International Registry of Healthcare Workers Exposed to COVID-19 Patients (UNITY Global)

Statistical Analysis Plan (SAP)

Document Type: Statistical Analysis Plan (SAP)

Project Code: BMGF-IDD-COVID19-2120

Draft Version: 6.0

Prepared for:

Bill and Melinda Gates Foundation

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Funder:	Bill and Melinda Gates Foundation
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1 Introduction

The purpose of this statistical analysis plan (SAP) is to provide an analytic framework for the study "International Registry of Healthcare Workers Exposed to COVID-19 Patients (UNITY Global)". This SAP addresses the statistical analyses that will be carried out in support of the protocol objectives. This analysis plan is based on the protocol version 1.0 of the study dated 08 June 2020.

2 Objectives of the study

This is an international registry of HCWs exposed to SARS-CoV-2 while caring for confirmed or clinically diagnosed COVID-19 patients. The aim of this registry is to generate real-world evidence in HCWs to potentially inform recommendations and policies on prevention measures, including prophylactic use of potential drug therapies in HCWs.

2.1 Primary objective

- To assess the association of potential prophylactic treatments with reduced risk of COVID-19 (or SARS-CoV-2 infection) in HCWs caring for COVID-19 patients.

2.2 Secondary objectives

- To characterize the type of potential prophylactic treatments, by dose and duration, overall, and by country/region/site.
- To explore the key factors (for example, use of PPE, HCW and healthcare facility characteristics, underlying co-morbidities, household history and COVID-19 exposure) modifying the risk of COVID-19 among HCWs.

3 Study overview

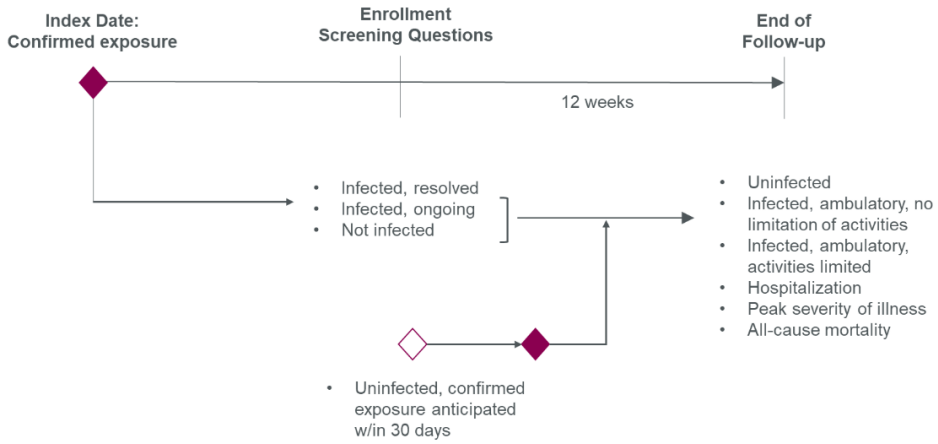
3.1 Study design

The UNITY Global Registry is designed to collect data on healthcare workers exposed to SARS-Cov-2 using longitudinal serial surveys implemented through a web/mobile application-based technology to encourage participation and facilitate rapid responses during this pandemic. Countries and healthcare facilities were selected based on the availability of potential prophylactic treatments to prevent workplace infection from SARS-CoV-2. Individuals with workplace exposure to confirmed or clinically diagnosed COVID-19 patients prior to enrollment, or anticipated within 30 days after enrollment, are eligible to participate. COVID-19 exposure is defined as per WHO classification[1]. The date of the HCW's first known exposure to a confirmed or clinically diagnosed case of COVID-19 is referred to as the "Index Date" (see Figure 1). Healthcare worker volunteers are ineligible if they had COVID-19 or symptoms highly suggestive of COVID-19 before the Index Date. However, at the time of enrollment, HCWs can be either SARS-CoV-2 positive (symptomatic or asymptomatic) or SARS-CoV-2 negative. Healthcare workers are identified for participation via a central contact at participating healthcare facilities and are directed to a website/mobile application allowing them to electronically consent and answer questions that help assess their eligibility to participate. Information on potential prophylactic treatments used by HCWs are also collected.

