COVID-19 in people with MS

Global data sharing initiative

Introduction and problem statement

We are in the middle of a global humanitarian crisis.

As the COVID-19 pandemic unfolds across the globe, the demand for data on the impact of the virus on people with Multiple Sclerosis (PwMS) grows rapidly. There is 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.

Efforts are already underway in a number of countries to start collecting data, but there are several advantages of collaborating now 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 Multiple Sclerosis International Federation (MSIF) and the Multiple Sclerosis Data Alliance (MSDA) have teamed up to set up a Global Data Sharing Initiative 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.

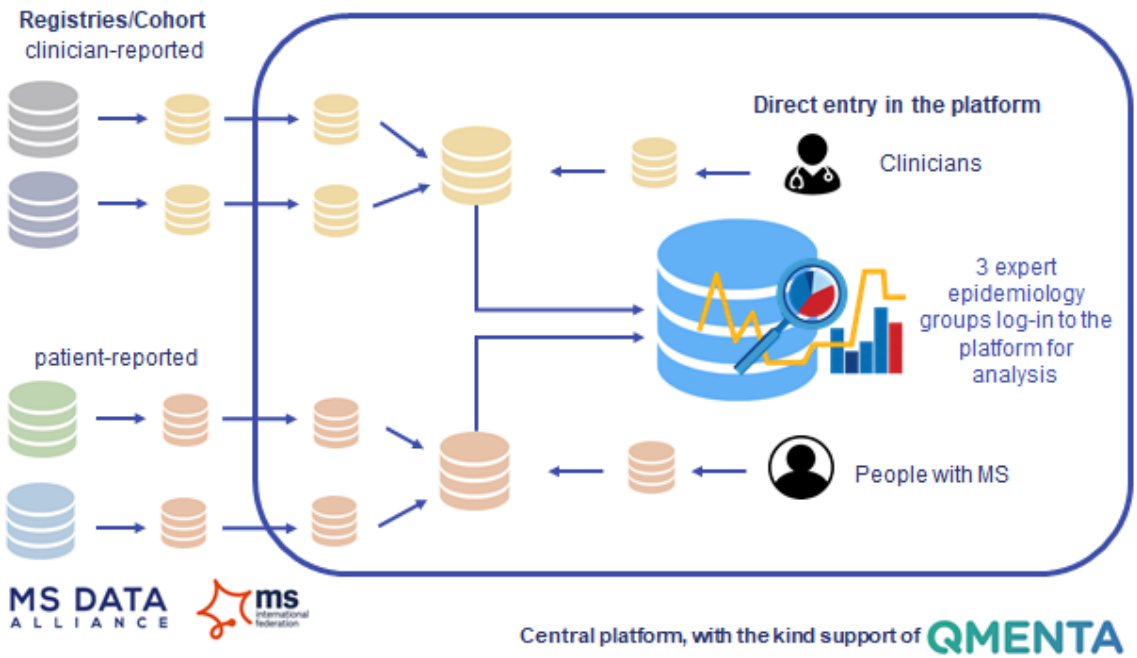
Summary approach

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 propose 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 are developing a user-friendly interface to allow a user-friendly fast module information collection

We propose the following stages.

The figure below visualizes this high-level approach:



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. This list is not exhaustive. *We invite all data custodians focusing on COVID19 and MS who want to be included to contact us (lotte.geys@uhasselt.be).*

