

**The COVID-19 Critical Care Consortium observational study:  
Design and rationale of a prospective, international, multicenter,  
observational study**

**SUPPLEMENTAL FILES**



**SUPPLEMENT 1**

**STUDY PROTOCOL**



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# Covid-19 Critical Care Consortium Observational Study

*Incorporating the  
ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus  
Acute Respiratory Disease*



**v. 1.2.8**

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## Summary

<b>Scientific Title</b>	<b>Covid-19 Critical Care Consortium</b> <b>Incorporating the</b> ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease (ECMOCARD)
<b>Study Design</b>	Prospective/Retrospective multi-centre short period incidence observational study of patients in participating hospitals and intensive care units (ICUs) with 2019 novel coronavirus (COVID-19).
<b>The Collaborative</b>	<b>In response to the COVID-19 outbreak and to assist in pandemic planning both locally and globally, a research collaborative has been assembled.</b> The collaborative consists of investigators from the Asia-Pacific extracorporeal life support organization (APELSO) in collaboration with centres within the SPRINT-SARI and ISARIC Network. In Australia, this study will be also complemented through collaboration with the “National registry on the treatment and outcomes of patients requiring ECMO” (EXCEL Registry).
<b>Study Aim and Objectives</b>	To describe clinical features; severity of pulmonary dysfunction; incidence of ICU admission and use of mechanical ventilation, coagulatory and thrombotic derangement, and ECMO technical characteristics; duration of ECMO; complications; and survival of patients with COVID-19.
<b>Inclusions/Exclusions</b>	All patients admitted to ICU with clinical suspicion or lab-confirmed COVID-19 infection by real-time PCR and/or next-generation sequencing will be included. Patients receiving mechanical ventilation or ECMO for other concomitant causes will be excluded.
<b>Consent</b>	Given the negligible risk associated with this study and the timely nature in which the data needs to be collected, a waiver of consent is sought.
<b>Study Setting</b>	International multi-centre study, conducted in all collaborating hospitals/ICU-based research networks in Asia, Australia and New Zealand, Europe.
<b>Sample Size</b>	All patients with confirmed COVID-19 infection admitted to ICUs at the collaborative centres
<b>Study Start Date</b>	From the commencement of COVID-19 global epidemic
<b>Study Duration</b>	Until completion of COVID-19 global epidemic, as judged by the World Health Organization

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<p><b>Data collection processes</b></p>	<p>Patients will be studied from time of ICU admission until hospital discharge or up to 28 days post ICU admission, whichever occurs later. All clinical information will only be recorded if taken as part of routine clinical practice at each site. Only re-identifiable data will be submitted centrally (REDCap hosted at Oxford University for International centres and at Monash University for Australian centres). A specific ECMOCARD Case Report Form (CRF) will be used by participating sites to collect a minimum data set of ICU, mechanical ventilation and ECMO data. Data for ECMOCARD and SPRINT SARI observational study will be concomitantly collected. Data will be recorded into REDcap through standard data collection or interactive augmented human experience via digital interaction by voice or touch monitors or digital transcription of CRF hard copies. In Australia, patients concomitantly included into the EXCEL registry, EXCEL data will be requested to complement ECMOCARD data and reduce daily workload.</p>
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## Introduction

The ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute Respiratory Disease (ECMOCARD Trial) will be carried out within the network and web-based case collection forms of the ISARIC consortium's SPRINT-SARI study and in Australian and New Zealand centres, upon conclusion of the epidemics, potentially complemented through the study "A comprehensive national registry on the treatment and outcomes of patients requiring ECMO" (EXCEL Registry).

### International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)

The International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) was formed in 2011, in response to global recognition of the unmet need for timely and effective clinical research during outbreaks of emerging infectious disease with epidemic or pandemic potential. ISARIC represents a new paradigm for effective, coordinated, and timely collaborative clinical research during rapidly emerging threats to public health. It is collaboration among clinicians, clinical researchers, epidemiologists, ethicists, statisticians, laboratory-based clinicians, basic scientists, and public health experts. The mission of ISARIC is to develop operational readiness and to co-ordinate the conduct of essential clinical research to characterise and respond to new epidemic or pandemic infectious disease threats, thereby informing and guiding evidence-based optimal management. ISARIC is facilitating the coordination of SPRINT-SARI, which supports ISARIC's goal of improving the effectiveness of clinical researching globally during a pandemic by:

1. Establishing protocols, with standardised definitions and study methods, for conducting time-critical research during outbreaks of emerging infectious diseases;
2. Coordinating a large number of globally diversified hospitals and/or ICU-based networks with pre-existing ethics, administrative, regulatory and logistics in place, sufficient to implement study protocols, especially including regions where this type of clinical research has traditionally not been performed;
3. Identifying and solving barriers to pandemic research, including those identified in SPRINT-SARI;
4. Studying SARI globally, providing evidence on SARI microbiology, treatment and outcome in both resource-rich and resource-poor settings;

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5. Allowing ISARIC to evaluate its research capacity and capabilities; and
6. Assisting ISARIC to maintain network stakeholders during inter-pandemic periods.

### Short PeRIod IncideNce sTudy of Severe Acute Respiratory Infection (SPRINT-SARI)

Severe acute respiratory infection (SARI) continues to be of major relevance to public health worldwide. In the last 10 years there have been multiple SARI outbreaks around the world. The 2009 H1N1 pandemic was estimated to result in more than 200,000 respiratory deaths globally<sup>1-3</sup>. The World Health Organization (WHO) defines SARI as an acute respiratory infection of recent onset (within 10 days) requiring hospitalisation, manifested by fever ( $\geq 38^{\circ}\text{C}$ ) or a history of fever and cough<sup>4-6</sup>. There is international consensus that it is important to undertake observational studies of patients with SARI as an essential component of pandemic and epidemic research preparedness.

The primary aim of the SPRINT-SARI study was to establish a research response capability for future epidemics / pandemics through a global SARI observational study. The secondary aim of this study was to describe the clinical epidemiology and microbiology profiles of patients with SARI. The tertiary aim of this study was to assess the Ethics, Administrative, Regulatory and Logistic (EARL) barriers to conducting pandemic research on a global level. SPRINT-SARI was designed as a multi-centre, prospective, short period incidence observational study of patients in participating hospitals and intensive care units (ICUs) with SARI. The study period was planned to occur, in both Northern and Southern hemispheric winters. The study period comprised a 5 to 7-day cohort study in which patients meeting a SARI case-definition, who are newly admitted to the hospitals/ICUs at participating sites, will be included in the study. The study was planned to be conducted in 20 to 40-hospital/ ICU-based research networks globally. All clinical information and sample data were planned to only be recorded if taken as part of the routine clinical practice at each site and only fully anonymised and re-identifiable data will be submitted centrally. The primary outcome of SPRINT-SARI was to test the feasibility of conducting a global study of SARI.

#### Secondary Outcomes:

1. Incidence of SARI
2. Disease severity and risk factors for severe disease due to SARI
3. Case Fatality Proportion of SARI
4. Duration of ICU/hospital stay due to SARI

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5. Microbiology of SARI, including variability in testing
6. Treatments received during hospitalization for SARI
7. Evaluate impact on incidence of alternative case-definitions of SARI
8. Evaluate the operational characteristics of this study, including CRF, Completion Guidelines, and entry criteria to provide information by which iterative improvement in study design can be achieved.
9. Explore the feasibility of extrapolation of results obtained at participating sites to population levels

### Coronaviruses

Coronaviruses are a family of enveloped, single-stranded, positive-strand RNA viruses classified within the Nidovirales. Coronaviruses may infect mammals and birds, triggering respiratory, enteric, hepatic, and neurologic diseases<sup>7</sup>. Six coronavirus species are known to cause human disease. The coronaviruses 229E, OC43, NL63, and HKU1 are prevalent worldwide and most commonly cause only marginal respiratory symptoms. Two other strains, the severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have originated from animal to human transmission and have caused more serious, sometimes fatal, respiratory illnesses. In previous years, SARS-CoV<sup>8,9</sup> and MERS-CoV<sup>10,11</sup>, have caused serious respiratory infections, with mortality rates of 10% for SARS-CoV<sup>12</sup> and 37% for MERS-CoV<sup>13</sup>.

### 2019 Novel Coronavirus (COVID-19)

In late December, 2019, in Wuhan, Hubei, China, a new respiratory syndrome emerged with clinical signs resembling viral pneumonia and person-to-person transmission<sup>14</sup>. Prompt diagnostic methods, through deep sequencing analysis from lower respiratory tract samples, corroborated emergence of a novel coronavirus, namely the 2019 novel coronavirus (COVID-19). In particular, Na Zhu and collaborators<sup>15</sup> were able to isolate the virus from bronchoalveolar lavage (BAL) from patients with pneumonia of unknown cause, who were in Wuhan on December 21, 2019 or later, and who had been present at the Huanan Seafood Market. RNA extracted from BAL fluid from the patients was used as a template to clone and sequence a genome using a combination of Illumina sequencing and nanopore sequencing. More than 20,000 viral reads from individual specimens were obtained, and most contigs



matched to the genome from lineage B of the genus betacoronavirus — showing more than 85% identity with a bat SARS-like CoV (bat-SL-CoVZC45, MG772933.1) genome. Virus isolation from the clinical specimens was performed with human airway epithelial cells and Vero E6 and Huh-7 cell lines. 2019-nCoV–infected human airway epithelial cultures were examined with light microscopy and with transmission electron microscopy 6 days after inoculation. Cytopathic effects were observed 96 hours after inoculation on surface layers of human airway epithelial cells and lack of cilium beating was seen with light microscopy (Fig. 1).

**Figure 1**

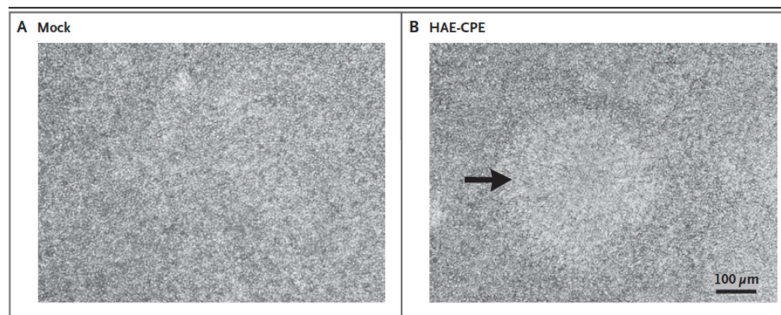


Figure 1: Cytopathic effect of the novel coronavirus, as reported in previous publication<sup>15</sup>

Through transmission electron microscopy, the authors were able to image the COVID-19 particles, that generally appeared spherical, of 60 to 140 nm, with some pleomorphism and distinctive spikes, about 9 to 12 nm (Fig. 3), and gave virions the appearance of a solar corona. This morphology corroborated the Coronaviridae family.

**Figure 2**

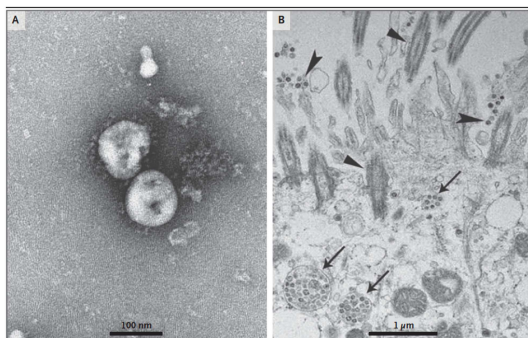


Figure 2: A: COVID-19 particles are depicted. B: COVID-19 in human airway epithelium, as reported in previous publication<sup>15</sup>.

Finally, investigators carried out inclusive phylogenetic analysis that showed that COVID-19 falls into the genus betacoronavirus, which includes coronaviruses as SARS-CoV, bat SARS-like CoV, and others from humans, bats, and other wild animals.

Thus far, more than 111,000 confirmed cases, including health-care workers, have been identified worldwide, and several exported cases have been confirmed in other provinces in China, Thailand<sup>16</sup>, Japan<sup>17</sup>, South Korea<sup>18</sup>, Germany, Italy<sup>19</sup>, France, Iran<sup>20</sup>, USA<sup>21</sup> and many other countries<sup>22</sup>. An early case report in 41 patients with laboratory-confirmed COVID-19 infection in Wuhan has been reported<sup>23</sup>. The median age of the patients was 49 years and mostly men (73%). Among those, 32% were admitted to the ICU because they required high-flow nasal cannula or higher-level oxygen support measures to correct hypoxaemia. Less than half had underlying diseases, including diabetes (20%), hypertension (15%), and cardiovascular diseases (15%). On admission, 98% of the patients had bilateral multiple lobular and subsegmental areas of consolidation (Figure 3)<sup>24</sup>.

**Figure 3**

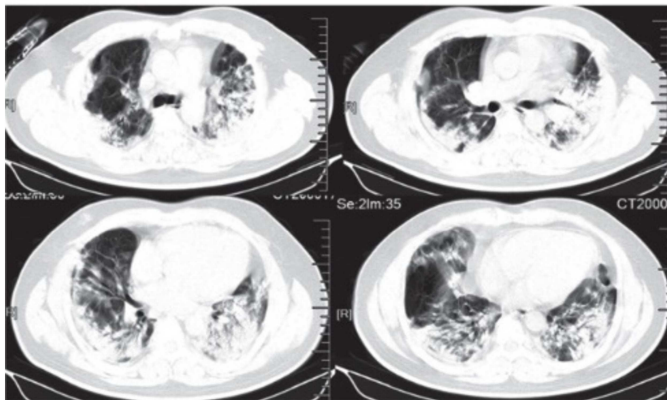


Figure 3 Caption: Transverse chest CT images from a 40-year-old man showing bilateral multiple lobular and subsegmental areas of consolidation on day 15 after symptom onset. Transverse chest CT images from a 53-year-old woman showing bilateral ground-glass opacity and subsegmental areas of consolidation on day 8 after symptom onset, adapted from<sup>23</sup>

Importantly, acute respiratory distress syndrome (ARDS) developed in 29% of the patients, while acute cardiac injury in 12%, and secondary infection in 10%. Invasive mechanical ventilation was required in 10% of those patients, **and two of them (5%) had refractory hypoxaemia and received extracorporeal membrane oxygenation (ECMO).**



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In a later retrospective report by Wang and collaborators<sup>25</sup>, clinical characteristics of 138 patients with COVID-19 infection were described. Those patients were admitted at Zhongnan Hospital of Wuhan University in Wuhan, China, from January 1 to January 28, 2020. The median age was 56 years and clinical signs of the infection comprised fever (98.6%), fatigue (69.6%), and dry cough (59.4%). Interestingly, lymphopenia occurred in 70.3% of the patients, prolonged prothrombin time 58%, and elevated lactate dehydrogenase 39.9%. ICU admission was required in 26.1% of the patients for acute respiratory distress syndrome (61.1%), arrhythmia (44.4%), and shock (30.6%). Among these patients, 11.1% received high-flow oxygen therapy, 41.7% noninvasive ventilation, and 47.2% invasive ventilation. ***ECMO support was needed in 11% of the patients admitted to the ICU.*** During the period of follow-up, overall mortality was 4.3%.

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## Objectives

### Hypothesis

We hypothesize that a significant percentage of patients with COVID-19 infection will require admission to the intensive care unit, mechanical ventilation and ECMO for refractory hypoxemia, in addition a substantial proportion of patients will present coagulation disorders and thrombosis.