All eligible HCWs in the study facilities are asked to enter the data in the registry via electronic data collection form. Data is collected at entry to the registry, and then weekly until 12 weeks after enrollment, death or lost to follow-up, whichever is earlier. A secondary contact is identified to be contacted to confirm status of HCWs in case of non-response/ loss to follow-up. In case of conflicts, responses by HCWs take precedence. Serology results from the laboratory will be loaded into the Local Data Store and merged with HCW contact information based on the participant identification numbers. Notification of results may be made available to the HCWs via secure access.

This is an observational cohort study; therefore, no preventive interventions, visits or laboratory tests are mandated. Dosing and duration of potential prophylactic treatment is at the discretion of the institution and/or healthcare provider, in accordance with regular local practice. However, serology testing for SARS-CoV-2 antibodies are being offered to the first 50% of participating HCWs per country, at enrollment and at the last follow-up (i.e. at Week 12).

Figure 1: Healthcare Worker Flow – Study Schematic



3.1.1 Study population and setting

The study population comprises male and female HCWs, aged 18 years or older, working in healthcare facilities (e.g., acute care hospital) or in a community healthcare setting (e.g., clinic) in Indonesia, Kenya, Nigeria, Pakistan, Sengal, South Africa, Uganda, Zimbabwe, and Zambia. Hospitals or healthcare facilities directly participating in the study in target countries of interest should have at least five COVID-19 cases at the time of establishing the registry. Institutions that participate in the study should be able to provide a list of HCWs exposed to COVID-19 patients. As per the WHO definition[2], HCWs eligible for enrollment are limited, based on the high likelihood of being exposed to COVID-19 patients during patient care, to the following positions:

- Medical doctors*
- Clinical officers*
- Licensed physician assistant or nurse practitioner*
- Registered nurse (or equivalent)*
- Assistant nurse, nurse technician (or equivalent)*
- Phlebotomist
- Clinical pharmacist
- Clinical physical therapist
- Respiratory therapist
- Community healthcare worker

*These should include the following primary specialties:

- Surgery (all sub-specialties)
- Internal medicine (general)
- Pulmonology/critical care
- Emergency medicine

- Geriatrics
- Cardiology
- Infectious disease
- Anesthesiology
- Pediatrics
- Obstetrics/Midwifery
- Other

3.1.1.1 Inclusion criteria

Healthcare workers are eligible for entry into this study only if they meet all the following criteria:

- Healthcare workers aged ≥ 18 years.
- Healthcare workers must be exposed through ongoing and recurrent contact to a confirmed or clinically diagnosed COVID-19 patient prior to enrollment, or anticipated within 30 days after enrollment.
- Healthcare workers must consent to provide data for the registry and must be willing to be contacted/reminded about data entry at each follow-up time point.
- Healthcare workers must agree to provide a secondary contact for follow-up.

3.1.1.2 Exclusion criteria

- A confirmed SARS-CoV-2 infection or clinically diagnosed COVID-19 prior to the first known exposure to confirmed or clinically diagnosed COVID-19 patient (Index Date).
- Participation in a 'blinded' clinical trial, i.e. unaware of exact treatment received as part of the clinical trial.

Date checks to confirm eligibility criteria will be completed for all subjects. Subsequently, healthcare workers that indicate first exposure to COVID-19 infected patients or COVID-19 symptoms/diagnosis/test results prior to 2020 will be dropped from any analysis. Similarly, healthcare workers that are not exposed to COVID-19 infected patients within 30 days following enrolment will be excluded from any analysis.

