COVID-19 in people with MS

Global Data Sharing Initiative

Introduction and problem statement

Mid-march 2020 the Multiple Sclerosis Data Alliance (MSDA) was contacted by the Multiple Sclerosis International Federation (MSIF). As the COVID-19 pandemic unfolded across the globe, there was an urgent demand for data on the impact of the virus on people with MS (PwMS). There was an urgent need to gather and share information to enable evidence-based decision making on the clinical management of Multiple Sclerosis (MS) during the pandemic, and to inform future research.

At that moment, efforts were already underway in a number of countries to start collecting data, but there were several advantages of collaborating and aligning data collection protocols. These advantages include:

- Providing a framework to enable data collection in a wider number of countries and regions
- Enabling comparative analysis of treatment regimes and outcomes across different countries
- Reducing the time and cost of future collaborative research using COVID-19 and MS case data (compared to using retrospective data harmonisation efforts)

The MSIF and the MSDA have teamed up together with many other stakeholders and data partners to set up a Global Data Sharing Initiative (GDSI) to achieve insights on the effect of COVID-19 in people with MS as fast as possible, with the intent to steer decision-making during the pandemic.

MS DATA ALLIANCE

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Summary approach

The goal of this initiative is to achieve insights on the effect of COVID-19 in people with MS as soon as possible. Therefore, we proposed a plan that:

- **Is compliant** with all legal and ethical restrictions of data collection and data sharing. We do this by providing a GDPR compliant platform. Next to this, we are being supported with legal and ethical guidance to clear the protocol.
- **Is as fast as possible.** We do this by building on the existing national and international data collection initiatives already underway and by reducing the administrative burden (ethical and legal restrictions) by using anonymous data flows.
- **Is sustainable** and also supports the **long-term need** for robust data. To achieve this, we recommend everyone to use and rely upon existing registries, cohorts and platforms as much as possible.
- **Is user-friendly**. To achieve this, we have chosen a central platform (kindly provided by QMENTA) that has extensive beyond state-of-the-art possibilities to allow easy data import, integration and data management. Next to this, we developed a user-friendly interface to allow a user-friendly fast module information collection.

  Three main "data-flows" are defined:

  - "*Direct entry in the platform*": We provide an option to directly enter data into our central platform (a distinction is made between a Clinician reported fast module for data entry by healthcare professionals and a Patient reported fast module for data entry by PwMS). The clinician-reported fast module might be of benefit to healthcare professionals who only have the resources to collect the core dataset.

  - "*Patient-level data sharing via participating registries/cohorts*": We invite all MS registries and cohorts to regularly share their COVID-19 core dataset* ('export') into the central platform.

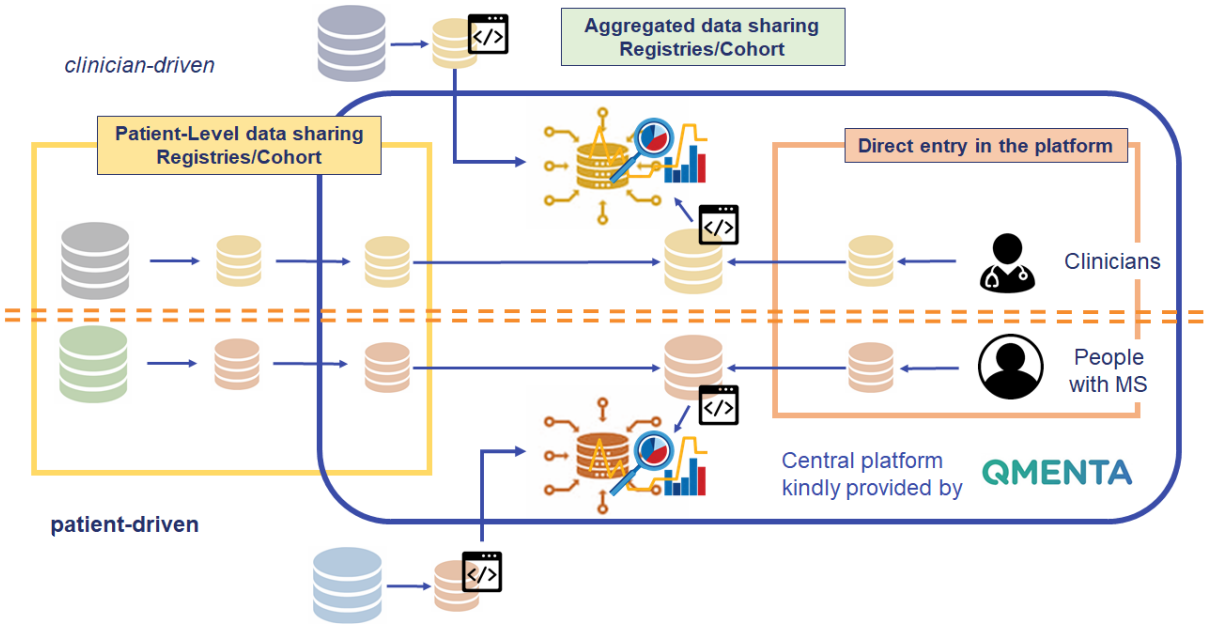
  - "*Aggregated data sharing via participating registries/cohorts*": Some registries do not share patient-level data, but share results of specific scripts. We refer to these registries as "federated registries". The script assumes the data is harmonized locally to the COVID-19 core dataset as described in the dictionary*. After running the scripts locally, the counts are shared and combined with the counts of the data inside the central platform. The advantage of this federated pipeline is that regulatory and privacy concerns are reduced. However, the main disadvantages of this approach are:

