Proposal Title:

Defining the Burden of COVID-19:

Incidence, Epidemiology & Clinical Outcomes of

Patients with COVID-19

Proposal Short Title:

"Burden of COVID-19"

Principal Investigator

Julio A. Ramirez[1] MD

Division of Infectious Diseases University of Louisville &

Center of Excellence for Research in Infectious Diseases (CERID), University of Louisville

Scientific Advisory Board

(See Appendix)

1. Abstract

1.1 Rationale. Early evaluation of the burden of disease that COVID-19 may produce in a community is critical to appropriately allocate resources for COVID-19 prevention and treatment.

1.2 Objective. The primary objective of this study is to observe the incidence, epidemiology, and clinical outcomes of patients with COVID-19 in the USA, as well as regions throughout the world.

1.3 Methods. This will be a retrospective observational study of patients with a diagnosis of COVID-19.

2. Background & Significance

The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020 (**1**). The virus that causes COVID-19 is SARS-CoV-2. It is expected that SARS-CoV-2 will reach global spread and will infect a significant number of the global population. The declaration of a pandemic refers primarily to the capability of SARS-CoV-2 to spread from person to person at a global level, but the declaration of pandemic is not related to the severity of SARS-CoV-2. The burden of patients with COVID-19 may vary from region to region. This variability is primarily due to the mutations that SARS-CoV-2 will accumulate as the virus moves through the population. When the virus mutates, it undergoes small changes in its genome. A common pattern of evolution for viral infections is that as the virus mutates, it may have the capability to spread more efficiently from person to person, and at the same time, the strain may become less aggressive, which results in better outcomes in patients with the disease. Even though this

is the most likely evolution of a virus, we do not know if the new mutations of SARS-CoV-2 will produce a virus more virulent or less virulent. At the present time, there are different patterns of burden of disease originating in China (**2**), Italy (**3**), and Germany (**4**). Why the clinical outcomes of patients with COVID-19 in these regions are different is unclear, but different viral mutations may partially explain the clinical outcomes.

Because of the above, it is clear that it will be difficult to predict the burden of COVID-19 in communities throughout the world. Defining burden of disease as soon as possible after SARS-CoV-2 arrives in a particular region is critical to properly inform public health authorities for development of effective preventive strategies, and healthcare professionals so they are able to appropriately and safely manage and treatment patients with COVID-19.

In an attempt to identify early burden of disease, the primary objective of this study is to define the incidence, epidemiology, and clinical outcomes of patients diagnosed with COVID-19 in regions throughout the USA, as well as other regions throughout the world and compare this data to one another.

3. Objectives

3.1 Primary Objectives

3.1.1 To define the incidence, epidemiology, and clinical outcomes of patients diagnosed with COVID-19 in the USA and throughout the world and compare the data collected to one another, to assess differences in the incidence, epidemiology, and clinical outcomes of these patients.

3.2 Secondary Objectives

3.2.1 To evaluate incidence of COVID-19 in special populations.

3.2.2 To evaluate better inform Public Health authorities of local COVID-19 activity.

3.2.3 To define areas of the community where surveillance activities should be increased.

3.2.4 To rapidly disseminate the new knowledge gained by this project.

4. Methods

4.1 Study Design and Subjects

The International Burden of COVID-19 study will be a retrospective study of patients diagnosed with COVID-19. We will invite all participants of the CAPO study (11.0613), but we will also advertise on our CERID website for other groups and investigators to apply. We will collect our data from the hospital EMRs, other sites who collect data will submit the protocol through their own IRB and will collect using the same CRF. The data will be de-identified and housed in UofL RedCap.

4.2 Inclusion and Exclusion Criteria

A patient will be defined as having COVID-19 when the virus SARS-CoV-2 was identified in a clinical specimen using Polymerase Chain Reaction (PCR) and/or a CT scan with bilateral ground glass opacities. All patients with diagnosis of COVID-19 will be evaluated. The study will have no exclusion criteria.

4.3 Incidence Calculations

The monthly COVID-19 incidence rates per 100,000 adults will be estimated for: unique patients (unadjusted and age-adjusted), total hospitalizations, unique patients by various age groups, unique patients by comorbid conditions and smoking status, as well as for white and

black/African American races. These incidence rate calculations will be performed only in areas where population based-data can be obtained.

