Appendix: Neurology CRF Data Entry Guide

The COVID-19 Critical Care Consortium (CCCC) Neurology Sub-study aims to assess the neurologic impact of severe SARS-COV-2 infection. All patients who have been enrolled in the main ECMOCard study can be enrolled in the neurology sub-study.

Please note the following points:

1. This study is investigating *new* neurologic manifestations which occur during the development and treatment of SARS-COV-2 infection. Data should only be entered which pertains to (1) neurologic complications which manifested concurrently with COVID-19 symptoms, or (2) neurologic complications which occurred during the patient's hospital stay (the period from hospital admission to discharge/death). Previous diagnoses of neurologic conditions should only be listed in *Section 1 – Patient Information*.
2. To determine the rate of complications, all patients should be added to the neurology sub-study *regardless* of whether they had neurologic complications or manifestations.
3. For questions regarding data entry and definitions, please refer to the data entry guide in this document. If you have any questions regarding the CCCC Neurology Sub-study CRF which are not addressed in this guide, please contact one of the study investigators listed below:

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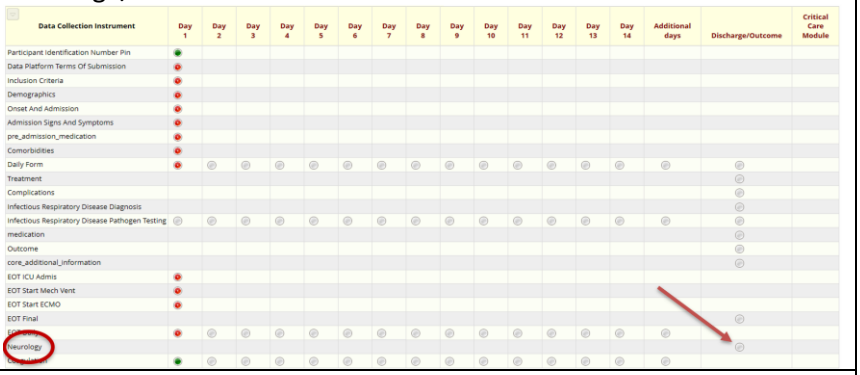
1. The neurology CRF only needs to be completed once for each patient. It is possible to enter all data retrospectively, or progressively update the form throughout the patient's clinical course.		
1.1	**ADDING AN ECMOCARD PATIENT TO THE SUB-STUDY**	To add a patient to the neurology substudy navigate to the patient's RedCap record and select the "**Neurology**" option in the Discharge/Outcome column. 
1.2	**PREVIOUS DIAGNOSIS OF CHRONIC NEUROLOGICAL DISORDER**	Only complete this section if you have selected 'yes' to chronic neurological condition on the SPRINT-SARI CRF. This section describes neurological diagnoses made *before* COVID-19 infection. New neurologic complications which have occurred concurrently with infection should be outlined in the subsequent sections. *Chronic neurodegenerative condition* includes any diseases associated with primary and progressive loss of neuronal structures or function. Common examples include: Parkinson's Disease, motor-neurone disease, cerebellar degeneration, Alzheimer's Disease, dementias, and Huntington's disease. *Previous diagnosis of psychological disorder* includes any illness defined in the DSM-5 handbook of psychiatric illness, including mood disorders. If the psychological disorder is a neurocognitive deficit due to a neurodegenerative condition such as dementia, do NOT tick this box, instead select *'Chronic neurodegenerative condition'.* Similarly, if delirium, select the *'Previous delirium'* box instead. *Previous delirium* as defined in the DSM-5 manual. *History of cerebrovascular disease* includes: ischaemic stroke, intracranial haemorrhage (including intracerebral hemorrhage, subarachnoid haemorrhage, and subdural hematoma, excluding epidural haematoma). Please also select this option if the patient has experienced a previous transient ischemic attack If any previous diagnoses for a patient do not fit into the above options, please specify in the *'Other'* option.

