Design and rationale of the COVID-19 Critical Care Consortium prospective, international, multicenter, observational study

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Design and rationale of the COVID-19 Critical Care Consortium prospective, international, multicenter, observational study

Short Title: COVID-19 CCC observational study protocol

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COVID-19 CCC observational study protocol   Li Bassi et al.

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2

COVID-19 CCC observational study protocol   Li Bassi et al.

ABSTRACT

Introduction: There is a paucity of data that can be used to guide the management of critically ill patients with coronavirus disease-2019 (COVID-19). In response, a research and data-sharing collaborative – The COVID-19 Critical Care Consortium – has been assembled to harness the cumulative experience of intensive care units (ICUs) worldwide. The resulting observational study provides a platform to rapidly disseminate detailed data and insights crucial to improving outcomes.

Methods and analysis: This is an international, multicenter, prospective, observational study of patients with confirmed or suspected SARS-CoV-2 infection admitted to ICUs. This is an evolving, open-ended study that commenced on January 1st, 2020 and currently includes more than 350 sites in over 48 countries. The study enrolls patients at the time of ICU admission and follows them to the time of death, hospital discharge, or 28 days post-ICU admission, whichever occurs last. Key data, collected via an electronic case report form devised in collaboration with the ISARIC/SPRINT-SARI networks, include: patient demographic data and risk factors, clinical features, severity of illness and respiratory failure, need for non-invasive and/or mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO), and associated complications, as well as data on adjunctive therapies.

Ethics and dissemination: Local principal investigators will ensure that the study adheres to all relevant national regulations, and that the necessary approvals are in place before a site may contribute data. In jurisdictions where a waiver of consent is deemed insufficient, prospective, representative or retrospective consent will be obtained, as appropriate. A web-based dashboard has been developed to provide relevant data and descriptive statistics to international collaborators in real-time. It is anticipated that, following study completion, all de-identified data will be made open access.

Clinical Trial Registration: ACTRN12620000421932. Available from: http://anzctr.org.au/ACTRN12620000421932.aspx.

3

COVID-19 CCC observational study protocol   Li Bassi et al.

STRENGTHS AND LIMITATIONS

- This protocol is of a pragmatic international, multicenter, observational clinical study of patients with confirmed or suspected SARS-CoV-2 infection admitted to ICUs around the world.

- This is an evolving clinical registry, which will facilitate the characterization of patients and their management and provide real-time information on associated characteristics and outcomes.

- These data will assist clinicians in deriving evidence-based practices for the care of critically ill patients infected by SARS-CoV-2.

- Patients will not receive identical treatments and care. While this will limit some aspects of data analysis, it will also give breadth to the scope of the investigation, as data on laboratory and patient characteristics, interventions and adjunct therapies, and outcomes will be available.

- This study relies on clinicians and support staff to accurately record data during a time of increased patient influx and ICU workload, raising concerns over data input error and completeness.

4

INTRODUCTION

The world is currently witnessing a viral pandemic. Cases of atypical pneumonia first emerged in Wuhan, China, in December 2019. [1] Investigation has identified the cause as a novel betacoronavirus, ultimately named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). [2] The virus, and the disease it causes – COVID-19 – has since spread internationally. The World Health Organization declared the outbreak a "Public Health Emergency of International Concern" on the 30th of January, 2020, and a "pandemic" on the 12th of March. There have now been more than 5.4 million confirmed infections globally, resulting in 340,000 deaths (as of the 26th of May, 2020). [3]

SARS-CoV-2, COVID-19, and critical illness

The mortality rate of COVID-19 among patients admitted to the intensive care unit (ICU) has been reported to be as high as 60%. [4-7] Early data and clinical experience indicate that this is caused primarily by acute hypoxemic respiratory failure (AHRF). [8-10] These same data have also prompted some authors to suggest that the pathobiology of COVID-19 – associated AHRF may differ from that of Acute Respiratory Distress Syndrome (ARDS). [11,12] This assertion hinges on reports of patients with severe COVID-19 associated AHRF and high pulmonary compliance, a presentation not thought to be typical of ARDS. Much has also been made of the high incidence of thromboembolic events in critically ill patients. [13,14] However, many reports are limited by either small numbers of patients or by geographic restrictions. These fail to account for variations in practices or for the variations between countries in patient, systemic, and organizational factors. Consequently, much of our current practice is driven by anecdotal cases or by limited case series.

Rationale for developing a worldwide registry of COVID-19 patients admitted to ICUs

We aim to improve conclusions robustness regarding the management, interventions and treatment of critically-ill COVID-19 patients around the world. We aim to do this by utilizing

5

combined data sets which detail a wide variety of patients entering the ICU at multiple stages of COVID-19 illness from diverse geographic locations. This ongoing research effort will aid in developing best practices based on evidence from a wide variety of ICUs throughout the world. This is especially important as there is currently a paucity of evidence-based guidelines and limited clinical resources globally. This data will also aid decision-making of clinicians working in healthcare systems that are currently managing or yet to face a surge in COVID-19 cases.

METHODS AND ANALYSIS

Study design

This is an international, multicenter, prospective, observational study. The study protocol v. 1.2.8 appears in [Supplement 1].

Study eligibility

The inclusion criteria are: (1) clinically suspected or laboratory-confirmed SARS-CoV-2 infection (by real time PCR and/or next generation sequencing), and (2) admission to an ICU. Patients admitted to an ICU for a reason other than SARS-CoV-2 infection are excluded. Patients of all ages from infants through adults can be enrolled into the study.

Enrolment and participating sites

This study commenced on January 1st, 2020. There is no fixed end date for the study. Currently, 350 centers are included, spanning 48 countries [Supplement 2], coordinated by regional leads and assistants [Supplement 3] and the operating team at the coordinating site [Supplement 3]. Co-enrolment with other studies, including interventional trials, is permitted.

Outcome measures

A summary of variables recorded by the study case report form (CRF) is presented in Table 1.

6

COVID-19 CCC observational study protocol   Li Bassi et al.

Data collection

Data collection methods

Streamlined data-collection instruments and procedures are used to minimize the workload at study centers. Data collection begins at the time of hospital admission using the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and Short Period Incidence Study of Severe Acute Respiratory Illness (SPRINT-SARI) data tools (https://isaric.tghn.org/COVID-19-CRF/). Data collection for the COVID-19 CCC observational study commences at the time of a patient's admission to an ICU, using a study specific adaptation of the ISARIC/SPRINT-SARI COVID-19 CRF [Supplement 4]. Figure 1 outlines the schedule of assessments used for patients included in the COVID-19 CCC study. De-identified study data are collected and managed using the REDCap electronic data capture tool hosted at the University of Oxford, United Kingdom. [15] Of note, an optional, interactive augmented data collection has been implemented through a platform developed specifically for the study by Amazon Web Services Australia (AWS, Sydney, Australia). A physical device and associated software tools assist with de-identified data collection and their transfer to the REDCap database. This approach has no impact on the ownership of data, which remains with the individual site. Full encryption is used, beginning from data ingestion into the Amazon cloud, through to transfer to the REDCap web application. Data will not be used for any purpose other than those described in the study protocol. Each site's principal investigator is responsible for ensuring data integrity. Regular written and web-based training is provided. In countries unable to upload data into a centralized database, the ability to retain a local database on a national server is available, with aggregated anonymized data exported centrally for analysis.

Inter-hospital transfer

If a patient is transferred from a facility participating in the COVID-19 CCC and ISARIC/SPRINT-SARI to another participating center, the patient's previously allocated

7

COVID-19 CCC observational study protocol   Li Bassi et al.

unique identifier transfers with them. However, sites will not have access to study 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. All sites will be asked to include a COVID-19 CCC and ISARIC/SPRINT-SARI study information sheet in any outgoing patient's documentation.

Data management

Several procedures are in place to optimize data quality and completeness. These include: (1) a detailed data dictionary, (2) quality assurance within the data management system, (3) quality assurance of key variables within the CRF, and (4) regular written and web-based training for local study investigators. A compendious CRF is fundamental to the success of this study. Extensive efforts have been made to limit data collection to essential variables. It is hoped that this will contribute to more complete data entry with a reduced burden on participating centers. Information that is not available to the investigator will not be treated as missing, and no assumptions will be made for missing data. An audit will be conducted on a randomly selected sample (approximately 5%) of cases. In-person site visits will not be feasible, given the nature of the study and pandemic. Sub-study projects will be accessed via the main CRF platform. Specific extensions will be used to collect additional variables, limiting the overall burden on data collectors, but allowing centers involved in sub-studies to enter data in the single REDCap format.

Data access

The coordinating team will have access to all collected data to assure integrity, provide oversight, and conduct the main study analyses. Individual sites will have access to all the data they collect. A multinational steering committee [Supplement 1] oversees registry operations worldwide and approves investigator-initiated or site-specific sub-studies, external requests for data, and reviews suggestions by participants. To date, several sub-studies have

8

COVID-19 CCC observational study protocol   Li Bassi et al.

been initiated focusing on the impact of COVID-19 on the brain, heart, kidneys, management and risks of ECMO, coagulation and thrombosis risks and long-term effects, all involving multi-center participation. Once approval is obtained, relevant de-identified data will be made available. It is anticipated that, following study completion, all de-identified data will be made open access.