4.4 Geospatial Epidemiology

To define specific hot areas with high density of COVID-19, initially the geomasked location of each patient's home address will be obtained through the US Census Bureau website. A Kernel Density heatmap will be created. Kuldorff's Spatial Scan Statistic will be used to calculate significant areas of risk for COVID-19. Choropleth maps will be created to compare census tract-level demographics and the spatial distribution of COVID-19 cases. These geospatial epidemiology calculations will be performed only in areas where population-based data can be obtained.

4.5 Mortality

All-cause mortality for all COVID-19 patients will be evaluated at 30-days, 6-months, and 1-year after diagnosis.

5. Scientific Advisory Board

A scientific advisory board has been established with leaders from health care systems around the world. The board has the following objectives: 1) To provide feedback for improvement of the Burden of COVID-19 study; 2) To support the dissemination of information. Regular meetings will be held by the principal investigator and members of the scientific advisory board.

6. Preliminary Studies

The principal investigators, Drs. Julio Ramirez, has vast experience in development and implementation of studies evaluating burden of particular infectious diseases.

Dr. Ramirez is the Chief of the Division of Infectious Diseases and Director of the Center of Excellence for Research in Infectious Diseases (ceridlouisville.org). He has led multiple surveillance programs in the State of Kentucky, including the Severe Influenza Pneumonia Surveillance (SIPS) Project. SIPS was funded by the Department of Homeland Security (**5**). He was also funded by the Centers for Disease Control and Prevention to study the role of oseltamivir in hospitalized patients with influenza in the city of Louisville. This was done in collaboration of CERID with all adult hospitals in Louisville (**6**). More recently, Pfizer Pharmaceuticals sponsored CERID to perform a population-based study of all hospitalized adult patients in the city of Louisville to define the burden of community-acquired pneumonia. Data from this study were used to estimate the burden of pneumonia in the United States (**7**). The successes of these studies led to the selection of CERID as the North American Center of Excellence for Vaccine Epidemiology, funded by Pfizer. This is the first such center in the world, and recognizes the unique infrastructure and capabilities of UofL CERID (Center of Excellence announcement).

7. Project Coordinating Center

The Burden of COVID-19 study will be coordinated by the Center of Excellence for Research in Infectious Diseases (CERID). The current structure of CERID is depicted in Figure 4.

The activities related to this project for each of the CERID units are as follows:

7.1 Data Management Unit: generate the data collection form and the REDCap database for this project.

7.2 Implementation Unit: responsible for data collection, and data entry into the REDCap database.

7.3 Laboratory Unit: No activity related to this retrospective study.

7.4 Biostatistics Unit: will be responsible for periodic and real-time analysis of incidence, epidemiological, and clinical outcomes data.

7.5 Medical Writing Unit: will support the generation of manuscripts.

7.6 Peer-Review Journals Unit: will facilitate rapid publication of new knowledge.

7.7 Informatics Unit: will support the data management unit and implementation unit in regard to computer and database maintenance.

7.8 Community Outreach Unit: will be responsible for maintaining open lines of communication with community leaders and coordinating activities of the Advisory Board.