1.3	**PREMORBID MODIFIED RANKIN SCALE (mRS)**	The premorbid modified Rankin Scale (mRS) should be calculated based on history acquired from the patient or from close contacts of the patient. The mRS describes the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability. If the patient is not impaired by a neurological disability or previous stroke then their score is '0'. The mRS can be calculated using the following online tool: https://www.mdcalc.com/modified-rankin-scale-neurologic-disability.
2. This section describes any central nervous system (CNS) complications experienced by the patient during their COVID-19 clinical course. The central nervous system is defined as the brain and spinal cord. While the olfactory and optic nerves are often considered part of the CNS, please specify any visual, gustatory, or olfactory manifestations in Section 3 – Peripheral Nervous System Complications.		
2.1	**DIAGNOSIS OF ISCHEMIC STROKE**	Ischemic stroke is defined as cerebrovascular occlusion leading to brain infarction and subsequent ischemia. While stroke can be identified based on clinical syndrome, only select yes for this option if the diagnosis has been confirmed with imaging (CT or MRI). Select this option regardless of the severity of the stroke or the size of the infarcted brain region.
2.1a	**DATE OF DIAGNOSIS**	Please enter the date when ischemic stroke was diagnosed with imaging confirmation. Use the **DD/MM/YYYY** configuration.
2.2	**DIAGNOSIS OF INTRACRANIAL HAEMORRHAGE**	Intracranial haemorrhage includes intracerebral, subarachnoid, and subdural haemorrhage. Intracerebral haemorrhage describes bleeding within brain tissue or ventricle resulting from rupture of a cerebral blood vessel. Subarachnoid haemorrhage is caused by bleeding in the subarachnoid space. Subdural haemorrhage describes bleeding beneath the dura mater but superficial to the arachnoid. Only select yes for this option if the diagnosis was confirmed with imaging.
2.2a	**DATE OF DIAGNOSIS**	Please enter the date when intracranial haemorrhage was diagnosed with imaging confirmation. Use the **DD/MM/YYYY** configuration.
2.3	**DIAGNOSIS OF HYPOXIC ISCHAEMIC BRAIN INJURY**	Hypoxic ischemic brain injury is described as diffuse injury secondary to prolonged disruption of blood flow or tissue oxygen supply. Only select yes if diagnosis confirmed by clinical assessment of comatose state, MRI, or somatosensory evoked potential.
2.3a	**DATE OF DIAGNOSIS**	Please enter the date when hypoxic ischemic brain injury was diagnosed using any of the above criteria. Use the **DD/MM/YYYY** configuration.
2.4	**DIAGNOSIS OF MENINGITIS/ENCEPHALITIS**	Select yes for this section if the patient was diagnosed with meningitis, encephalitis, or both. Encephalitis describes infection of the brain parenchyma which is be diagnosed based on a combination of clinical and CSF criteria (https://www.ncbi.nlm.nih.gov/pubmed/23861361). Meningitis describes infection of the meninges classified based on clinical and CSF findings (https://www.aafp.org/afp/2010/1215/p1491.html).
2.4a	**DATE OF DIAGNOSIS**	Please enter the date when meningitis/encephalitis was diagnosed. Use the **DD/MM/YYYY** configuration.
2.5	**DIAGNOSIS OF TRANSVERSE MYELITIS (TM)/SPINAL CORD PATHOLOGY:**	Transverse myelitis (TM) describes inflammation of the spinal cord. Diagnosis can be based on clinical identification of spinal cord