Statistical considerations

Initial characterization will be descriptive, including all eligible patients at participating centers enrolled within defined timeframes. Where analysis is hypothesis-driven, sample size calculations and power analysis (where appropriate) will depend on the specific outcome or endpoint under consideration and will be pre-defined. Results that aim to show an association or test a hypothesis will include 95% confidence intervals. These intervals and associated means will be interpreted in terms of their clinical and statistical significance, and discussion may include whether a comparison is under-powered.

For discharge, mortality, and length-of-stay outcomes, we will use a survival analysis with competing risks approach. [16] We will graphically depict the risks of death and discharge over time using cumulative incidence plots. We will estimate which patient variables influence the risk of death and discharge using Cox regression, with separate models for death and discharge. In addition to Cox models, we will construct non-linear predictive models for both outcomes using Random Forest models, which will be externally validated on a hold-out test set. Comparison of the predictive performance of both the Cox regression and Random Forest modelling approaches will be made using: (1) a Brier score, [17] (2) area under the receiver operating characteristic (ROC) curves using a 2-sided DeLong test, and (3) calibration plots, characterized by visual inspection and reporting of slope and intercept. [17] For the Random Forest models, a Shapley Tree Explainer will be used to identify variables that are highly predictive of each outcome. [18] This analysis will follow the Transparent Reporting of a

9

COVID-19 CCC observational study protocol

Li Bassi et al.

Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) reporting guideline for prediction model development and validation. [19]

To show within-patient trends, we will plot continuous longitudinal variables over time using line plots. We will summarize each trend using daily averages and will estimate trends over time and the influence of patient variables using a linear mixed model with a random intercept per patient to control for repeated data. For binary variables, we will use panel bar charts to show the average change over time, and will model these variables using a generalized linear mixed model with a binomial distribution. A smooth estimation using cubic spline will be explored to estimate potential non-linear trends of the continuous longitudinal variables and binary variables.

Patient and public involvement in research

The data collection methodology of this study has been designed without patient or public input due to the urgent need for inclusion of prospective data from critically ill COVID-19. However, a consultative approach is planned via structured interviews, workshops and surveys to develop research questions, refine methods and ensure public voice helps to shape consumer focused outcomes.

ETHICS AND DISSEMINATION

Ethical considerations

Chief investigators and the study management team are responsible for ensuring that the study is conducted in accordance with both the protocol, Declaration of Helsinki and the Principles of Good Clinical Practice. The study management team will continue to work with local principal investigators to ensure that the study adheres to all relevant national regulations, and that the necessary approvals are in place before a site may contribute data. The principal investigator at each site is responsible for maintaining a securely-held enrolment log, linking each patient's hospital record number with the COVID-19 CCC study number, if

10

required. The original protocol and subsequent amendments will be translated into the main language of the collaborating institutions and submitted for institutional review board approval or an equivalent. Patients will not be enrolled under the conditions of an amended protocol, until after approval has been granted.

It is expected that this study will not require informed consent in most jurisdictions. This study is, in effect, a large-scale clinical audit, as all data are collected routinely. This may justify a waiver of consent. Any jurisdiction that deems informed consent necessary may use forms provided on our website (https://www.elso.org/COVID19/ECMOCARD.aspx). Within such jurisdictions, patients who meet the eligibility criteria will be approached directly. If this is not possible, due to the patient's incapacity, a model of retrospective or representative consent may be used, per local requirements.

Dissemination

Due to the evolving nature of the pandemic and the uncertainty surrounding its impact, this study was designed to be responsive to the international call for swift characterization of COVID-19 patients. Hence, in collaboration with University of Queensland and extramural collaboration with IBM Australia (St. Leonard's, Australia), a web-based dashboard has been developed to provide relevant data and descriptive statistics to international collaborators in real-time.

DISCUSSION

Herein we have described the rationale and design of an international, multicenter, observational registry of COVID-19 patients admitted to an ICU. To date, the characterization of patients admitted to ICUs with COVID-19 has been limited to national or single-center series. This study, using a large collaborative network, attempts to overcome the limitations induced by small patient numbers and geographic restrictions, by providing real-time global data. In a pandemic of an emerging pathogen, high-quality, real-time information is crucial to guide an optimal response. The speed of this response and cumulative experience of ICUs

11

worldwide offer the best framework for determining evidence-based best practices and, therefore, improving outcomes for those requiring critical care.

The design of the COVID-19 CCC study has several strengths. First, the care of patients admitted to the ICU, specifically those who are mechanically ventilated, is dependent on regional resources and may vary. [20,21] This potential heterogeneity is mitigated by the international composition of the consortium. Second, the study leverages novel data acquisition methods, which may improve and expedite data collection. Third, the registry-based, collaborative, and open-source approach of the study lends itself to the conduct of multiple prospective sub-studies. Fourth, the study incorporates the provision of a web-based dashboard, which provides real-time data in an accessible format.

Limitations

Patients will not receive identical treatments and care. While this will limit some aspects of data analysis, it will also give breadth to the scope of the investigation, as data on laboratory and patient characteristics, interventions and adjunct therapies, and outcomes will be available.

This study relies on clinicians and support staff to accurately record data during a time of increased patient influx and ICU workload, raising concerns over data input error and completeness. To overcome this, coordinators at each site have access to regular training, as well as 'drop-in' query sessions on-line.

This study will provide inclusive global characterization of critically ill patients with COVID-19. As the study is open-ended, continued data accrual will result in increased power to answer hypothesis-led questions over time and guide the development of evidence-based patient management tools to improve outcomes.

12

COVID-19 CCC observational study protocol   Li Bassi et al.

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14

Authors' contributions

GL, JS and JF conceived study. GL, JS, JF, AB, BL, SS and HD designed study. GL, JS, AC, IL, JF will coordinate study. Statistical analysis will be performed by AB, BL, SH and SS. JF, JM, SC, KW, SL, GA prepared the manuscript. All authors provided edits and critiqued manuscript for intellectual content.

Competing interests statement

None declared

Word count

2,305

TABLES AND FIGURES

Figure 1. Schematic study overview

The study ends at death, hospital discharge/transfer, or 28 days, whichever occurs latest.

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COVID-19 CCC observational study protocol   Li Bassi et al.

	Screening	ICU Admission	Start MV	Start ECMO	Daily	Outcomes
Eligibility criteria	x					
Demographics		x				
Co-morbidities		x				
Severity scoring		x				
Symptoms		x				
ABG and biochemistry		x	x	x	x	
Respiratory support			x	x	x	
Adjunctive therapies			x	x	x	
ECMO parameters				x	x	
Pulmonary mechanics				x	x	
Microbiology					x	
Blood transfusion					x	
Length of stay						x
Survival						x

Table 1. Assessment schedule

MV – mechanical ventilation; ECMO – extracorporeal membrane oxygenation; ABG – arterial

blood gas.

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

SUPPLEMENTAL FILES

SUPPLEMENT 1

STUDY PROTOCOL

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

Scientific Title	**Covid-19 Critical Care Consortium** **Incorporating the** **E**xtra**C**orporeal **M**embrane **O**xygenation for 2019 novel **C**oronavirus **A**cute **R**espiratory **D**isease (ECMOCARD)
Study Design	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).
The Collaborative	**In response to the COVID-19 outbreak and to assist in pandemic planning both locally and globally, a research collaborative has been assembled.** 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).
Study Aim and Objectives	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.
Inclusions/Exclusions	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.
Consent	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.
Study Setting	International multi-centre study, conducted in all collaborating hospitals/ICU-based research networks in Asia, Australia and New Zealand, Europe.
Sample Size	All patients with confirmed COVID-19 infection admitted to ICUs at the collaborative centres
Study Start Date	From the commencement of COVID-19 global epidemic
Study Duration	Until completion of COVID-19 global epidemic, as judged by the World Health Organization

CONFIDENTIAL

Data collection processes	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.

Table of contents

ACTRN12620000421932
Version 1.2.8
23 May 2020

10

ACTRN12620000421932
Version 1.2.8
23 May 2020

11

CONFIDENTIAL

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;

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[1–3]. The World Health Organization (WHO) defines SARI as an acute respiratory infection of recent onset (within 10 days) requiring hospitalisation, manifested by fever (≥38oC) or a history of fever and cough [4–6]. 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

ACTRN12620000421932
Version 1.2.8
23 May 2020

13

CONFIDENTIAL

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[7]. 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[8,9] and MERS-CoV[10,11], have caused serious respiratory infections, with mortality rates of 10% for SARS-CoV[12] and 37% for MERS-CoV[13].

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[14]. 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[15] 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

ACTRN12620000421932
Version 1.2.8
23 May 2020

14

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 microcopy (Fig. 1).

Figure 1

Figure 1: Cytopathic effect of the novel coronavirus, as reported in previous publication[15]

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 publicaition[15].

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[16], Japan[17], South Korea[18], Germany, Italy[19], France, Iran[20], USA[21] and many other countries[22]. An early case report in 41 patients with laboratory-confirmed COVID-19 infection in Wuhan has been reported[23]. 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)[24].

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[23]

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)***.

In a later retrospective report by Wang and collaborators[25], 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

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 (APELSO) 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.

CONFIDENTIAL

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

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). 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[5,26]. 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[27]. The CRF has previously been used in Singapore, New

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***

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

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

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***

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

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

ACTRN12620000421932
Version 1.2.8
23 May 2020

31

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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

ACTRN12620000421932
Version 1.2.8
23 May 2020

33

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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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ACTRN12620000421932
Version 1.2.8
23 May 2020

37

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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.

