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.

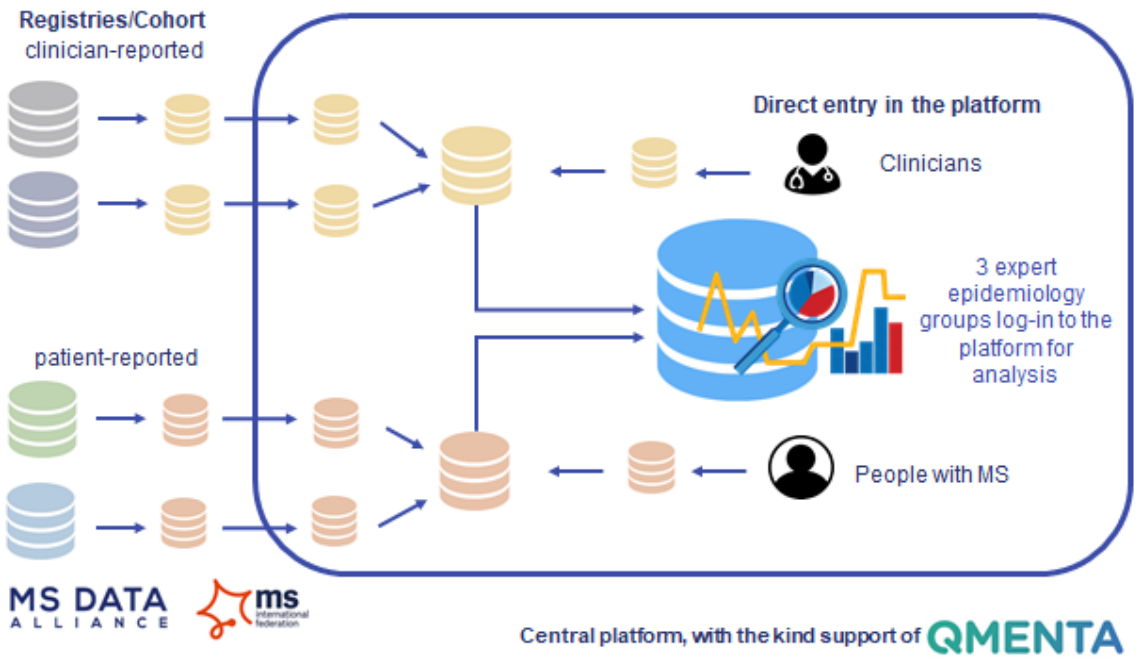
Summary approach

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. 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/).

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

Clinician reported data initiatives			
Swedish MS Registry COVID-19 module	Open to clinicians across Sweden	Open	Link
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.
COViMS Registry	Open to clinicians across North America	Open	Link
Cleveland Clinic Registry	Open to clinicians to capture data on patients of Cleveland Clinic population.	Open	
German MS Register COVID-19 survey	Open to clinicians who are already part of the registry	Open	Link
RELACONEM	Open to Latin American countries	Opening soon	Link
OptimiseMS	Open to clinicians of UK participating sites	Open	
Australia and New Zealand COVID19 Data Set	Open to Australian and New Zealand neurologists	Open	Link
MSBase COVID-19 Substudy	Open to reporting anywhere in the world from MSBase centres	Opening soon	Link to follow
UK MS Register COVID-19 CRF	Open to UK clinicians for laboratory confirmed COVID-19 cases only	Open	Link
The Spanish MS Registry	Restricted to neurologists	Open	Link is provided to all

	members of the Spanish Society of Neurology		members of the Spanish Society of Neurology by e-mail
The Danish Multiple Sclerosis Registry	Open to Danish clinicians	Open	Link
REDONE - Brazilian Registry of multiple sclerosis and neuromyelitis optica spectrum disorders	Open to clinicians of countries that use Portuguese as mother tongue	Opening soon	Link
International MuSC-19 Case Reporting platform linked to the Italian MS Register	Open to reporting anywhere in the world	Open	Link
LEOSS (Lean European Open survey on SARS-CoV-2 Infected Patients: based in Germany	Open to participating hospitals worldwide	Open	Link
Bulgarian SmartMS COVID-19 data set	Open to clinicians in Bulgaria	Opening soon	Link to follow
French COVISEP	Open to neurologists across France	Open	To submit data contact Yanica Mathieu (yanica.mathieu@icm-institute.org)
Patient reported data initiatives			
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
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
German MS Register COVID-19 survey	Open to German speaking patients from all over the world	Open	Link
Cleveland Clinic Registry	Open to PwMS already in Cleveland Clinic population	Open	
UK MS Register COVID-19 substudy	Open to people with MS in the UK	Open	Sign up to MS Register to take part
Australian MS Longitudinal Study (AMSLS)	Open to people with MS anywhere in the world, but focus on Australian people	Open	Link

	with MS		
Bulgarian SmartMS COVID-19 data set	Open to people with MS in Bulgaria	Opening soon	Link to follow
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.
ABEM - Brazilian MS Patients Association	Open to Portuguese speaking people with MS anywhere in the world	Open	Link
Esclerosis Multiple Argentina (EMA) COVID-19 survey	Open to Spanish speaking people with MS across Latin America	Open	Link
RADAR-CNS	Open to MS patients recruited for the programme	Open	More information on the programme

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. 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. **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 24h, every week, 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.

CALL-TO-ACTION for Data custodians:

We are looking for 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 was 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.

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)

This 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.

MS DATA ALLIANCE

ms international federation

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 When did you have the first signs of MS?	**ms_onset_date**	Date (**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		**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.

			fumarate (**dimethyl_fumarate**) Teriflunomide (**teriflunomide**) Alemtuzumab (**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			