### Aims

This is a multi-centre international study in patients with suspected or confirmed COVID-19 who require admission to the intensive care unit, mechanical ventilation and/or ECMO to characterize the following features:

1. Incidence of ICU admission, use of mechanical ventilation and ECMO
2. Risk factors
3. Clinical features
4. Coagulation disorders and thrombosis
5. Severity of respiratory failure
6. Need for non-invasive and invasive mechanical ventilation and ECMO
7. Settings of invasive mechanical ventilation
8. ECMO technical characteristics
9. Duration of ECMO
10. Complications
11. ICU survival
12. Hospital survival.
13. Requirements and the time frame for approvals in each participating network region

## Materials and Methods

### Study Design

This is an international multi-centre, prospective/retrospective observational study of patients in participating hospitals and ICUs with suspected or confirmed COVID-19 infection. The study will be conducted at 20 to 90 hospital networks globally and will aim to recruit as many patients as possible. The aim is to recruit all eligible patients at each study location and

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there is no maximum number of patients that can be recruited from any one site. Patients will be studied from time of ICU admission up to 28 days or until hospital discharge, whichever occurs later. Information will be collected on demographics, co-existing illnesses, severity of illness, source and type of clinical specimens (upper versus lower respiratory tract and collection date), results of microbiological tests. ECMOCARD will specifically focus on collecting data of mechanical ventilation and ECMO and administration of other major therapies (including vasoactive therapies, hypoxaemia rescue therapies, and dialysis), administration of antibiotics and antivirals (and adjunctive therapies, e.g. immunomodulators, corticosteroids) and outcomes at ICU (if applicable), hospital discharge and 28 days.

### Research centres

This is a collaborative effort among investigators of the Asia-Pacific extracorporeal life support organization (APELISO) in collaboration with centres within the SPRINT-SARI and ISARIC Network.

### Study Population

We plan to recruit as many patients as possible of the patients with COVID-19 infection admitted to the ICU, in as many locations as possible, who meet the inclusion criteria with no-exclusion criteria at the participating sites. It is anticipated that each participating Institution could contribute between 5 and 50 patients. Each site's recruitment will be determined by the incidence of the disease during the study period, and their ability to collect the required data.

### Inclusion Criteria

1. Clinical suspicion or laboratory-confirmed COVID-19 infection by real-time PCR and/or next-generation sequencing
2. Admission to an intensive care unit

### Exclusion Criteria

3. Patients treated with mechanical ventilation for other concomitant causes
4. Patients treated with ECMO for other concomitant causes

### Co-enrolment

This is an observational study. Co-enrolment with other studies including interventional clinical trials is accepted.

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## Ethics

### Guiding Principles

The Chief Investigators and study management team are responsible for ensuring the study is performed in accordance with the protocol. This study is to be performed in accordance with the ethical principles of the Declaration of Helsinki (June 1964, most recently amended in October 2013), and the most recent, relevant ethical conduct of research guidelines published in the country of the participating site. The Principal Investigator at each site is responsible for maintenance of a securely held enrolment log linking the patient hospital record number and the study number as per their countries research guidelines.

### Comply with all local requirements

National or regional Co-ordinators in their defined location will be responsible for clarifying the requirements for ethics approval. It is the responsibility of the site Chief Investigator and Research Co-ordinator to ensure ethics approval has been granted prior to commencing the study and all local requirements are addressed. Each participating site will require ethics approval for this protocol and data collection of the ECMOCARD and ISARIC SPRINT-SARI CRF (RAPID, CORE, SUPPLEMENTARY TO CORE, DAILY and EPIDEMIOLOGY) and any other study documents relevant to their region. When possible, each participating study site will be supported by the ECMOCARD, Project Officer with their application. The Principal Investigator will produce progress reports, and any other required documentation for the local independent Ethics Committee in accordance with their guidelines. It is the responsibility of the Chief Investigator at each participating hospital to keep an up to date record of all correspondence and applicable documentation with the local Independent Ethics Committee. We will be collecting data on the requirements and the time frame for approvals in each participating network region.

### Confidentiality of patient data

No identifying data will be entered into the central database. Participants' names will not be collected, and confidentiality of information in medical records will be preserved. The confidentiality of the participant will be maintained unless disclosure is to comply with the law. To adhere to international ethical review board requirements and facilitate global ECMOCARD and SPRINT-SARI ISARIC data polling/sharing the CLiRes Data Management



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System will convert all dates entered (DD/MM/YYYY) into the eCRF into a re-identifiable format (D1, D2) at a system level. The original entered data (DD/MM/YYYY) will only be accessible by the site Research Co-ordinator and the site Principal Investigator using their unique database account details. ***In Australia, re-identifiable data will be entered into a central REDCap database hosted by Monash University and harmonised with the SPRINT-SARI study.***

#### Rule of Transfer

It is proposed that if a patient is transferred from a facility participating in ECMOCARD and SPRINT-SARI to another facility that is also participating, the patient's previously allocated patient ID number will be documented in the CRF completed by the receiving hospital at time of admission. All sites participating in SPRINT-SARI will be asked to include a ECMOCARD and SPRINT-SARI study information sheet in the patients transferring documents, notifying the new hospital of the patient's inclusion in ECMOCARD and SPRINT-SARI, the patients re-identifiable participation number, the contact details of the Principle Investigator of ECMOCARD and SPRINT-SARI in the country and the ECMOCARD and SPRINT-SARI coordinating centre. If you are unsure if a patient has previously been enrolled in ECMOCARD and SPRINT-SARI please check to see if the patients transferring hospital and ward/unit are included in the participating sites list on the ECMOCARD and SPRINT-SARI website ([www.sprintsari.org](http://www.sprintsari.org)). Please use the patients existing ECMOCARD and SPRINT-SARI participant number at the new hospital when entering data into the paper and/or eCRF. Sites will not have access to any data collected outside their hospital; it is the responsibility of each hospital to enter data pertaining to their component of the patient's hospital admission. If a patient is transferred to a non-participating hospital, there will be no further data collection.

#### International waiver of informed consent

It is expected that this study will not require individual patient consent. This study is in effect a large-scale clinical audit, as all data is already recorded as part of routine clinical care, therefore justifying participant enrolment using a waiver of consent. Waiver of consent may be available for studies that submit only re-identifiable information and where involvement in the research carries no more than low risk. Any location that deems individual consent necessary can use potential forms reported in the Appendix A. In particular, only in

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patients who meet the inclusion/exclusion criteria, informed consent will be obtained directly from the patient, either before the study or retrospectively in case the patient is unconscious at the time of enrolment. If the patient is unable to provide a consent form upon admission, informed consent will be obtained by his/her next of kin.

### Informed Consent in Australia

In Australia all patients admitted to the ICU and meeting all inclusion and no exclusion criteria will be included in ECMOCARD observational study. Their hospital data will be included under a waiver of consent, in line with the National Statement (chapter 2.3) and the NHMRC *Ethical Considerations in Quality Assurance and Evaluation Activities, 2014*.

Data for ECMOCARD and SPRINT SARI observational study will be concomitantly collected. In addition, to minimise workload for site staff, whenever possible, EXCEL data will be requested to complement ECMOCARD data. SPRINT-SARI and EXCEL have both been approved to recruit patients under a waiver of consent. Yet, it is important to emphasize that ethics approval certificate for Project 202/16 has the following special condition: "A waiver of the requirement for consent was granted for the collection and use of identifiable information during relevant epidemics and pandemics. An opt-out approach will be used at all other times."

## Data Collection

### ISARIC Data Collection

As detailed in following paragraphs, we will collect data prospectively or retrospectively on patient demographics including age, sex, height, weight, and ethnicity, as well as the presence of predefined comorbidities. **General data will be collected from each site using the SPRINT-SARI data tool, namely the WHO and ISARIC NOVEL CORONAVIRUS (nCoV) ACUTE RESPIRATORY INFECTION CLINICAL CHARACTERISATION (<https://isaric.tghn.org/novel-coronavirus/>)**. As shown in figure 4, SPRINT-SARI data collection will start upon admission to the Hospital. The CRF was assembled by ISARIC members on the basis of the WHO natural history protocol, INFINITE (ANZICS), MOSAIC and others<sup>5,26</sup>. The CRF was assembled to be a basic CRF with the aims of avoiding data duplication, and with the intention of being user friendly and applicable in all settings, regardless of the resources available<sup>27</sup>. The CRF has previously been used in Singapore, New



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Zealand, Saudi Arabia, Vietnam, and North America and adapted by a working group for the purposes of this study with ISARIC approval to all changes made. In 2020, with the emergence of the COVID-19 epidemics, the ISARIC CRF eCRF were modified in order to characterize patients with this infection. In addition, Chief Investigators of the ECMOCARD trial further improved the ISARIC CRF eCRF to specifically describe COVID-19 patients admitted to the ICU and undergoing mechanical ventilation and ECMO.

### ECMOCARD Data Collection

Streamlined data-collection instruments and procedures will be used in an attempt to minimise the work in study centres. Specifically, we will collect data on the timing of ICU admission, endotracheal intubation, mechanical ventilation and ECMO commencement in relation to presumed onset of symptoms and hospital admission. We will investigate whether invasive mechanical ventilation and ECMO treatment was commenced in the participating hospital or whether the patient was retrieved and transferred while receiving invasive mechanical ventilation and/or ECMO from a referral centre. Severity of illness before endotracheal intubation and before ECMO will be investigated by respiratory rate, severity of hypoxemia, hypercapnia, non-pulmonary vital organ support, ventilator settings, and use of rescue ARDS therapies in the 12 hours before ECMO commencement. Dynamics of invasive mechanical ventilation and ECMO treatment will be recorded and characterized from commencement of invasive mechanical ventilation up to discontinuation (Figure 4). We will also collect administration of antiviral and antibiotic medications. Finally, duration of mechanical ventilation, ECMO, ICU and hospital stay, ICU and hospital mortality will be documented. In patients who died during hospital admission, we characterized the mode of death from a list of predefined options. ***Of note, In Australian centres, patients enrolled into the study “A comprehensive national registry on the treatment and outcomes of patients requiring ECMO) (EXCEL Study) will be identified by the ECMOCARD eCRF. Likewise, in the EXCEL study eCRF, a specific question will be added to identify patients enrolled in the ECMOCARD. Thus, we will complement ECMOCARD CRF with data collected through the EXCEL study.***

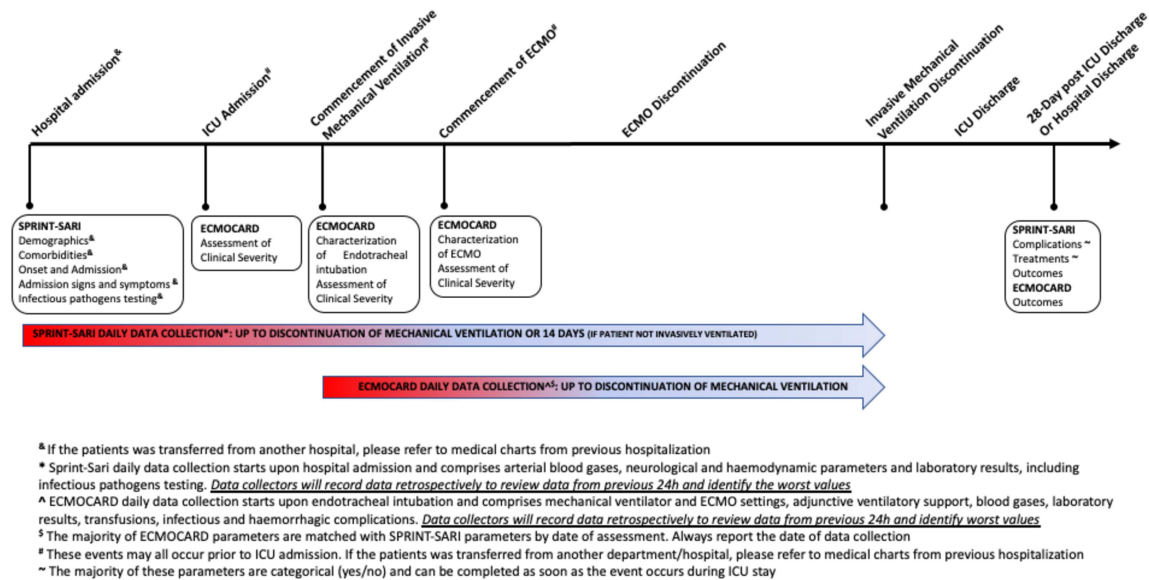
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Figure 4



**Figure 4 Caption:** Follow-up schedule and assessments. ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation.

### Coagulation Disorders and Thrombosis Sub-study Data Collection

In collaborative centres that routinely perform rotational thromboelastometry (ROTEM) or thromboelastography (TEG) in their clinical practice, we will carry out an additional observational sub-study to appraise coagulation disorders and/or pro-thrombotic risks in COVID-19 patients in the ICU. As detailed in following paragraphs, upon admission to ICU, and every 24 hours thereafter, we will collect data prospectively or retrospectively on coagulation disorders and pro-thrombotic risks until discontinuation of mechanical ventilation or in case of patients who are not mechanically ventilated, until 7 days post-ICU discharge. In addition, in centres that routinely use ROTEM, within 1h from a clinically relevant thrombosis/embolism or bleeding event, and 6h prior to commencement of ECMO, we will perform an additional ROTEM assessment to record TRAPTEM AUC, A6 and MS parameters. **Data for the Coagulation Disorders and Thrombosis Sub-study will be collected**

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*from each collaborating site using the dedicated REDcap CRF, hosted at the University of Queensland.*

#### Data collection methods

Each site will have the option to collect data via Option 1 alone **OR** Option 1 +2. The method chosen will be a decision made at a site level. The options for data collection are as follows:

#### **OPTION 1: Standard Data Collection**

Both the SPRINT-SARI ISARIC and ECMOCARD CRF will be made available at all participating sites as a paper CRF. The SPRINT-SARI ISARIC and ECMOCARD CRFs will be available in a variety of languages and will be translated into languages appropriate for all participating sites. The translation of the paper and electronic CRFs from English into the required language will be the responsibility of the national lead investigators and collaborators of the Critical Care Research group and checked for consistency by an appropriate investigator in the relevant country. All data will be collected by trained staff at each study site and these individuals will enter all required data described in the protocol into the CRFs directly from the source data. Trained staff at sites with the IT capabilities can enter all required data directly into the protected online database, known as the eCRF; paper CRFs are the alternative option for direct data entry with subsequent transcription, upon completion, into the eCRF. Information recorded in the CRF should accurately reflect the participants' medical/hospital notes. The Research Coordinator or Site Investigator will have the ability to choose the process they use to enter data into the eCRF, where data may be entered at one time or intermittently. If used, the original paper based CRF will be stored within a locked office in each study site. The intent of this process is to improve the quality of the clinical study by providing prompt feedback to the Investigators on the progress of the submitted data and to enhance the ability to collect early safety information in a more timely fashion to fully comply with the intent of GCP requirements. ***Data from International countries will be entered into an online eCRF database managed by the Oxford University Clinical Research Unit, Vietnam (OUCRU) for the SPRINT-SARI ISARIC and ECMOCARD tiers. Data from Australia will be entered into an online eCRF database managed by Monash University, and will be complemented with data from SPRINT SARI observational study (ALFRED HREC Reference 202/16) and EXCEL (ALFRED HREC Reference 534/18)).*** In Countries unable to upload data on a centralised database the right to retain a local database on a

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national server is available with aggregated completely anonymised data exported centrally for analysis. Each site will be identified via a 3-digit network code, a 3-digit site code, and each patient will be assigned a 4-digit sequential patient code making up the patient ID number at time of originally enrolment in SPRINT- SARI. The site-code will be specified as to whether it is an ICU, hospital ward, or other facility. The site code is obtained by registering on the eCRF, data management system. Patient numbers should be assigned sequentially for each site beginning with 0001. In the case of a single site recruiting patients on different wards, or where it is otherwise difficult to assign sequential numbers, it is acceptable to assign numbers in blocks. Alpha characters can also be used (e.g. Intensive Care Unit will assign A001 onwards, in-patient ward will assign B001 onwards). ***The full patient identification number will therefore be a 10-digit number, with the format of the following: network code - site code – individual patient code [ ][ ][ ]-[ ][ ][ ]-[ ][ ][ ][ ](eg. 001-012-0001).*** ***The register of patient names and study numbers will not leave the participating hospital. Access to the data entry system will be protected by username and password.*** Username and password will be assigned during the registration process for individual Research Coordinators or Site Investigators. All electronic data transfer between study site and database will be username and password protected. Each centre will maintain a trial file including a protocol, ethics approval documentation, and paper CRFs. A participant list will be used in each study site to match identifier codes in the database to individual patients in order to record clinical outcomes and supply any missing data points. The Participant List is maintained locally and is not to be transferred to any other location. The Research Coordinator will compile an enrolment log including the patient's name, age, hospital identification number and unique study number. Subsequent data will be identified by the unique study number only. The enrolment log and study data will be kept separately.

