COVID-19 Data Platform - Data Access Application Form

Please review the Data Access Guidelines and the Data Transfer Agreement before completing this form. A complete application should address all of the Review Considerations outlined in the Data Access Guidelines. Note that the details of all approved applications will be made publicly available on the COVID-19 Data Platform website.

Complete all sections of this form fully and return to covid19@iddo.org.

SECTION A: RESEARCHER / RESEARCH TEAM INFORMATION	
Lead Applicant Details	
Title	Project Leader
First name (given name)	Zhongshi
Surname (family name)	Huang
Gender	Male
Position at employing organisation/ institution	- Regular employee, Attending Physician of Critical Care Medicine, Clinical researcher - *Affiliated Hospital of Youjiang Medical University for Nationalities*
ORCID ID (https://orcid.org) or URL to academic profile	*https://orcid.org/0000-0002-3621-0750* *(if no ORCID or URL, please attach a short academic CV)*
Email	*anhtie@163.com*
Employing Organisation/Institution *Institution with a remit including health, research or academic pursuit, and with legal status which includes the scope to sign the **Data Transfer Agreement.***	
Institution name	*Affiliated Hospital of Youjiang Medical University for Nationalities*
City, Country	*Baise, China*
Does your institution agree to execute the Data Transfer Agreement? (if your application is approved)	**YES** (delete as appropriate)
Co-applicants *ALL individuals accessing the data must be listed. Any additions must be notified to the COVID-19 Data Access Committee. Add rows as necessary.*	
1. Name	*Pinhu Liao*
1. Position / Role in analysis	*professor/ Mentor*
1. Organisation/Institution	*Youjiang Medical University for Nationalities*
2. Name	*Sican Xiong*
2. Position / Role in analysis	*professor/ Medical Statistics*
2. Organisation/Institution	*East China University of Technology*
3. Name	
3. Position / Role in analysis	
3. Organisation/Institution	
Conflicts of Interest *List details of any existing or perceived conflicts of interest (financial or non-financial) that exist relating to the use of the requested data by the data requestor and/or co-applicants (see ICMJE.org for the definition of conflicts of interest)*	
None	

SECTION B: RESEARCH PLAN

Title of Proposed Research	Sepsis in Covid-19
Is this a re-submission of a previous application to the COVID-19 DAC? If yes, provide the submission date of the previous application.	NO

Summary of Research in Lay Language *(suggested ~ 100 words)*

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Many patients affected by COVID-19 will die from sepsis and its complications. Therefore, it is essential to understand and recognize the early signs of sepsis and to treat and intervene immediately after diagnosis to save lives and organ function. This is a multicenter international observational study of patients with COVID-19 based on the **COVID-19 Data Platform** to report and describe the demographic characteristics, clinical features, prevalence, risk factors, and sepsis prognosis.

Summary of Research Objectives and Scientific Value *(suggested maximum 400 words)*

- To summarize the demographic and clinical characteristics of patients with sepsis hospitalized for COVID-19.
- To investigate the incidence of sepsis in non-ICU and ICU patients.
- To identify the time variation at different ICU stay stages, including treatments received, time in the intensive care unit, and mechanical ventilation time.
- To describe the complications and clinical outcomes associated with sepsis in patients with COVID-19.
- To explore the risk factors and protective factors associated with mortality in these patients.
- To construct clinical prediction models for the risk of sepsis and death in COVID-19 patients and perform external validation.

Primary and Secondary Outcome Measures *(suggested maximum 200 words)*

- **Primarily:** morbidity, mortality.
- **Secondary:**risk factors and protective factors for the development of sepsis in Covid-19 patients, length of ICU stay, duration of high-flow oxygenation, duration of mechanical ventilation, duration of ECMO, duration of CRRT, frequency of complications, determine the impact of these complications on clinical outcomes, and identify risk factors.