3.2 Study period

This registry will remain open and will continue to enroll HCWs until target country level quotas have been reached, or until otherwise determined by the Sponsor.

3.3 Baseline period

Baseline period is defined as timeframe prior to or at index date, i.e. date of the HCW's first known exposure to a confirmed or clinically diagnosed case of COVID-19.

3.4 Follow-up period

The HCWs will be followed up for 12 weeks upon enrollment in the study.

3.5 Study outcomes

3.5.1 Primary Outcome

- Occurrence of SARS-CoV-2 infection among HCWs caring for COVID-19 patients, in terms of time, geography, healthcare setting, and type of HCW. SARS-CoV-2 infection will be defined as a composite outcome diagnosed via the following methods:
    - By test – positive test results – confirmed diagnosis
    - Clinical diagnosis
    - By symptoms
    - Hospitalisation due to COVID-19 illness

Sensitivity analyses will be conducted using confirmed (by positive test results) diagnosis only, and diagnosis by other means, as specified above.

3.5.2 Secondary Outcomes

For the following outcomes, infection status will be defined as per the composite primary outcome. Ambulatory status and hospitalisation will be based on responses to the relevant questions in the survey. Mortality will be based on the survey response of each subject's secondary contact. Prophylactic treatment will be based on relevant questions from healthcare worker's surveys.

- Occurrence of SARS-CoV-2 uninfected HCWs
- Occurrence of SARS-CoV-2 infection with ambulatory status and no limitation of activities. This will be defined as subjects reporting COVID-19 related symptoms, clinical diagnosis of COVID-19 or positive test results but reporting "No" limitation of activities due to their symptoms and no hospitalisation.
- Occurrence of SARS-CoV-2infection with ambulatory status and limitation of activities. This will be defined as subjects reporting COVID-19 symptoms, clinical diagnosis of COVID-19 or positive test results and reporting "Yes" to having their usual activities limited being limited due to their symptoms, but no hospitalisation.
- Occurrence of hospitalisation due to COVID-19 illness with mild disease. This is defined as being hospitalised without being admitted to the ICU or without ventilation
- Occurrence of hospitalization due to COVID-19 illness with severe disease. This is defined as being hospitalised with either admittance to the ICU and/or receiving ventilation.
- Occurrence of all-cause mortality

- Type of prophylactic treatments (Chloroquine, Hydroxychloroquine, Azithromycin, Lopinavir/ritonavir, Ivermectin, others) by dose, frequency and duration, overall and by country/region/site. To note, prophylactic treatment use will be defined by relevant indication from 'prophylactic treatment' section of the survey; in addition, if there is an indication of drugs in 'concomitant medications' section that are also listed but not selected under 'prophylactic treatment' section, those indications will be added too.

3.6 Other study variables

All of the following variables are collected at baseline and for each week of follow-up up to 12 weeks.

3.6.1 Clinical Outcomes Variables

- WHO Ordinal Scale for Clinical Improvement of COVID-19 (adapted, abbreviated version)
  - SARS-CoV-2 (uninfected/infected)
  - Ambulatory status (limitation/no limitation of activities)
  - Hospitalized with no intensive care unit (ICU) or mechanical ventilation (mild)
  - Hospitalized with ICU and/or mechanical ventilation (severe)
  - Death

3.6.2 Prophylactic treatment (treatment exposure)

- Types, intake frequency, and doses of prophylactic treatments
  - Treatment name: Chloroquine, Hydroxychloroquine, Azithromycin, Lopinavir/ritonavir, Ivermectin, others
  - Date started
  - Date stopped
  - Dose (intake)
  - Duration of treatment
  - Dose frequency and dosing interval
  - Status (stopped/ongoing)
  - Reason for stopping (not available/side effects/expense/other)
  - Number of missed doses and reason (not available/side effects/expense/other)