## OPTION 2: Interactive augmented data collection

We will use platforms and solutions provided by Amazon to collect data and transfer data into the REDcap web application. Data will be collected through 1) voice commands; 2) digital video monitor interface and 3) through digital transcription of parameters collected via SPRINT-SARI/ECMOCARD paper CRFs. Similar to option 1, only de-identified information will be collected, encrypted and transferred directly to the REDCAP database. No data or

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information of any kind will be directed elsewhere. Amazon Web Services will not have any direct interaction with the enhanced user-interface once it is implemented and will only act in an external consultancy capacity. Data will be fully encrypted from data ingestion into Amazon cloud, up to de-encryption into the REDcap web application. Thus Amazon platform will only channel, without being able to codify, data from hospitals into the REDcap system.

#### Data collection methods (Coagulation Disorders and Thrombosis sub-study)

As for the Coagulation Disorders and Thrombosis Sub-study, the CRF will be made available at all collaborating sites as a paper CRF. The Coagulation Disorders and Thrombosis Sub-study CRF will be only available in English. Data will be collected by trained staff at each study site and these individuals will enter all required data described in the protocol into the CRFs directly from laboratory results, ROTEM or TEG reports. Trained staff at sites with the IT capabilities can enter all required data directly into the protected online database hosted at UQ, known as the eCRF; paper CRFs are the alternative option for direct data entry with subsequent transcription, upon completion, into the eCRF. Information recorded in the CRF should accurately reflect the participants' laboratory results, ROTEM or TEG reports. The Research Coordinator or Site Investigator will have the ability to choose the process they use to enter data into the eCRF, where data may be entered at one time or intermittently. If used, the original paper based CRF will be stored within a locked office in each study site. The intent of this process is to improve the quality of the clinical study by providing prompt feedback to the Investigators on the progress of the submitted data and to enhance the ability to collect early safety information in a more timely fashion to fully comply with the intent of GCP requirements. **Data will be entered into an online eCRF database managed by the University of Queensland.** In Countries unable to upload data on a centralised database the right to retain a local database on a national server is available with aggregated completely anonymised data exported centrally for analysis. **The full patient SPRINT-SARI/ECMOCARD identification number will be recorded to match results of the Coagulation Disorders and Thrombosis Sub-study with SPRINT-SARI/ECMOCARD records. The register of patient names and study numbers will not leave the participating hospital. Access to the data entry system will be protected by username and password.** Username and password will be assigned by the University of Queensland during the registration process for individual Research Coordinators or Site Investigators. All electronic data transfer between study site and

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database will be username and password protected. The Participant List of the Coagulation Disorders and Thrombosis Sub-study is maintained locally and is not to be transferred to any other location.

### Screening log

No screening log will be maintained.

### Data quality

Several procedures to ensure data quality and protocol standardisation will help to minimise bias. These include:

1. Online meetings for all research coordinators will be held to ensure consistency in procedures;
2. A detailed data dictionary will define the data to be collected on the case report form;
3. Quality checks will be built into the data management system and there will be quality checks of critical data points entered into the CRFs to ensure standardization and validity of the data collected;

An achievable data set will be fundamental to the success of the study. We have identified the key data points whilst not discouraging centres from participating through an excessive burden of data collection. Data queries may be generated, depending on resource availability. Any information that is not available for the investigator will not be considered as missing. No assumptions will be made for missing data.

### Data management

Data entry and data management will be coordinated by ISARIC and ECMOCARD steering committee, including programming and data management support. On behalf of the management committee, ANZIC-RC and ISARIC will act as custodian of the data. The University of Queensland will receive data from the data custodians via data sharing agreements. The management committee of the trial will take responsibility for the content and integrity of any data. There will be periodic assessments of data burden to ensure that the infrastructure is organized to handle large amounts of incoming data in small time periods. SPRINT-SARI and ECMOCARD will adhere to the research and data sharing policies of ISARIC, Sample and Data Sharing Policy, Version 4, 21 July 2014. ***Clinical investigators contributing to the research efforts will be given full recognition for their efforts and will be***

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**given the opportunity to access data. Ownership of any data transferred to the eCRF will be retained by the site that contributed it.** Networks will retain the right to request raw data for all sites included in their network for research purposes, provided that the research proposal has been reviewed and approved by the management committee, ISARIC and ECMOCARD following publication of the primary manuscript. All analysis of pooled data will be undertaken with the explicit agreement of each site who contributed. ISARIC and ECMOCARD will retain the right to use all pooled data for scientific and other purposes. All members of the study group will have the right to access the pooled data for research purposes provided the research proposal has been reviewed and deemed satisfactory by the management committee following publication of the primary manuscript. Only summary data will be presented publicly. Individual patient data provided by participating sites will remain the property of the respective institution. Of note, a data management plan will be developed to address researchers' intentions related to generation, collection, access, use, analysis, disclosure, storage, retention, disposal, sharing and re-use of data and information, the risks associated with these activities and any strategies for minimising those risks.

### Monitoring

Data monitoring will be conducted on a randomly selected subset (up to 5%) of cases, through discussion with the local site investigator to discuss data collection techniques. Direct site visits will not be feasible, given the scope of the study.

### Collected Parameters

The following parameters will be assessed and recorded based on the follow-up schedule and assessments reported in Figure 4. All the mandatory variables to be assessed are highlighted in red:

#### Demographics and Medical History

1. Personal Data
2. Medical History and comorbidities, including type of anti-hypertensive medications
3. Smoking habits
4. Chronic alcohol abuse
5. Intravenous drug abuse
6. Immuno-competency status

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#### COVID-19 infection

1. Date of first signs of infection
2. Date of hospital admission
3. Date of ICU admission
4. Date of invasive mechanical ventilation
5. Blood gases before commencement of invasive mechanical ventilation
6. Use of continuous renal replacement therapy before commencement of invasive mechanical ventilation
7. Use of vasoactive drugs before commencement of invasive mechanical ventilation
8. Use of cardiac-assist devices before commencement of invasive mechanical ventilation
9. Acute physiology and chronic health evaluation (APACHE II) score upon ICU admission
10. Use of anti-viral treatment
11. Use of antibiotics
12. Cutaneous manifestations

#### Clinical parameters upon commencement of invasive mechanical ventilation

1. Date of invasive mechanical ventilation commencement
2. Use of prone position
3. Use of neuromuscular blockade
4. Use of recruitment manoeuvres
5. Use of inhaled nitric oxide
6. Use of bicarbonate
7. Blood gases
8. Ventilatory mode
9. Inspiratory fraction of oxygen
10. Respiratory rate
11. Tidal volume (ml/Kg of ideal body weight)
12. Positive end-expiratory pressure
13. Airway plateau pressure

#### Daily assessment of clinical parameters during invasive mechanical ventilation

1. Date of assessment

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2. Use of prone position
3. Use of neuromuscular blockade
4. Use of recruitment manoeuvres
5. Use of inhaled nitric oxide
6. Blood gases
7. Ventilatory mode
8. Inspiratory fraction of oxygen
9. Respiratory rate
10. Tidal volume (ml/Kg of ideal body weight)
11. Positive end-expiratory pressure
12. Airway plateau pressure
13. Haemoglobin
14. White blood cells
15. AST
16. ALT
17. Lactate
18. Creatinine
19. Ferritin
20. D-dimer
21. Troponins
22. BNP
23. Use of continuous renal replacement therapy
24. Use of vasoactive drugs
25. Use of anticoagulants
26. Transfused blood products
27. Infectious complications
28. Haemorrhagic complications

#### Clinical features before commencement of ECMO

1. Date of ECMO commencement
2. Use of prone position
3. Use of neuromuscular blockade

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4. Use of recruitment manoeuvres
5. Use of inhaled nitric oxide
6. Use of bicarbonate
7. Blood gases
8. Ventilatory mode
9. Inspiratory fraction of oxygen
10. Respiratory rate
11. Tidal volume (ml/Kg of ideal body weight)
12. Positive end-expiratory pressure
13. Airway plateau pressure

#### ECMO characteristics

1. Type and manufacturer of centrifugal blood pump driven circuit
2. Type and manufacturer of low-resistance oxygenator
3. Type of ECMO: venous-venous or venous-arterial
4. Peripheral access: femoral, jugular, both
5. ECMO blood flow rate day 0, and every 24 hours thereafter
6. ECMO gas flow rate day 0, and every 24 hours thereafter
7. Anticoagulation during ECMO
8. Frequency of ECMO circuit change
9. Ventilatory settings on ECMO
10. Vasoactive support on ECMO
11. Organ dysfunctions on ECMO

#### ECMO adverse effects

1. Transfused blood during ECMO
2. Transfused plasma during ECMO
3. Transfused platelets during ECMO
4. Transfused cryoprecipitates during ECMO
5. Type and source of infectious complications
6. Type and source of haemorrhagic complications
7. Other complications

#### ECMO adverse effects

1. Transfused blood during ECMO
2. Transfused plasma during ECMO
3. Transfused platelets during ECMO
4. Transfused cryoprecipitates during ECMO
5. Type and source of infectious complications
6. Type and source of haemorrhagic complications
7. Other complications

#### Daily assessments for Coagulation Disorders and Thrombosis Sub-study

1. SPRINT-SARI/ECMOCARD patient number
2. Date of assessment
3. Lactate dehydrogenase
4. Ferritin
5. D-dimer
6. Fibrinogen
7. Activated clotting time
8. Activated partial thromboplastin time
9. International normalised ration
10. Plasma free haemoglobin
11. ROTEM parameters (EXTEM, FIBTEM, INTEM, HEPTEM, TRAPTEM, NATEM if patients undergoing treatment with low molecular weight heparin and ECATEM if patients undergoing treatment with direct thrombin inhibitors)
12. TEG parameters

#### Main outcomes

1. Date of ECMO discontinuation
2. Date of invasive mechanical ventilation discontinuation
3. Date of ICU Discharge
4. Date of Hospital Discharge
5. Mortality at 28 days
6. Main cause of death





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## Data Analysis

The global analysis of SPRINT-SARI/ECMOCARD and Coagulation Disorders and Thrombosis Sub-study categorical variables will be described as proportions and will be compared using chi-square or Fisher's exact test. Continuous variables will be described as mean and standard deviation if normally distributed or median and inter-quartile range if not normally distributed. Comparisons of continuous variables will be performed using one-way ANOVA or Mann-Whitney test, as appropriate. A logistic regression model will be performed to assess independent association between prognostic factors and outcomes, taking into account the hierarchical nature of the data. Significance will be set at  $p < 0.05$ .

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## Reference List

1. Bolotin S, Pebody R, White PJ, et al. A new sentinel surveillance system for severe influenza in England shows a shift in age distribution of hospitalised cases in the post-pandemic period. *PLoS One*. 2012;7(1). doi:10.1371/journal.pone.0030279
2. Dawood FS, Iuliano AD, Reed C, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: A modelling study. *Lancet Infect Dis*. 2012;12(9):687-695. doi:10.1016/S1473-3099(12)70121-4
3. Simonsen L, Spreeuwenberg P, Lustig R, et al. Global Mortality Estimates for the 2009 Influenza Pandemic from the GLaMOR Project: A Modeling Study. *PLoS Med*. 2013;10(11). doi:10.1371/journal.pmed.1001558
4. Huang QS, Baker M, McArthur C, et al. Implementing hospital-based surveillance for severe acute respiratory infections caused by influenza and other respiratory pathogens in New Zealand. *West Pacific Surveill response J WPSAR*. 2014;5(2):23-30. doi:10.5365/WPSAR.2014.5.1.004
5. Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand. *N Engl J Med*. 2009;361(20):1925-1934. doi:10.1056/NEJMoa0908481
6. Guery B, Poissy J, El Mansouf L, et al. Clinical features and viral diagnosis of two cases of infection with Middle East Respiratory Syndrome coronavirus: A report of nosocomial transmission. *Lancet*. 2013;381(9885):2265-2272. doi:10.1016/S0140-6736(13)60982-4
7. Weiss SR, Navas-Martin S. Coronavirus Pathogenesis and the Emerging Pathogen Severe Acute Respiratory Syndrome Coronavirus. *Microbiol Mol Biol Rev*. 2005;69(4):635-664. doi:10.1128/membr.69.4.635-664.2005
8. Drosten C, Günther S, Preiser W, et al. Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome. *N Engl J Med*. 2003;348(20):1967-1976. doi:10.1056/NEJMoa030747
9. Ksiazek TG, Erdman D, Goldsmith CS, et al. A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome. *N Engl J Med*. 2003;348(20):1953-1966. doi:10.1056/NEJMoa030781
10. Zaki AM, Van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med*.



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- 2012;367(19):1814-1820. doi:10.1056/NEJMoa1211721
11. de Groot RJ, Baker SC, Baric RS, et al. Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Announcement of the Coronavirus Study Group. *J Virol*. 2013;87(14):7790-7792. doi:10.1128/jvi.01244-13
  12. WHO | Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. *WHO*. 2015.
  13. WHO | Middle East respiratory syndrome coronavirus (MERS-CoV). *WHO*. 2020.
  14. Chan JF-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. January 2020. doi:10.1016/S0140-6736(20)30154-9
  15. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*. January 2020:NEJMoa2001017. doi:10.1056/NEJMoa2001017
  16. WHO | Novel Coronavirus – Thailand (ex-China). *WHO*. 2020.
  17. WHO | Novel Coronavirus – Japan (ex-China). *WHO*. 2020.
  18. WHO | Novel Coronavirus – Republic of Korea (ex-China). *WHO*. 2020.
  19. Spina S, Marrazzo F, Migliari M, Stucchi R, Sforza A, Fumagalli R. The response of Milan's Emergency Medical System to the COVID-19 outbreak in Italy. *Lancet (London, England)*. 2020;0(0). doi:10.1016/S0140-6736(20)30493-1
  20. Ebrahim SH, Memish ZA. COVID-19: preparing for superspreader potential among Umrah pilgrims to Saudi Arabia. *Lancet*. 2020;0(0). doi:10.1016/S0140-6736(20)30466-9
  21. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med*. January 2020. doi:10.1056/nejmoa2001191
  22. Sun K, Chen J, Viboud C. Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowdsourced data: a population-level observational study. *Lancet Digit Heal*. 2020;0(0). doi:10.1016/S2589-7500(20)30026-1
  23. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. January 2020. doi:10.1016/S0140-6736(20)30183-5
  24. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19

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- pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis.* 2020;0(0). doi:10.1016/S1473-3099(20)30086-4
25. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA.* February 2020. doi:10.1001/jama.2020.1585
26. André T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med.* 2004;350(23):2343-2351. doi:10.1056/NEJMoa032709
27. Dunning JW, Merson L, Rohde GGU, et al. Open source clinical science for emerging infections. *Lancet Infect Dis.* 2014;14(1):8-9. doi:10.1016/S1473-3099(13)70327-X

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## Regulation, Ethics and Governance

Protocol and any following amendment to the original protocol will be translated to the main language of the collaborative institution and submitted for the approval of each institutional review board (IRB). All protocols of the study will require approval by each institutional review board, before enrolment of patients. Sites should apply for a waiver of consent to be granted given the negligible risk nature of the study and the need for rapid data collection to inform pandemic responses globally.

### Conflict of interest

The investigators of the APELSO network DO NOT have any significant financial or personal interest that would reasonably appear to be affected by the proposed research activities.