ACTRN12620000421932
Version 1.2.8
23 May 2020

38

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 resides 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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Authorship policy

Authorship will be determined according to the internationally agreed criteria for authorship (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

1

	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
New Zealand	Auckland	Auckland City Hospital	Shay McGuinness (CVICU)
Hong Kong	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
Indonesia	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

2

	West Java	Hasan Sadikin Hospital	Gezy Giwangkancana (Adult)
			Dadang H Somasetia (Paeds)
	Surabya	Airlanna University	Dr Neurinda Permata Kusumastuti
	Medan	Adam Malik Hospital	Bastian Lubis
	Semarang	Dr Kariadi Hospital Semarang	Moh Supriatna
	Yogyakarta	Sardjito Hospital	Desy Rusmawatiningtyas (Paeds)
			Dr. Bhirowo (Adult)
Japan	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

3

	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
	Kuyshu	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
Singapore	Singapore	National Centre for Infectious Diseases	Sennen Low
			Shawn Vasoo
		Tan Tock Seng Hospital	Chia Yew Woon
			Benjamin Ho

4

		National University Hospital	Kollengode Ramanathan
		KK Women's and Children's Hospital	Yee Hui Mok
South Korea	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 Unviersity Hostpital	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
Taiwan	Taipei	National Taiwan University Hospital	Yih-Sharng Chen, Jung-Yien Chien, Chih-Hsie
Thailand	Bangkok	Siriraj Hospital	Pranya Sakiyalak
Vietnam	Ho Chi Minh City	Hospital for Tropical Diseases	Trieu Huynh Trung
			Thuy Duong Bick
Italy	Milan	Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico	Mauro Panigada
			Antonio Pesenti
		Ospedale San Paolo	Davide Chiumello
	Rome	Children's Hospital Bambino Gesù	Matteo Di Nardo
		Policlinico Umberto, Sapienza University of Rome	Francesco Alessandri

5

	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
			Denise Battaglini
	Parma	Azienda Ospedaliero Universitaria Parma	Sandra Rossi Marta
			Velia Antonini
	Turin	Le Molinette Hospital (Ospedale Molinette Torino)	Luca Brazzi
			Gabriele Sales
	Palermo	ISMETT	Antonio Arcadipane
	Florence	Careggi Hospital	Adriano Peris
	Pisa	Azienda Ospedaliero Universitaria Pisana	Fabio Guarracino
	Verona	Verona Integrated University Hospital	Katia Donadello
	Padua	Padua University Hospital (Policlinico of Padova)	Andrea Dellamore and Paolo Navales
	Trento	Ospedale di Arco (Trento hospital)	MArco Cavana and Alberto Cucino
	Monza	Ospedale San Gerardo	Marco Giani
	Borgo	Borgo San Lorenzo Hospital	Vieri Parrini
USA	New York City	Columbia University Medical Centre	Dan Brodie
			Alexis Serra
			Darryl Abrams
		Northwell Health	Effe Mihelis
		Presbyterian Hospital, New York/ Weill Cornell Medical Centre	Debra Burns
	Los Angeles	Cedars-Sinai Medical Centre	Dominic Emerson

6

		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 Sichting
	Buffalo	Mercy Hospital of Baffalo	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

8

	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

9

	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
			Wanda Fikes (CRC)
		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

Scotland	Edinburgh	Royal Infirmary Edinburgh	Kenneth Baillie
	Aberdeen	Aberdeen Royal Infirmary (Foresterhill Health Campus)	Emma Hartley
Wales	Swansea	Swansea Hospital	Lenny Ivatt
Netherlands	Nijmegen	Radboud University Medical Centre	Tim Frenzel
	St. Antonious	St. Antonius Hospital	Nicole Van Belle
	Maastricht	Maastricht University Medical Centre	Roberto Lorusso
Belgium	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
Kuwait	Hadiya	Al-Adan Hospital	Tala Al-Dabbous
	Kuwait City	Kuwait ECLS program, Al-Amiri & Jaber Al-Ahmed Hospitals	Abdulrahman Al-Fares
Saudi Arabi	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
Austria	Vienna	Sozialmedizinisches Zentrum Süd - Kaiser-Franz-Josef-Spital	Tamara Seitz
		Medical University of Vienna	Nina Buchtele (ICU)
			Michael Schwameis (ED)
Philippines	Quezon City	National Kidney and Transplant Institute	Joselito Chavez
Estonia	Tallinn	North Estonia Medical Centre	Indrek Ratsep

11

	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 Aberta (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 Máñez 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

12

			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
Argentina	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
Colombia	Bucaramanga	Fundación Cardiovascular de Colombia	Leonardo Salazar
	Cali	Clinica Valle de Lilli	Diego Fernando Bautista Rincón
	Bogota	Fundación Clinica Shaio	Estefania Giraldo
Chile	Las Condes	Clinica Las Condez	Roderigo Diaz
	Santiago	Hospital del Tórax	Francisco Arancibia
	Santiago	Clinica Alemana De Santiago	Jerónimo Graf
Germany	Regensburg	Universitätsklinikum Regensburg (Klinik für Innere Medizin II)	Maximilian Malfertheiner
	Donaustauf	Donaustauf Hospital	Annette Schweda
	Regensburg	Barmherzige Bruder Regansburg	Stephan Schroll
	Munich	Medizinische Klinik und Poliklinik II	Stephanie Stecher
	Berlin	Charite-Univerrsitatsmedizi n Berlin	Roland Francis
	Passau	Klinikum Passau	Johannes Gebauer
	Nuremberg	Paracelsus Medical University Nuremberg	Matthias Baumgaertel

13

	Frankfurt	Universitätsklinikum Frankfurt (University Hospital Frankfurt)(Uniklinik)	Gösta Lotz
	Stockwerk	Universitätsspital Bern, Universitätsklinik für Herz- und Gefässchirurgie	Beate Hugi-Mayr
Brazil	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
Ireland	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
Poland	Krakow	University Hospital in Krakow	Konstanty S. Szuldrzynski
	Ghansk	Gdansk Medical University	Wojtek Karolak
South Africa	Johannesburg	Nelson Mandela Children's Hospital	Krubin Naidoo
		Netcare Unitas ECMO Centre	Marlice van Dyk
	Cape Town	Groote Schuur Hospital	David Thomson
Qatar	Qatar	Hamad General Hospital - Weill Cornell Medical College in Qatar	Ibrahim Hassan and Ali Hssain
Egypt	Cairo	Cairo University Hospital	Ahmad Abdelaziz
Sweden	Gothenburg	Sahlgrenska University Hospital	Pia Watson
Croatia	Zagreb	University Hospital Dubrava	Nikola Bradic
Luxembourg	Barble	Luxembourg Heart Center	Katja Ruck
Ukraine	Kyiv	Heart Institute Ministry of Health of Ukraine	Serhii Sudakevych
Switzerland	Bern	Inselspital University Hospital	Beate Hugi-Mayr
Turkey	Izmir	Dr. Suat Seren Chest Diseases and Surgery Practice and Training Centre	Cenk Kirakli
Mexico	Zapopan	Hospital Puerta de Hierro	Anna Greti

14

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

15

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SUPPLEMENT 3

REGIONAL LEADS/ASSISTANTS

OPERATIONAL TEAM

16

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	

17

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

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

19

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

20

SUPPLEMENT 4

CASE REPORT FORM

21

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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

Version 1.2.7
8 May 2020

1

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 PaO2/FiO2 ratio.**

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

Version 1.2.7
8 May 2020

2

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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.□ Not available

1.18 ARTERIAL BICARBONATE (HCO3⁻) 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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

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

☐ Truck

☐ Upper limbs

☐ Hands

☐ Lower limbs

☐ Feet

4

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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 PaO2/FiO2 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 PaO2/FiO2 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)

Version 1.2.7
8 May 2020

5

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 PaO2/FiO2 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 PaO2/FiO2 ratio.

□ Not available

2.9 ARTERIAL HCO3⁻ 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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

Ceftaroline
Ceftazidime
Ceftibuten
Ceftizoxime
Ceftobiprole
Ceftriaxone
Cefuroxime
Cephalexin
Cephalothin
Cephapirin
Cephradine
Chloramphenicol
Cinoxacin
Ciprofloxacin
Clarithromycin
Clindamycin
Cloxacillin
Colistimethate
Cycloserine
Daptomycin
Demeclocycline
Dicloxacillin
Dirithromycin
Doripenem
Doxycycline
Enoxacin
Ertapenem
Erythromycin
Fosfomycin
Gatifloxacin
Gemifloxacin
Gentamicin
Grepafloxacin
Imipenem/Cilastatin
Imiquimod
Kanamycin
Levofloxacin
Lincomycin
Linezolid
Lomefloxacin
Loracarbef
Mafenide
Meropenem
Methenamine hippurate
Methicillin
Metronidazole
Mezlocillin
Minocycline
Moxifloxacin
Mupirocin
Nafcillin
Nalidixic Acid

Neomycin
Netilmicin
Nitrofurantoin
Nitrofurazone
Norfloxacin
Novobiocin
Ofloxacin
Oxacillin
Oxytetracycline
Penicillin
Piperacillin
Piperacillin +
Tazobactam
Podofilox
Polymyxin B
Quinupristin +
Dalfopristin
Retapamulin
Rifapentine
Rifaximin
Saturated Solution of
Potassium Iodide (SSKI)
Sparfloxacin
Spectinomycin
Streptomycin
Sulfadiazine
Sulfamethoxazole
Sulfisoxazole
Sulphur, precipitated in
petrolatum
TCA (trichloroacetic
acid), BCA
(bichloroacetic acid).
Teicoplanin
Telavancin
Telithromycin
Terbinafine
Tetracycline
Ticarcillin
Ticarcillin + Clavulanic
Acid
Tigecycline
Tobramycin
Trimethoprim
Trimethoprim +
Sulfamethoxazole
Trovafloxacin
Vancomycin

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CORE CASE RECORD FORM (EOT Start ECMO)

3. UPON COMMENCMENT 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:

Version 1.2.7
8 May 2020

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)
Bylevel 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.