Proposed Methodology and Statistical Analysis Plan *(suggested maximum 400 words)*

Continuous measures were expressed as median and interquartile spacing, while categorical variables were expressed as frequencies and percentages. Differences in severity of COVID-19 cases were compared using the Mann-Whitney U test and Fisher's exact test, respectively. Univariate and multivariate logistic regression analyses were used to analyze risk or protective factors associated with sepsis at admission. Variables from demographics, clinical history and assessment, laboratory and imaging tests, and therapeutic interventions were selected for inclusion in multivariate logistic regression analyses based on clinical rationale and statistical inference from univariate analyses. Variables with $p < 0.05$ were selected from univariate analyses for use in multivariate logistic regression models. A stepwise approach of multiple logistic regression was used to construct clinical prediction models for sepsis and death risk. For all analyses in this study, the bivariate statistical significance level p-value was set at 0.05. All analyses will be performed in Python 3.7.

Ethics *(suggested maximum 300 words)*
Provide details of any ethical considerations relating to the research proposal.
Additionally, list any approvals required by your institution to undertake this work, list reference numbers of any approved proposals, or explain why no approvals are required.

The ethics committee of our institution states that "for retrospective studies of scientific and social value, if they do not violate relevant laws and regulations, if they only collect clinical patient data, do not interfere with the patient's treatment plan, do not pose a risk to the patient's physiology, and if the investigator ensures that every effort is made to protect patient information, they may apply for an ethical review exemption."
This study was an analytical study based on anonymized data and followed the above policy provisions, therefore the ethics committee of our institution approved the application for ethical review exemption for this study.

Publication and Dissemination Plan *(suggested maximum 300 words)*
Provide details of plans for authorship/acknowledgement of data contributors.
Provide details of timelines for publication and dissemination of research findings.

Findings will be published in Chinese or international medical journals in critical care medicine or immunology. When a representative from the UK ISARIC group actively helps with the analysis, this person will be invited as co-author.
All findings are the property of all data contributors and we promise not to register any exclusive intellectual property rights with the findings.

Research Priorities Addressed (*suggested maximum 300 words)*
Provide details of how this research aligns with nationally or internationally set research priorities.

The Global Sepsis Alliance clearly states that COVID-19 does cause sepsis. After about 8-10 days, about 5% of people infected with COVID-19 will develop the multi-organ damage symptoms typical of sepsis. Many patients affected by COVID-19 will die from sepsis and its complications. The 3rd Annual Meeting of the European Sepsis Alliance on 16 March 2020 also focused on this topic and featured a lively academic discussion. Therefore, it is vital to understand and recognize the early signs of sepsis and treat the disease as soon as possible after diagnosis. Timely intervention can save lives and organ function. Most of the studies reported to date on sepsis in hospitalized patients with COVID-19 are single-center studies and are not representative of the global experience of COVID-19 sepsis since the pandemic. Therefore, studying the demographic and clinical characteristics of Covid-19 sepsis, its incidence, and its risk factors for complications and prognosis is essential for our knowledge, understanding, prevention, and treatment of Covid-19 sepsis.

Collaboration and Knowledge Sharing *(suggested maximum 300 words)*
Provide details of how this research will collaborate, support and/or share knowledge with appropriate partners. The platform is particularly interested in research that builds capacity in low-resource settings.

We will collaborate with computing and medical statistics experts to improve the big data analysis's efficacy and accuracy.
This work's output will be disseminated as widely as possible to inform patient care and public health policy. We will submit a paper for publication in an international peer-reviewed journal.

Funding *(suggested maximum 100 words)*
Provide details of how this research will be funded/resourced. Please name the source of funding.

- We have been researching sepsis for a long time. At present, we have received a special research fund (90000.00 RMB) for the COVID-19 study from the Science and Technology Bureau of Baise City. This fund applies to this project.
- If this application is approved, we will apply to the government health department for higher-level Covid-19 special research funding without worrying about the source and access of the research data.