### Data collection and Site Monitoring plan

#### Data Collection

Data will be collected in dedicated electronic forms and/or hard copies as provided by the SPRINT-SARI and ISARIC Organisations (APPENDIX B) and the ECMOCARD Steering Committee (APPENDIX C). Data for Coagulation Disorders and Thrombosis Sub-study can be found in the APPENDIX D. A custom-designed electronic case report form has been developed in REDcap, which is hosted at the University of Oxford and for all Australian centres will be hosted at Monash University, Melbourne, Australia. A custom-designed electronic case report form has been developed in REDcap for the Coagulation Disorders and Thrombosis Sub-study, which is hosted at the University of Queensland. Hard copies and electronic data will be kept for at least 7 years following the conclusion of the study. Each investigator will be responsible to collect and preserve data obtained at his/her collaborative institution.

#### Site Monitoring

Periodic conference calls will be organized with all investigators or investigators of specific collaborative centres to monitor the quality of the data collected, address specific issues in data collection and prepare future publications

#### Compensations

No compensation will be offered to collaborating institutions.





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## Data Access

All essential documentation of the SPRINT-SARI/ECMOCARD and the Coagulation Disorders and Thrombosis Sub-study will be stored in an Investigator Study File (ISF), which will be held by the Critical Care Research Group (CCRG), University of Queensland. On completion of the study, this information will be archived by the CCRG. Following the publication of the primary and secondary outcomes, additional analyses could be undergone on the data collected. In the event of publications arising from these analyses, those responsible will need to provide the Chief Investigator with a copy of the manuscript for approval prior to submission.

## Feasibility

This is a multi-centre study performed within the COVID-19 Critical Care Consortium, which comprises the SPRINT-SARI, ISARIC, ELSO and APELSO networks of clinical research institutions, during an emergent new respiratory infection caused by the new COVID-19 virus. The study will be conducted in intensive care units with broad experience in mechanical ventilation, ECMO and coagulation disorders and thrombosis. Further intra-mural and extra-mural collaborations beyond the COVID-19 Critical Care Consortium and SPRINT-SARI, ISARIC and APELSO networks will be potentially pursued to promptly achieve goals. In summary, the COVID-19 Critical Care Consortium multidisciplinary and international research team of collaborators provides ideal conditions to perform reported study.

## Dissemination and Publication

### Publication policy

Ownership of the data arising from the study resides with the study teams. Data requested from SPRINT-SARI and EXCEL investigators will reside with their own study teams. After the study, results will be analysed and tabulated, and a study report will be prepared. This report will be made available to the study collaborators and the relevant IRBs. The study findings will be presented at national and international meetings. We plan to publish our study findings in a high-quality peer reviewed journal. SPRINT-SARI and EXCEL studies will be fully acknowledged in all publications and presentations.

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CONFIDENTIAL



### Authorship policy

Authorship will be determined according to the internationally agreed criteria for authorship ([www.icmje.org](http://www.icmje.org)). Authorship of parallel studies conducted outside of the main trial will be according to the individuals involved in the study but must acknowledge the contribution of the involved investigators.

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# **SUPPLEMENT 2**

## **COLLABORATING SITES**

## COLLABORATING SITES

Country	City	Site Name	Principal Investigator
Australia	Brisbane	The Prince Charles Hospital	Kiran Shekar
	Melbourne	The Alfred Hospital	Carol Hodgson
	Gold Coast	Gold Coast University Hospital	James Winearls
	South Brisbane	Princess Alexandra Hospital	James Walsham
		Queensland Children's Hospital	Adrian Mattke
	Canberra	Canberra Hospital	Hemanth Hurkadli Veerendra
	Perth	Perth Children's Hospital	Simon Erickson
	Sydney	St Vincent's Hospital	Hergen Buscher
		Royal North Shore Hospital	Perre Janin
		Westmead Hospital	Benjamin Davidson
		Prince of Wales Hospital	Gavin Salt
		St George Hospital	Swapnil Pawar
			Andrew Cheng
		Royal Prince Alfred Hospital	Richard Totaro
	Nepean Hospital	Ian Mark Seppelt	
	Newcastle	John Hunter Hospital	Jorge Brieva
	Melbourne	Box Hill Hospital	Diarmuid O'Briain
	Geelong	Geelong Hospital	Joseph McCaffrey
Hervey Bay	Hervey Bay Hospital (Wide Bay HHS)	Angela Ratsch	
Bundaberg	Bundaberg Hospital (Wide Bay HHS)	Angela Ratsch	
Adelaide	Royal Adelaide Hospital	Michael Farquharson	

	Caboolture	Caboolture Hospital	Mahesh Ramanan
	Redcliffe	Redcliffe Hospital	Alexis Tabah
	Rockhampton	Rockhampton Hospital	Antony Attokaran
	Launceston	Launceston General Hospital	Matt Brain
	Melbourne	Royal Children's Hospital	Warwick Butt
<b>New Zealand</b>	Auckland	Auckland City Hospital	Shay McGuinness (CVICU)
<b>Hong Kong</b>	Hong Kong	Tuen Mun Hospital	Kenny Chan King-Chung
		Princess Margaret Hospital	Dominic So
		Queen Mary Hospital	Pauline Yeung, Simon Wai Ching Sin
		Queen Elizabeth Hospital	George Ng
		Pamela Youde Nethersole Eastern Hospital	Hoi Ping Shum
<b>Indonesia</b>	Jakarta	National Cardiovascular Center Harapan Kita	Eva Marwali
		Sulianti Saroso Hospital	Surya Oto Wijaya
		Persahabatan Hospital	Erlina Burhan
		Pelni Hospital	Amelya Hutahaean
		Fatmawati Hospital	Azhari Taufik
		Cipto Mangunkusumo Hospital	Yogi Prawira (Paeds)
			Dr Anas Alatas (Adult)
		Cengkareng Hospital	Dr Kamal
		Sanglah General Hospital	Dr. Sajinadiyasa (adult)
		Dyah Kanya Wati (pead)	
	East Java	Soetomo Hospital, Surabaya	Neurinda Permata Kusumastuti
Saiful Anwar Malang Hospital (Brawijaya University)		Dr Saptadi Yularito	



	West Java	Hasan Sadikin Hospital	Gezy Giwangkencana (Adult)
			Dadang H Somasetia (Paeds)
	Surabaya	Airlanna University	Dr Neurinda Permata Kusumastuti
	Medan	Adam Malik Hospital	Bastian Lubis
	Semarang	Dr Kariadi Hospital Semarang	Moh Supriatna
	Yogyakarta	Sardjito Hospital	Desy Rusmawatingtyas (Paeds)
			Dr. Bhirowo (Adult)
<b>Japan</b>	Sapporo	Teine Keijinkai Hospital	Takako Akimoto
	Tokyo	Nippon Medical School Hospital	Singo Ichiba
	Kawasaki	St Marianna Medical University Hospital	Shigeki Fujitani (Adults)
			Shimizu Naoki (Paeds)
	Utsunomiya	Saiseikai Utsunomiya Hospital	Keibun Liu
	Hokkaido	Hokkaido University	Dr Koji Hoshino
			Dr Yuk Uchinami
	Kyoto	Kyoto Medical Centre	Hiro Tanaka
	Yokohama	Yokohama City University Medical Center	Hayato Taniguci
	Aichi	Tosei Hospital	Dr Yokoyama
	Maebashi	Japan Red Cross Maebashi Hospital	Hiroyuki Suzuki
	Gunma	Gunma University Graduate School of Medicine	Kanamoto Masafumi
	Chiba	Chiba University Graduate School of Medicine	Ryuzo Abe
	Hiroshima	Hiroshima University	Shinichiro Ohshimo
	Tokyo	Tokyo Metropolitan Medical Center	Keiki Shimizu
Hakodate	Hakodate City hospital	Yoshihiro Takeyama	
Ryukyo	Ryukyu Univesity	Ichiro Kukita	

	Yokohama	Saiseikai Yokohamashi Tobu Hospital	Kenji Tamai
	Okayama	Okayama University Hospital	Toshiyuki Aokage
	Miyagi	Tohoku Medical and pharmaceutical university	Tomoyuki Endo
	Osaka	Rinku general medical center (and Senshu trauma and critical care center)	Shingo Adachi (PI)
			Shota Nakao
	Kyushu	Fukuoka University	Kota Hoshino
	Kyoto	Kyoto Prefectural University of Medicine	Satoru Hashimoto
	Osaka	Osaka City General Hospital	Kazuaki Shigemitsu
	Chiba	Kimitsu Chuo Hospital	Shinya Kitamura
			Takashi Shimazui
	Sapporo	KKR Medical center	Masahiro Yamane
	Hyogo	Hyogo Prefectural Kakogawa Medical Center	Akihiro Shimizu
	Hyogo	Hyogo Prefectural Kobe Children's Hospital	Hiroshi Kurosawa
	Nagoya	Nagoya University Graduate School of Medicine	Kasugai Daisuke
	Mie	Mie University Hospital	Asami Ito
	Fujieda	Fujieda Municipal General Hospital	Motohiro Asaki
	Osaka	Saiseikai Senri Hospital	Masahiro Fukuda
	Shimane	Shimane University Hospital	Yoshiaki Iwashita
	Osaka	National Cerebral and Cardiovascular Center	Dr. Koji Iihara
	Miyagi	Tohoku Medical and Pharmaceutical University	Tomoyuki Endo
<b>Singapore</b>	Singapore	National Centre for Infectious Diseases	Sennen Low
			Shawn Vasoo
		Tan Tock Seng Hospital	Chia Yew Woon
			Benjamin Ho

		National University Hospital	Kollengode Ramanathan
		KK Women's and Children's Hospital	Yee Hui Mok
<b>South Korea</b>	Gwangju	Chonnam National University Hospital	Hwa Jin Cho
			In Seok Jeong
	Anyang	Hallym University Sacred Heart Hospital	Sunghoon Park
	Cheongju	Chungbuk National University Hospital	Hye Won Jeong
	Daegu	Kyungbuk National University Hospital	Tak-hyuck Oh
		Keimyung University Dong San Hospital	Jae Burm Kim
	Seoul	The Catholic University of Seoul St Mary Hospital	Hyun Mi Kang
		Seoul National University Children's Hospital	Bongjin Lee
		Anam Korea University Hospital	Jae-Seung Jung
		Severance Hospital	Su Hwan Lee
Seoul national university hospital		Sang Min Lee	
		Seoul National University Bundang Hospital	Young-Jae Cho
<b>Taiwan</b>	Taipei	National Taiwan University Hospital	Yih-Sharng Chen, Jung-Yien Chien, Chih-Hsie
<b>Thailand</b>	Bangkok	Siriraj Hospital	Pranya Sakiyalak
<b>Vietnam</b>	Ho Chi Minh City	Hospital for Tropical Diseases	Trieu Huynh Trung
			Thuy Duong Bick
<b>Italy</b>	Milan	Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico	Mauro Panigada
		Ospedale San Paolo	Antonio Pesenti
	Rome	Children's Hospital Bambino Gesù	Matteo Di Nardo
		Policlinico Umberto, Sapienza University of Rome	Francesco Alessandri

	Bologna	Policlinico di S. Orsola, Università di Bologna	Antonio Loforte
	Bergamo	Bergamo Hospital	Lorenzo Grazioli and Prof Lorini
	Rome	Fondazione Policlinico Universitario Agostino Gemelli IRCCS	Massimo Antonelli and Domenico Grieco
	Genoa	Ospedale Gaslini	Andrea Moscatelli
		San Martino Hospital	Paolo Pelosi
	Parma	Azienda Ospedaliero Universitaria Parma	Denise Battaglini
			Sandra Rossi Marta
	Turin	Le Molinette Hospital (Ospedale Molinette Torino)	Velia Antonini
			Luca Brazzi
	Palermo	ISMETT	Gabriele Sales
	Florence	Careggi Hospital	Antonio Arcadipane
	Pisa	Azienda Ospedaliero Universitaria Pisana	Adriano Peris
	Verona	Verona Integrated University Hospital	Fabio Guarracino
	Padua	Padua University Hospital (Policlinico of Padova)	Katia Donadello
	Trento	Ospedale di Arco (Trento hospital)	Andrea Dellamore and Paolo Navales
	Monza	Ospedale San Gerardo	MARCO Cavana and Alberto Cucino
	Borgo	Borgo San Lorenzo Hospital	Marco Giani
USA	New York City	Columbia University Medical Centre	Vieri Parrini
			Dan Brodie
			Alexis Serra
	Los Angeles	Cedars-Sinai Medical Centre	Darryl Abrams
			Effe Mihelis
		Presbyterian Hospital, New York/ Weill Cornell Medical Centre	Debra Burns

		Ochsner LSA Health Shreveport	Kristi Lofton
		Children's Hospital	Kimberly Kyle
		UCLA Medical Centre (Ronald Regan)	Vadim Gudzenko
Virginia		Carilion Clinic	Mark Joseph
		INOVA Fairfax Hospital	Steven Nathan
Arizona		Dignity Health St. Joseph's Hospital and Medical Center (SJHMC)	Rajat Walia
Albuquerque		Presbyterian Hospital Services, Albuquerque	Irfan Khan
San Diego		University of California at San Diego	Cassia Yi
		Scripps Memorial Hospital La Jolla	Scott McCaul
Newark		Christiana Care Health System's Centre for Heart and Vascular Health	Ray A Blackwell
Santa Cruz		Dignity Health Medical Group- Dominican	Marsha Moreno
Florida		Cleveland Clinic	Nicolas Brozzi
		University of Florida	Giles John Peek
St Louis		Washington University in St. Louis/ Barnes Jewish Hospital	Christy Kay
Pittsburgh		University of Pittsburgh Medical Centre	Raj Padmanabhan
Omaha		University of Nebraska Medical Centre	Lace Sindt
Louisville		Norton Children's Hospital	Teka Siebenaler
		Baptist Health Louisville	Emily Coxon
Columbia		University of South Carolina	Luca Paoletti
			Laura Hollinger
Indianapolis		Peyton Manning Children's Hospital	Kay A Sighting
Buffalo		Mercy Hospital of Buffalo	Harsh Jain
Indiana		Indiana University Health	Juan Salgado
Washington		George Washington University Hospital	Elizabeth Pocock



Washington	MedStar Washington Hospital Centre	Akram Zaaqoq
Cincinnati	University of Cincinnati Medical Centre	Suzanne Bennett
Irvine	University of California, Irvine	Jennifer Elia
Salt Lake City	University of Utah Hospital	Matthew Griffee
Durham	Duke University Hospital	Melissa Williams
Cincinnati	The Christ Hospital	Timothy Smith
Cleveland	University Hospital Cleveland Medical Centre (UH Cleveland hospital)	Colin McCloskey
Hartford	Hartford Healthcare	Ethan Kurtzman
Atlanta	Emory University Healthcare System	Gabrielle Ragazzo
Atlanta	Children's Healthcare of Atlanta- Egleston Hospital	Micheal Heard
Stanford	Stanford University Hospital	Clark Owyang
Hershey	Penn State Heath S. Hershey Medical Centre	Holly Roush
Pittsburgh	Allegheny General Hospital	Subbarao Elapavaluru
Colorado	Billings Clinic	Daniel Loverde D.O
Boston	Massachusetts General Hospital	Lorenzo Berra
		Yuval Raz
Poughkeepsie	Vassar Brothers Medical Center (VBMC)	Jennifer Osofsky
Kansas	The University of Kansas Medical Centre	Brigid Flynn
Santa Monica	Providence Saint John's Health Centre	Anna Jung
Columbus	Ohio State University Medical Centre	Veena Satyapriya
Portland	Oregon Health and Science University Hospital (OHSU)	Bishoy Zakhary
Washington	Providence Sacred Heart Children's Hospital	Carl P. Garabedian
Lancaster	Lancaster General Health	Cathleen Forney
Philadelphia	Penn Medicine	Asad Usman