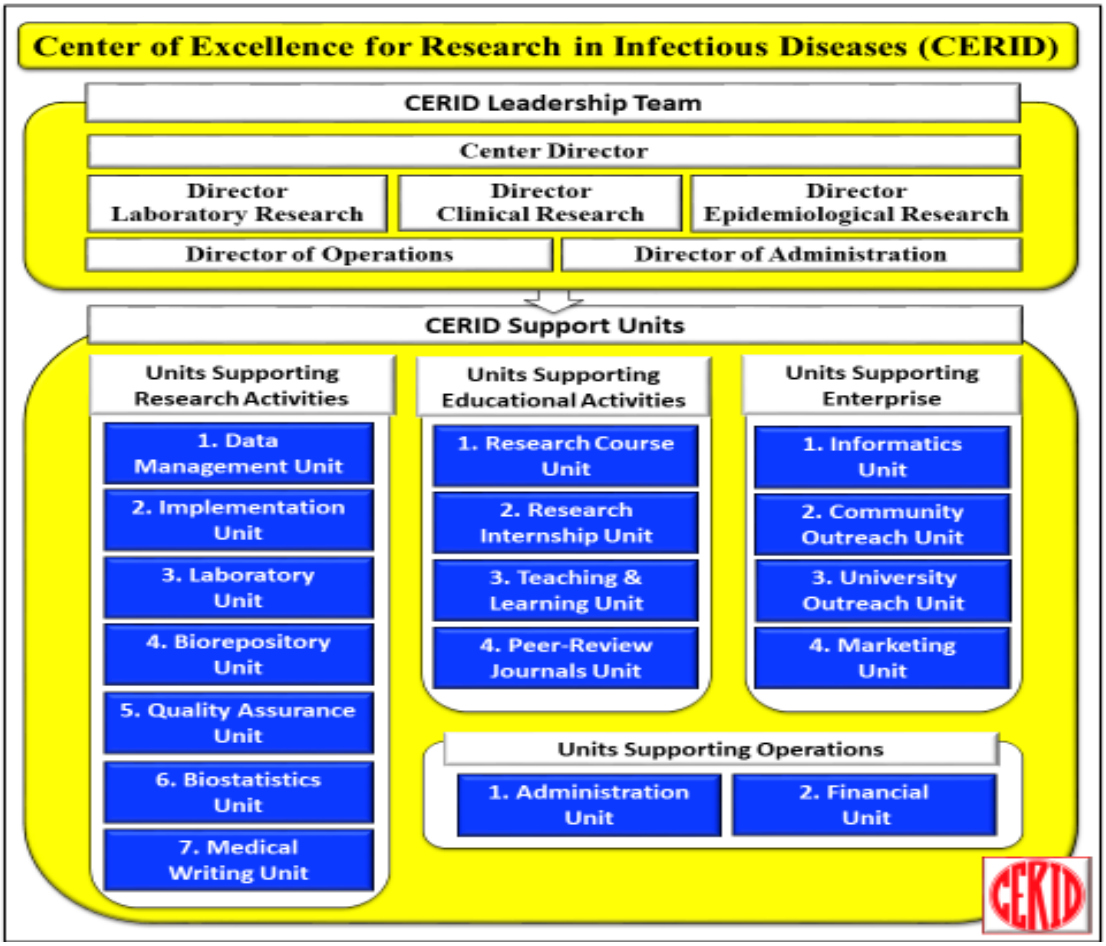

Figure 4. Structure of the Project Coordinating Center

7.9 University Outreach Unit: will be responsible for maintaining open lines of communication with UofL leaders and will work with the Community Outreach Unit to coordinate the activities of the Advisory Board.

7.10 Marketing Unit will collaborate with investigators to develop education and response communications.

8. Protection of Human Subjects

All patient information will be entered into REDCap databases that are HIPAA-compliant. All surveillance information will be considered to be protected health information and standard data safety processes will be followed.

9. Authorship

Individuals/organizations contributing data to the International Observational Study to Evaluate Incidence, Epidemiology, & Clinical Outcomes of Patients with COVID-19 will have two separate pathways to publication; 1.) Publication rights for data entered into the database by the individual/organization directly is controlled by that individual/organization and can be used for any publication topic of their choice. 2.) If the participating individual/organization would like to write a publication using data from the full international database, then the idea for publication can be submitted through the REDCap survey process and it will be evaluated by the study evaluation team. The reason for the evaluation team is to prevent duplication of topics for publication, the evaluation team will not reject any new ideas.

10. Data Collection

Data on patient demographics, past medical history, course of the disease, clinical management/therapy, laboratory and radiographic, course of hospitalization, cardiovascular events, clinical outcomes, tests will be transferred from the medical record to a data collection form. Data will be de-identified by assigning a code to each patient. Each study center will be given a data collection manual with clear rules for data entry.

11. Data Management & Quality

Each study site will be given access to REDCap. Data will be entered in a local computer into REDCap hosted at the Division of Infectious Diseases, University of Louisville. Data quality will be evaluated for consistency among variables by the quality assurance unit. Missing, out-of-range, or illogical data will generate queries for corrective actions. Descriptive statistics will be performed at periodic intervals during the study to evaluate for unexpected distributions. Data will be analyzed by descriptive and analytic statistics at the end of study period.

12. References

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Appendix 1:

Burden of COVID-19 Scientific Advisory Board

University of Louisville Center of Excellence for Research in Infectious Diseases

Ruth Carrico, PhD; Leslie Wolf, PhD

University of Louisville Center for Predictive Medicine

Kenneth E. Palmer PhD; Donghoon Chung, PhD

University of Louisville School of Public Health

William McKinney, MD

Louisville Public Health

Sarah Moyer, MD

University of Louisville Health

Jason Smith, MD; Forest W. Arnold, DO

Norton Healthcare Louisville

James Frazer, MD; Paul Schulz, MD; Ashley Wilde, PharmD

Baptist Health Louisville

Kenneth Anderson, MD; Anna Hart, MD

Clark Memorial Health

Klaus Boel, MD

Floyd Memorial Hospital

Krishna Konijeti, MD