Version 1.2.7
8 May 2020

Ideal Body Weight formula:

Male patients: 50 + (0.91 x [height in cm – 152.4])

Female patients: 45.5 + (0.91 x {height in cm – 152.4])

□   Not available

3.20 POSITIVE END EXPIRATORY PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH2O):
_____ (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 PaO2/FiO2 ratio.

□   Not available

3.21 PEAK AIRWAY PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH2O): _____
(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 PaO2/FiO2 ratio.

□   Not available

3.22 AIRWAY PLATEAU PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH2O): _____
(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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.

□   Not available

3.26 ARTERIAL HCO3⁻ IN THE 6 HOURS BEFORE START OF ECMO _____mEq/L

Version 1.2.7
8 May 2020

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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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	Cefonicid
Amoxicillin +	sodium	Cefoperazone
Clavulanate	Cefaclor	Cefotaxime
Ampicillin	Cefadroxil	Cefotetan
Ampicillin + Sulbactam	Cefamandole	Cefoxitin
Atovaquone	Cefazolin	Cefpodoxime Proxetil
Azithromycin	Cefdinir	Cefprozil
Aztreonam	Cefditoren	Ceftaroline
Bacampicillin	Cefepime	Ceftazidime
Bacitracin	Cefixime	Ceftibuten

Version 1.2.7
8 May 2020

CONFIDENTIAL

1
2
3 Ceftizoxime
4 Ceftobiprole
5 Ceftriaxone
6 Cefuroxime
7 Cephalexin
8 Cephalothin
9 Cephapirin
10 Cephradine
11 Chloramphenicol
12 Cinoxacin
13 Ciprofloxacin
14 Clarithromycin
15 Clindamycin
16 Cloxacillin
17 Colistimethate
18 Cycloserine
19 Daptomycin
20 Demeclocycline
21 Dicloxacillin
22 Dirithromycin
23 Doripenem
24 Doxycycline
25 Enoxacin
26 Ertapenem
27 Erythromycin
28 Fosfomycin
29 Gatifloxacin
30 Gemifloxacin
31 Gentamicin
32 Grepafloxacin
33 Imipenem/Cilastatin
34 Imiquimod
35 Kanamycin
36 Levofloxacin
37 Lincomycin
38 Linezolid
39 Lomefloxacin
40 Loracarbef
41 Mafenide
42 Meropenem
43 Methenamine hippurate
44 Methicillin
45 Metronidazole
46 Mezlocillin
47 Minocycline
48 Moxifloxacin
49 Mupirocin
50 Nafcillin
51 Nalidixic Acid

Neomycin
Netilmicin
Nitrofurantoin
Nitrofurazone
Norfloxacin
Novobiocin
Ofloxacin
Oxacillin
Oxytetracycline
Penicillin
Piperacillin
Piperacillin +
Tazobactam
Podofilox
Polymyxin B
Quinupristin +
Dalfopristin
Retapamulin
Rifapentine
Rifaximin
Saturated Solution of
Potassium Iodide (SSKI)
Sparfloxacin
Spectinomycin
Streptomycin
Sulfadiazine
Sulfamethoxazole
Sulfisoxazole
Sulphur, precipitated in
petrolatum
TCA (trichloroacetic
acid), BCA
(bichloroacetic acid).
Teicoplanin
Telavancin
Telithromycin
Terbinafine
Tetracycline
Ticarcillin
Ticarcillin + Clavulanic
Acid
Tigecycline
Tobramycin
Trimethoprim
Trimethoprim +
Sulfamethoxazole
Trovafloxacin
Vancomycin

52
53
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57
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60

Version 1.2.7
8 May 2020

12

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 NEUROMUSCOLAR 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)
    Bylevel Positive Airway Pressure (BiPAP)
    Continuous Positive Airway Pressure (CPAP)

Version 1.2.7
8 May 2020

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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.Ideal Body Weight formula:

Male patients: 50 + (0.91 x [height in cm – 152.4])

Female patients: 45.5 + (0.91 x {height in cm – 152.4])

☐ Not available

4.13 POSITIVE END EXPIRATORY PRESSURE IN THE LAST 24h (cmH2O): _____ (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 PaO2/FiO2 ratio.☐ Not available

4.14 AIRWAY PLATEAU PRESSURE IN THE LAST 24h (cmH2O): _____ (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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.☐ Not available

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

Version 1.2.7
8 May 2020

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 PaO2/FiO2 ratio.□ Not available

4.18 ARTERIAL HCO3‾ 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 □

Version 1.2.7
8 May 2020

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:

Version 1.2.7
8 May 2020

16

Yes
No

ANTIBIOTICs:

Amikacin
Amoxicillin
Amoxicillin   +
Clavulanate
Ampicillin
Ampicillin + Sulbactam
Atovaquone
Azithromycin
Aztreonam
Bacampicillin
Bacitracin
Capreomycin
Carbenicillin   indanyl
sodium
Cefaclor
Cefadroxil
Cefamandole
Cefazolin
Cefdinir
Cefditoren
Cefepime
Cefixime
Cefmetazole
Cefonicid
Cefoperazone
Cefotaxime
Cefotetan
Cefoxitin
Cefpodoxime Proxetil
Cefprozil
Ceftaroline
Ceftazidime
Ceftibuten
Ceftizoxime
Ceftobiprole
Ceftriaxone
Cefuroxime
Cephalexin
Cephalothin
Cephapirin
Cephradine
Chloramphenicol
Cinoxacin

Ciprofloxacin
Clarithromycin
Clindamycin
Cloxacillin
Colistimethate
Cycloserine
Daptomycin
Demeclocycline
Dicloxacillin
Dirithromycin
Doripenem
Doxycycline
Enoxacin
Ertapenem
Erythromycin
Fosfomycin
Gatifloxacin
Gemifloxacin
Gentamicin
Grepafloxacin
Imipenem/Cilastatin
Imiquimod
Kanamycin
Levofloxacin
Lincomycin
Linezolid
Lomefloxacin
Loracarbef
Mafenide
Meropenem
Methenamine hippurate
Methicillin
Metronidazole
Mezlocillin
Minocycline
Moxifloxacin
Mupirocin
Nafcillin
Nalidixic Acid
Neomycin
Netilmicin
Nitrofurantoin
Nitrofurazone

Norfloxacin
Novobiocin
Ofloxacin
Oxacillin
Oxytetracycline
Penicillin
Piperacillin
Piperacillin   +
Tazobactam
Podofilox
Polymyxin B
Quinupristin   +
Dalfopristin
Retapamulin
Rifapentine
Rifaximin
Saturated   Solution   of
Potassium Iodide (SSKI)
Sparfloxacin
Spectinomycin
Streptomycin
Sulfadiazine
Sulfamethoxazole
Sulfisoxazole
Sulphur,   precipitated   in
petrolatum
TCA   (trichloroacetic
acid), BCA (bichloroacetic acid).
Teicoplanin
Telavancin
Telithromycin
Terbinafine
Tetracycline
Ticarcillin
Ticarcillin + Clavulanic
Acid
Tigecycline
Tobramycin
Trimethoprim
Trimethoprim   +
Sulfamethoxazole
Trovafloxacin
Vancomycin

Version 1.2.7
8 May 2020

17

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 10^9/L
X 10^3/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

Version 1.2.7
8 May 2020

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

Gastro-intestinal

Genito-urinary

Skin and soft tissue

Central nervous system

Osteoarticular and bone

Cardiac

Bloodstream

Not known

4.45 CAUSATIVE PATHOGEN 1:

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

Chlamydophila pneumoniae

Chlamydophila 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

Version 1.2.7

8 May 2020

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 lusitaniae
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
Chlamydophila pneumoniae
Chlamydophila 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

Version 1.2.7
8 May 2020

CONFIDENTIAL

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
Basidiobolomycosis
Blastomyces dermatitidis
Candida albicans
Candida glabrata
Candida guilliermondii
Candida krusei
Candida lusitaniae
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

Version 1.2.7
8 May 2020

21

4.51 CAUSATIVE PATHOGEN 3:

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
Chlamydophila pneumoniae
Chlamydophila 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/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 lusitaniae
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

Version 1.2.7
8 May 2020

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

Version 1.2.7
8 May 2020

CONFIDENTIAL

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Version 1.2.7
8 May 2020

24

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

Version 1.2.7
8 May 2020

25

□　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

Version 1.2.7
8 May 2020

26

Design and rationale of the COVID-19 Critical Care Consortium, international, multicenter, observational study: A study protocol

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Design and rationale of the COVID-19 Critical Care Consortium, international, multicenter, observational study: A study protocol

Short Title: COVID-19 CCC observational study protocol

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2

COVID-19 CCC observational study protocol   Li Bassi et al.