New Haven	Yale New Haven Hospital	Andres Oswaldo Razo Vazquez
Cincinnati	Cincinnati Children's	Reanna Smith
Macon	The Medical Centre Navicent Health	James Erskine
Philadelphia	Main Line Health Lankenau Medical Center)	Eric Gnall
Columbia	University of Missouri	Shyam Shankar
Oklahoma City	Oklahoma University Medical Center (OU)	Ryan Kennedy
Oklahoma City	INTEGRIS Baptist Medical Center	Michael Harper
Charlotte	Novant Health (NH) Presbyterian Medical Centre	Hannah Flynn
Minnesota	M Health Fairview	Rhonda Bakken
Fresno	University of California, San Francisco-Fresno Clinical Research Centre	Mohamed Fayed
Boston	Tufts Medical Centre (and Floating Hospital for Children)	Leslie Lussier
	Beth Israel Deaconess Medical Centre	Wilson Grandin
Seattle	University of Washington in Seattle	Jenelle Badulak
Charleston	Medical University of South Carolina	Monika Cardona
Atlanta	Piedmont Atlanta Hospital	Peter Barrett
Chicago	University of Chicago Cardiac Surgery	Pamela Combs
	Northwestern Medicine	Randy McGregor
Tulsa	Oklahoma Heart Institute	Rita Moreno
Phoenix	John C Lincoln Medical Centre	Celina Adams
	Banner University Medical Centre	Stacey Gerle
Norfolk	Sentara Norfolk General Hospital	Xian Qiao
York	WellSpan Health - York Hospital	Josh Fine
Rochester	University of Rochester Medical Centre (UR Medicine)	Bill Hallinan
	Rochester General Hospital	Meghan Nicholson

	Kentucky	University of Kentucky Medical Center	Thomas Tribble	
	Madison	University of Wisconsin & American Family Children's Hospital	Jillian Koch	
	Milwaukee	Medical College of Wisconsin (Froedtert Hospital)	Cassandra Seefeldt	
	New Orleans	Ochsner Clinic Foundation	Julia Garcia-Diaz, Derek Vonderhaar	
	Philadelphia	St. Christopher's Hospital for Children	Daniel Marino	
	Alabama	University of Alabama at Birmingham Hospital (UAB)	Keith Wille	
	Portland	Legacy Emanuel Medical Center	Tawnya Ogston	
	Scottsdale	Mayo Clinic College of Medicine	Ayan Sen	
	Iowa	University of Iowa	Lovkesh Arora	
	Texas		Baylor All Saints Medical Centre, Forth Worth	Dr. Gonzo Gonzalez-Stawinski
			The Heart Hospital Baylor Plano, Plano	Dr Timothy George (PI)
			Baylor University Medical Centre, Dallas	Dr Dan Meyer (PI)
			Baylor Scott & White Health - Temple	Dr Jorge Velazco (PI)
				Margarite Grable
		Doernbecher Children's Hospital	Amit Mehta	
		University of Texas Medical Branch	Yolanda Leyva	
		Cedar Park Regional Medical Center	Mark Sanders	
	UTHealth (University of Texas)	Lisa Janowaik		
England	London	Guy's and St Thomas NHS Foundation Trust Hospital	Nicholas Barrett/Luigi Camporota	
		Royal Brompton & Harefield NHS Foundation Trust	Brij Patel	
	Cambridge	Papworth Hospitals NHS Foundation Trust	Alain Vuysteke	
	Leicester	University Hospitals of Leicester NHS Trust	Yusuff Hakeem	
	Manchester	Manchester University NHS Foundation Trust - Wythenshawe	Tim Felton/Miguel Garcia	

<b>Scotland</b>	Edinburgh	Royal Infirmary Edinburgh	Kenneth Baillie
	Aberdeen	Aberdeen Royal Infirmary (Foresterhill Health Campus)	Emma Hartley
<b>Wales</b>	Swansea	Swansea Hospital	Lenny Ivatt
<b>Netherlands</b>	Nijmegen	Radboud University Medical Centre	Tim Frenzel
	St. Antonious	St. Antonius Hospital	Nicole Van Belle
	Maastricht	Maastricht University Medical Centre	Roberto Lorusso
<b>Belgium</b>	Edegem	University of Antwerp	Gerdy Debeuckelaere
	Brussels	Universite Libre de Bruxelles	Fabio Taccone
	Lodelinsart	Hospital Civil Marie Curie	Anne Joosten
	Leuven	Collaborative Centre Department Cardiac Surgery, UZ Leuven	Klaartje Van den Bossche and Bart Mey
<b>Kuwait</b>	Hadiya	Al-Adan Hospital	Tala Al-Dabbous
	Kuwait City	Kuwait ECLS program, Al-Amiri & Jaber Al-Ahmed Hospitals	Abdulrahman Al-Fares
<b>Saudi Arabi</b>	Mecca	King Abdullah Medical City Specialist Hospital	Jihan Fatani
	Jeddah	King Abdullah Medical Complex	Husam Baeissa;Dr. Mohamed Azzam;Dr. S Ashgar
	Tabuk	King Salman Hospital Nwaf	Ayman AL Masri
	Riyadh	Prince Mohammed bin Abdulaziz Hospital	Ahmed Rabie
		King Faisal Specialist Hospital and Research Center	Abdullah Al-Hudaib Alyaa Elhazmi
<b>Austria</b>	Vienna	Sozialmedizinisches Zentrum Süd - Kaiser-Franz-Josef-Spital	Tamara Seitz
		Medical University of Vienna	Nina Buchtele (ICU) Michael Schwameis (ED)
<b>Philippines</b>	Quezon City	National Kidney and Transplant Institute	Joselito Chavez
<b>Estonia</b>	Tallinn	North Estonia Medical Centre	Indrek Ratsep

	Tartu	Tartu University Hospital	Olavi Maasikas
Canada	Toronto	Toronto General Hospital	Eddy Fan, Kathleen Exconde
	Toronto	Mount Sinai Hospital	Eddy Fan
	Winnipeg	University of Manitoba	Rohit Singal
			Rakesh Arora
	Edmonton	University of Alberta (Mazankowski Heart Institute)	Gurmeet Singh
			Sean Bagshaw
	Hamilton	Hamilton General Hospital	Faizan Amin
	Montreal	McGill University Health Centre	Gordan Samoukoviv
		University de Montreal	Yoan Lamarche
	New Westminster	Royal Columbian Hospital	Derek Gunning
Calgary	University of Calgary (Peter Lougheed Centre, Foothills Medical Centre, South Health Campus and Rockyview General Hospital)	Ken Parhar and Cassidy Codan	
Manitoba	St Boniface Hospital	Rakesh Arora	
India	Kolkata	Medica Superspeciality Hospital	Arpan Chakraborty
Spain	Alicante	Hospital Universitario Sant Joan d'Alacant	Angel Sanchez
	Lugo	Hospital Universitario Lucus Augusti	Ignacio Martinez
	Zaragoza	Hospital Nuestra Señora de Gracia	Ruth Jorge García
	Barcelona	Hospital Universitario de Bellvitge	Rafael Mánñez Mendiluce
		Hospital Clinic, Barcelona	Antoni Torres
		Hospital Universitari Sagrat Cor	Adrian Ceccato
		Hospital de Sant Pau	Ferran Roche-Campo
		Clínica Sagrada Família	Arturo Huerta Garcia
	Vall d'Hebron University Hospital, Barcelona	Ricard Ferrer	



			Jordi Riera
	Valladolid	Rio Hortega University Hospital	Pablo Blanco
	Caceres	San Pedro de Alcantara Hospital	Juan Fernando Masa Jiménez
	Cadiz	Hospital Universitario Virgen de Valme	Ana Loza Vazquez
	Navarra	Clinica Universidad de Navarra	Nahikari Saltera
<b>Argentina</b>	Buenos Aires	Hospital de Clinicas	Carlos Luna
	Buenos Aires	National University of Comahue	Gustavo Zabert
	Buenos Aires	Hospital Alemán	Javier Osatnik
	Buenos Aires	Clinica Bazterrica	Fernando Palizas
	Lisbon	University Hospital CHLN	Joao Miguel Ribeiro
	Portugal	São João Hospital Centre, Porto	Sérgio Gaião
<b>Colombia</b>	Bucaramanga	Fundación Cardiovascular de Colombia	Leonardo Salazar
	Cali	Clinica Valle de Lilli	Diego Fernando Bautista Rincón
	Bogota	Fundación Clinica Shaio	Estefania Giraldo
<b>Chile</b>	Las Condes	Clinica Las Condez	Roderigo Diaz
	Santiago	Hospital del Tórax	Francisco Arancibia
	Santiago	Clinica Alemana De Santiago	Jerónimo Graf
<b>Germany</b>	Regensburg	Universitätsklinikum Regensburg (Klinik für Innere Medizin II)	Maximilian Malfertheiner
	Donaustauf	Donaustauf Hospital	Annette Schweda
	Regensburg	Barmherzige Bruder Regensburg	Stephan Schroll
	Munich	Medizinische Klinik und Poliklinik II	Stephanie Stecher
	Berlin	Charite-Universitätsmedizin Berlin	Roland Francis
	Passau	Klinikum Passau	Johannes Gebauer
	Nuremberg	Paracelsus Medical University Nuremberg	Matthias Baumgaertel

	Frankfurt	Universitätsklinikum Frankfurt (University Hospital Frankfurt)(Uniklinik)	Gösta Lotz
	Stockwerk	Universitätsspital Bern, Universitätsklinik für Herz- und Gefässchirurgie	Beate Hugi-Mayr
<b>Brazil</b>	Belo Horizonte	Hospital Mater Dei	Ana Luiza Valle Martins
	São Paulo	Universidade de São Paulo	Marcelo Amato
	São Paulo	Hospital das Clínicas da Faculdade de Medicina da USP (HCFMUSP)	Suely Pereira Zeferino
	Rio de Janeiro	Universidade Federal Fluminense	Marcello Salgado
<b>Ireland</b>	Galway	National University of Ireland Galway	John Laffey
	Dublin	St James's University Hospital	Ignacio Martin-Loeches
		Mater Misericordiae University Hospital	Ed Carton
Crumlin	Children's Health Ireland (CHI) at Crumlin	Sunimol Joseph	
<b>Poland</b>	Krakow	University Hospital in Krakow	Konstanty S. Szuldrzynski
	Ghansk	Gdansk Medical University	Wojtek Karolak
<b>South Africa</b>	Johannesburg	Nelson Mandela Children's Hospital	Krubin Naidoo
		Netcare Unitas ECMO Centre	Marlice van Dyk
	Cape Town	Groote Schuur Hospital	David Thomson
<b>Qatar</b>	Qatar	Hamad General Hospital - Weill Cornell Medical College in Qatar	Ibrahim Hassan and Ali Hssain
<b>Egypt</b>	Cairo	Cairo University Hospital	Ahmad Abdelaziz
<b>Sweden</b>	Gothenburg	Sahlgrenska University Hospital	Pia Watson
<b>Croatia</b>	Zagreb	University Hospital Dubrava	Nikola Bradic
<b>Luxembourg</b>	Barble	Luxembourg Heart Center	Katja Ruck
<b>Ukraine</b>	Kyiv	Heart Institute Ministry of Health of Ukraine	Serhii Sudakevych
<b>Switzerland</b>	Bern	Inselspital University Hospital	Beate Hugi-Mayr
<b>Turkey</b>	Izmir	Dr. Suat Seren Chest Diseases and Surgery Practice and Training Centre	Cenk Kirakli
<b>Mexico</b>	Zapopan	Hospital Puerta de Hierro	Anna Greti



<b>UAE</b>	Dubai	American Hospital	Balu Bhaskar
<b>Lebanon</b>	Beirut	Pediatric and Neonatal Cardiac intensive care at the American University	Jana Assy
<b>Kenya</b>	Nairobi	Kenyatta National Hospital (KNH)	George Nyale
	Nairobi	Kenyatta University Teaching, Referral & Research Hospital	George Nyale
<b>Tunisia</b>	Tunis	Charles Nicolle University Hospital	Ali Cherif
<b>Zimbabwe</b>	Harare	St Annes Hospital	Jackie Stone
<b>Morocco</b>	Oujda	Mohammed VI university hospital	Brahim Housni
	Rabat	Rabat university hospital	Younes Oujidi
			Jawad Tadili





**SUPPLEMENT 3**

**REGIONAL LEADS/ASSISTANTS**

**OPERATIONAL TEAM**



### REGIONAL LEADS/ASSISTANTS

Country	Regional Lead	Regional Lead Affiliation	Regional Coordinator/Assistant
Australia	Hergen Buscher	St Vincent's Hospital, Sydney	India Lye
Australia	Carol Hodgson	The Alfred Hospital, Melbourne	
New Zealand	Shay McGuinness	Auckland City Hospital	Rachael Parke
Hong Kong	Simon Wai Ching Sin	Queen Mary Hospital, Hong Kong	Pauline Yeung
Indonesia	Eva Marwali	National Cardiovascular Center Harapan Kita, Jakarta	
Indonesia	Erlina Burhan	Persahabatan Hospital, Jakarta	
Japan	Shingo Ichiba	Nippon Medical School Hospital, Tokyo	Keibun Liu, Takako Akimoto
Singapore	Kollengode Ramanathan	National University Hospital, Singapore	
South Korea	Young-Jae Cho	Seoul National University Bundang Hospital	Hwa Jin Cho, Jae-Seung Jung
Taiwan	Yih-Sharng Chen, Jung-Yien Chien, Chih-Hsien Wang	National Taiwan University Hospital	
Vietnam	Vinh Chau	Hospital for Tropical Diseases, Ho Chi Minh City	Trieu Huynh, Sophie Yacoub, Angela McBride
Italy	Antonio Pesenti, Mauro Panigada	Fondazione IRCCS Policlinico of Milan	Michela Leone and Sebastiano Colombo
USA	Robert Bartlett	University of Michigan Medical School	Leticia Helms
USA	Daniel Brodie	Columbia University Medical Centre	
USA	Phillip Mason	Brooke Army Medical Center, San Antonio	
USA	Archit Sharma	University of Iowa Hospitals & Clinics	

<b>USA</b>	Christian Bermudez	Hospital of the University of Pennsylvania	
<b>USA</b>	Vadim Gudzenko	UCLA Medical Centre (Ronald Regan)	
<b>USA</b>	Bishoy Zakhary	Oregon Health and Science University Hospital, Portland	
<b>England</b>	Brij Patel	Royal Brompton & Harefield NHS Foundation Trust	Johnny Millar
<b>Scotland Wales</b>	Johnny Millar	University of Glasgow	
<b>Netherlands</b>	Roberto Lorusso	Maastricht University Medical Centre	
<b>Belgium</b>	Fabio Taccone	Universite Libre de Bruxelles	
<b>Kuwait</b>	Abdulrahman Al-Fares	Al-Amiri & Jaber Al-Ahmed Hospitals	
<b>Saudi Arabi</b>	Alyaa Elhazmi	King Faisal Specialist Hospital and Research Center	
<b>Saudi Arabi</b>	Ahmed Rabie	Prince Mohammed bin Abdulaziz Hospital	
<b>Austria</b>	Nina Buchtele	Medical University of Vienna	
<b>Philippines</b>	Joselito Chavez	National Kidney and Transplant Institute	
<b>Estonia</b>	Indrek Ratsep	North Estonia Medical Centre	Silver Heinsar
<b>Canada</b>	Eddy Fan	Toronto General Hospital Research Institute	Kathleen Exconde
<b>India</b>	Arpan Chakraborty	Medica Superspeciality Hospital	Kiran Shekar
<b>Spain</b>	Antoni Torres	Hospital Clinic, Barcelona	
<b>Spain</b>	Ricard Ferrer	Hospital Vall d'Hebron	Jordi Riera Del Brio
<b>Argentina</b>	Carlos Luna	Hospital de Clinicas	
<b>Colombia</b>	Leonardo Salazar	Fundación Cardiovascular de Colombia	
<b>Germany</b>	Maximilian Malferteiner	Universitätsklinikum Regensburg	





<b>Brazil</b>	Marcelo Amato	Universidade de São Paulo	
<b>Brazil</b>	Marcello Salgado	Federal University of Rio de Janeiro	
<b>Ireland</b>	John Laffey	National University of Ireland Galway	
<b>Poland</b>	Konstanty S. Szuldrzynski	University Hospital in Krakow	
<b>South Africa</b>	David Thomsom	Groote Schuur Hospital	
<b>Qatar</b>	Ibrahim Hassan, Ali Hssain	Hamad General Hospital	
<b>Egypt</b>	Ahmad Abdelaziz	Cairo University Hospital	
<b>Sweden</b>	Pia Watson	Sahlgrenska University Hospital	
<b>Zimbabwe</b>	Jackie Stone	St Annes Hospital	





## COORDINATING CENTRE OPERATIONAL TEAM

1. Cooper Ansicar
2. Chris Chan
3. William Crawford
4. Gaenor Cross
5. Courtney Dwyer
6. Alessandro Ferraioli
7. Halah Hassan
8. Samuel Huth
9. Lacey Irvine
10. Christine Jackman
11. Varun Karnik
12. Katrina Ki
13. Niki McGuinness
14. Hollier O'Neill
15. Janice Reid
16. Kei Sato
17. Declan Sela
18. Yvgeniy Shek
19. Emily Wood
20. Stephanie Yerkovich
21. Taylor Zhang





# SUPPLEMENT 4

# CASE REPORT FORM



## Data Collection Form

## CORE CASE RECORD FORM (EOT ICU Admis)

**1. UPON ICU ADMISSION – Please complete the below data as of the date and time of the patient's admission to the ICU**

DATE OF ICU ADMISSION: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 14/12/2019)

1.1 HEIGHT (cm): \_\_\_\_\_

If this data has already been entered into the 'Signs and Symptoms' section of the ISARIC CRF, please DO NOT re-enter the data here. Leave this '1.1 Height' box blank.