    - We lose some of the ability to explore and fish in a fully combined dataset, so looking for patterns and forming hypotheses is more difficult.

    - Also the running of localised data queries can become time consuming as the data analysis evolves.

**The core variable set/dictionary can be downloaded via the MSDA website (link)*

The figure below visualizes this high-level approach:



How can data custodians join the Global Data Sharing Initiative?

We invite all data custodians focusing on COVID-19 and MS who want to be included to contact us (lotte.geys@uhasselt.be).

STAGE 1: DATA COLLECTION

We recommend data collection takes place through the existing and emerging COVID-19 initiatives and MS Registers.

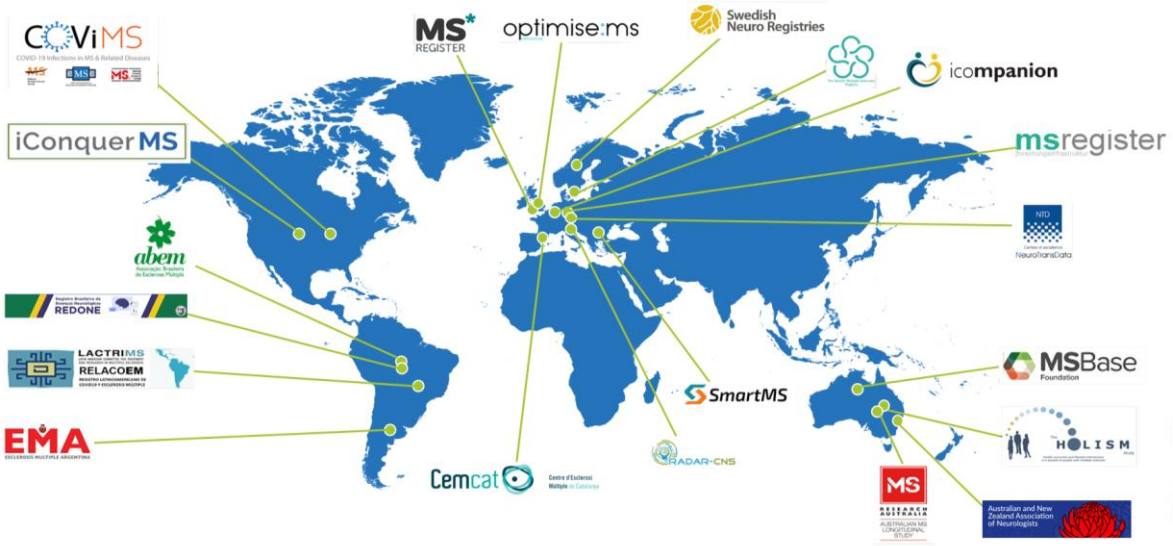
This is because the registries and cohorts are able to deliver the highest quality of data (including patient history and trajectory data). We need this high-quality data to deliver fine-tune results during, but specifically after the pandemic. Some of these initiatives are already available for international COVID-19 and MS data collection.