Clinician reported data initiatives			
International MuSC-19 Case Reporting platform linked to the Italian MS Register	Open to reporting anywhere in the world	Opening week of 30th March	Link to follow
MSBase COVID-19 Substudy	Open to reporting anywhere in the world from MSBase centres	Opening week of 4th April	Link to follow
Australia and New Zealand COVID19 Data Set	Open to Australian and New Zealand neurologists	Open	Link
Swedish MS Registry COVID-19 module	Open to clinicians across Sweden	Opening week of 30th March	Link
UK MS Register COVID-19 CRF	Open to UK clinicians for laboratory confirmed COVID-19 cases only	Open	Link
German MS Register COVID-19 survey	Open to German clinicians	Opening week of 30th March	Link to follow
French COVISEP	Open to neurologists across France	Open	To submit data contact Yanica Mathieu
RelevarEM COVID-19 data set	Open to Latin American countries	Opening April 7th	Link to follow
LEOSS register for hospitalized COVID-19 patients (not MS specific)	Open to European countries only	Open	Link
Patient reported data initiatives			
iConquer MS COVID-19 survey	Open to people with MS anywhere in the world	Opening week of 30th March	Link to follow
UK MS Register COVID-19 substudy	Open to people with MS in the UK	Open now	Sign up to MS Register to take part
German MS Register COVID-19 survey	Open to people with MS in Germany	Opening week of 30th March	Link to follow

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.

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. Currently, millions of people with MS are living in self-isolation and in great fear to become infected with the virus. People with MS and their doctors have little or no information about whether medication should be adjusted, stopped or not started in first place. The validated and high-quality data collected in this global initiative can therefore be of great value, and will potentially save people's lives.
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 are 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

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 COVID19 core dataset from other registers and cohorts into the central platform.

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

1. **Create an anonymous 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 24h, every week, every month) depending on what is feasible.

2. **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.

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

CALL-TO-ACTION for Data custodians:

We are looking for pioneer registries to start preparing for the first data dump and import into the QMENTA platform. If interested, 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. 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 will be selected to form the Analysis taskforce to work on a list of predefined hypotheses and analysis plans. A small hack-a-thon will be organized between these epidemiology groups to speed-up the analysis as well as to incorporate immediate validation of the first analysis. We aim to have the taskforce assembled by 1st April 2020.

STAGE 5: FEEDING BACK THE RESULTS TO THE COMMUNITY

As soon as the first analysis results from stage 4 are considered **trustworthy** and **accurate**, the platform will become interactive. This way we aim to feed back all insights using an interactive platform, allowing the platform to become a true decision-support-tool for people with MS and clinicians during the pandemic.

We aim to have the first results ready to release by the end of April, but this will depend on the speed at which we can set up data dumps and the quality of the data.

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** (+32 496 46 69 39; 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 **Clare Walton** (Clare@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 **Jan Samyn (**+32 475 34 31 20; jan.samyn@seauton-international.com)
- For questions on the International MuSC-19 Case Reporting platform linked to the Italian MS Register - **Maria Pia Sormani** (mariapia.sormani@unige.it)
- For questions on the UK MS Register COVID-19 substudy - **Rodden Middleton** (r.m.middleton@swansea.ac.uk)
- For questions on the iConquer MS COVID-19 survey - **Hollie Schmidt** - (hollie@acceleratedcure.org)
- For questions on COVISEP in France - **Yanica Mathieu** - yanica.mathieu@icm-institute.org

This initiative is chaired by **Liesbet M. Peeters** (+32 479 78 67 27; Liesbet.peeters@uhasselt.be)

MS DATA ALLIANCE

ms international federation

APPENDIX 1: RECOMMENDATIONS COVID19 CORE DATASET

The table below summarizes our recommendations for the COVID19 core dataset.

- 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 COVID19 core dataset to be implemented in registries that use either clinician reported or patient reported data. However, sometimes we give suggestions for changes in the way variables are reported based on who reports (indicated in the column "clinician reports" and "patient reports"). The ideal solution is if clinician reported data can be linked to data reported directly by people with MS.