1.2 BODY WEIGHT (Kg): \_\_\_\_\_

If this data has already been entered into the 'Signs and Symptoms' section of the ISARIC CRF, please DO NOT re-enter the data here. Leave this '1.2 Body Weight' box blank.

## 1.3 Arterial Hypertension

Yes

No

If this data has already been entered into the 'Co-Morbidities & Risk Factors' section of the ISARIC CRF, please DO NOT re-enter the data here. Leave this '1.3 Hypertension' box blank.

## 1.3a Chronic anti-hypertensive therapy (if 'Yes' to 1.3. Please select up to three)

Diuretics

Calcium channel blockers

ACE inhibitors

If this data has already been entered in the 'Pre-Admission Medication' section of the ISARIC CRF, please DO NOT re-enter the data here. Leave this 'ACE inhibitors' box blank.

Angiotensin II receptor antagonists

If this data has already been entered in the 'Pre-Admission Medication' section of the ISARIC CRF, please DO NOT re-enter the data here. Leave this 'Angiotensin II receptor antagonists' box blank.

Renin inhibitors

Beta blockers

Alpha blockers

Vasodilators

Aldosterone receptor antagonist

Alpha-2 adrenergic receptor agonists

Not applicable

## 1.4 GASTROINTESTINAL AND PANCREATIC COMORBIDITIES

Yes

No



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**1.5 HEPATIC AND BILIARY COMORBIDITIES**

Yes  
No

**1.6 HAEMATOLOGIC AND SPLEEN COMORBIDITIES**

Yes  
No

**1.7 IMMUNOLOGICAL AND TRANSPLANT COMORBIDITIES**

Yes  
No

**1.8 ENDOCRINOLOGICAL COMORBIDITIES**

Yes  
No

**1.9 GENITO-URINARY COMORBIDITIES**

Yes  
No

**1.10 CHRONIC ALCOHOL ABUSE**

Yes  
No

**1.11 INTRAVENOUS DRUGS ABUSE**

Yes  
No

**1.12 IMMUNO-COMPETENT**

Yes  
No

**1.13 APACHE II SCORE:** \_\_\_\_\_ (ONLY NUMBERS FROM 0 to 71)

APACHE II score can be calculated at the following link <https://www.mdcalc.com/apache-ii-score>

Not available

**1.14 SOFA SCORE:** \_\_\_\_\_ (ONLY NUMBERS FROM 0 to 24)

SOFA score can be calculated at the following link <https://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score>

Not available

**BLOOD GAS ANALYSIS (Qs 1.15 – 1.20) – Please document the values associated with the ‘worst’ blood gas analysis in the 6 hours prior to ICU admission. ‘Worst’ blood gas is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.**

**1.15 ARTERIAL pH IN THE LAST 6h:** \_\_\_\_\_ (ONLY NUMBERS FROM 6.500 TO 7.600)

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Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to ICU admission. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**1.16 ARTERIAL PARTIAL PRESSURE OF OXYGEN IN THE LAST 6h (mmHg):** \_\_\_\_\_ (ONLY NUMBERS FROM 20 TO 500)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to ICU admission. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**1.17 ARTERIAL PARTIAL PRESSURE OF CARBON DIOXIDE IN THE LAST 6h (mmHg):** \_\_\_\_\_ (ONLY NUMBERS FROM 10 TO 100)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to ICU admission. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**1.18 ARTERIAL BICARBONATE (HCO<sub>3</sub><sup>-</sup>) IN THE LAST 6h** \_\_\_\_\_ mEq/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to ICU admission. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**1.19 ARTERIAL Base excess IN THE LAST 6h** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to ICU admission. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**1.20 Lactate IN THE LAST 6h** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to ICU admission. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**1.21 Ferritin in the last 12 hours:** \_\_\_\_\_ (ng/mL)

Only numbers from 0-1000

Not available

**1.22 D-dimer in the last 12 hours:**

\_\_\_\_\_ (ng/mL or mcg/mL)

Only numbers from 0-15000

Not available

**1.23 Troponin in the last 12 hours:**

- Troponin T: \_\_\_\_\_ (ng/mL or ng/L)
- Troponin I: \_\_\_\_\_ (ng/mL or ng/L)
- High sensitivity troponin T: \_\_\_\_\_ (ng/mL or ng/L)
- High sensitivity troponin I: \_\_\_\_\_ (ng/mL or ng/L)
- Not available

**1.24 Cardiac BNP in the last 12 hours:**

\_\_\_\_\_ (picograms/mL)

Only numbers between 0-1000

Not available





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**1.25 Upon ICU admission, did the patient present with cutaneous manifestations?**

- Yes
- No
- Not available

**If yes to 1.25, type of cutaneous manifestations (please select up to three (3) options)**

- Bullae
- Macules
- Nodules
- Papules
- Plaques
- Purpura
- Pustules
- Rash
- Scale
- Urticaria
- Vesicles
- Other: \_\_\_\_\_

**If yes to 1.25, specify the involved regions (please select up to three (3) options):**

- Face
- Trunk
- Upper limbs
- Hands
- Lower limbs
- Feet



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## CORE CASE RECORD FORM (EOT Mech Vent)

**2. UPON COMMENCEMENT OF MECHANICAL VENTILATION - 'Mechanical ventilation' includes invasive mechanical ventilation via an endotracheal tube or tracheostomy only. Importantly, this module will be active only when you click 'YES' in the field '1.17 Invasive ventilation?' of the SPRINT-SARI form.**

**2.1 DATE OF START OF MECHANICAL VENTILATION:** \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 14/12/2019)

### 2.2 SITE OF INTUBATION

- Outside hospital
- Intensive Care Unit
- Emergency Department
- Hospital Ward
- Different hospital, then patient was transferred
- Other

### 2.3 TYPE OF INTUBATION

- Elective
- Emergent

### 2.4 CARDIAC ARREST

- Yes
- No

### 2.5 VENTILATORY SUPPORT BEFORE INTUBATION

- High-Flow Oxygen Ventilation
- Mask non-invasive ventilation
- Full Face-mask non-invasive ventilation
- Helmet non-invasive ventilation
- Simple face mask oxygen therapy
- Venturi mask oxygen therapy
- Non re-breather face mask oxygen therapy
- Nasal prongs oxygen therapy
- Other
- Not available

**BLOOD GAS ANALYSIS (Qs 2.6 – 2.11) – Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' blood gas is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.**

**2.6 ARTERIAL pH IN THE 6 HOURS BEFORE START OF MV:** \_\_\_\_\_ (ONLY NUMBERS FROM 6.500 TO 7.600)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**2.7 ARTERIAL PARTIAL PRESSURE OF OXYGEN (mmHg) IN THE 6 HOURS BEFORE START OF MV:** \_\_\_\_\_ (ONLY NUMBERS FROM 20 TO 500)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**2.8 ARTERIAL PARTIAL PRESSURE OF CARBON DIOXIDE (mmHg) IN THE 6 HOURS BEFORE START OF MV:** \_\_\_\_\_ (ONLY NUMBERS FROM 10 TO 100)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**2.9 ARTERIAL HCO<sub>3</sub><sup>-</sup> IN THE 6 HOURS BEFORE START OF MV** \_\_\_\_\_ mEq/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**2.10 ARTERIAL Base excess IN THE 6 HOURS BEFORE START OF MV** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**2.11 Lactate IN THE 6 HOURS BEFORE START OF MV** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of mechanical ventilation. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**2.12 USE OF CONTINUOUS RENAL REPLACEMENT THERAPY BEFORE START OF MV**

Yes

No

**2.13 USE OF VASOACTIVE DRUGS BEFORE START OF MV**

Yes

No

**2.14 USE OF CARDIAC ASSIST DEVICES BEFORE START OF MV**

Yes

No

**2.15 ANTIBIOTICS BEFORE START OF MV**

Amikacin	Bacitracin	Cefepime
Amoxicillin	Capreomycin	Cefixime
Amoxicillin +	Carbenicillin indanyl	Cefmetazole
Clavulanate	sodium	Cefonicid
Ampicillin	Cefaclor	Cefoperazone
Ampicillin + Sulbactam	Cefadroxil	Cefotaxime
Atovaquone	Cefamandole	Cefotetan
Azithromycin	Cefazolin	Cefoxitin
Aztreonam	Cefdinir	Cefpodoxime Proxetil
Bacampicillin	Cefditoren	Cefprozil



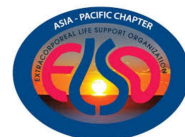
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Ceftaroline	Neomycin
Ceftazidime	Netilmicin
Ceftibuten	Nitrofurantoin
Ceftizoxime	Nitrofurazone
Ceftobiprole	Norfloxacin
Ceftriaxone	Novobiocin
Cefuroxime	Ofloxacin
Cephalexin	Oxacillin
Cephalothin	Oxytetracycline
Cephapirin	Penicillin
Cephradine	Piperacillin
Chloramphenicol	Piperacillin +
Cinoxacin	Tazobactam
Ciprofloxacin	Podofilox
Clarithromycin	Polymyxin B
Clindamycin	Quinupristin +
Cloxacillin	Dalfopristin
Colistimethate	Retapamulin
Cycloserine	Rifapentine
Daptomycin	Rifaximin
Demeclocycline	Saturated Solution of
Dicloxacillin	Potassium Iodide (SSKI)
Dirithromycin	Sparfloxacin
Doripenem	Spectinomycin
Doxycycline	Streptomycin
Enoxacin	Sulfadiazine
Ertapenem	Sulfamethoxazole
Erythromycin	Sulfisoxazole
Fosfomycin	Sulphur, precipitated in
Gatifloxacin	petrolatum
Gemifloxacin	TCA (trichloroacetic
Gentamicin	acid), BCA
Grepafloxacin	(bichloroacetic acid).
Imipenem/Cilastatin	Teicoplanin
Imiquimod	Telavancin
Kanamycin	Telithromycin
Levofloxacin	Terbinafine
Lincomycin	Tetracycline
Linezolid	Ticarcillin
Lomefloxacin	Ticarcillin + Clavulanic
Loracarbef	Acid
Mafenide	Tigecycline
Meropenem	Tobramycin
Methenamine hippurate	Trimethoprim
Methicillin	Trimethoprim +
Metronidazole	Sulfamethoxazole
Mezlocillin	Trovafloxacin
Minocycline	Vancomycin
Moxifloxacin	
Mupirocin	
Nafcillin	
Nalidixic Acid	



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## CORE CASE RECORD FORM (EOT Start ECMO)

**3. UPON COMMENCEMENT OF ECMO. Importantly, this module will be active only when you click 'YES' in the field '1.18 ECLS?' of the SPRINT-SARI form.**

**3.1 DATE OF START OF ECMO:** \_\_\_/\_\_\_/\_\_\_ (ONLY DATE FROM 14/12/2019)

**3.2 Is this patient enrolled in the EXCEL study?**

Yes  
No

**3.3 If Yes, what is the patients EXCEL study number** \_\_\_\_\_

**3.4 LOCATION OF ECMO CANNULATION:**

Same Hospital  
Other Hospital, then patient was retrieved and transferred

**3.5 Type and Manufacturer of centrifugal blood pump driven circuit:** \_\_\_\_\_ (TEXT)

**3.6 Type and Manufacturer of low-resistance oxygenator:** \_\_\_\_\_ (TEXT)

**3.7 TYPE OF ECMO:**

Venous-venous  
Venous-arterial

**3.8 DRAINAGE CANNULA INSERTION SITE:**

Left femoral vein  
Left internal jugular vein  
Right femoral vein  
Right internal jugular vein

**3.9 RETURN CANNULA INSERTION SITE:**

Left femoral vein  
Left internal jugular vein  
Right femoral vein  
Right internal jugular vein  
Left femoral artery  
Right femoral artery

**3.10 CARDIAC ARREST BEFORE START OF ECMO**

Yes  
No

**3.11 USE OF PRONE POSITION BEFORE START OF ECMO:**

Yes  
No

**3.12 USE OF NEUROMUSCULAR BLOCKADE BEFORE START OF ECMO:**

Yes  
No

**3.13 USE OF RECRUITMENT MANOEUVRES BEFORE START OF ECMO:**



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Yes

No

**3.14 USE OF INHALED NITRIC OXIDE BEFORE START OF ECMO:**

Yes

No

**3.15 USE OF BICARBONATE BEFORE START OF ECMO**

Yes

No

**3.16 VENTILATORY MODE BEFORE START OF ECMO:**

Synchronized Intermittent Mandatory Ventilation – Volume-Controlled (SIMV-V)

Synchronized Intermittent Mandatory Ventilation – Pressure-Controlled (SIMV-P)

Volume Controlled Ventilation

Pressure Controlled Ventilation

Pressure Regulated Volume Control (PRVC)

Airway Pressure Release Ventilation (APRV)

Pressure Support Ventilation (PSV)

Volume Support Ventilation (VSV)

High Frequency Oscillatory (HFO)

Bilevel Positive Airway Pressure (BiPAP)

Continuous Positive Airway Pressure (CPAP)

Proportional Assist Ventilation (PAV)

Neurally Adjusted Ventilatory Assist (NAVA)

Other: \_\_\_\_\_ (TEXT)

**MECHANICAL VENTILATION & BLOOD GAS ANALYSIS (Qs 3.17- 3.28) – Please document the ‘worst’ value in the 6 hours before the commencement of ECMO. ‘Worst’ means the values associated with the arterial blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio. Please report ventilatory settings associated with the worst arterial blood gas.**

**3.17 INSPIRATORY FRACTION OF OXYGEN IN THE 6 HOURS BEFORE START OF ECMO:** \_\_\_\_\_  
(ONLY NUMBERS, BETWEEN 21 and 100)

Please document the values associated with the ‘worst’ blood gas analysis in the 6 hours prior to commencement of ECMO. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

 Not available**3.18 RESPIRATORY RATE IN THE 6 HOURS BEFORE START OF ECMO (breaths/min):** \_\_\_\_\_  
(ONLY NUMBERS, BETWEEN 2 and 60)

Please document the values associated with the ‘worst’ blood gas analysis in the 6 hours prior to commencement of ECMO. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

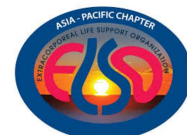
 Not available**3.19 TIDAL VOLUME (ml/Kg of Ideal Body Weight):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 1 and 14)

Please document the values associated with the ‘worst’ blood gas analysis in the 6 hours prior to commencement of ECMO. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.