Scientific Review *(suggested maximum 200 words)*
If the project has been scientifically reviewed, please provide details. This could be by your institution, a funder/donor or review committee.

Our institution's academic committee has reviewed our draft study. When data access is granted, it will be formally approved.

SECTION C: DATA

Data Variables

*Provide a list of the **data variables** required to achieve the research objectives.*
Note: Please go to www.iddo.cognitive.city to explore the interactive COVID-19 data inventory and to identify the variables, populations and data volumes required for your analysis. You can select the data variables from this inventory and copy it to this section.

The standard definition of sepsis is based on the Sequential Organ Failure Assessment (SOFA) score. SOFA variables:

Table 1

The Sequential Organ Failure Assessment (SOFA) score

SOFA score	1	2	3	4
Respiration[a]				
PaO_2/FIO_2 (mm Hg)	<400	<300	<220	<100
SaO_2/FIO_2	221-301	142-220	67-141	<67
Coagulation				
Platelets $\times 10^3/mm^3$	<150	<100	<50	<20
Liver				
Bilirubin (mg/dL)	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular[b]				
Hypotension	MAP <70	Dopamine ≤5 or dobutamine (any)	Dopamine >5 or norepinephrine ≤0.1	Dopamine >15 or norepinephrine >0.1
CNS				
Glasgow Coma Score	13-14	10-12	6-9	<6
Renal				
Creatinine (mg/dL) or urine output (mL/d)	1.2-1.9	2.0-3.4	3.5-4.9 or <500	>5.0 or <200

MAP, mean arterial pressure; CNS, central nervous system; SaO_2, peripheral arterial oxygen saturation.

[a]PaO_2/FIO_2 ratio was used preferentially. If not available, the SaO_2/FIO_2 ratio was used

[b]vasoactive mediations administered for at least 1 hr (dopamine and norepinephrine μmg/kg/min).

SOFA Score ≥ 2 in setting of infection strongly supports the diagnosis of sepsis.

Septic shock: Vasopressors needed to maintain MAP ≥ 65 mmHg and serum lactate level ≥ 2 mmo1/L (18 mg/dL) despite volume resuscitation.

This proposed analysis will marshal the eligible population from the ISARIC dataset based on the sepsis diagnostic criteria (**SOFA score**) described above. **As the number of people meeting the diagnostic criteria for sepsis is unknown, We apply for access to as many variables, populations, and data volumes as possible.**

List of the data variables

Clinical Classification:

Comorbidities (126836)
Signs and Symptoms (23085)
Clinical and Adverse Event:
Glasgow Coma Score (GCS) (14718)
AVPU Scale (Alert, Voice, Pain, Unresponsive) (9338)
Richmond Agitation-Sedation Scale (RASS) (2579)
Demographics:
COUNTRY (128018)
SEX (128018)
AGE (125842)
Healthcare Encounters:
INTENSIVE CARE UNIT (22346)
HOSPITAL (14359)
Interventions:
SUPPORTIVE CARE (13178),
CORTICOSTEROIDS FOR SYSTEMIC USE (10883),
ANTIBACTERIALS FOR SYSTEMIC USE (10824),
ANTIVIRALS FOR SYSTEMIC USE (10646),
OXYGEN (10242),
ANTIMYCOTICS FOR SYSTEMIC USE (10143),
MEDICATION (8423),
ANTIFUNGAL AGENTS (8247),
CARDIAC THERAPY (7838),
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS,
NON-STEROIDS (7783),
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM (7609),
ANTITHROMBOTIC AGENTS (3794),
OTHER RESPIRATORY SYSTEM PRODUCTS (3578),
ANTIVIRAL AGENTS (3158),
MEDICAL HISTORY (3013),
ANTIMALARIALS (2885),
ANTIMALARIAL AGENTS (2765),
INVASIVE VENTILATION (2747),
EXTRACORPOREAL (2746),
PRONE POSITIONING (2746),
NON-INVASIVE VENTILATION (2746),
RENAL REPLACEMENT THERAPIES (2739),
ANTIBIOTIC AGENTS (1972),
CORTICOSTEROIDS (1865),
NSAIDS (268),
EXPERIMENTAL AGENTS **(268)**
Laboratory Test Results:
Hemoglobin (20780), Platelets (20713), Leukocytes (20694), Creatinine (20370), Hematocrit (20347), Potassium (19893), Sodium (19874), Alanine Aminotransferase (18461), Urea Nitrogen (18359), C Reactive Protein (17715), Aspartate Aminotransferase (17630), Bilirubin (17471), Lymphocytes (16788), Neutrophils (16457), Lactate Dehydrogenase (10719), Glucose (10495), Prothrombin Intl. Normalized Ratio (8684), Lactic Acid (7445), Prothrombin Time (6575), Fraction of Inspired Oxygen (5762), Partial Pressure Carbon Dioxide (5720), pH (5696), Bicarbonate (5602), Partial Pressure Oxygen