	Definition/Format	**Clinician reports**	**Patient reports**
COVID INCIDENCE			
Date of reporting/visit	yyyy-MM-dd		
Suspected COVID case	Yes/No		
Recommended self-Isolation	Yes/No ● *If Yes,* Start Date: yyyy-MM-dd ● *If Yes,* Duration of self-isolation (in days)	Did you recommend self-isolating?	Have you been recommended to self-isolate?
Confirmed COVID case	Yes/No ● *If Yes,* Date of lab test confirmation: yyyy-MM-dd		
Date of (suspected) COVID onset	Defined as the date the first suspicious symptom occurred: yyyy-MM-dd		
Geographical location at time of onset	Provide list of countries if possible (instead of free text)		

Symptoms	Suspicious COVID 19 symptoms: Yes/No/Unknown ● *If yes or Unknown*: Fever: Yes/No Dry Cough: Yes/No Fatigue: Yes/No Pain (joint,bone,muscle): Yes/No Sore Throat: Yes/No Shortness of breath: Yes/No Nasal congestion: Yes/No Chills: Yes/No Loss of smell or taste: Yes/No Pneumonia: Yes/No		
COVID19 Severity			
Hospital admission	Admission in hospital: Yes/No ● *If yes:* Admission date: yyyy-MM-dd ● *If yes:* Release date: yyyy-MM-dd		
Duration of stay in ICU	In ICU: Yes/No ● *If yes:* Still in ICU?: Yes/No ○ *if yes:* current number of days in ICU (in days) ○ *if no*: total number of days in ICU (in days)		
Ventilation	Ventilation necessary: Yes/No ● *If yes:* Non-invasive? Yes/No ● *If yes:* Invasive? Yes/No		Have you been given assistance to breath?
ECMO	Yes/No		
Outcome	Ongoing: Yes/No ● *If No:* Recovered: Yes/No ● *If No:* Death: Yes/No ○ *If Yes, D*ate of death: yyyy-MM-dd		
Demographics			
Age	In years		
Sex	female/male/non-binary		
Pregnancy	if female, currently pregnant: yes/no		

Smoker history	Current smoker (Yes/No) Former smoker (Yes/No)		
Height	in centimeter		
Weight	in kg		
Are you a healthcare professional?	Yes/No		
MS History and severity			
MS Type	CIS/RRMS/SPMS/PPMS		
MS Onset	= Date of first symptoms: yyyy-MM-dd		
MS Diagnosis	=Date of formal MS diagnosis: yyyy-MM-dd		
EDSS	Date of evaluation: yyyy-MM-dd Value		PDSS
Blood Data	Last White Blood Cell Count before COVID19 (number + unit) Last Lymphocyte Cell Count before COVID19 (number + unit) Last B Cell Count before COVID19 (number + unit)		
DMT information			
Current DMT	Yes/No/Never Treated		
Type of last/current DMT	Generic names (for clinicians) || brand names (for PwMS) Interferons || Betaferon, Betaseron, Extavia, Avonex, Rebif Glatiramer || Copaxone, Glatopa Natalizumab || Tysabri Fingolimod || Gilenya		

	Dimethyl fumarate || Tecfidera Teriflunomide || Aubagio Alemtuzumab || Lemtrada Ocrelizumab || Ocrevus Cladribine || Mavenclad Siponimod || Mayzent Rituximab || Mabthera, Rituxan, Rixathon, Blitzima, Ritemvia and Rituzena		
Start Date	yyyy-MM-dd	Allow yyyy-MM	Allow yyyy-MM
Date of last dose	yyyy-MM-dd		
Stop Date	yyyy-MM-dd	Allow yyyy-MM	Allow yyyy-MM
Reason for stop	We recommend the use of check boxes if possible (instead of free text) Suggestion: Adverse event/side effect; pregnancy (planning); lack of efficacy; patient's decision; onset of COVID		
Glucocorticoid during the past 2 months	Yes/No ● *If yes*: Date Start: yyyy-MM-dd ● *If yes*: Stop: yyyy-MM-dd ● *If yes:* Dosage (incl. units!)		
Comorbidities			
Comorbidities	Yes/No		
Cardiovascular disease	Yes/No		
Hypertension	Yes/No		
Diabetes	Yes/No		
Chronic liver disease	Yes/No		

Chronic kidney disease	Yes/No		
Chronic neurological and neuromuscular disease	Yes/No		
Chronic lung disease	Yes/No		
Immunodeficiency disease	Yes/No		
Malignancy	Yes/No		
Other	Free text		