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Ideal Body Weight formula:

Male patients:  $50 + (0.91 \times [\text{height in cm} - 152.4])$

Female patients:  $45.5 + (0.91 \times [\text{height in cm} - 152.4])$

Not available

**3.20 POSITIVE END EXPIRATORY PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH<sub>2</sub>O):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 0 and 25)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.21 PEAK AIRWAY PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH<sub>2</sub>O):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 0 and 85)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.22 AIRWAY PLATEAU PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH<sub>2</sub>O):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 0 and 50)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.23 ARTERIAL pH IN THE 6 HOURS BEFORE START OF ECMO:** \_\_\_\_\_ (ONLY NUMBERS FROM 6.500 TO 7.600)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.24 ARTERIAL PARTIAL PRESSURE OF OXYGEN IN THE 6 HOURS BEFORE START OF ECMO (mmHg):** \_\_\_\_\_ (ONLY NUMBERS FROM 20 TO 500)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.25 ARTERIAL PARTIAL PRESSURE OF CARBON DIOXIDE IN THE 6 HOURS BEFORE START OF ECMO (mmHg):** \_\_\_\_\_ (ONLY NUMBERS FROM 10 TO 150)

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

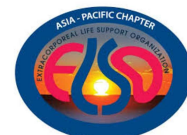
Not available

**3.26 ARTERIAL HCO<sub>3</sub><sup>-</sup> IN THE 6 HOURS BEFORE START OF ECMO** \_\_\_\_\_ mEq/L



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Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.27 ARTERIAL Base excess IN THE 6 HOURS BEFORE START OF ECMO** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.28 Lactate IN THE 6 HOURS BEFORE START OF ECMO** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the 6 hours prior to commencement of ECMO. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**3.29 USE OF CONTINUOUS RENAL REPLACEMENT THERAPY BEFORE START OF ECMO:**

Yes  
No

**3.30 USE OF VASOACTIVE DRUGS BEFORE START OF ECMO:**

Yes  
No

**3.31 USE OF CARDIAC ASSIST DEVICE BEFORE START OF ECMO:**

Yes  
No

**3.32 USE OF ANTIBIOTICS BEFORE START OF ECMO:**

Yes  
No

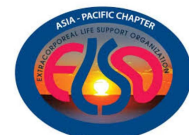
**3.33 ANTIBIOTICS BEFORE START OF ECMO:**

Yes  
No

Amikacin	Capreomycin	Cefmetazole
Amoxicillin	Carbenicillin indanyl sodium	Cefonicid
Amoxicillin + Clavulanate	Cefaclor	Cefoperazone
Ampicillin	Cefadroxil	Cefotaxime
Ampicillin + Sulbactam	Cefamandole	Cefotetan
Atovaquone	Cefazolin	Cefoxitin
Azithromycin	Cefdinir	Cefpodoxime Proxetil
Aztreonam	Cefditoren	Cefprozil
Bacampicillin	Cefepime	Ceftaroline
Bacitracin	Cefixime	Ceftazidime
		Ceftibuten



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Ceftizoxime	Neomycin
Ceftobiprole	Netilmicin
Ceftriaxone	Nitrofurantoin
Cefuroxime	Nitrofurazone
Cephalexin	Norfloxacin
Cephalothin	Novobiocin
Cephapirin	Ofloxacin
Cephradine	Oxacillin
Chloramphenicol	Oxytetracycline
Cinoxacin	Penicillin
Ciprofloxacin	Piperacillin
Clarithromycin	Piperacillin +
Clindamycin	Tazobactam
Cloxacillin	Podofilox
Colistimethate	Polymyxin B
Cycloserine	Quinupristin +
Daptomycin	Dalfopristin
Demeclocycline	Retapamulin
Dicloxacillin	Rifapentine
Dirithromycin	Rifaximin
Doripenem	Saturated Solution of
Doxycycline	Potassium Iodide (SSKI)
Enoxacin	Sparfloxacin
Ertapenem	Spectinomycin
Erythromycin	Streptomycin
Fosfomycin	Sulfadiazine
Gatifloxacin	Sulfamethoxazole
Gemifloxacin	Sulfisoxazole
Gentamicin	Sulphur, precipitated in
Grepafloxacin	petrolatum
Imipenem/Cilastatin	TCA (trichloroacetic
Imiquimod	acid), BCA
Kanamycin	(bichloroacetic acid).
Levofloxacin	Teicoplanin
Lincomycin	Telavancin
Linezolid	Telithromycin
Lomefloxacin	Terbinafine
Loracarbef	Tetracycline
Mafenide	Ticarcillin
Meropenem	Ticarcillin + Clavulanic
Methenamine hippurate	Acid
Methicillin	Tigecycline
Metronidazole	Tobramycin
Mezlocillin	Trimethoprim
Minocycline	Trimethoprim +
Moxifloxacin	Sulfamethoxazole
Mupirocin	Trovafloxacin
Nafcillin	Vancomycin
Nalidixic Acid	



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**4. DAILY CASE RECORD FORM**

**Complete one form 24 hours after commencement of mechanical ventilation, and daily up to discontinuation of mechanical ventilation or death, whichever occurs first. Importantly, parameters related to mechanical ventilation or ECMO will be active only when you click 'YES' in the field '1.17 Invasive ventilation?' or when you click 'YES' in the field '1.18 ECLS?', respectively, of the SPRINT-SARI form.**

**4.1 DATE:** \_\_\_\_\_ (ONLY DATE, FROM 14/12/2019)

**4.2 PATIENT POSITION IN THE LAST 24h:**

Please report the position applied predominantly during the 24 hours.

Supine  
Prone

**4.3 HIGHEST ECMO FLOW RATE IN THE LAST 24h (L/min):** \_\_\_\_\_

**4.4 HIGHEST ECMO GAS FLOW RATE IN THE LAST 24h (L/min):** \_\_\_\_\_

**4.5 ECMO CIRCUIT CHANGE IN THE LAST 24h:**

Yes  
No

**4.6 USE OF NEUROMUSCULAR BLOCKADE IN THE LAST 24h:**

Yes  
No

**4.7 USE OF RECRUITMENT MANOEUVRES IN THE LAST 24h:**

Yes  
No

**4.8 USE OF INHALED NITRIC OXIDE IN THE LAST 24h:**

Yes  
No

**4.9 MOST FREQUENT VENTILATORY MODE IN THE LAST 24h:**

Synchronized Intermittent Mandatory Ventilation – Volume-Controlled (SIMV-V)  
Synchronized Intermittent Mandatory Ventilation – Pressure-Controlled (SIMV-P)  
Volume Controlled Ventilation  
Pressure Controlled Ventilation  
Pressure Regulated Volume Control (PRVC)  
Airway Pressure Release Ventilation (APRV)  
Pressure Support Ventilation (PSV)  
Volume Support Ventilation (VSV)  
High Frequency Oscillatory (HFO)  
Bilevel Positive Airway Pressure (BiPAP)  
Continuous Positive Airway Pressure (CPAP)



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Proportional Assist Ventilation (PAV)  
 Neurally Adjusted Ventilatory Assist (NAVA)  
 Other: \_\_\_\_\_ (TEXT)

**MECHANICAL VENTILATION & BLOOD GAS ANALYSIS (Qs 4.10 – 4.21) – Please document the ‘worst’ value in the last 24 hours. ‘Worst’ means the values associated with the arterial blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio. Please report ventilatory settings associated with the worst arterial blood gas.**

**4.10 INSPIRATORY FRACTION OF OXYGEN IN THE LAST 24h:** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 21 and 100)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

**4.11 RESPIRATORY RATE IN THE LAST 24h (breaths/min):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 2 and 60)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.12 TIDAL VOLUME IN THE LAST 24h (ml/Kg of Ideal Body Weight):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 1 and 14)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio. Ideal Body Weight formula:

Male patients:  $50 + (0.91 \times [\text{height in cm} - 152.4])$

Female patients:  $45.5 + (0.91 \times \{\text{height in cm} - 152.4\})$

Not available

**4.13 POSITIVE END EXPIRATORY PRESSURE IN THE LAST 24h (cmH<sub>2</sub>O):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 0 and 25)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.14 AIRWAY PLATEAU PRESSURE IN THE LAST 24h (cmH<sub>2</sub>O):** \_\_\_\_\_ (ONLY NUMBERS, BETWEEN 0 and 50)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.15 ARTERIAL pH IN THE LAST 24h:** \_\_\_\_\_ (ONLY NUMBERS FROM 6.500 TO 7.600)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.16 ARTERIAL PARTIAL PRESSURE OF OXYGEN IN THE LAST 24h: (mmHg):** \_\_\_\_\_ (ONLY NUMBERS FROM 20 TO 500)

Please document the values associated with the ‘worst’ blood gas analysis in the last 24 hours. ‘Worst’ is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.17 ARTERIAL PARTIAL PRESSURE OF CARBON DIOXIDE IN THE LAST 24h: (mmHg):** \_\_\_\_\_ (ONLY NUMBERS FROM 10 TO 100)



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Please document the values associated with the 'worst' blood gas analysis in the last 24 hours. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.18 ARTERIAL HCO<sub>3</sub><sup>-</sup> IN THE LAST 24h:** \_\_\_\_\_ mEq/L

Please document the values associated with the 'worst' blood gas analysis in the last 24 hours. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.19 ARTERIAL Base excess IN THE LAST 24h:** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the last 24 hours. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.  Not available

**4.20 Lactate IN THE LAST 24h:** \_\_\_\_\_ mmol/L

Please document the values associated with the 'worst' blood gas analysis in the last 24 hours. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.20 Lactate' blank.

**4.21 CREATININE IN THE LAST 24h (mg/dL):** \_\_\_\_\_

Please document the values associated with the 'worst' blood gas analysis in the last 24 hours. 'Worst' is defined as the blood gas with the lowest PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.21 Creatinine' blank.

**4.22 USE OF CONTINUOUS RENAL REPLACEMENT THERAPY:**

Yes

No

**4.23 USE OF VASOACTIVE DRUGS IN THE LAST 24h:**

Yes

No

**4.24 TYPE OF VASOACTIVE DRUG 1:**

Dobutamine

Dopamine

Enoximone

Epinephrine: YES  NO

Esmolol

Levosimendan

Metaraminol

Metoprolol

Milrinone

Nicardipine

Nitroglycerin

Nitroprusside

Norepinephrine: YES  NO

Phenylephrine

Tolazoline

Vasopressin



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**4.25 HIGHEST DOSE OF VASOACTIVE DRUG 1 IN THE LAST 24h (mcg/Kg/min):** \_\_\_\_\_

**4.26 TYPE OF VASOACTIVE DRUG 2:**

- Dobutamine
- Dopamine
- Enoximone
- Epinephrine: YES  NO
- Esmolol
- Levosimendan
- Metaraminol
- Metoprolol
- Milrinone
- Nicardipine
- Nitroglycerin
- Nitroprusside
- Norepinephrine: YES  NO
- Phenylephrine
- Tolazoline
- Vasopressin

**4.27 HIGHEST DOSE OF VASOACTIVE DRUG 2 IN THE LAST 24h (mcg/Kg/min):** \_\_\_\_\_

**4.28 TYPE OF VASOACTIVE DRUG 3:**

- Dobutamine
- Dopamine
- Enoximone
- Epinephrine: YES  NO
- Esmolol
- Levosimendan
- Metaraminol
- Metoprolol
- Milrinone
- Nicardipine
- Nitroglycerin
- Nitroprusside
- Norepinephrine: YES  NO
- Phenylephrine
- Tolazoline
- Vasopressin

**4.29 HIGHEST DOSE OF VASOACTIVE DRUG 3 IN THE LAST 24h (mcg/Kg/min):** \_\_\_\_\_

**4.30 USE OF CARDIAC ASSIST DEVICES IN THE LAST 24h:**

- Yes
- No

**4.31 USE OF ANTIBIOTICS IN THE LAST 24h:**



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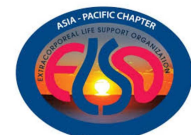
Yes  
No

## ANTIBIOTICS:

Amikacin		Ciprofloxacin	Norfloxacin	
Amoxicillin		Clarithromycin	Novobiocin	
Amoxicillin	+	Clindamycin	Ofloxacin	
Clavulanate		Cloxacillin	Oxacillin	
Ampicillin		Colistimethate	Oxytetracycline	
Ampicillin + Sulbactam		Cycloserine	Penicillin	
Atovaquone		Daptomycin	Piperacillin	
Azithromycin		Demeclocycline	Piperacillin	+
Aztreonam		Dicloxacillin	Tazobactam	
Bacampicillin		Dirithromycin	Podofilox	
Bacitracin		Doripenem	Polymyxin B	
Capreomycin		Doxycycline	Quinupristin	+
Carbenicillin	indanyl	Enoxacin	Dalfopristin	
sodium		Ertapenem	Retapamulin	
Cefaclor		Erythromycin	Rifapentine	
Cefadroxil		Fosfomycin	Rifaximin	
Cefamandole		Gatifloxacin	Saturated Solution of	
Cefazolin		Gemifloxacin	Potassium Iodide (SSKI)	
Cefdinir		Gentamicin	Sparfloxacin	
Cefditoren		Grepafloxacin	Spectinomycin	
Cefepime		Imipenem/Cilastatin	Streptomycin	
Cefixime		Imiquimod	Sulfadiazine	
Cefmetazole		Kanamycin	Sulfamethoxazole	
Cefonicid		Levofloxacin	Sulfisoxazole	
Cefoperazone		Lincomycin	Sulphur, precipitated in	
Cefotaxime		Linezolid	petrolatum	
Cefotetan		Lomefloxacin	TCA (trichloroacetic	
Cefoxitin		Loracarbef	acid), BCA (bichloroacetic acid).	
Cefpodoxime Proxetil		Mafenide	Teicoplanin	
Cefprozil		Meropenem	Telavancin	
Ceftaroline		Methenamine hippurate	Telithromycin	
Ceftazidime		Methicillin	Terbinafine	
Ceftibuten		Metronidazole	Tetracycline	
Ceftizoxime		Mezlocillin	Ticarillin	
Ceftobiprole		Minocycline	Ticarillin + Clavulanic	
Ceftriaxone		Moxifloxacin	Acid	
Cefuroxime		Mupirocin	Tigecycline	
Cephalexin		Nafcillin	Tobramycin	
Cephalothin		Nalidixic Acid	Trimethoprim	
Cephapirin		Neomycin	Trimethoprim	+
Cephradine		Netilmicin	Sulfamethoxazole	
Chloramphenicol		Nitrofurantoin	Trovafoxacin	
Cinoxacin		Nitrofurazone	Vancomycin	



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**4.32 Haemoglobin IN THE LAST 24h** g/dL \_\_\_\_\_ Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.32 Haemoglobin' blank.

**4.33 White Blood Cells IN THE LAST 24h** Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.33 White Blood Cells' blank.

**4.34 White Blood Cells Unit**X 10<sup>9</sup>/LX 10<sup>3</sup>/microL**4.35 AST/SGOT IN THE LAST 24h** U/L \_\_\_\_\_ Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.34 AST' blank.

