INTERNATIONAL COVID-19 CLINICAL EVALUATION REGISTRY:

HOPE-2.

(Health Outcome Predictive Evaluation for COVID 19- 2)

PROTOCOL VERSION 2

ENGLISH VERSION.

NCT04778020

INTRODUCTION.

Since December 2019, when a new respiratory virus (coronavirus) designated as SARS-CoV-2 was detected in China, millions of people worldwide have been infected. This condition was named coronavirus 2019 disease (COVID-19) and has produced a pandemic with millions of casualties.

With an increasing number of confirmed cases in most countries worldwide, it is responsible for a relevant morbidity and mortality and has motivated the implementation of measures at national and international levels with a great impact on the way of life of people throughout the whole planet.

One year after the beginning of the outbreak, several reports and trials have been produced reporting important data about the acute phase of the disease. In this field the International registry HOPE COVID-19 (NCT04334291) has provided several publications with collaborative data from more than 45 centers in 9 countries.

The registry, as well, produced an online mortality calculator based in a few clinical variables (https://hopeprojectmd.com/en/tool).

However, limited follow-up information is available and the existing evidence point out frequent lasting effects after the acute phase of COVID-19. This persistent condition has been baptized by several authors with different terms such Post-acute COVID-19, Persistent COVID-19, Post COVID- syndrome, Long haulers, Long COVID-19, etc..

Since COVID-19 have involved and unprecedented numbers of people is possible the sequelae would be important form the socioeconomic and scientific point of view.

Thus, we propose here the international Registry HOPE 2, aiming to produce clinically relevant data regarding the longstanding outcomes after discharge after COVID-19.

PURPOSE.

The main objective of the present study is to carefully characterize the clinical profile of individuals with lasting sequelae after a COVID-19 admission.

As secondary objectives, the analysis of the risk-adjusted influence of COVID-19 severity, previous comorbidities and management of patients discharged after COVID-19 will be performed.

DESIGN AND STATISTICAL ANALYSIS

Cross-sectional and prospective registry, a real life "all comers" type, with voluntary participation, without specific funding or conflicts of interest.

It is a study initiated by researcher that will have advanced statistical support from the IMAS foundation (Institute for the Improvement of Health Care, Madrid, Spain) and the Fundación para la Investigacion Cardiovascular (FIC, Madrid, Spain).

International level.

PARTICIPANTS PROTOCOL.

The study has been approved by Hospital Clinico San Carlos Ethic´s Committee (**21/128-E**) and the institutional board of each participating center.

The present study proposes the continuation in time of the work previously carried out in the HOPE registry.

We propose to select all the patients attended in any health center (with in hospital beds), who have been discharged or have died up to 30th september 2020.

All will be considered eligible with a positive COVID 19 test (any type) or if their attending physicians consider them highly likely to have presented the infection.

Given the anonymous characteristics of the registry and the health alarm situation generated by the virus, in principle, it is not considered necessary to provide written informed consent.

- **Inclusion criteria**

Patients discharged (deceased or alive) from any hospital center with a confirmed diagnosis or a COVID-19 high suspicion.

There are no exclusion criteria, except for the patient's explicit refusal to participate.

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Same inclusion/exclusion as HOPE COVID-19. We propose the long-term follow-up of patients discharged after a COVID-19 admission up to 30th september 2020.

Consecutive inclusion and the completion of patients previously included in HOPE registry is strongly warranted.

DATA BASE.

An anonymized HOPE 2 database is presented, in electronic format, to be filled in at each participating center (www.HopeProjectMD.com).

In theory, most information could be obtained from electronic records (medical history).

Probably, the investigator should call or use in office visits in order to establish the vital the long-term management and follow-up outcomes (warranted).

For variables definition, please see protocol appendix.

SAMPLE SIZE.

We consider it would not be possible to estimate for the sample size based on literature reports. Thus, HOPE2 will aim to get the maximum numbers of patients possible.

Researchers are warranted to recruit their patients in a consecutive manner.

OUTCOMES.

Primary: All-cause mortality. The major contributors of increased mortality will be assessed.

Secondary: Cause of death and Outcomes after discharge.

See protocol appendix for precise definitions.

Depending the results of the main interim analysis, the main DB could be slightly modified and several sub analyses could be proposed after sensitivity analyses.

The objectives and event variables would vary with the precise analysis performed.

RESEARCHERS AND AUTHORSHIP.

Following HOPE rules, to avoid potential duplicates, an unique online account is accepted per hospital. Within each center, the researchers will decide themselves the main researcher (maximum 2 principal investigators,) and the collaborators (maximum 15).

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They are accepted as collaborators, physicians, nurses, students, and other personnel under the supervision of local MD/DO/PhD investigators.

The order of authorship will be established based on the recruitment (valid cases) in HOPE 2. All study researchers and collaborators will be included in the HOPE 2 group.

HOPE or HOPE 2 are not audited records, so each researcher is responsible and vouch for the veracity and accuracy of their included data.

The database will be made available to participating researchers who wish to carry out sub-analyzes of their interest, upon reasonable request.

PRELIMINARY AGENDA AND ROADMAP.

10th February 2021: Research Ethics committee approval.

February-15th March: DB design and preparation.

15-25th March 2021: National and international invitations to participate submission.

15-31st March 2021: Activation of HOPE 2 study invitation links. Once participation in the study is approved, your center will be registered and the researcher will be able to set a login and password. Then, you could enter the data on the web. For center previously participating in HOPE, the researcher's account will be reactivated.

May 2021: DB exportation. Query resolution phase. Interim analysis.

16-30th June: Analysis and development of statistical models, (propensity scores, etc.).

30th June- 15th July 2021: preliminary results.

31st september 2021: Final HOPE 2 enrollment period.

1-15th October: DB exportation. Query resolution phase. DB closure.

15 th October-15th november 2021: Analysis and development of statistical models. Manuscripts.

January 2022: Final HOPE 2results.

The final date of registration/follow up is sept 31st, 2021

SCIENTIFIC COORDINATION: Iván J. Núñez-Gil, MD, PhD. Carlos Macaya, MD, PhD.

SCIENTIFIC COMMITTEE AND LIST OF PARTICIPATING HOSPITALS: Available updated at www.HopeProjectMD.com.

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COORDINATOR CENTRE: HOSPITAL CLINICO SAN CARLOS, MADRID, SPAIN.

PROMOTER: Fundación interhospitalaria para la Investigación cardiovascular, **FIC**. Paseo del Pintor Rosales, N18, izq. 28008, Madrid. Spain. CIF: G-81563801.

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