Table 1: COVID-19 and MS data collection initiatives: this table summarizes the MS data initiatives we are currently aware of. The initiatives can be checked online as well (www.msif.org/covid19data and https://msdataalliance.com/covid-19/covid-19-and-ms-global-data-sharing-initiative/).

Clinician reported data initiatives			
Australia and New Zealand COVID-19 Data Set	Open to Australian and New Zealand neurologists	Open	Link
Bulgarian SmartMS COVID-19 data set	Open to clinicians in Bulgaria	Open	Link
Centre d'Esclerosi Múltiple de Catalunya (CEMCAT)	Open to clinicians across Catalonia	Open	
COViMS Registry	Open to clinicians across North America	Open	Link
German MS Register COVID-19 survey	Open to clinicians who are already part of the registry	Open	Link
MSBase COVID-19 Substudy	Open to reporting anywhere in the world from MSBase centres	Open	
Neurotransdata (NTD)	Open to German clinicians that are members of NTD	Open	Clinicians can submit data only via the NTD system DESTINY – this is only possible if they are members of NTD.
OptimiseMS	Open to clinicians of UK participating sites	Open	Link
REDONE.BR - Brazilian MS Registry	Open to clinicians of countries that use Portuguese as mother tongue	Open	Link
RELACOEM	Open to Latin American countries	Open	Link
Swedish MS Registry COVID-19	Open to clinicians across	Open	Link

module	Sweden		
The Danish Multiple Sclerosis Registry	Open to Danish clinicians	Open	Link
UK MS Register COVID-19 CRF	Open to UK clinicians for laboratory confirmed COVID-19 cases only	Open	Link
Patient reported data initiatives			
ABEM - Brazilian MS Patients Association	Open to Portuguese speaking people with MS anywhere in the world	Open	Link
Australian MS Longitudinal Study (AMSLS)	For people with MS anywhere in the world, but focus on Australian people with MS	Currently not open	Link
Bulgarian SmartMS COVID-19 data set	Open to people with MS in Bulgaria	Open	Link
Esclerosis Múltiple Argentina (EMA) COVID-19 survey	Open to Spanish speaking people with MS across Latin America	Open	Link
German MS Register COVID-19 survey	Open to German speaking patients from all over the world	Open	Link
HOLISM (Health Outcomes and Lifestyle in a Sample of People with Multiple Sclerosis)	open to existing participants spread over 66 countries	Open	Existing participants will be contacted to complete a survey, the link to which will be provided.
icompanion	Open to people with MS from anywhere in the world (in English, German, French and Dutch)	Opening soon	Link: please log in on the website to share your data or install the app on your smartphone
iConquer MS COVID-19 survey	Open to people with MS anywhere in the world	Open	Sign up to iConquerMS to take part
Neurotransdata (NTD)	Open to German patients	Open	German patients can submit data via the patient portal / app featured by Vitabook – i.e. patients need a Vitabook account to use this possibility. More information
RADAR-CNS	Open to MS patients recruited for the programme	No new patients will be recruited	More information on the programme
UK MS Register COVID-19 substudy	Open to people with MS in the UK	Open	Sign up to MS Register to take part

A global map visualising the contributing data partners of the GDSI:



Together with a global data taskforce, we established recommendations for a "**COVID-19 core dataset"**. This is based on a data subset of the Italian MuSC-19 Case Reporting platform and UK MS Register substudy protocols. It represents a list of variables that can be the common denominator across all initiatives and is provided in Appendix 1. A distinction is made between clinician reported and patient reported COVID-19 core dataset.

CALL-TO-ACTION for Data custodians:

1. **We invite all MS registries and cohorts to join this global data sharing initiative.** All initiatives that contribute will be acknowledged for their participation. We can work with both clinician reported and patient reported data on COVID-19 in MS.
2. **We recommend all data custodians wanting to work on COVID-19 and MS to implement the core data set within their protocols**, even if they do not plan to participate in the global data sharing initiative in the short-term.

If you have any questions on the COVID-19 core data set or want to join the global data sharing initiative, please contact Lotte Geys: lotte.geys@uhasselt.be.