**4.36 ALT/SGPT IN THE LAST 24h** U/L \_\_\_\_\_ Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.36 ALT' blank.

**4.37 ANTICOAGULANTS IN THE LAST 24h**

Yes

No

**4.38 TYPE OF ANTICOAGULANTS IN THE LAST 24h**

Continuous infusion of unfractionated heparin

Subcutaneous unfractionated heparin only

Low molecular heparin

Danaparoid Lepirudin

Argatroban

Hirulog and bivalirudin

Desirudin

Nafamostat Mesilate

Other

**4.39 TRANSFUSED PACKED RED BLOOD CELL CONCENTRATE IN THE LAST 24 HOURS**

Yes

No

**4.40 TRANSFUSED PLATELETS CONCENTRATE IN THE LAST 24 HOURS**

Yes

No



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**4.41 TRANSFUSED FRESH FROZEN PLASMA IN THE LAST 24 HOURS**

Yes  
No

**4.42 TRANSFUSED CRYOPRECIPITATES IN THE LAST 24 HOURS**

Yes  
No

**4.43 INFECTION COMPLICATION 1:**

Yes  
No

**4.44 SOURCE OF INFECTIOUS COMPLICATION 1**

Lungs	Central nervous system	Cardiac
Gastro-intestinal	Osteoarticular and bone	Bloodstream
Genito-urinary		Not known
Skin and soft tissue		

**4.45 CAUSATIVE PATHOGEN 1:**

Acinetobacter baumannii	Clostridium tetani (Tetanus)	Lymphogranuloma venereum (LGV)
Actinomyces	Corynebacterium diphtheriae	Methicillin Resistant Staphylococcus aureus
Aeromonas	Coxiella burnetii	Moraxella catarrhalis
Bacillus anthracis	Ehrlichia species	Morganella
Bacillus species	Eikenella corrodens	Mycobacterium abscessus
Bacteroides fragilis	Enterobacter species	Mycobacterium avium-complex (MAC, MAI, non-HIV)
Bacteroides species	Enterococcus	Mycobacterium chelonae
Bartonella species	Erysipelothrix rhusiopathiae	Mycobacterium fortuitum
Bordetella species	Escherichia coli	Mycobacterium gordonae
Borrelia burgdorferi	Francisella tularensis	Mycobacterium kansasii
Borrelia species	Haemophilus ducreyi (Chancroid)	Mycobacterium leprae
Brucella Species	Haemophilus influenzae	Mycobacterium marinum
Burkholderia cepacia	Helicobacter cinaedi and related species	Mycobacterium scrofulaceum
Burkholderia mallei	Helicobacter pylori	Mycobacterium tuberculosis
Burkholderia pseudomallei	Klebsiella granulomatis (Antibiotic Guide)	Mycobacterium ulcerans
Campylobacter and related species	Klebsiella species	Mycobacterium xenopi
Campylobacter jejuni	ESBL Klebsiella pneumoniae	
Capnocytophaga canimorsus	Lactobacillus	
Chlamydia trachomatis	Legionella pneumophila	
Chlamydomphila pneumoniae	Legionella species	
Chlamydomphila psittaci	Leptospira interrogans	
Citrobacter species	Listeria monocytogenes	
Clostridium botulinum		
Clostridium difficile		
Clostridium species		



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Mycoplasma pneumoniae (Antibiotic Guide)  
 Neisseria gonorrhoeae  
 Neisseria meningitidis  
 Nocardia  
 Other atypical mycobacteria  
 Pasteurella multocida  
 Peptostreptococcus/Peptococcus  
 Plesiomonas  
 Propionibacterium species  
 Proteus species  
 Providencia  
 Pseudomonas aeruginosa  
 Rhodococcus equi  
 Rickettsia rickettsii  
 Rickettsia species  
 Salmonella species  
 Serratia species  
 Shigella dysenteriae  
 Shigella species  
 Staphylococci, coagulase negative

Staphylococcus aureus  
 Stenotrophomonas maltophilia  
 Streptobacillus moniliformis  
 Streptococcus pneumoniae  
 Streptococcus pyogenes (Group A)  
 Streptococcus species  
 Treponema pallidum (syphilis)  
 Tropheryma whipplei  
 Vancomycin Resistant Enterococcus species  
 Vancomycin Resistant Staphylococcus aureus  
 Vibrio cholerae  
 Vibrio species (noncholera)  
 Yersinia pestis  
 Yersinia species (non-plague)  
 Absidia  
 Aspergillus  
 Basidiobolomycosis  
 Blastomyces dermatitidis

Candida albicans  
 Candida glabrata  
 Candida guilliermondii  
 Candida krusei  
 Candida lusitanae  
 Candida parapsilosis  
 Candida species  
 Candida tropicalis  
 Chromomycosis  
 Coccidioides immitis  
 Cryptococcus neoformans  
 Cunninghamella  
 Dermatophytes  
 Fusarium  
 Histoplasma capsulatum  
 Mucor  
 Mycetoma  
 Pneumocystis carinii  
 Pneumocystis jirovecii  
 Pseudallescheria boydii  
 Rhizomucor  
 Rhizopus  
 Saksanea  
 Sporothrix schenckii  
 Zygomycetes

**4.46 INFECTION COMPLICATION 2:**

Yes  
 No

**4.47 SOURCE OF INFECTIOUS COMPLICATION 2:**

Lungs  
 Gastro-intestinal  
 Genito-urinary  
 Skin and soft tissue

Central nervous system  
 Osteoarticular and bone

Cardiac  
 Bloodstream  
 Not known

**4.48 CAUSATIVE PATHOGEN 2:**

Acinetobacter baumannii  
 Actinomyces  
 Aeromonas  
 Bacillus anthracis  
 Bacillus species  
 Bacteroides fragilis  
 Bacteroides species  
 Bartonella species  
 Bordetella species  
 Borrelia burgdorferi  
 Borrelia species  
 Brucella Species  
 Burkholderia cepacia

Burkholderia mallei  
 Burkholderia pseudomallei  
 Campylobacter and related species  
 Campylobacter jejuni  
 Capnocytophaga canimorsus  
 Chlamydia trachomatis  
 Chlamydomydia pneumoniae  
 Chlamydomydia psittaci  
 Citrobacter species  
 Clostridium botulinum

Clostridium difficile  
 Clostridium species  
 Clostridium tetani (Tetanus)  
 Corynebacterium diphtheriae  
 Coxiella burnetii  
 Ehrlichia species  
 Eikenella corrodens  
 Enterobacter species  
 Enterococcus  
 Erysipelothrix rhusiopathiae  
 Escherichia coli

Francisella tularensis  
Haemophilus ducreyi  
(Chancroid)  
Haemophilus influenzae  
Helicobacter cinaedi and  
related species  
Helicobacter pylori  
Klebsiella granulomatis  
(Antibiotic Guide)  
Klebsiella species  
ESBL Klebsiella  
pneumoniae  
Lactobacillus  
Legionella pneumophila  
Legionella species  
Leptospira interrogans  
Listeria monocytogenes  
Lymphogranuloma  
venereum (LGV)  
Methicillin Resistant  
Staphylococcus aureus  
Moraxella catarrhalis  
Morganella  
Mycobacterium  
abscessus  
Mycobacterium avium-  
complex (MAC, MAI,  
non-HIV)  
Mycobacterium  
chelonae  
Mycobacterium  
fortuitum  
Mycobacterium  
gordonae  
Mycobacterium kansasii  
Mycobacterium leprae  
Mycobacterium  
marinum  
Mycobacterium  
scrofulaceum  
Mycobacterium  
tuberculosis

Mycobacterium ulcerans  
Mycobacterium xenopi  
Mycoplasma  
pneumoniae (Antibiotic  
Guide)  
Neisseria gonorrhoeae  
Neisseria meningitidis  
Nocardia  
Other atypical  
mycobacteria  
Pasteurella multocida  
Peptostreptococcus/Pep-  
tococcus  
Plesiomonas  
Propionibacterium  
species  
Proteus species  
Providencia  
Pseudomonas  
aeruginosa  
Rhodococcus equi  
Rickettsia rickettsii  
Rickettsia species  
Salmonella species  
Serratia species  
Shigella dysenteriae  
Shigella species  
Staphylococci, coagulase  
negative  
Staphylococcus aureus  
Stenotrophomonas  
maltophilia  
Streptobacillus  
moniliformis  
Streptococcus  
pneumoniae  
Streptococcus pyogenes  
(Group A)  
Streptococcus species  
Treponema pallidum  
(syphilis)  
Tropheryma whipplei

Vancomycin Resistant  
Enterococcus species  
Vancomycin Resistant  
Staphylococcus aureus  
Vibrio cholerae  
Vibrio species  
(noncholera)  
Yersinia pestis  
Yersinia species (non-  
plague)  
Absidia  
Aspergillus  
Basidiobolomyces  
Blastomyces dermatitidis  
Candida albicans  
Candida glabrata  
Candida guilliermondii  
Candida krusei  
Candida lusitanae  
Candida parapsilosis  
Candida species  
Candida tropicalis  
Chromomycosis  
Coccidioides immitis  
Cryptococcus  
neoformans  
Cunninghamella  
Dermatophytes  
Fusarium  
Histoplasma capsulatum  
Mucor  
Mycetoma  
Pneumocystis carinii  
Pneumocystis jirovecii  
Pseudallescheria boydii  
Rhizomucor  
Rhizopus  
Saksanea  
Sporothrix schenckii  
Zygomycetes

**4.49 INFECTION COMPLICATION 3:**

Yes  
No

**4.50 SOURCE OF INFECTIOUS COMPLICATION 3:**

Lungs  
Gastro-intestinal  
Genito-urinary  
Skin and soft tissue

Central nervous  
system  
Osteoarticular and  
bone

Cardiac  
Bloodstream  
Not known



**4.51 CAUSATIVE PATHOGEN 3:**

Acinetobacter baumannii	Legionella species	Stenotrophomonas maltophilia
Actinomyces	Leptospira interrogans	Streptobacillus moniliformis
Aeromonas	Listeria monocytogenes	Streptococcus pneumoniae
Bacillus anthracis	Lymphogranuloma venereum (LGV)	Streptococcus pyogenes (Group A)
Bacillus species	Methicillin Resistant Staphylococcus aureus	Streptococcus species
Bacteroides fragilis	Moraxella catarrhalis	Treponema pallidum (syphilis)
Bacteroides species	Morganella	Tropheryma whippelii
Bartonella species	Mycobacterium abscessus	Vancomycin Resistant Enterococcus species
Bordetella species	Mycobacterium avium-complex (MAC, MAI, non-HIV)	Vancomycin Resistant Staphylococcus aureus
Borrelia burgdorferi	Mycobacterium chelonae	Vibrio cholerae
Borrelia species	Mycobacterium fortuitum	Vibrio species (noncholera)
Brucella Species	Mycobacterium gordonae	Yersinia pestis
Burkholderia cepacia	Mycobacterium kansasii	Yersinia species (non-plague)
Burkholderia mallei	Mycobacterium leprae	Absidia
Burkholderia pseudomallei	Mycobacterium marinum	Aspergillus
Campylobacter and related species	Mycobacterium scrofulaceum	Basidiobolomycosis
Campylobacter jejuni	Mycobacterium tuberculosis	Blastomyces dermatitidis
Capnocytophaga canimorsus	Mycobacterium ulcerans	Candida albicans
Chlamydia trachomatis	Mycobacterium xenopi	Candida glabrata
Chlamydophila pneumoniae	Mycoplasma pneumoniae (Antibiotic Guide)	Candida guilliermondii
Chlamydophila psittaci	Neisseria gonorrhoeae	Candida krusei
Citrobacter species	Neisseria meningitidis	Candida lusitanae
Clostridium botulinum	Nocardia	Candida parapsilosis
Clostridium difficile	Other atypical mycobacteria	Candida species
Clostridium species	Pasteurella multocida	Candida tropicalis
Clostridium tetani (Tetanus)	Peptostreptococcus/Peptococcus	Chromomycosis
Corynebacterium diphtheriae	Plesiomonas	Coccidioides immitis
Coxiella burnetii	Propionibacterium species	Cryptococcus neoformans
Ehrlichia species	Proteus species	Cunninghamella
Eikenella corrodens	Providencia	Dermatophytes
Enterobacter species	Pseudomonas aeruginosa	Fusarium
Enterococcus	Rhodococcus equi	Histoplasma capsulatum
Erysipelothrix rhusiopathiae	Rickettsia rickettsii	Mucor
Escherichia coli	Rickettsia species	Mycetoma
Francisella tularensis	Salmonella species	Pneumocystis carinii
Haemophilus ducreyi (Chancroid)	Serratia species	Pneumocystis jirovecii
Haemophilus influenzae	Shigella dysenteriae	Pseudallescheria boydii
Helicobacter cinaedi and related species	Shigella species	Rhizomucor
Helicobacter pylori	Staphylococci, coagulase negative	Rhizopus
Klebsiella granulomatis (Antibiotic Guide)	Staphylococcus aureus	Saksanea
Klebsiella species		Sporothrix schenckii
ESBL Klebsiella pneumoniae		Zygomycetes
Lactobacillus		
Legionella pneumophila		

**4.52 HAEMORRHAGIC COMPLICATION 1:**

Yes  
No

**4.53 SOURCE OF HAEMORRHAGIC COMPLICATION 1:**

Lungs	Central nervous system	Not known
Gastro-intestinal	Osteoarticular and bone	
Genito-urinary	Cardiac	
Skin and soft tissue	Bloodstream	

**4.54 HAEMORRHAGIC COMPLICATION 2:**

Yes  
No

**4.55 SOURCE OF HAEMORRHAGIC COMPLICATION 2:**

Lungs	Skin and soft tissue	Cardiac
Gastro-intestinal	Central nervous system	Bloodstream
Genito-urinary	Osteoarticular and bone	Not known

**4.56 OTHER NON-HAEMORRHAGIC COMPLICATION (Please describe):**

\_\_\_\_\_ (TEXT)

**4.57 Ferritin in the last 24 hours: \_\_\_\_\_ (ng/mL)**

Only numbers from 0-1000

- Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.57 Ferritin' blank.

**4.58 D-dimer in the last 24 hours:**

\_\_\_\_\_ (ng/mL or mcg/mL)

Only numbers from 0-15000

- Not available

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.58 D-dimer' blank.

**4.59 Troponin in the last 24 hours:**

- Troponin T: \_\_\_\_\_ (ng/mL or ng/L)  
 Troponin I: \_\_\_\_\_ (ng/mL or ng/L)

If this data has already been entered in the 'Daily Case Report Form – Laboratory Results' section of the ISARIC CRF, please DO NOT re-enter the data here. Please leave '4.59 Troponin I' blank.

- High sensitivity troponin T: \_\_\_\_\_ (ng/mL or ng/L)  
 High sensitivity troponin I: \_\_\_\_\_ (ng/mL or ng/L)  
 Not available

**4.60 Cardiac BNP in the last 24 hours:**

\_\_\_\_\_ (picograms/mL)

Only numbers between 0-1000

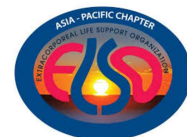
- Not available



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## CORE CASE RECORD FORM (EOT Final)

### 5 OUTCOMES

**5.1 DATE OF ECMO DISCONTINUATION:** \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 14/12/2019)

**5.2 DATE OF INVASIVE MECHANICAL VENTILATION DISCONTINUATION:** \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 14/12/2019)

**5.3 DATE OF ICU DISCHARGE:** \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 01/01/2019)

**5.4 DATE OF HOSPITAL DISCHARGE:** \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 01/01/2019)

**5.5 DATE OF DEATH:** \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (ONLY DATE, FROM 01/01/2019)

Not applicable

**5.6 SITE OF DEATH**

ICU

HOSPITAL

OUTSIDE HOSPITAL

Not applicable

**5.7 MAIN CAUSE OF ICU DEATH**

Respiratory Failure

Cardiac Failure

Liver Failure

Cardio-vascular accident

Septic shock

Haemorrhagic shock

Other

Not applicable

**5.8 ALIVE AT 28 DAYS POST ICU ADMISSION?**

Yes

No

**5.9 FINAL ASSESSMENT NOTES**

TEXT)

**5.10 At any time post ICU admission and until ICU discharge, did the patient present new cutaneous manifestations?**

- Yes
- No
- Not available

**If yes to 5.10, type of cutaneous manifestations (please select up to three (3) options)**

- Bullae



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- Macules
- Nodules
- Papules
- Plaques
- Purpura
- Pustules
- Rash
- Scale
- Urticaria
- Vesicles
- Other: \_\_\_\_\_

**If yes to 5.10, specify the involved regions (please select up to three (3) options):**

- Face
- Truck
- Upper limbs
- Hands
- Lower limbs
- Feet



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