PROTOCOL

EuroCOV Study

Risk stratification of patients with suspected COVID-19 presenting to the ED

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CONFIDENTIAL

Statement of Compliance

This study will be conducted in compliance with all stipulation of this protocol, ethical and regulatory approvals will be obtained in each European country for all participating sites.

1. SYNOPSIS

Title:	Risk stratification of patients with suspected COVID-19 presenting to the ED
Short Title:	EuroCOV
Design:	Retropective multicentre observational study Descriptive study of patients with suspected COVID-19 upon ED arrival of European hospitals between March 09 and April 08 2020.
Study Centres:	Emergency Departments in Europe
Co-ordinating centre:	Emergency Medicine Department, CHU de Tours, France
Justification:	Over the past 3 months, the world has faced a novel infection disease outbreak, due to a novel coronavirus, the severe acute respiratory syndrome coronavirus (SARS-CoV2), with a massive impact on healthcare resource. In Europe, numbers of confirmed cases continue to rise. Europe is currently one of the regions with the highest number of Covid-19 cases and deaths due to this emergent diseases. Most COVID-19 infected patients present with mild to moderate acute respiratory symptoms, including cough, fever, dyspnea and pneumonia. About 20% will present with severe or critical manifestations of the disease, including pneumonia, respiratory failure and acute respiratory distress syndrome (ARDS). Anticipating the needs for hospitalization in ward and/or intensive care is crucial. Emergency departments are at the front line for triaging patients with suspected Covid-19 and referring them to the appropriate level of care. In Europe, the number of ED patients with suspected Covid-19 is variable; rate of hospitalization from ED reaches 40% for this population. Risk stratification and management decisions of patients presenting to the ED with suspected COVID-19 is a challenge for emergency physicians.

Study Objectives:	Main Objectives 1. Evaluate the prognostic performances of clinical and biological parameters measured at ED arrival to risk stratify patients with suspected COVID-19 based on the following outcomes : hospitalization, length of hospital stay, in-hospital death, ICU admission Secondary objectives 2. Describe clinical presentation and management of patients with suspected COVID-19 infection following ED arrival 3. Evaluate the accuracy of pneumonia severity scores (CURB65, Pneumonia Severity Index (PSI), qSOFA and News2 scores…) as risk stratification tools
Methodology	Design and setting Multicenter retrospective observational study Descriptive study of patients with suspected COVID-19 admitted to European EDs between March 09 and April 08 2020. Vital signs, clinical and biological parameters and radiology findings will be collected as part of standard care in the participating centers A follow-up period of 30 days post ED management will allow to collect the followings : new ED visit, rehospitalization, and all cause death Risk stratification will be based on the performance for distinguishing patients who can be discharged from the ED from those who require hospital admission Outcomes Endpoint of interest • discharge home after ED evaluation with no readmission or serious outcome during the 30 days follow up period • Hospitalization following index ED visit • All-cause mortality at 30 days following index ED visit Other criteria of interest Diagnosis of COVID-19 will be based on clinical signs, SARS-CoV RT-PCR results or chest CT Imaging RT-PCR testing for COVID-19 will be performed from nasal swab

	according to central laboratory testing at each center.
Study population	Adult patients (>= 18 years old) attending the ED with a clinical suspicion of COVID-19 based on the presence of the following criteria - Fever >= 38 °*C* - respiratory symptoms (dyspnea, cough, expectorations) - any other symptoms suggestive of COVID-19 including digestive signs (diarrhea, anosmia…)
Study sites	Emergency Departments (ED) in Europe. EDs will be approached by researchers who are members of the steering committee via the EUSEM research network. Both public and private hospitals are eligible to participate. Sites will be recruited by expression of interest.
Number of Planned Subjects:	20-40 patients per day are expected at each participating ED.
Study period	From March 9th to April 8th 2020
Recruitment methodology	Consecutive adult patients (18 years old or older) presenting to the ED with suspected COVID-19 without trauma during the study period will be identified from ED data management systems and included in the study. Patients will be identified and data will be collected retrospectively from hospital chart records.
Data collection	Data will be collected as part of standard care in the participating EDs and retrieved from hospital chart records Data collected: Patient characteristics, presenting signs and symptoms, comorbidities, laboratory results, Imaging results, ED and hospital management, 30 days outcome (ED visit, hospital admission, ICU admission, hospital length of stay and all-cause all-cause mortality) Data will be de-identified and collected into an electronic CRF provided by the EUSEM research network
Statistical Methods:	Analyses will be descriptive. Binary outcomes will be analyzed using a hierarchical logistical regression model to allow for partial pooling. Partial pooling enables simultaneous estimation of dis-similarity (variation) between centres as well as estimation of the grand mean. Data will be analyzed by the coordinating centre. Analyses will be descriptive.