		dysfunction, detection of active infection by lumbar puncture, or MRI identification of spinal lesions with gadolinium contrast.
2.5a	**DATE OF DIAGNOSIS**	Please enter the date when transverse myelitis/spinal cord pathology was diagnosed. Use the **DD/MM/YYYY** configuration.
2.6	**OCCURRENCE OF SEIZURE**	A seizure is defined as a sudden, uncontrolled electrical disturbance in the brain. This can manifest with generalised or focal motor convulsions, or transient non-motor deficits. Non-convulsive seizure is defined as cerebral ictal activity with no obvious clinical sign of motor activity. Select yes if the patient had at least one (1) clinically identified seizure or abnormal EEG activity consistent with seizure.
2.6a	**DATE OF DIAGNOSIS**	Please enter the date when *the first* seizure occurred. Use the **DD/MM/YYYY** configuration.
2.7	**DIAGNOSIS OF DELIRIUM**	Delirium is defined as an acutely disturbed mental status typically characterised by 4 features characterized in the DSM-5: changes from baseline cognitive function, inattention and either altered/fluctuant level of consciousness or disorganized thinking. The may included hyperactive symptoms (agitation, confusion, hallucinations), hypoactive symptoms (slowness, sleepiness) or mixed of both hyperactive and hypoactive symptoms. The screen for delirium should be determined using on the currently commonly used systematic screening tools at least once per day; either 1. Confusion Assessment Method for the ICU (CAM-ICU) (**https://www.mdcalc.com/confusion-assessment-method-icu-cam-icu**) 2. Intensive Care Unit Delirium Screening Checklist (ICDSC) definition (**https://www.lhsc.on.ca/media/8367/download**) *A paired sedation score should be used in conjunction with the delirium screening tool; the level of arousal should be a RASS (Richmond Agitiation Sedation Score) of > -3 (https://www.mdcalc.com/richmond-agitation-sedation-scale-rass#:~:text=The%20Richmond%20Agitation%20and%20Sedation,to%20patients%20with%20intracranial%20processes.)
2.7a	**DATE OF DIAGNOSIS**	Please enter the date when delirium was first diagnosed using either the CAM-ICU. ICDSC. Use the **DD/MM/YYYY** configuration.
2.8	**DIAGNOSIS OF OTHER CNS COMPLICATIONS**	Specify any other diagnoses relating to the central nervous system (brain or spinal cord) which don't fit any of the above categories.
2.8a	**DATE OF DIAGNOSIS**	Please enter the date when the other neurological condition was diagnosed. Use the **DD/MM/YYYY** configuration.
3. The peripheral nervous system (PNS) is the portion of the nervous system outside of the brain and spinal cord. Please include visual, olfactory or gustatory conditions in this section.		
3.1	**DIAGNOSIS OF GUILLAN-BARRE SYNDROME (GBS)**	Demyelinating inflammation of the peripheral nerves triggered by acute viral or bacterial infection. Clinically diagnosed based on multiple motor and sensory neurological deficits (https://www.nature.com/articles/nrneurol.2013.138). Ancillary testing, such as nerve conduction studies and CSF analysis, can aid in diagnosis.