CALL-TO-ACTION for Industry partners:

We encourage all industry partners to support the individual MS registries with extra resources. Adjusting the platforms and being ready to start collecting the COVID19 core dataset is both time and resource consuming.

FAST MODULE - Direct entry into the central platform is provided if needed

For occasions when it is not possible to collect data via an existing register or cohort, there is the option to directly enter data into the central platform. QMENTA is kindly providing us with the platform and have developed a user-friendly interface for both clinician-reported and patient reported data.

- Clinician reported fast module
- Patient report fast module

The patient reported fast module is also available in French and Spanish.

These options should be used minimally, but have been developed to ensure no-one is excluded from submitting data. The clinician reported fast module might be of benefit to healthcare professionals who only have time to collect and input the minimal data set. Regarding privacy and data protection matters, we were assisted by a specialized external firm (P-95). Additionally, QMENTA is ISO certified to handle medical data. Security and privacy are taken very seriously in this initiative and the system is therefore able to contain personal health information (PHI).

STAGE 2: DATA SHARING and TRANSFERS

We have secured legal and ethical approval to receive de-identified subsets of the COVID-19 core dataset from other registers and cohorts into the central platform.

- Any registry that is collecting COVID-19 data, that wants to take part in the global data sharing initiative and share their data in the central platform will be asked to take the following actions:

1. **Sign an agreement** to make sure that the import and the use of the data is agreed upon between all parties involved.

2. **Create a de-identified subset of your COVID-19 and MS data set (a "dump").** The MS Data Alliance team will work with each register to support this process as much as possible. We recommend creating this dump using a transformation code that would allow regular updates (e.g. every month) depending on what is feasible.

3. **Import the dump into the QMENTA central platform.** The MS Data Alliance and QMENTA team will work one on one with each data custodian to support import of the dump and will provide data custodians access to the central platform.

Once data is uploaded into QMENTA, the data will not leave the QMENTA environment. The system is locked and data cannot be downloaded out of the system. QMENTA also has tracking of all users activity as well as fine grained permissions on an individual user level. Access to the patient level data is restricted to the members of the task forces only.

- Any registry that is collecting COVID-19 data, and does want to contribute to the global data sharing initiative without sharing patient-level data will be asked to run a Python script. We will provide you with a docker, and a manual. Next to this, a video "**Video - How to run the python script using the docker**" can be consulted in this link.

CALL-TO-ACTION for Data custodians:

Please contact Lotte Geys (lotte.geys@uhasselt.be):

- If you are interested in preparing a first data dump and import into the QMENTA platform, or
- If you are interested in sharing aggregated data (=results of specific scripts).

CALL-TO-ACTION for Industry partners:

We encourage all industry partners to support the individual MS registries with extra resources. Creating a dump is both time and resource consuming.

STAGE 3: DATA CLEANING AND PREPROCESSING

A task force of 6 data scientists referred to as the 'wrangling task force' has been established and will work on cleaning and preprocessing the data to make it ready for downstream analysis. In addition, two people from each registry will be given access to their data within the platform.

STAGE 4: DATA ANALYSIS

A small set of epidemiology experts was selected to form the Analysis taskforce to work on a list of predefined hypotheses and analysis plans.

STAGE 5: FEEDING BACK THE RESULTS TO THE COMMUNITY

Due to this wonderful collaboration between data custodians, technical people, analysts, researchers, clinicians, data scientists, patients with MS, etc., we were able to steer global advice for people with MS and their clinicians (link), and publish/submit scientific publications.

Interesting links and reads regarding the GDSI:

- General information regarding de GDSI can be found on the MSDA website.
- "COVID-19 in people with multiple sclerosis: A global data sharing initiative" was published last year as a scientific paper in MS Journal: link.
- In February 2021 the scientific paper entitled "Associations of DMT therapies with COVID-19 severity in multiple sclerosis" was submitted in Neurology (currently under review) and the pre-print on MedRxiv of the paper can be found on this link.
- We will keep you up to date if you'll subscribe to the Regular updates on the Global Data Sharing Initiative and/or the newsletter of the MSDA .

Contact information

If you have questions on the global data sharing initiative or any of the data collection initiatives for COVID-19 and MS, please contact the relevant person below:

- If you are a data custodian or represent a COVID-19 data initiative and have question about the core data set or how to get involved, please contact **Lotte Geys** (lotte.geys@uhasselt.be).