Monitor responsible	Not applicable
Treatment	Not applicable
Adverse events	There is no intervention. No change to usual management is involved. Adverse events registry and declaration are not applicable.
Patient consent	This study involves no change to patient care so there are no clinical risks. There is no inconvenience. The only risks involved are related to privacy and confidentiality. There will be mechanisms at the local level to minimize this (separate identifier – case number logs and case report forms without identifiers). All data submitted centrally will be non-identifiable, making this risk negligible. As discussed the risks are very low. While there is no direct benefit for participants at the time of the study, there is potential benefit in improved management for them and other patients in future. It is impracticable to obtain consent. Many patients attending ED are experiencing moderate/ severe dyspnea and often unpleasant associated features such as fever. Their distress is such that usual consent processes such as reading and signing a PICF is impractical. Also the process of obtaining consent may cause them distress and confusion by delaying treatment and potentially giving the (false) impression that consent is required for treatment. Limiting consent to only those able to participate in a consent process would severely bias our sample towards suspected Covid-19 in EDs. There is no known or likely reason for thinking that participants would not have consented if they had been asked. All data is routinely collected (and given by the patient) as part of clinical care. We have no reason to suspect that patients would decline consent. There is sufficient protection of their privacy. There are data and privacy protections at both local and central levels as described above. There is an adequate plan to protect the confidentiality of data. Our results will be presented at conferences and published so that important data, particularly about investigations and treatment is widely disseminated.

	In the unlikely event that the data collection process at the local level identifies a risk to an individual patient, such as a missed or misinterpreted investigation result, this will be directed to the site investigator who will manage the issue according to usual quality assurance / clinical follow-up processes which may include informing the patient, arranging further investigations and/or specialist referral. ED routinely checks results to identify similar issues, so these processes are already established. There is no possibility of commercial exploitation of derivatives of the study. The waiver is not prohibited by State, federal, or international law. Note, the requirement for ethical approval may vary in different countries and, where required, consent will be obtained according to local practices.
Privacy and confidentiality	Data will be collected by local clinicians who would usually have access to the data as part of clinical care. Data entered to the on-line database will be non-identifiable. The on-line database will be password secured and stored on a server in the European union. Local data collectors will only have access to their own site data. Local data will be collected and stored according to local research ethics requirements
Risk and benefits	There is no direct benefit to participants from their data being included in this study.
Data security and handling	Data storage and destruction will comply with ethics standards of the European union.
Dissemination of results	It is our intention that this data will be presented at internal and external educational/ academic meetings and in a publication in a medical journal. In all presentations and publications only non-identifiable, pooled results will be presented.
Publication rules	All publications and presentations must be approved by the EuroCOV study steering committee. Any publication will be communicated to local leads of each participating site. Authorship The EuroCOV study steering committee will be responsible for the coordination of all articles that will be published. The first author will be the one who has made the largest

	contribution to all aspects of the project, analysis and manuscript preparation. Authorship will be decided by members of the EuroCOV study steering Committee using ICMJE principles. All papers will name the EUSEM Research Network group as an author and all site leads will be listed as members of the group in the acknowledgement section.
Data sharing	On request, each site will be provided with a summary of its own data and be able to compare it with EuroCOV study pooled data. Data sharing with other researchers will be considered on a case-by-case basis and subject to additional ethics approval.

2. GLOSSARY OF ABBREVIATIONS

Abbreviation	Description (using lay language)
ED	Emergency Department
CT	Computed tomography
RT-PCR	Reverse transcriptase – Polymerase chain reaction

3. ATTACHMENTS

Document Name	Version Number	Date (e.g., 18 January 2012)
Data collection form (with coding)	1	(insert date)
List of sites expressing interest to participate	1	

4. BUDGET

Database preparation and management will be provided by EUSEM.

Item	Amount
Management of ethical approvals and reporting	Local researchers responsible for any ethics approval lodgement fees
Database preparation and management	€5,000
Data analysis	
Publication costs	
Total	€5,000

14. REFERENCES

- Wu, Z. and J.M. McGoogan, Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA, 2020

- Guan, W.-j., et al., Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine, 2020.
- Zhou, F., et al., Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet.
- Wu, C., et al., Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Internal Medicine, 2020.
- Young, B.E., et al., Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. JAMA, 2020.