ABSTRACT

Introduction: There is a paucity of data that can be used to guide the management of critically ill patients with coronavirus disease-2019 (COVID-19). In response, a research and data-sharing collaborative – The COVID-19 Critical Care Consortium – has been assembled to harness the cumulative experience of intensive care units (ICUs) worldwide. The resulting observational study provides a platform to rapidly disseminate detailed data and insights crucial to improving outcomes.

Methods and analysis: This is an international, multicenter observational study of patients with confirmed or suspected SARS-CoV-2 infection admitted to ICUs. This is an evolving, open-ended study that commenced on January 1st, 2020 and currently includes more than 350 sites in over 48 countries. The study enrolls patients at the time of ICU admission and follows them to the time of death, hospital discharge, or 28 days post-ICU admission, whichever occurs last. Key data, collected via an electronic case report form devised in collaboration with the ISARIC/SPRINT-SARI networks, include: patient demographic data and risk factors, clinical features, severity of illness and respiratory failure, need for non-invasive and/or mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO), and associated complications, as well as data on adjunctive therapies.

Ethics and dissemination: Local principal investigators will ensure that the study adheres to all relevant national regulations, and that the necessary approvals are in place before a site may contribute data. In jurisdictions where a waiver of consent is deemed insufficient, prospective, representative or retrospective consent will be obtained, as appropriate. A web-based dashboard has been developed to provide relevant data and descriptive statistics to international collaborators in real-time. It is anticipated that, following study completion, all de-identified data will be made open access.

3

Clinical Trial Registration: ACTRN12620000421932. Available from: http://anzctr.org.au/ACTRN12620000421932.aspx.

STRENGTHS AND LIMITATIONS

- This protocol is of a pragmatic international, multicenter, observational clinical study of patients with confirmed or suspected SARS-CoV-2 infection admitted to ICUs around the world.

- This is an evolving clinical registry, which will facilitate the characterization of patients and their management and provide real-time information on associated characteristics and outcomes.

- These data will assist clinicians in deriving evidence-based practices for the care of critically ill patients infected by SARS-CoV-2.

- Patients will not receive identical treatments and care. While this will limit some aspects of data analysis, it will also give breadth to the scope of the investigation, as data on laboratory and patient characteristics, interventions and adjunct therapies, and outcomes will be available.

- This study relies on clinicians and support staff to accurately record data during a time of increased patient influx and ICU workload, raising concerns over data input error and completeness.

4

INTRODUCTION

The world is currently witnessing a viral pandemic. Cases of atypical pneumonia first emerged in Wuhan, China, in December 2019. [1] Investigation has identified the cause as a novel betacoronavirus, ultimately named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). [2] The virus, and the disease it causes – COVID-19 – has since spread internationally. The World Health Organization declared the outbreak a "Public Health Emergency of International Concern" on the 30th of January, 2020, and a "pandemic" on the 12th of March. There have now been more than 39 million confirmed infections globally, resulting in 1.1 million deaths (as of the 17th of October, 2020). [3]

SARS-CoV-2, COVID-19, and critical illness

The mortality rate of COVID-19 among patients admitted to the intensive care unit (ICU) has been reported around 30% [4] and substantially higher for mechanically ventilated patients [5–9] Early data and clinical experience indicate that this is caused primarily by acute hypoxemic respiratory failure (AHRF). [10,11] These same data have also prompted some authors to suggest that the pathobiology of COVID-19 – associated AHRF may differ from that of Acute Respiratory Distress Syndrome (ARDS). [12,13] This assertion hinges on reports of patients with severe COVID-19 associated AHRF and high pulmonary compliance, a presentation not thought to be typical of ARDS. Much has also been made of the high incidence of thromboembolic events in critically ill patients. [14,15] However, many reports are limited by either small numbers of patients or by geographic restrictions. These fail to account for variations in practices or for the variations between countries in patient, systemic, and organizational factors. Consequently, much of our current practice is driven by anecdotal cases or by limited case series.

Rationale for developing a worldwide registry of COVID-19 patients admitted to ICUs

5

We aim to improve conclusions robustness regarding the management, interventions and treatment of critically-ill COVID-19 patients around the world. We aim to do this by utilizing combined data sets which detail a wide variety of patients entering the ICU at multiple stages of COVID-19 illness from diverse geographic locations. This ongoing research effort will aid in developing best practices based on evidence from a wide variety of ICUs throughout the world. This is especially important as there is currently a paucity of evidence-based guidelines and limited clinical resources globally. This data will also aid decision-making of clinicians working in healthcare systems that are currently managing or yet to face a surge in COVID-19 cases.

METHODS AND ANALYSIS

Study design

This is an international, multicenter, prospective, observational study. The study protocol v. 1.2.8 appears in [Supplement 1].

Study eligibility

The inclusion criteria are: (1) clinically suspected (as determined by attending physician) or laboratory-confirmed SARS-CoV-2 infection (by real time PCR and/or next generation sequencing), and (2) admission to an ICU. Patients admitted to an ICU for a reason other than SARS-CoV-2 infection are excluded. In addition, patients who were recently diagnosed with SARS-CoV-2 infection and later admitted to the ICU for reasons not related to the SARS-CoV-2 infection will be excluded. Patients of all ages from infants through adults can be enrolled into the study.

Enrolment and participating sites

6

This study commenced on January 1st, 2020. There is no fixed end date for the study. Currently, 350 centers are included, spanning 48 countries [Supplement 2], coordinated by regional leads and assistants [Supplement 3] and the operating team at the coordinating site [Supplement 3]. Co-enrolment with other studies, including interventional trials, is permitted.

Outcome measures

A summary of variables recorded by the study case report form (CRF) is presented in Table 1.

Data collection

Data collection methods

Streamlined data-collection instruments and procedures are used to minimize the workload at study centers. Data can be collected and entered prospectively (preferred) or retrospectively dependent on the participating site's resources. Data collection begins at the time of hospital admission using the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and Short Period Incidence Study of Severe Acute Respiratory Illness (SPRINT-SARI) data tools (https://isaric.tghn.org/COVID-19-CRF/). Data collection for the COVID-19 CCC observational study commences at the time of a patient's admission to an ICU, using a study specific adaptation of the ISARIC/SPRINT-SARI COVID-19 CRF [Supplement 4]. Figure 1 outlines the schedule of assessments used for patients included in the COVID-19 CCC study. De-identified study data are collected and managed using the REDCap electronic data capture tool hosted at the University of Oxford, United Kingdom. [16] Data will not be used for any purpose other than those described in the study protocol. Each site's principal investigator is responsible for ensuring data integrity. Regular written and web-based training is provided. In countries unable to upload data into a centralized database, the ability

7

to retain a local database on a national server is available, with aggregated anonymized data exported centrally for analysis.

Inter-hospital transfer

If a patient is transferred from a facility participating in the COVID-19 CCC and ISARIC/SPRINT-SARI to another participating center, the patient's previously allocated unique identifier transfers with them. However, sites will not have access to study 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. All sites will be asked to include a COVID-19 CCC and ISARIC/SPRINT-SARI study information sheet in any outgoing patient's documentation.

Data management

Several procedures are in place to optimize data quality and completeness. These include: (1) a detailed data dictionary, (2) quality assurance within the data management system, (3) quality assurance of key variables within the CRF, and (4) regular written and web-based training for local study investigators. A compendious CRF is fundamental to the success of this study. Extensive efforts have been made to limit data collection to essential variables. It is hoped that this will contribute to more complete data entry with a reduced burden on participating centers. Information that is not available to the investigator will not be treated as missing, and no assumptions will be made for missing data. An audit will be conducted on a randomly selected sample (approximately 5%) of cases. In-person site visits will not be feasible, given the nature of the study and pandemic. Sub-study projects will be accessed via the main CRF platform. Specific extensions will be used to collect additional variables, limiting the overall burden on

data collectors, but allowing centers involved in sub-studies to enter data in the single REDCap format.

Data access

The coordinating team will have access to all collected data to assure integrity, provide oversight, and conduct the main study analyses. Individual sites will have access to all the data they collect. A multinational steering committee [Supplement 1] oversees registry operations worldwide and approves investigator-initiated or site-specific sub-studies, external requests for data, and reviews suggestions by participants. To date, several sub-studies have been initiated focusing on the impact of COVID-19 on the brain, heart, kidneys, management and risks of ECMO, coagulation and thrombosis risks and long-term effects, all involving multi-center participation. Once approval is obtained, relevant de-identified data will be made available. It is anticipated that, following study completion, all de-identified data will be made open access.

Statistical considerations

Initial characterization will be descriptive, including all eligible patients at participating centers enrolled within defined timeframes. Where analysis is hypothesis-driven, sample size calculations and power analysis (where appropriate) will depend on the specific outcome or endpoint under consideration and will be pre-defined. Results that aim to show an association or test a hypothesis will include 95% confidence intervals. These intervals and associated means will be interpreted in terms of their clinical and statistical significance, and discussion may include whether a comparison is under-powered.

