
# EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE COVID-19 Project (UNITE-COVID)

**Study protocol**
Version 19MAY2020

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# SUMMARY OF THE STUDY

## Study title

- EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE COVID-19 Project (UNITE-COVID-19)

## Study design

- Multicenter, international point prevalence study

## Patient population

- Critically ill patients diagnosed with COVID-19 present in the ICU or any other area in the hospital under the care of the critical care team on the on the day between February 15$^{th}$ and May 15$^{th}$ 2020 with the highest number of COVID-19 patients in the unit.

## Study duration

- 1 day (with 60 day follow up)

## Primary objective

- To describe the burden of COVID-19 admissions to ICUs worldwide including regional differences, and variability in treatment
- To describe the clinical characteristics, management and outcomes of critically ill COVID-19 patients in the ICU

## Secondary objective(s)

- To describe respiratory characteristics
- To describe co- and super-infections
- To describe thromboembolic events and the use of antithrombotic therapy
- To describe frequency and timing of tracheotomy
- To describe mobilization and rehabilitation in critically ill patients with COVID-19

# INTRODUCTION

## RATIONALE FOR THE STUDY.

COVID-19 is arguably the biggest challenge critical care medicine has been confronted with since its conception. Critical care services around the world are flooded by patients presenting with severe respiratory failure who require prolonged treatment in the ICU. Despite the support provided, outcomes are poor, particularly in ventilated patients.

Many unanswered questions remain regarding the pathophysiology of COVID-19, particularly in severely ill patients. No evidence-based treatment is currently available, yet different often experimental therapies are administered to patients.

As experience grows, new phenotypes are recognized, and unreported complications are observed in the most severely ill patients. Although many registries are currently including patients, few of them focus on ICU patients and their specific treatments and newly observed complications and challenges.

Although the pandemic may appear on its return in many countries that are now easing the restrictions that were put in place to limit the spread of the disease, it can be expected that COVID-19 will be a continued challenge in ICUs globally until a safe and effective vaccine is found. Efforts to study the disease should continue in order to advance our understanding of the disease as well as improve treatment options.

## AIM OF THE STUDY.

This study will provide answers to the following questions from a global perspective

- What is the burden of COVID-19 in ICUs around the world?
- How are patients with COVID-19 now managed around the world?
- What are the outcomes of ICU patients with COVID-19?
- What is the incidence of specific patterns such as
    - Respiratory phenotypes
    - AKI
    - Infectious complications

- Thromboembolic events (venous and arterial)
- Neurological complications
- Cardiac complications

# STUDY OBJECTIVES

## PRIMARY OBJECTIVE

- To describe the burden of COVID-19 admissions to ICUs worldwide including regional differences, and variability in treatment
- To describe the clinical characteristics, management and outcomes of critically ill C19 patients in the ICU

## SECONDARY OBJECTIVES

- To describe respiratory characteristics
- To describe co- and super-infections
- To described thromboembolic events
- To describe frequency and timing of tracheotomy
- To describe mobilization and rehabilitation in critically ill patients with COVID-19

# STUDY POPULATION

Patients with confirmed COVID-19 infection present in the ICUs or any other area in the hospital under the care of the critical care team on the day between February 15$^{th}$ and May 15$^{th}$ 2020 with the highest number of COVID-19 patients in the unit (date to be decided by local investigator).

## INCLUSION CRITERIA.

For inclusion in the study, subjects must fulfill all of the following criteria:

- Age 18 or older
- Patient is present in an ICU or any other area in the hospital under the care of the critical care team on the day between February 15th and May 15th 2020 with the highest number of COVID-19 patients in the unit. The exact date can be decided by the local investigator.
- COVID-19 confirmed diagnosis through PCR or equivalent diagnostic technique

## EXCLUSION CRITERIA.

Any of the following is regarded as a criterion for exclusion from the study:

- SARS-CoV2 positive without COVID-19.

# STUDY DESIGN

This is a multicenter, international, anonymized point prevalence study.

Patients who were present in the ICU on the day between February 15th and May 15th 2020 with the highest number of COVID-19 patients in the unit. Data can be entered in the database until August 2020. Retrospective data collection and entry is allowed.

Subjects believed to fulfill all eligibility criteria, and none of the exclusion criteria, detailed in the relevant section of this protocol, will be included in the study.

Data will be entered in the database anonymously.

Data will consist of two core elements:

1. Center data (to be completed once)
2. Patient data

For different domains with specific, highly relevant and un(der)explored ICU research questions, an focused data set is to be completed. These domains include:

- Respiratory (group lead: Giacomo Grasselli)
- Coagulation and thrombo-embolic events (group lead: Andrea Lavinio)
- Infectious complications (group lead Andy Conway Morris)
- Rehabilitation (group lead Stefan Schaller)
- Renal (group lead Marlies Ostermann)

# DATA COLLECTION

## CENTER DATA

For each participating center we will collect center data as detailed in **CenterData CRF.** Data will be recorded regarding current nurse/patient ratio, MD/patient ratio,number of beds, 24h intensivist staffing, and hospital type, as well as resources available and capacity including surge capacity.

