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Master Thesis

**Landscaping of COVID-19 Clinical Trials for the Discovery of Insightful Patterns on Ethnicities**

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|  |  |
| --- | --- |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus-2 |
| ICTRP | International Clinical Trials Registry Platform |
| WHO | World Health Organization |
| ECRIN | European Clinical Research Infrastructure Network |
| MDR | Metadata Repository |
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**ABSTRACT**

**INTRODUCTION**

**THEORETICAL BACKGROUND**

2.1 SARS-CoV-2 a novel coronavirus

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) a novel strain and fatal coronavirus was first identified in Wuhan city of China in December 2019. The common symptoms include increased body temperature, dry cough, nausea and body pains. The rapid spread of the virus posed a threat of life to the global environment. According to the records maintained by Worldometer, the top ten most affected nations include USA, India, Brazil, France, Russia, UK, Turkey, Italy, Spain and Germany (*COVID Live Update: Worldometer*, n.d.).

The coronaviruses generally is classified under the family Coronoviridae and subfamily Coronavirinae which is subdivided into four genera namely Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus (Mittal et al., 2020). The SARS-CoV-2, a member of Betacoronavirus genera whose sequence is 96% homologous to the bat coronavirus. Its primary reservoir is considered to be bats and transmitted to human beings through an intermediate host called Pangolin (Zhao et al., 2020).

The SARS-CoV-2 also called by COVID-19 is spherical in structure with positively stranded RNA genome packed inside the nucleocapsid protein (N) and enveloped by the membrane glycoprotein protein (M), envelope protein (E), and the spike protein (S). The typical virus lengths between 26.4 and 31.7 kb with the GC content ranging between 32% and 43% thus indicating to be the largest RNA virus (Mousavizadeh & Ghasemi, 2020).

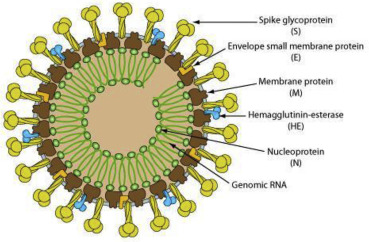


Figure 1 Structure of novel coronavirus SARS-CoV-2, Adapted from (Mousavizadeh & Ghasemi, 2020)

2.2 Clinical trials

Clinical trials are experimental studies performed using volunteers with the objective of examining different interventions like medical, surgical or behavioral ones. They can be classified into interventional studies and observational studies. These studies are led by a medical doctor assisted by other doctors, nurses carried out in hospitals, universities and research institutes (*Learn About Clinical Studies - ClinicalTrials.Gov*, n.d.).

The United States Food and Drug Administration (FDA) has defined the different stages of clinical trial phases to determine whether the drug could be employed for public usage. They are described as follows:

Phase I: During the initial phase, around 20 to 80 participants are enrolled having no underlying medical complications to evaluate the highest dosage levels that can be administrated without serious side effects.

Phase II: During this phase, around 100 to 300 participants are enrolled to evaluate the effectiveness of the medication along with short time side effects if occurred. This is carried out up to several years.

Phase III: During this phase, around 3000 participants are enrolled to evaluate the effectiveness of the medication across diverse population and varied dosage thus studying both the drug safety and efficacy. The rare and long time effects are observed during this phase. The medications are approved by the FDA if the trial results are positive.

Phase IV: During this final phase, long time side effects and efficacy of the approved medications are evaluated across the thousands of participants (*What Are Clinical Trials and Studies? | National Institute on Aging*, n.d.).

2.3 Clinical Trial Registries

The results of the clinical studies are recorded and published in a repository called Clinical Trial Registries. They are open source and their accession is available for scientific community and public. Each nation has their own trial registry systems centrally maintained by their Government or other approved institution. Some notable registries are described as follows:

2.3.1 ClinicalTrials.gov

ClinicalTrials.gov is an US based trial registry maintained by the National Library of Medicine (NLM) at the National Institute of Health (NIH), made available in February 2000. It holds both interventional and observational studies carried in 50 US states and 220 countries. The records contains information pertaining to the disease under investigation; the type of interventions employed; meta information like ethnicity of the participants, demographic data, inclusion/exclusion criteria for the study, location, list of comorbidities if any, clinical variables and laboratory variables. The results are included sometimes if the trials are subject to Section 801 of FDAAA (FDAAA 801) (*ClinicalTrials.Gov Background - ClinicalTrials.Gov*, n.d.).

The ClinicalTrials.gov registry could be accessed via <https://clinicaltrials.gov/>. The registry actually recorded 5,420 studies for the novel COVID 19 virus as of 21st April 2021.

2.3.2 ICTRP

International Clinical Trials Registry Platform (ICTRP) is a project of World Health Organization (WHO) is to ensure the registration of *WHO Trial Registration Data Set* and its accessibility to the public. In order for the clinical study to be considered as fully registered, it must contain atleast minimum amount of information called as Trial Registration Data Set (TRDS). Some of them include title of the study, disease conditions investigated, participant’s location, type of the study, duration of the study and outcome of the study etc. (*About ICTRP*, n.d.).

The ICTRP could be accessed via <https://apps.who.int/trialsearch/>. It was established in August 2005 in Geneva, Switzerland.

2.3.3 EU Clinical Trials Register

The EU Clinical Trials Register records the interventional studies conducted in the European Union (EU) or the European Economic Area (EEA) started after May 01, 2004. In this registry, the description of phase II to phase IV along with its summary results are available. The summary results include the trial information, endpoints, adverse effects identified in patients if available with the additional information. The registry doesn’t contain any information on non-interventional studies, surgical procedures, medical devices and psychotherapeutic procedures (*About the EU Clinical Trials Register*, n.d.). The EU Clinical Trials Register could be accessed via <https://www.clinicaltrialsregister.eu/ctr-search/search>.

2.3.4 ECRIN-MDR

European Clinical Research Infrastructure Network (ECRIN) is an EU based non-profit organization built to facilitate multinational clinical research across twelve EU countries. To support the COVID-19 research, ECRIN developed the Metadata Repository (MDR). It standardizes the metadata about the clinical studies and thus it could be accessed by a web interface. This portal is an open source enabling researchers to access worldwide with the results directing to the open access journal article or a trial registry entry if the results are publicly available (*Clinical Research Metadata Repository | ECRIN*, n.d.). The ECRIN-MDR could be accessed via <https://ecrin.org/tools/clinical-research-metadata-repository>.

2.3.5 Global Coronavirus COVID-19 Clinical Trial Tracker

This is a specialized real time dashboard of clinical trial for COVID-19. The results are gathered from International Clinical Trials Registry Platform (ICTRP), Chinese Clinical Trial Registry (ChiCTR), ClinicalTrials.gov, EU Clinical Trials Register, Clinical Research Information Service – Republic of Korea (CRiS), Iranian Registry of Clinical Trials (IRCT), Japan Primary Registries Network (JPRN) and German Clinical Trials Register (DRKS) . To identify potential clinical studies Artificial Intelligence (AI) based methods are employed. COVID-19 trials are mapped based on geographical, patient and intervention characteristics whose results are visualized in a convincing plots (Thorlund et al., 2020). The real time dashboard could be accessed via <https://www.covid-trials.org/>.

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