3.1a	**DATE OF DIAGNOSIS**	Please enter the date when Guillan-Barre was diagnosed. Use the **DD/MM/YYYY** configuration.
3.2	**DIAGNOSIS OF CRITICAL ILLNESS MYOPATHY/NEUROPATHY**	Critical illness myopathy and neuropathy are overlapping syndromes describing sensorimotor deficits secondary to prolonged intensive care. These conditions are typified by symmetric, flaccid weakness, reduced deep tendon reflexes and muscle atrophy. Recommendations for diagnosis vary (https://www.ncbi.nlm.nih.gov/pubmed/21939902).
3.2a	**DATE OF DIAGNOSIS**	Please enter the date when critical illness myopathy/neuropathy was diagnosed. Use the **DD/MM/YYYY** configuration.
3.3	**HYPOGEUSIA OR HYPOSMIA**	Please indicate whether the patient has presented with any new deficits in taste or smell.
3.3a	**DATE OF DIAGNOSIS**	Please enter the date when taste/smell deficit was noted. Use the **DD/MM/YYYY** configuration.
3.4	**DIAGNOSIS OF OTHER NEUROPATHY OR MYOPATHY**	Please specify any other peripheral nervous system conditions which were diagnosed in this patient.
3.4a	**DATE OF DIAGNOSIS**	Please enter the date when other PNS complication was noted. Use the **DD/MM/YYYY** configuration.
4. Please provide further details regarding any diagnoses listed. Options will only appear when a diagnosis has been indicated in section 2 or 3.		
4.1	**TOAST STROKE CLASSIFICATION**	Classification of the stroke based on clinical syndrome, aetiology, and imaging findings. Details available at the following link: https://radiopaedia.org/articles/toast-classification-in-acute-ischemic-stroke
4.1a	**National Institutes of Health Stroke Score (NIHSS)**	If available, calculate the NIHSS for the patient: https://www.mdcalc.com/nih-stroke-scale-score-nihss
4.1b	**IMAGING CONFIRMATION OF ISCHEMIC STROKE**	Specify which imaging modality was used to confirm diagnosis of ischaemic stroke.
4.1c	**MANAGEMENT OF ISCHAEMIC STROKE**	Specify which of the management strategies were used to treat ischemic stroke.
4.2	**HEMORRHAGIC CONVERSION**	Select 'yes' to this option if the hemorrhage occurred as a complication subsequent to cerebral infarction, i.e. hemorrhagic conversion of infarct.
4.2a	**INTRACRANIAL HAEMORRHAGE CLASSIFICATION**	Select the classification(s) of intracranial haemorrhage. Intracerebral haemorrhage describes haemorrhagic stroke resulting from rupture of an intracerebral blood vessel. Subarachnoid haemorrhage is caused by bleeding between the brain and the arachnoid mater. Subdural haemorrhage describes bleeding beneath the dura mater but superficial to the pia.
4.2b	**IMAGING CONFIRMATION OF INTRACRANIAL HAEMORRHAGE**	Specify which imaging modality was used to confirm diagnosis of intracranial haemorrhage.
4.2c	**TREATMENT OF INTRACRANIAL HAEMORRHAGE**	Specify the management strategies which were used to treat intracranial haemorrhage.
4.2d	**INTRACEREBRAL HAEMORRHAGE (ICH) SCORE**	Estimate of mortality based on age and CT findings: https://www.mdcalc.com/intracerebral-hemorrhage-ich-score.
4.3	**ANCILLARY TESTING FOR HYPOXIC ISCHAEMIC BRAIN INJURY**	Select each of the modalities that were used to test for hypoxic ischemic brain injury.
4.4	**INVESTIGATIONS FOR MENINGITIS/ENCEPHALITIS**	Select each of the investigations which were used for assessing meningitis/encephalitis.