For discharge, mortality, and length-of-stay outcomes, we will use a survival analysis with competing risks approach. [17] We will graphically depict the risks of death and discharge over time using cumulative incidence plots. We will estimate which patient variables influence the

9

risk of death and discharge using Cox regression, with separate models for death and discharge. In addition to Cox models, we will construct non-linear predictive models for both outcomes using Random Forest models, which will be externally validated on a hold-out test set. Comparison of the predictive performance of both the Cox regression and Random Forest modelling approaches will be made using: (1) a Brier score, [18] (2) area under the receiver operating characteristic (ROC) curves using a 2-sided DeLong test, and (3) calibration plots, characterized by visual inspection and reporting of slope and intercept. [18] For the Random Forest models, a Shapley Tree Explainer will be used to identify variables that are highly predictive of each outcome. [19] This analysis will follow the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) reporting guideline for prediction model development and validation. [20]

To show within-patient trends, we will plot continuous longitudinal variables over time using line plots. We will summarize each trend using daily averages and will estimate trends over time and the influence of patient variables using a linear mixed model with a random intercept per patient to control for repeated data. For binary variables, we will use panel bar charts to show the average change over time, and will model these variables using a generalized linear mixed model with a binomial distribution. A smooth estimation using cubic spline will be explored to estimate potential non-linear trends of the continuous longitudinal variables and binary variables.

Patient and public involvement in research

The data collection methodology of this study has been designed without patient or public input due to the urgent need for inclusion of prospective data from critically ill COVID-19. However, a consultative approach is planned via structured interviews, workshops and surveys to develop

10

COVID-19 CCC observational study protocol   Li Bassi et al.

research questions, refine methods and ensure public voice helps to shape consumer focused outcomes.

ETHICS AND DISSEMINATION

Ethical considerations

Chief investigators and the study management team are responsible for ensuring that the study is conducted in accordance with both the protocol, Declaration of Helsinki and the Principles of Good Clinical Practice. The study management team will continue to work with local principal investigators to ensure that the study adheres to all relevant national regulations, and that the necessary approvals are in place before a site may contribute data. The principal investigator at each site is responsible for maintaining a securely-held enrolment log, linking each patient's hospital record number with the COVID-19 CCC study number, if required. The original protocol and subsequent amendments will be translated into the main language of the collaborating institutions and submitted for institutional review board approval or an equivalent. Patients will not be enrolled under the conditions of an amended protocol, until after approval has been granted.

It is expected that this study will not require informed consent in most jurisdictions. This study is, in effect, a large-scale clinical audit, as all data are collected routinely. This may justify a waiver of consent. Any jurisdiction that deems informed consent necessary may use forms provided on our website (https://www.elso.org/COVID19/ECMOCARD.aspx). Within such jurisdictions, patients who meet the eligibility criteria will be approached directly. If this is not possible, due to the patient's incapacity, a model of retrospective or representative consent may be used, per local requirements.

Dissemination

11

Due to the evolving nature of the pandemic and the uncertainty surrounding its impact, this study was designed to be responsive to the international call for swift characterization of COVID-19 patients. Hence, in collaboration with University of Queensland and extramural collaboration with IBM Australia (St. Leonard's, Australia), a web-based dashboard has been developed to provide relevant data and descriptive statistics to international collaborators in real-time. The collected data will also eventually be made available and shared on a public open access platform once core research questions have been answered.

DISCUSSION

Herein we have described the rationale and design of an international, multicenter, observational registry of COVID-19 patients admitted to an ICU. To date, the characterization of patients admitted to ICUs with COVID-19 has been limited to national or single-center series. This study, using a large collaborative network, attempts to overcome the limitations induced by small patient numbers and geographic restrictions, by providing real-time global data. In a pandemic of an emerging pathogen, high-quality, real-time information is crucial to guide an optimal response. The speed of this response and cumulative experience of ICUs worldwide offer the best framework for determining evidence-based best practices and, therefore, improving outcomes for those requiring critical care.

The design of the COVID-19 CCC study has several strengths. First, the care of patients admitted to the ICU, specifically those who are mechanically ventilated, is dependent on regional resources and may vary. [21,22] This potential heterogeneity is mitigated by the international composition of the consortium. In addition, we are planning to further characterize individual ICUs, collecting data on nurse/doctor to patient ratio, capacity, and potential expanded capacity. Second, the study leverages novel data acquisition methods, which may improve and expedite data collection. Third, the registry-based, collaborative, and

12

open-source approach of the study lends itself to the conduct of multiple prospective sub-studies. Fourth, the study incorporates the provision of a web-based dashboard, which provides real-time data in an accessible format.

Limitations

Patients will not receive identical treatments and care. While this will limit some aspects of data analysis, it will also give breadth to the scope of the investigation, as data on laboratory and patient characteristics, interventions and adjunct therapies, and outcomes will be available.

This study relies on clinicians and support staff to accurately record data during a time of increased patient influx and ICU workload, raising concerns over data input error and completeness. To overcome this, coordinators at each site have access to regular training, as well as 'drop-in' query sessions on-line.

This study will provide inclusive global characterization of critically ill patients with COVID-19. As the study is open-ended, continued data accrual will result in increased power to answer hypothesis-led questions over time and guide the development of evidence-based patient management tools to improve outcomes.

13

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15

Authors' contributions

We hereby confirm that all authors listed below have provided substantial contributions to either the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND Drafting the work or revising it critically for important intellectual content; AND Final approval of the version to be published. In addition, all authors listed below agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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16

Word count

2,322

TABLES AND FIGURES

Figure 1. Schematic study overview

The figure shows in detail periods of data collection into the ISARIC case report form (dark blue), COVID-19 Critical Care Consortium (COVID-19 CCC) case report form (red) and for both case report forms (light blue). As shown, data for the COVID-19 Critical Care Consortium can be collected and entered prospectively (preferred) or retrospectively dependent on the participating site's resources. The study ends at death, hospital discharge/transfer, or 28 days, whichever occurs latest.

18

COVID-19 CCC observational study protocol   Li Bassi et al.

	Screening	ICU Admission	Start MV	Start ECMO	Daily	Outcomes
Eligibility criteria	x					
Demographics		x				
Co-morbidities		x				
Severity scoring		x				
Symptoms		x				
ABG and biochemistry		x	x	x	x	
Respiratory support			x	x	x	
Adjunctive therapies			x	x	x	
ECMO parameters				x	x	
Pulmonary mechanics				x	x	
Microbiology					x	
Blood transfusion					x	
Length of stay						x
Survival						x

Table 1. Assessment schedule

MV – mechanical ventilation; ECMO – extracorporeal membrane oxygenation; ABG – arterial

blood gas.

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Death,
hospital discharge,
or 28 days

Prospective/Retrospective data collection

ICU admission

Retrospective data collection

Hospital admission

COVID-19 CCC Observational Study

ISARIC/SPRINT-SARI

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

SUPPLEMENTAL FILES

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
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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

Scientific Title	**Covid-19 Critical Care Consortium** **Incorporating the** **E**xtra**C**orporeal **M**embrane **O**xygenation for 2019 novel **C**oronavirus **A**cute **R**espiratory **D**isease (ECMOCARD)
Study Design	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).
The Collaborative	**In response to the COVID-19 outbreak and to assist in pandemic planning both locally and globally, a research collaborative has been assembled.** 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).
Study Aim and Objectives	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.
Inclusions/Exclusions	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.
Consent	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.
Study Setting	International multi-centre study, conducted in all collaborating hospitals/ICU-based research networks in Asia, Australia and New Zealand, Europe.
Sample Size	All patients with confirmed COVID-19 infection admitted to ICUs at the collaborative centres
Study Start Date	From the commencement of COVID-19 global epidemic
Study Duration	Until completion of COVID-19 global epidemic, as judged by the World Health Organization

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Data collection processes	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.

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Table of contents

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11

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;

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[1–3]. The World Health Organization (WHO) defines SARI as an acute respiratory infection of recent onset (within 10 days) requiring hospitalisation, manifested by fever (≥38oC) or a history of fever and cough [4–6]. 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

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[7]. 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[8,9] and MERS-CoV[10,11], have caused serious respiratory infections, with mortality rates of 10% for SARS-CoV[12] and 37% for MERS-CoV[13].

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[14]. 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[15] 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 microcopy (Fig. 1).

Figure 1

Figure 1: Cytopathic effect of the novel coronavirus, as reported in previous publication[15]

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 publicaition[15].

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[16], Japan[17], South Korea[18], Germany, Italy[19], France, Iran[20], USA[21] and many other countries[22]. An early case report in 41 patients with laboratory-confirmed COVID-19 infection in Wuhan has been reported[23]. 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)[24].

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[23]

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)***.

In a later retrospective report by Wang and collaborators[25], 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

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 (APELSO) 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

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). 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

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[5,26]. 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[27]. The CRF has previously been used in Singapore, New

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***

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

ACTRN12620000421932
Version 1.2.8
23 May 2020

27

CONFIDENTIAL

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***

CONFIDENTIAL

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

ACTRN12620000421932
Version 1.2.8
23 May 2020

29

CONFIDENTIAL

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

ACTRN12620000421932
Version 1.2.8
23 May 2020

30

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

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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Page 56 of 108

SPRINT SARI
2019 n-CoV

ISARIC

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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.