- If you are a person with MS or a patient organisation and want to find out how to take part or to promote the initiative, please contact **Anne Helme** (anne@msif.org).

- If you have questions about the central data sharing platform and how it works, please contact **Landon McKenna** (landon@qmenta.com).

- If you have questions relating to legal concerns of data sharing, please contact **Lotte Geys** (lotte.geys@uhasselt.be).

This Global Data Sharing Initiative is chaired by Liesbet M. Peeters (+32 479 78 67 27; Liesbet.Peeters@uhasselt.be).

APPENDIX 1: RECOMMENDATIONS COVID-19 CORE DATASET

The tables below summarize our recommendations for the COVID-19 core dataset (clinician reported and patient reported).

- We *empathise* greatly with the fact that your platform cannot be adapted for all of these variables within a short timeframe. All of us are doing the best we can. Therefore, use these recommendations as YOU see fit for YOUR specific initiative. If necessary, we can provide more detailed information. Please consult with tina.parciak@med.uni-goettingen.de if you have any questions on this topic.
- We *encourage* this COVID-19 core dataset to be implemented in registries that use either clinician reported or patient reported data. The ideal solution is if clinician reported data can be linked to data reported directly by people with MS.

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COVID-19 Incidence

Title	Variable_ID	Data Type	Options Label (Value)	Do you collect this variable? Y/N	Comments Please elaborate on the original ID (=name of the variables) as well as the original format
Date of Visit/Reporting (This date refers to (last) date of COVID19 reporting. It serves to assess how up-to-date the COVID19 information is.)	**covid19_date_reporting**	Date (**YYYY-MM-DD**)			
COVID-19 Symptoms	**covid19_has_symptoms**	Single choice	YES (**yes**) NO (**no**)		
What COVID19 symptoms did/does the patient/ do you have?					
Fever	**covid19_sympt_fever**	Single choice	YES (**yes**) NO (**no**)		
Dry Cough	**covid19_sympt_dry_cough**	Single choice	YES (**yes**) NO (**no**)		
Fatigue	**covid19_sympt_fatigue**	Single choice	YES (**yes**) NO (**no**)		
Pain (joint,bone,muscle)	**covid19_sympt_pain**	Single choice	YES (**yes**) NO (**no**)		
Sore Throat	**covid19_sympt_sore_throat**	Single choice	YES (**yes**)		

			NO (**no**)		
Shortness of breath	**covid19_sympt_shortness_breath**	Single choice	YES (**yes**) NO (**no**)		
Nasal congestion	**covid19_sympt_nasal_congestion**	Single choice	YES (**yes**) NO (**no**)		
Chills	**covid19_sympt_chills**	Single choice	YES (**yes**) NO (**no**)		
Loss of smell or taste	**covid19_sympt_loss_smell_taste**	Single choice	YES (**yes**) NO (**no**)		
Pneumonia	**covid19_sympt_pneumonia**	Single choice	YES (**yes**) NO (**no**)		
Do you suspect the patient has or had COVID-19? Do you suspect that you have/had COVID-19?	**covid19_suspected_case**	Single choice	YES (**yes**) NO (**no**)		
Did you recommend self-isolation for the patient? Have you been recommended to self-isolate?	**covid19_self_isolation**	Single choice	YES (**yes**) NO (**no**)		

I'm self-isolated anyways:	**covid19_self_isolation_by_self_patient**	Single choice	YES (**yes**) NO (**no**)		
Isolation start date	**covid19_self_isolation_date**	Date (**YYYY-MM-DD**)			
Duration of self-isolation (in days)	**covid19_self_isolation_duration**	Number			
Was the COVID-19 case confirmed by a lab test? Have you been tested positive for COVID-19?	**covid19_confirmed_case**	Single choice	YES (**yes**) NO (**no**)		
Date of lab test confirmation	**covid19_date_lab_test**	Date (**YYYY-MM-DD**)			
What is the country in which the patients' first COVID-19 (suspicious) symptoms occurred? If the patient does not have or had any (suspicious symptoms), please select the country of residence? What is the country in which your first COVID-19 (suspicious) symptoms occurred? If you do not have or had	**covid19_country**	Single choice	COUNTRY NAME		

any (suspicious symptoms), please select your country of residence?					
Date of COVID-19 symptom onset When have you had the first COVID-19 symptoms?	**covid19_date_suspected_onset**	Date (**YYYY-MM-DD**)			