(5590), Base Excess (5017), Creatine Kinase (4902), Ferritin (4731), D-Dimer (4652), Procalcitonin (4207), Lymphocytes/Leukocytes (4052), Neutrophils/Leukocytes (3996), Activated Partial Thromboplastin Time (3726), Erythrocyte Sedimentation Rate (3633), Ery. Mean Corpuscular Hemoglobin (3448), Erythrocytes (3448), Monocytes/Leukocytes (3448), Ery. Mean Corpuscular HGB Concentration (3448), Monocytes (3448), Basophils/Leukocytes (3448), Erythrocytes Distribution Width (3448), Eosinophils/Leukocytes (3443), Eosinophils (3260), Ery. Mean Corpuscular Volume (3032), Protein (2804), Troponin (2800), Basophils (2629), Fibrinogen (2593), Albumin (2443), Prothrombin Time Actual/Control (2167), Direct Bilirubin (1540), Urate (1309), Platelet Hematocrit (1265), Mean Platelet Volume (1265), Cholesterol (1103), Amylase (924), Interleukin 6 (891), Iron (853), Alkaline Phosphatase (816), Gamma Glutamyl Transferase (801), Activated PTT/Standard (563), Fibrinogen, Functional (498), Troponin I (488), Chloride (482), Calcium (406), PP Arterial O2/Fraction Inspired O2 (276), Oxygen Saturation (223), Thrombin Time (176), Calcium, Ionized pH Adjusted (146), Calcium, Ionized (146), Carbon Dioxide (126), Deoxyhemoglobin (124), Oxyhemoglobin (124), Methemoglobin (124), Carboxyhemoglobin (124), Hemoglobin A1C (115), Magnesium (18), Urea (7), Troponin T (4)

Microbiology Specimen Test Result:

Microbial Organism Identification (117626),
Coronavirus test result (111988),
Other respiratory pathogens (8735),
Influenza Virus (6970),
Bacteria test result (5852),
Respiratory Syncytial Virus (RSV) test result (4984),
Adenovirus test result (4619),
SARS CoV2 test result (3938),
Other pathogens of public health importance (1051),
HIV-1/2 Antibody + HIV-1 p24 Antigen (602),
Human Immunodeficiency Virus (HIV) test result (491),
Malaria test result (165),
Plasmodium (164),
Coronavirus (32)

Reproductive System Findings:

Pregnancy status (4601)
Estimated Gestational Age (182)

Vital Signs:

Temperature (21996)
Oxygen Saturation (19690)
Systolic Blood Pressure (18499)
Diastolic Blood Pressure (18490)
Respiratory Rate (17537)
Heart Rate (12507)
Weight (7075)
Height (6513)
Pulse Rate (6387)
Mean Arterial Pressure (5447)
Body Mass Index (3141)
Mid-Upper Arm Circumference (64)