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 resides 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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Authorship policy

Authorship will be determined according to the internationally agreed criteria for authorship (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

1

	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
New Zealand	Auckland	Auckland City Hospital	Shay McGuinness (CVICU)
Hong Kong	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
Indonesia	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

2

	West Java	Hasan Sadikin Hospital	Gezy Giwangkancana (Adult)
			Dadang H Somasetia (Paeds)
	Surabya	Airlanna University	Dr Neurinda Permata Kusumastuti
	Medan	Adam Malik Hospital	Bastian Lubis
	Semarang	Dr Kariadi Hospital Semarang	Moh Supriatna
	Yogyakarta	Sardjito Hospital	Desy Rusmawatiningtyas (Paeds)
			Dr. Bhirowo (Adult)
Japan	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

3

	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
	Kuyshu	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
Singapore	Singapore	National Centre for Infectious Diseases	Sennen Low
			Shawn Vasoo
		Tan Tock Seng Hospital	Chia Yew Woon
			Benjamin Ho

4

		National University Hospital	Kollengode Ramanathan
		KK Women's and Children's Hospital	Yee Hui Mok
South Korea	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 Unviersity Hostpital	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
Taiwan	Taipei	National Taiwan University Hospital	Yih-Sharng Chen, Jung-Yien Chien, Chih-Hsie
Thailand	Bangkok	Siriraj Hospital	Pranya Sakiyalak
Vietnam	Ho Chi Minh City	Hospital for Tropical Diseases	Trieu Huynh Trung
			Thuy Duong Bick
Italy	Milan	Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico	Mauro Panigada
			Antonio Pesenti
		Ospedale San Paolo	Davide Chiumello
	Rome	Children's Hospital Bambino Gesù	Matteo Di Nardo
		Policlinico Umberto, Sapienza University of Rome	Francesco Alessandri

5

	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 Grie
	Genoa	Ospedale Gaslini	Andrea Moscatelli
		San Martino Hospital	Paolo Pelosi
			Denise Battaglini
	Parma	Azienda Ospedaliero Universitaria Parma	Sandra Rossi Marta
			Velia Antonini
	Turin	Le Molinette Hospital (Ospedale Molinette Torino)	Luca Brazzi
			Gabriele Sales
	Palermo	ISMETT	Antonio Arcadipane
	Florence	Careggi Hospital	Adriano Peris
	Pisa	Azienda Ospedaliero Universitaria Pisana	Fabio Guarracino
	Verona	Verona Integrated University Hospital	Katia Donadello
	Padua	Padua University Hospital (Policlinico of Padova)	Andrea Dellamore and Paolo Navales
	Trento	Ospedale di Arco (Trento hospital)	MArco Cavana and Alberto Cucino
	Monza	Ospedale San Gerardo	Marco Giani
	Borgo	Borgo San Lorenzo Hospital	Vieri Parrini
USA	New York City	Columbia University Medical Centre	Dan Brodie
			Alexis Serra
			Darryl Abrams
		Northwell Health	Effe Mihelis
		Presbyterian Hospital, New York/ Weill Cornell Medical Centre	Debra Burns
	Los Angeles	Cedars-Sinai Medical Centre	Dominic Emerson

6

		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 Sichting
	Buffalo	Mercy Hospital of Baffalo	Harsh Jain
	Indiana	Indiana University Health	Juan Salgado
	Washington	George Washington University Hospital	Elizabeth Pocock

7

	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

8

	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

9

	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
		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)
	Texas	Baylor Scott & White Health - Temple	Dr Jorge Velazco (PI)
			Margarite Grable
			Wanda Fikes (CRC)
		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

10

Scotland	Edinburgh	Royal Infirmary Edinburgh	Kenneth Baillie
	Aberdeen	Aberdeen Royal Infirmary (Foresterhill Health Campus)	Emma Hartley
Wales	Swansea	Swansea Hospital	Lenny Ivatt
Netherlands	Nijmegen	Radboud University Medical Centre	Tim Frenzel
	St. Antonious	St. Antonius Hospital	Nicole Van Belle
	Maastricht	Maastricht University Medical Centre	Roberto Lorusso
Belgium	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
Kuwait	Hadiya	Al-Adan Hospital	Tala Al-Dabbous
	Kuwait City	Kuwait ECLS program, Al-Amiri & Jaber Al-Ahmed Hospitals	Abdulrahman Al-Fares
Saudi Arabi	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
Austria	Vienna	Sozialmedizinisches Zentrum Süd - Kaiser-Franz-Josef-Spital	Tamara Seitz
		Medical University of Vienna	Nina Buchtele (ICU)
			Michael Schwameis (ED)
Philippines	Quezon City	National Kidney and Transplant Institute	Joselito Chavez
Estonia	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 Aberta (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 Máñez 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

12

			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
Argentina	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
Colombia	Bucaramanga	Fundación Cardiovascular de Colombia	Leonardo Salazar
	Cali	Clinica Valle de Lilli	Diego Fernando Bautista Rincón
	Bogota	Fundación Clinica Shaio	Estefania Giraldo
Chile	Las Condes	Clinica Las Condez	Roderigo Diaz
	Santiago	Hospital del Tórax	Francisco Arancibia
	Santiago	Clinica Alemana De Santiago	Jerónimo Graf
Germany	Regensburg	Universitätsklinikum Regensburg (Klinik für Innere Medizin II)	Maximilian Malfertheiner
	Donaustauf	Donaustauf Hospital	Annette Schweda
	Regensburg	Barmherzige Bruder Regansburg	Stephan Schroll
	Munich	Medizinische Klinik und Poliklinik II	Stephanie Stecher
	Berlin	Charite-Univerrsitatsmedizi n Berlin	Roland Francis
	Passau	Klinikum Passau	Johannes Gebauer
	Nuremberg	Paracelsus Medical University Nuremberg	Matthias Baumgaertel

13

	Frankfurt	Universitätsklinikum Frankfurt (University Hospital Frankfurt)(Uniklinik)	Gösta Lotz
	Stockwerk	Universitätsspital Bern, Universitätsklinik für Herz- und Gefässchirurgie	Beate Hugi-Mayr
Brazil	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
Ireland	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
Poland	Krakow	University Hospital in Krakow	Konstanty S. Szuldrzynski
	Ghansk	Gdansk Medical University	Wojtek Karolak
South Africa	Johannesburg	Nelson Mandela Children's Hospital	Krubin Naidoo
		Netcare Unitas ECMO Centre	Marlice van Dyk
	Cape Town	Groote Schuur Hospital	David Thomson
Qatar	Qatar	Hamad General Hospital - Weill Cornell Medical College in Qatar	Ibrahim Hassan and Ali Hssain
Egypt	Cairo	Cairo University Hospital	Ahmad Abdelaziz
Sweden	Gothenburg	Sahlgrenska University Hospital	Pia Watson
Croatia	Zagreb	University Hospital Dubrava	Nikola Bradic
Luxembourg	Barble	Luxembourg Heart Center	Katja Ruck
Ukraine	Kyiv	Heart Institute Ministry of Health of Ukraine	Serhii Sudakevych
Switzerland	Bern	Inselspital University Hospital	Beate Hugi-Mayr
Turkey	Izmir	Dr. Suat Seren Chest Diseases and Surgery Practice and Training Centre	Cenk Kirakli
Mexico	Zapopan	Hospital Puerta de Hierro	Anna Greti

14

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

15

SUPPLEMENT 3

REGIONAL LEADS/ASSISTANTS

OPERATIONAL TEAM

16

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	

17

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

18

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

19

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

20

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60

SUPPLEMENT 4

CASE REPORT FORM

21

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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

Version 1.2.7
8 May 2020

1

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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 PaO2/FiO2 ratio.

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

Version 1.2.7
8 May 2020

2

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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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.□ Not available

1.18 ARTERIAL BICARBONATE (HCO3⁻) 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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

Version 1.2.7
8 May 2020

3

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

- ☐ Truck

- ☐ Upper limbs

- ☐ Hands

- ☐ Lower limbs

- ☐ Feet

Version 1.2.7
8 May 2020

4

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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 PaO2/FiO2 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 PaO2/FiO2 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)

Version 1.2.7
8 May 2020

5

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 PaO2/FiO2 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 PaO2/FiO2 ratio.

□ Not available

2.9 ARTERIAL HCO3⁻ 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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
Ceftazidime
Ceftibuten
Ceftizoxime
Ceftobiprole
Ceftriaxone
Cefuroxime
Cephalexin
Cephalothin
Cephapirin
Cephradine
Chloramphenicol
Cinoxacin
Ciprofloxacin
Clarithromycin
Clindamycin
Cloxacillin
Colistimethate
Cycloserine
Daptomycin
Demeclocycline
Dicloxacillin
Dirithromycin
Doripenem
Doxycycline
Enoxacin
Ertapenem
Erythromycin
Fosfomycin
Gatifloxacin
Gemifloxacin
Gentamicin
Grepafloxacin
Imipenem/Cilastatin
Imiquimod
Kanamycin
Levofloxacin
Lincomycin
Linezolid
Lomefloxacin
Loracarbef
Mafenide
Meropenem
Methenamine hippurate
Methicillin
Metronidazole
Mezlocillin
Minocycline
Moxifloxacin
Mupirocin
Nafcillin
Nalidixic Acid

Neomycin
Netilmicin
Nitrofurantoin
Nitrofurazone
Norfloxacin
Novobiocin
Ofloxacin
Oxacillin
Oxytetracycline
Penicillin
Piperacillin
Piperacillin +
Tazobactam
Podofilox
Polymyxin B
Quinupristin +
Dalfopristin
Retapamulin
Rifapentine
Rifaximin
Saturated Solution of
Potassium Iodide (SSKI)
Sparfloxacin
Spectinomycin
Streptomycin
Sulfadiazine
Sulfamethoxazole
Sulfisoxazole
Sulphur, precipitated in
petrolatum
TCA (trichloroacetic
acid), BCA
(bichloroacetic acid).
Teicoplanin
Telavancin
Telithromycin
Terbinafine
Tetracycline
Ticarcillin
Ticarcillin + Clavulanic
Acid
Tigecycline
Tobramycin
Trimethoprim
Trimethoprim +
Sulfamethoxazole
Trovafloxacin
Vancomycin

Version 1.2.7
8 May 2020

7

CORE CASE RECORD FORM (EOT Start ECMO)

3. UPON COMMENCMENT 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:

Version 1.2.7
8 May 2020

8

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)
Bylevel 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.