COVID-19 Severity

Title	**Variable_ID**	**Data Type**	**Options** **Label (Value)**	**Do you collect this variable?** **Y/N**	**Comments** Please elaborate on the original ID (=name of the variables) as well as the original format
Admission in Hospital because of COVID-19 (suspicious) infection?	**covid19_admission_hospital**	Single choice	YES (**yes**) NO (**no**)		
Admission date	**covid19_admission_hospital_date**	Date (**YYYY-MM-DD**)			
Discharge date	**covid19_admission_hospital_release**	Date (**YYYY-MM-DD**)			
Stay in ICU because of COVID-19 (suspicious) infection?	**covid19_icu_stay**	Single choice	YES (**yes**) NO (**no**)		

Still in ICU?	**covid19_still_icu_stay**	Single choice	YES (**yes**) NO (**no**)		
Current number of days in ICU (in days)	**covid19_icu_current_duration**	Number			
Total number of days in ICU (in days)	**covid19_icu_total_duration**	Number			
Ventilation needed during hospital stay? Have you been given assistance to breath because of COVID-19 (suspicious) infection?	**covid19_ventilation**	Single choice	YES (**yes**) NO (**no**)		
Non-invasive? (clinicians only)	**covid19_ventilation_non_invasive**	Single choice	YES (**yes**) NO (**no**)		
Invasive? (clinicians only)	**covid19_ventilation_invasive**	Single choice	YES (**yes**) NO (**no**)		
Did the patient receive ECMO because of COVID-19 (suspicious) infection? (clinicians only)	**covid19_ecmo**	Single choice	YES (**yes**) NO (**no**)		
Has the patient recovered from the (suspected) COVID-19 infection?	**covid19_outcome_recovered**	Single choice	YES (**yes**) NO (**no**) NOT APPLICABLE		

Have you recovered yet from the COVID-19?			(**not_applicable**)		
Did the patient die because of the (suspected) COVID-19 infection?	**covid19_outcome_death**	Single choice	YES (**yes**) NO (**no**)		
Date of death	**covid19_outcome_death_date**	Date (**YYYY-MM-DD**)			

Demographics

Title	**Variable_ID**	**Data Type**	**Options** **Label (Value)**	**Do you collect this variable?** **Y/N**	**Comments** Please elaborate on the original ID (=name of the variables) as well as the original format
Age (years)	**age_years**	Number			
Sex	**sex**	Single choice	MALE (**male**) FEMALE (**female**) NON-BINARY (**non-binary**)		
Currently pregnant	**pregnancy**	Single choice	YES (**yes**) NO (**no**)		
Current Smoker	**current_smoker**	Single choice	YES (**yes**) NO (**no**)		

Former Smoker	**former_smoker**	Single choice	YES (**yes**) NO (**no**)		
Height (in cm)	**height**	Number			
Weight (in kg)	**weight**	Number			
Is the patient's profession in healthcare? Are you a healthcare professional?	**is_healthcare_profession**	Single choice	YES (**yes**) NO (**no**)		

MS history and severity

Title	**Variable_ID**	**Data Type**	**Options** **Label (Value)**	**Do you collect this variable?** **Y/N**	**Comments** Please elaborate on the original ID (=name of the variables) as well as the original format
MS Type	**ms_type**	Single choice	CIS (**CIS**) RRMS (**RRMS**) SPMS (**SPMS**) PPMS (**PPMS**) Not sure (**not_sure**)		
MS onset	**ms_onset_date**	Date			

When did you have the first signs of MS?		(**YYYY-MM-DD**)			
MS diagnosis When were you formally diagnosed with MS?	**ms_diagnosis_date**	Date (**YYYY-MM-DD**)			
EDSS/PDSS					
Date of evaluation	**edss_date_diagnosis**	Date (**YYYY-MM-DD**)			
Value PDSS value	**edss_value**	Number	Values: **[0.0, 10.0]**		
LABORATORY RESULTS (clinicians only)					
Last White Blood Cell Count before COVID-19					
value	**last_white_blood_cell**	Number			
unit	**last_white_blood_cell_unit**	Text			
Last Lymphocyte Cell Count before COVID-19					
value	**last_lympho_cell**	Number			
unit	**last_lympho_cell_unit**	Text			
Last B Cell Count before COVID-19					
value	**last_b_cell**	Number			
unit	**last_b_cell_unit**	Text			

