WHO Global Clinical Platform
for COVID-19

Data for public health response

WHO Global Clinical Platform for the Clinical Characterization of COVID-19

Statistical Analysis Plan

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World Health Organization

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Data contributors

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Abbreviations

ACE	angiotensin-converting enzyme
ALT	alanine aminotransferase
APTR	activated Partial Thromboplastin Time Ratio
aPTT	activated partial thromboplastin time
ARB	angiotensin receptor blocker
ARDS	acute respiratory distress syndrome
AST	aspartate aminotransferase
AVPU	alert, verbal, pain, unresponsive
BiPAP	bi-level positive airway pressure
BMI	body mass index
BP	blood pressure
BUN	blood urea nitrogen
CI	confidence interval
CPAP	continuous positive airway pressure
CRP	c-reactive protein
CT	computed tomography
ECMO	extracorporeal membrane oxygenation
ESR	erythrocyte sedimentation rate
FiO2	fraction of inspired oxygen
GCS	Glasgow Coma Scale
HF	high-flow
HR	heart rate
ICU	intensive care unit
IL-6	interleukin-6
IQR	interquartile range
LDH	lactate dehydrogenase
NCDs	non-communicable diseases
NEWS2	national early warning score 2
NSAID	non-steroidal anti-inflammatory drug
PaCO2	partial pressure of carbon dioxide
PaO2	partial pressure of oxygen
PEEP	positive end-expiratory pressure
P/F ratio	ratio of the partial pressure of oxygen to the fraction of inspired oxygen
RR	respiratory rate
RRT	renal replacement therapy
SBP	systolic blood pressure
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SpO2	peripheral oxygenation saturation
WBC	white blood cell
WHO	World Health Organization

Chapter 1. Background and Objectives

Introduction: Concerted epidemiological surveillance strategies are needed to better characterize the clinical presentations of COVID-19 in different demographic groups and in the context of varying management approaches worldwide. At this juncture, it is also critical to gain a more comprehensive understanding of the risk factors portending severe COVID-19 so that appropriate preventative or mitigating strategies may be put into place.

Intended purpose: To gather this information, the World Health Organization (WHO) has devised data collection tools for its Member States and a global COVID-19 clinical platform to enable harmonized data collection system submissions. The purpose of this document is to present a succinct description of the proposed analytic plan to generate statistics at global, regional and national levels including among subpopulation on the different clinical characteristics associated with COVID-19 and risk factors associated with poor clinical outcomes. The reports generated and published from these proposed analyses will help clinicians and national programs prepare appropriate management and response strategies.

Rationale: The World Health Organization has launched a Global COVID-19 Clinical Platform, which is intended to provide Member States with a standardized approach and platform to collect clinical data to better characterize the natural history of the disease, identify risk factors for severe disease and describe treatment interventions. The use of a single standardized clinical data tool enables clinical data from around the world to be aggregated and analyzed to gain a better understanding of the disease, inform the public health response and prepare for large-scale clinical trials. See https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform for more information.

Objectives of the analysis

1. Description of clinical characteristics
To describe the demographic features, clinical features, underlying conditions, medications, therapeutic interventions, supportive care, laboratory markers, and clinical outcomes (hereafter, collectively called clinical characteristics) among:

- the general population hospitalized with COVID-19
- specific subpopulations such as children, pregnant women, people living with HIV, people infected with tuberculosis (TB) or malaria, individuals with non-communicable diseases or other underlying conditions, severe/critically ill patients, and those from different geographic settings (hereafter, subgroups).

2. Variations in clinical characteristics
To assess variations in clinical characteristics among and between subgroups, as described above.

3. Association of clinical characteristics with outcomes
To identify clinical characteristics associated with disease severity at admission, ICU admission and in-hospital mortality globally, regionally, and nationally using regression models in both:

- the general population hospitalized with COVID-19
- in subgroups, as described above.

Time-to-event analyses for ventilation, ICU admission, and death will also be conducted.

4. Temporal trends
To describe temporal trends in clinical characteristics.

Please refer to **Table 1** entitled "**Overview of Analytic Schema**" below for more details.

Registry design: The WHO Global Clinical Platform is an open platform where Members States and individual facilities are invited to contribute anonymized patient data. Data contributors include a convenience sample of facilities willing to contribute data to the WHO Global Clinical Platform for COVID-19, research networks including multiple facilities and national registries. Increasing attempts will be made to include a representative sample of clinics.

Study population: Anonymized patients hospitalized with clinically suspected or laboratory-confirmed COVID-19.

Participant inclusion criteria: All patients, regardless of age, admitted to a hospital or health facility with laboratory-confirmed or clinically suspected COVID-19, will be included in the analytic sample. Patients with a negative laboratory result for SARS-CoV2 will be excluded.

Contribution to the Data Platform: All Member States are invited by WHO to participate and contribute clinical data through official communication from WHO Regional Offices. The extent of data contribution and data representativeness was expected to vary greatly among countries. In countries where funding is available to support data collection and data entry, a large network of clinics (up to 50 clinics per country) was trained to contribute data to the WHO Global Clinical Platform. In countries where a national registry of clinical data from hospitalized cases was established, the data shared with WHO is a population of hospitalized patient census in the country. In other countries, data contribution is limited to conveniently selected hospitals. Through regular review of the literature, authors of studies of clinical characterization of COVID-19 are invited to contribute data.

Main parameters/endpoints: Primary descriptive parameters include demographics (age, gender), presence of underlying conditions, use of chronic medications, clinical features on admission and during the hospitalization, laboratory findings on admission and during hospitalization, clinical interventions on admission and during hospitalization (oxygen use, ventilator use, use of therapeutics) and patient outcomes (dead, discharged, referral).

The patient outcomes described above will be used for secondary analysis to determine associations between baseline characteristics and severity of disease and outcomes.

Standardized data collection tool: Case report forms can be found at https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform

Table 1. Overview of Analytic Schema

Objective 1: Description of Clinical Characteristics	**Objective 2:** Variations of Clinical characteristics	**Objective 3:** Association of clinical characteristics with outcomes	**Objective 4:** Temporal trends
Descriptive Analysis of variables 1. Demographics 2. Clinical features 3. Underlying conditions and co-infections 4. Medications received 5. Therapeutic interventions 6. Supportive care 7. Laboratory markers 8. Clinical outcomes Stratified by: 1. Age 2. Gender 3. Severity of illness at admission To be applied to subpopulations (see sample size section).	**Bivariate analysis** to assess differences among and between subpopulations 1. Pregnant women compared to non-pregnant women 2. Children compared to adults 3. HIV+ compared to HIV - 4. TB co-infected patients compared to non-TB patients 5. Malaria co-infected pts compared to non-malaria patients 6. Other subpopulations, including people with NCDs or other underlying conditions, or co-infections will be considered 7. Populations from different geographic areas	**Regression analysis** to estimate odds ratio/relative risk or hazards ratio for clinical outcomes Specified outcomes include: 1. Disease severity at hospital admission 2. Mortality 3. ICU admission To be applied to subpopulations (see sample size section).	**Time-series analysis** to assess temporal trends in clinical characterization and management

Chapter 2. Sample Size

Study design

This study design may be described as passive clinical surveillance. It was pre-determined that the minimal sample size to conduct descriptive analysis per country was 300 patients. For regional reports, the minimal sample size required was at least 1200 patients from four countries (300 patients in each country). For global reports, the minimal sample size was at least 7200 patients derived from at least