Version 1.2.7
8 May 2020

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Ideal Body Weight formula:

Male patients: 50 + (0.91 x [height in cm – 152.4])

Female patients: 45.5 + (0.91 x {height in cm – 152.4])

□ Not available

3.20 POSITIVE END EXPIRATORY PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH2O): _____ (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 PaO2/FiO2 ratio.

□ Not available

3.21 PEAK AIRWAY PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH2O): _____ (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 PaO2/FiO2 ratio.

□ Not available

3.22 AIRWAY PLATEAU PRESSURE IN THE 6 HOURS BEFORE START OF ECMO (cmH2O): _____ (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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.

□ Not available

3.26 ARTERIAL HCO3$^-$ IN THE 6 HOURS BEFORE START OF ECMO _____ mEq/L

Version 1.2.7
8 May 2020

10

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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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	Cefonicid
Amoxicillin +	sodium	Cefoperazone
Clavulanate	Cefaclor	Cefotaxime
Ampicillin	Cefadroxil	Cefotetan
Ampicillin + Sulbactam	Cefamandole	Cefoxitin
Atovaquone	Cefazolin	Cefpodoxime Proxetil
Azithromycin	Cefdinir	Cefprozil
Aztreonam	Cefditoren	Ceftaroline
Bacampicillin	Cefepime	Ceftazidime
Bacitracin	Cefixime	Ceftibuten

Version 1.2.7
8 May 2020

Ceftizoxime
Ceftobiprole
Ceftriaxone
Cefuroxime
Cephalexin
Cephalothin
Cephapirin
Cephradine
Chloramphenicol
Cinoxacin
Ciprofloxacin
Clarithromycin
Clindamycin
Cloxacillin
Colistimethate
Cycloserine
Daptomycin
Demeclocycline
Dicloxacillin
Dirithromycin
Doripenem
Doxycycline
Enoxacin
Ertapenem
Erythromycin
Fosfomycin
Gatifloxacin
Gemifloxacin
Gentamicin
Grepafloxacin
Imipenem/Cilastatin
Imiquimod
Kanamycin
Levofloxacin
Lincomycin
Linezolid
Lomefloxacin
Loracarbef
Mafenide
Meropenem
Methenamine hippurate
Methicillin
Metronidazole
Mezlocillin
Minocycline
Moxifloxacin
Mupirocin
Nafcillin
Nalidixic Acid

Neomycin
Netilmicin
Nitrofurantoin
Nitrofurazone
Norfloxacin
Novobiocin
Ofloxacin
Oxacillin
Oxytetracycline
Penicillin
Piperacillin
Piperacillin +
Tazobactam
Podofilox
Polymyxin B
Quinupristin +
Dalfopristin
Retapamulin
Rifapentine
Rifaximin
Saturated Solution of
Potassium Iodide (SSKI)
Sparfloxacin
Spectinomycin
Streptomycin
Sulfadiazine
Sulfamethoxazole
Sulfisoxazole
Sulphur, precipitated in
petrolatum
TCA (trichloroacetic
acid), BCA
(bichloroacetic acid).
Teicoplanin
Telavancin
Telithromycin
Terbinafine
Tetracycline
Ticarcillin
Ticarcillin + Clavulanic
Acid
Tigecycline
Tobramycin
Trimethoprim
Trimethoprim +
Sulfamethoxazole
Trovafloxacin
Vancomycin

Version 1.2.7
8 May 2020

12

CONFIDENTIAL

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 NEUROMUSCOLAR 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)
    Bylevel Positive Airway Pressure (BiPAP)
    Continuous Positive Airway Pressure (CPAP)

Version 1.2.7
8 May 2020

CONFIDENTIAL

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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.Ideal Body Weight formula:

Male patients: 50 + (0.91 x [height in cm – 152.4])

Female patients: 45.5 + (0.91 x {height in cm – 152.4])

□ Not available

4.13 POSITIVE END EXPIRATORY PRESSURE IN THE LAST 24h (cmH2O): _____ (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 PaO2/FiO2 ratio.□ Not available

4.14 AIRWAY PLATEAU PRESSURE IN THE LAST 24h (cmH2O): _____ (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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 ratio.□ Not available

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

Version 1.2.7
8 May 2020

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 PaO2/FiO2 ratio.□ Not available

4.18 ARTERIAL HCO3⁻ 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 PaO2/FiO2 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 □

Version 1.2.7
8 May 2020

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:

Version 1.2.7
8 May 2020

Yes
No

ANTIBIOTICs:

Amikacin
Amoxicillin
Amoxicillin   +
Clavulanate
Ampicillin
Ampicillin + Sulbactam
Atovaquone
Azithromycin
Aztreonam
Bacampicillin
Bacitracin
Capreomycin
Carbenicillin   indanyl
sodium
Cefaclor
Cefadroxil
Cefamandole
Cefazolin
Cefdinir
Cefditoren
Cefepime
Cefixime
Cefmetazole
Cefonicid
Cefoperazone
Cefotaxime
Cefotetan
Cefoxitin
Cefpodoxime Proxetil
Cefprozil
Ceftaroline
Ceftazidime
Ceftibuten
Ceftizoxime
Ceftobiprole
Ceftriaxone
Cefuroxime
Cephalexin
Cephalothin
Cephapirin
Cephradine
Chloramphenicol
Cinoxacin

Ciprofloxacin
Clarithromycin
Clindamycin
Cloxacillin
Colistimethate
Cycloserine
Daptomycin
Demeclocycline
Dicloxacillin
Dirithromycin
Doripenem
Doxycycline
Enoxacin
Ertapenem
Erythromycin
Fosfomycin
Gatifloxacin
Gemifloxacin
Gentamicin
Grepafloxacin
Imipenem/Cilastatin
Imiquimod
Kanamycin
Levofloxacin
Lincomycin
Linezolid
Lomefloxacin
Loracarbef
Mafenide
Meropenem
Methenamine hippurate
Methicillin
Metronidazole
Mezlocillin
Minocycline
Moxifloxacin
Mupirocin
Nafcillin
Nalidixic Acid
Neomycin
Netilmicin
Nitrofurantoin
Nitrofurazone

Norfloxacin
Novobiocin
Ofloxacin
Oxacillin
Oxytetracycline
Penicillin
Piperacillin
Piperacillin   +
Tazobactam
Podofilox
Polymyxin B
Quinupristin   +
Dalfopristin
Retapamulin
Rifapentine
Rifaximin
Saturated   Solution   of
Potassium Iodide (SSKI)
Sparfloxacin
Spectinomycin
Streptomycin
Sulfadiazine
Sulfamethoxazole
Sulfisoxazole
Sulphur, precipitated in
petrolatum
TCA   (trichloroacetic
acid), BCA (bichloroacetic acid).
Teicoplanin
Telavancin
Telithromycin
Terbinafine
Tetracycline
Ticarcillin
Ticarcillin + Clavulanic
Acid
Tigecycline
Tobramycin
Trimethoprim
Trimethoprim   +
Sulfamethoxazole
Trovafloxacin
Vancomycin

Version 1.2.7
8 May 2020

17

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 10^9/L
X 10^3/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

Version 1.2.7
8 May 2020

18

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
Gastro-intestinal
Genito-urinary
Skin and soft tissue

Central nervous
system
Osteoarticular and
bone

Cardiac
Bloodstream
Not known

4.45 CAUSATIVE PATHOGEN 1:

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
Chlamydophila
pneumoniae
Chlamydophila 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

Version 1.2.7
8 May 2020

19

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 lusitaniae
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
Chlamydophila pneumoniae
Chlamydophila 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

Version 1.2.7
8 May 2020

CONFIDENTIAL

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
Basidiobolomycosis
Blastomyces dermatitidis
Candida albicans
Candida glabrata
Candida guilliermondii
Candida krusei
Candida lusitaniae
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

Version 1.2.7
8 May 2020

21

CONFIDENTIAL

4.51 CAUSATIVE PATHOGEN 3:

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
Chlamydophila pneumoniae
Chlamydophila 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/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 lusitaniae
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

Version 1.2.7
8 May 2020

22

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
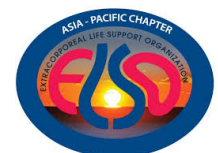
Version 1.2.7

8 May 2020

23

CONFIDENTIAL

1
2
3
4
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59
60

Version 1.2.7
8 May 2020

24

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

Version 1.2.7
8 May 2020

CONFIDENTIAL

□   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

Version 1.2.7
8 May 2020

26