Disease-Modifying Therapy information

Title	Variable_ID	Data Type	Options Label (Value)	Do you collect this variable? Y/N	Comments Please elaborate on the original ID (=name of the variables) as well as the original format
Disease-Modifying Therapy (DMT) current usage	**current_dmt**	Single choice	YES (**yes**) NO, but was in the past (**no**) NEVER TREATED (**never_treated**)		
Type of last/current DMT What is the name of the current/last disease modifying therapy you are/were taking?	**type_dmt**	Single choice	Interferons (**interferons**) Glatiramer (**glatiramer**) Natalizumab (**natalizumab**) Fingolimod (**fingolimod**) Dimethyl fumarate (**dimethyl_fumarate**) Teriflunomide (**teriflunomide**) Alemtuzumab		**Comment** from MSDA/QMENTA: you can change the names of the DMT's, the options the patients/clinicians have in your survey. However, the labels (values in bold between brackets) should be the same in order to be able to do the import into the platform. For example, you may offer several interferon options to the user but they all are saved as "interferons" in your import file for the platform.

			(**alemtuzumab**) Ocrelizumab (**ocrelizumab**) Cladribine (**cladribine**) Siponimod (**siponimod**) Rituximab (**rituximab**)		
Other/Comment Any comments concerning the question above about your current/last disease modifying therapy	**type_dmt_other**	Text			
Start Date	**dmt_start_date**	Date (**YYYY-MM-DD**)			
Date of last dose	**dmt_end_date**	Date (**YYYY-MM-DD**)			
Stop date	**dmt_stop_date**	Date (**YYYY-MM-DD**)			
Reason for stop/discontinuation	**dmt_stop_reason**	Multiple choice	Adverse event/side effect		

			(**adverse_event**) Pregnancy (planning) (**pregnancy**) Lack of efficacy (**lack_efficacy**) Patient's decision (**patient_decision**) Onset of COVID (**onset_covid**)		
Glucocorticoid during the past 2 months Have you received a glucocorticoid in the last 2 months?	**dmt_glucocorticoid**	Single choice	YES (**yes**) NO (**no**)		
Start date	**dmt_glucocorticoid_start_date**	Date (**YYYY-MM-DD**)			
Stop date	**dmt_glucocorticoid_stop_date**	Date (**YYYY-MM-DD**)			
Dosage					
value	**dmt_glucocorticoid_dosage_value**	Number			

unit	**dmt_glucocorticoid_dosage_unit**	Text			

Comorbidities

Title	**Variable_ID**	**Data Type**	**Options** **Label (Value)**	**Do you collect this variable?** **Y/N**	**Comments** Please elaborate on the original ID (=name of the variables) as well as the original format
Comorbidities	**has_comorbidities**	Single choice	YES (**yes**) NO (**no**)		
Cardiovascular disease	**com_cardiovascular_disease**	Single choice	YES (**yes**) NO (**no**)		
Hypertension	**com_hypertension**	Single choice	YES (**yes**) NO (**no**)		
Diabetes	**com_diabetes**	Single choice	YES (**yes**) NO (**no**)		
Chronic liver disease	**com_chronic_liver_disease**	Single choice	YES (**yes**) NO (**no**)		
Chronic kidney disease	**com_chronic_kidney_disease**	Single choice	YES (**yes**) NO (**no**)		
Chronic neurological and neuromuscular disease	**com_neurological_neuromuscular**	Single choice	YES (**yes**) NO (**no**)		

Chronic lung disease	**com_lung_disease**	Single choice	YES (**yes**) NO (**no**)		
Immunodeficiency disease	**com_immunodeficiency**	Single choice	YES (**yes**) NO (**no**)		
Malignancy	**com_malignancy**	Single choice	YES (**yes**) NO (**no**)		
Other	**com_other**	Text			