This will be completed only once per center

## INDIVIDUAL DATA

Data collection will consist of

- Demographic characteristics: age, sex, weight, length, pregnancy
- Comorbidities and chronic medication
- Duration of symptoms and previous hospital stay
- Data on admission: diagnoses, clinical parameters (temperature), lab values (WBCC, neutrophil count, lymphocyte count, CRP, procalcitonin, ferritin, troponin, fibrinogen, platelet count, aPTT, D-dimers, prothrombin time), respiratory support
- Complications during ICU stay
- Drug use during ICU stay including antimicrobials, sedatives, neuromuscular blockers, anticoagulation, anti-inflammatory therapies
- Supportive care during ICU stay
- Clinical and lab values during ICU stay (worst value during stay: temperature, WBCC, neutrophil count, lymphocyte count, CRP, procalcitonin, ferritin, troponin, fibrinogen, platelet count, aPTT, D-dimers, prothrombin time)
- Length of stay in ICU, hospital and outcome
- Use of respiratory support strategies
- Use of rehabilitation strategies

# ETHICS

Where required by local legislation or regulation, the study protocol will be submitted to the local ethics committee for approval.

# STUDY MEASUREMENTS

## MEASUREMENTS DURING STUDY

There will be no additional interventions or measurements other than those that are standard of care.

# DATA MANAGEMENT AND STATISTICS

## DATA MANAGEMENT

Case report forms will be provided for the recording of the data and a web-based electronic CRF will be used (ClinFile, France).
Access to the data entry system will be possible using a username and password, which will be provided to local investigators. Local investigators will only have access to the data from their unit. The full data will be accessible for the principle investigator, the steering committee and their collaborators.
Pseudonymized data will be collected. No personal details such as date of birth or initials will be recorded in the CRF.

## STATISTICAL ANALYSIS.

Statistical analysis will be performed by the principal investigator and the steering committee using a statistical software program and assisted by expert statisticians when necessary.

## GDPR COMPLIANCE

The data collection is necessary for scientific research purposes. In this sense, the processing of the data is in accordance with Article 9 §2 j) of the General Data Protection Regulation.

# ORGANIZATION

## PRINCIPAL INVESTIGATOR

- Jan J. De Waele – Ghent, Belgium

## STEERING COMMITTEE (ALHPABETICAL ORDER)

- Massimo Antonelli – Rome, Italy
- Maurizio Cecconi – Milano, Italy
- Giuseppe Citerio – Monza, Italy
- Andy Conway Morris - Cambridge, United Kingdom
- Frantisek Duska – Prague, Czech Republic
- Sharon Einav - Jerusalem, Israel
- Lui Forni – Guildford, United Kingdom
- Laura Galarza – Castellon, Spain
- Armand R J Girbes – Amsterdam, The Netherlands
- Giacomo Grasselli – Milano, Italy
- Jozef Kesecioglu – Utrecht, The Netherlands
- Andrea Lavinio - Cambridge, United Kingdom
- Maria Martin Delgado - Madrid, Spain
- Johannes Mellinghoff – London, United Kingdom
- Sheila Myatra – Mumbai, India
- Marlies Ostermann – London, UK
- Mariangela Pellegrini – Uppsala, Sweden
- Stefan Schaller – Berlin, Germany
- Jean-Louis Teboul – Paris, France
- Adrian Wong – Guildford, United Kingdom

## NATIONAL COORDINATORS

- National coordinators will be appointed by the steering committee.

## LOCAL INVESTIGATORS

There will be one local investigator per hospital (or ICU when applicable).

The Local investigator(s) will have the following role/responsibilities:

- Lead the study in their hospital.
- Ensure accurate data collection and accurate and timely eCRF completion.
- Guarantee the integrity, consistency and quality of data collection.

## INSURANCE

The need for insurance may vary depending on the region or country where patients are recruited. Where required by local legislation or regulation, insurance will be provided by the local investigator and/or the national coordinator.

# DATA MANAGEMENT

## DATA PROPERTY

Data provided by the local investigators are primarily the property of the ICU that collected the data. Local investigators shall have access to their data after they have been entered in the central database.

## DATA CONTROL

Automatic entry checks will be programmed. Local investigators may be contacted by the PI for queries in case of excessive missing values and other reasons deemed relevant by the PI.

## USE OF DATA BY THE PRINCIPAL INVESTIGATOR AND STEERING COMMITTEE

The PI and Steering Committee have the right to use the data in the central database for scientific purposes. Investigators will be informed about ongoing analyses and related study activities such as presentations at meetings.

All investigators have the right to submit study questions after the analyses described in the protocol have been completed. The Steering Committee will decide whether the proposed analysis can be performed, and only if there is no conflict with other ongoing or completed analysis.

Data in the database will not be distributed to third parties without explicit and written agreement of the local investigator.

## ARCHIVING

Local investigators will keep the CRFs according to local regulations.

## PUBLICATION RULES

Steering Committee members will be part of the writing committee and listed as authors of the final manuscript.

The primary analysis of the study will be submitted preferentially to a journal that allows all local investigators to be added as authors or collaborator if the former is not possible, albeit that a minimum of 10 patients should have been included in the study.

# REFERENCES.