4.5	**INVESTIGATIONS FOR TRANVERSE MYELITIS/SPINAL CORD PATHOLOGY**	Select each of the relevant investigations used for investigating transverse myelitis/spinal cord pathology.
4.5a	**CLASSIFICATION OF TRANSVERSE MYELITIS/SPINAL CORD PATHOLOGY**	Acute partial transverse myelitis (APTM) describes an asymmetrical/incomplete spinal neuropathy. Acute complete transverse myelitis (ACTM) indicates symmetrical and complete spinal neuropathy. Longitudinally extensive transverse myelitis (LETM) indicates that the spinal involvement is beyond 3 vertebral body segments in length. Acute flaccid myelitis (AFM) is severe and flaccid paralysis occurring due to involvement of the spinal grey matter.
4.6	**NUMBER OF DAYS WITH SEIZURES**	Number of days where seizures occurred (if solitary seizure, then 1 day).
4.6a	**SIMULTANEOUS DRUG USE FOR DRUG SEIZURE MANAGEMENT**	Indicate which drugs were used in combination when the treatment of the seizure was most intensive.
4.7	**INVESTIGATIONS FOR GUILLAIN BARRE SYNDROME**	Specify which testing modalities were used in the assessment of Guillain-Barre syndrome.
4.7a	**TREATMENT OF GUILLAIN BARRE SYNDROME**	Specify which treatments were used for Guillain-Barre Syndrome.
4.8	**INVESTIGATIONS FOR CIM/CIN**	Specify which investigations were conducted for chronic-illness myopathy/neuropathy.
4.8a	**TREATMENT OF CIM/CIN**	Specify which treatments were used for CIM/CIN.
4.9	**WHICH COMPONENTS OF TASTE PERCEPTION ARE AFFECTED?**	Select which components of taste perception were affected. Both subjective reports from patients and formal clinical testing are acceptable.
4.9a	**OLFACTORY CHANGES**	Indicate which olfactory changes have been experienced by the patient.
5. Please indicate which imaging investigations were performed and provide de-identified PDF/Word files of the radiology reports.		
5.1	**COMPUTED TOMOGRAPHY (CT) HEAD RADIOLOGY REPORT(S) AVAILABLE**	Was a CT scan of the head performed and is the radiology report available for upload?
5.1a	**DATE OF CT HEAD**	Please enter the date when the CT head was performed. Use the **DD/MM/YYYY** configuration.
5.1b	**CT HEAD RADIOLOGY REPORT(S)**	Please upload a de-identified copy of the radiology report for the CT head.
5.2	**MAGNETIC RESONANCE IMAGING (MRI) BRAIN RADIOLOGY REPORT(S) AVAILABLE**	Was an MRI of the brain performed and is the radiology report available for upload?
5.2a	**DATE OF MRI BRAIN**	Please enter the date when the MRI brain was performed. Use the **DD/MM/YYYY** configuration.
5.2b	**MRI BRAIN REPORT(S)**	Please upload a de-identified copy of the radiology report for the MRI brain.
5.3	**MRI SPINE RADIOLOGY REPORT(S) AVAILABLE**	Was an MRI of the spine performed and is the radiology report available for upload?
5.3a	**DATE OF MRI SPINE**	Please enter the date when the MRI spine was performed. Use the **DD/MM/YYYY** configuration.
5.3b	**MRI SPINE REPORT(S)**	Please upload a de-identified copy of the radiology report for the MRI spine.

5.4	**ISCHEMIC STROKE LATERALITY**	Indicate whether the stroke was lateralised to the right or left side or if it affected both hemispheres.
6. Please complete the below details regarding serum biochemistry.		
6.1	**SERUM BIOMARKERS OF NEURONAL INJURY ASSESSED**	Please indicate if S100 calcium-binding protein B (S100B) or neuron specific enolase (NSE) were analysed in this patient.
6.1b	**MAXIMUM S100 CALCIUM BINDING PROTEIN (S100B) CONCENTRATION AND DATE OF TEST**	Specify the date when S100B was tested and the respective concentration measured in nanograms per millilitre (ng/mL).
6.1c	**MAXIMUM NEURON SPECIFIC ENOLASE (NSE) CONCENTRATION AND DATE OF TEST**	Specify the date when NSE was tested and the respective concentration measured in nanograms per millilitre (ng/mL).
7. Complete the following details regarding patient outcomes.		
7.1	**WITHDRAWAL OF LIFE-SAVING THERAPY**	Did the patient die due to withdrawal of life-saving therapy?
7.1a	**REASON FOR WITHDRAWAL OF LIFE-SAVING THERAPY**	Failure of which organ/system instigated withdrawal of life-saving therapy?
7.2	**MODIFIED RANKIN SCALE (mRS) AT ICU DISCHARGE**	The mRS should be calculated based on the patient's status at discharge, either self-reported, observed, or reported by close contact of patient. https://www.mdcalc.com/modified-rankin-scale-neurologic-disability
7.3	**MODIFIED RANKIN SCALE (mRS) AT 28 DAYS POST-DISCHARGE**	If available, please report the mRS at 28-days post-discharge. https://www.mdcalc.com/modified-rankin-scale-neurologic-disability.