vollaro** | Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy | Site Investigator | Data collection |
| **Mauro Zaffaroni** | Centro Sclerosi Multipla Ospedale di Gallarate, ASST della Valle Olona | Site Investigator | Data collection |
| **Mauro Zampolini** | Neurologia, Ospedale San Giovanni, Foligno | Site Investigator | Data collection |
| **Ignazio Roberto Zarbo** | Dipartimento di Scienze Mediche, Chirurgiche e Sperimentali - Università di Sassari | Site Investigator | Data collection |
| **Luigi Zuliani** | Department of Neurology - Ospedale San Bortolo - AULSS8 Berica Vicenza | | Data collection |

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**COVID-19 Severity in Multiple Sclerosis: Putting Data Into Context**

Maria Pia Sormani, Irene Schiavetti, Luca Carmisciano, et al.

*Neurol Neuroimmunol Neuroinflamm* 2022;9;
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