3.6.3 History of exposure to COVID-19 patients

- At enrollment
  - Self-reported ongoing and recurrent exposure (yes/no)
  - WHO exposure definition (3 questions) (yes/no)
    - Direct patient care (yes/no)
    - Face-to-face contact (yes/no)
    - Present during aerosol-generating procedure (yes/no)

- Weekly follow-up
    - Self-reported ongoing and recurrent exposure (yes/no)
    - WHO exposure definition (3 questions) for past week
    - Days worked past week
    - Number of COVID-19 cases exposed to in the past week

3.6.4 Personal Protective Equipment Use

- At enrollment
    - Type and use of PPE (yes always, yes not always, no) prior to enrollment
- Weekly follow-up
    - Type and use of PPE (yes always, yes not always, no) at time of confirmed exposure(s) in the past week
    - Number of COVID-19 exposures in the absence of a mask
    - Longest COVID-19 exposure in the absence of a mask

Details on the following types of PPE will be captured:

- Mask (type of mask—N95 respirator mask, other)
- Eye protection/goggles/face shield
- Gown
- Gloves

3.6.5 Other Covariates

- COVID-19 symptoms (and date the symptoms begin)
    - Fever (temperature over 38°C)
    - Subjective fever (felt feverish)
    - Chills
    - Myalgia (muscles hurt or ache)
    - Rhinorrhea (runny or drippy nose)
    - Pharyngitis (sore throat)
    - Cough (new onset or worsening of chronic cough)
    - Dyspnea (hard to breathe or difficulty breathing)
    - Pneumonia
    - Nausea or vomiting
    - Headache or migraine
    - Abdominal pain (pain in tummy)
    - Asthenia (weakness or loss of strength)
    - Arthralgia (joint pain)
    - Anosmia (loss of smell)

  - Ageusia (loss of taste)
  - Blue coloring in toes
  - Diarrhea (two or more looser-than-normal stools in 24 hours)
- SARS-CoV-2testing
  - Type of test, if known
    - PCR (positive/negative)
    - Antigen test (positive/negative)
    - Serology (IgG and/or IgM, positive/negative or titer)
  - Date of test
- Household history (COVID-19)
  - Number of household contacts
  - Additional household member(s)exposed to COVID-19(yes/no). If yes, how many
  - Additional household member(s) with symptoms consistent with COVID-19 (yes/no). If yes, how many?
  - Additional household member(s) diagnosed withCOVID-19(yes/no). If yes, how many
- Healthcare worker-level covariates
  - Demographics at entry
  - Underlying conditions and key comorbidities
  - Job characteristics
  - Concomitant medications
  - Blood type
- Healthcare facility characteristics
  - Country, region
  - Urban or rural setting
  - Type of facility (public/private/community healthcare)
  - Teaching/university hospital or non-teaching
  - Capacity
    - number of patients tested for COVID-19
    - number of COVID-19 patients treated
    - number of hospitalized beds (overall, ICU, emergency department)
    - number of exposed HCWs
    - number of HCWs tested for COVID-19
  - Number of HCWs who developed confirmed or clinically diagnosed COVID-19
  - Number of HCWs who died from COVID-19
  - Approved PPE use policy, and experience of PPE shortage
  - Approved prophylactic treatment policy
  - Shortage of COVID-19 related tests
  - BCG vaccination policy
- Concomitant medications (other than for COVID-19)
  - Antibiotics (yes/no). If yes, please specify.

    - Azithromycin
    - Trimethoprim/sulphamethoxazole
    - Macrolide antibiotics (roxithromycin, clarithromycin, erythromycin)
    - Other antibiotics
- Antimalarials (yes/no). If yes, please specify.
    - Hydroxychloroquine
    - Chloroquine
    - Sulfadoxine-pyrimethamine (SP)
    - Other antimalarials
- Antiparasitics (yes/no). If yes, please specify.
    - Ivermectin(yes/no)
    - Other antiparasitics
- Antiretrovirals for Human Immunodeficiency Virus (HIV) (yes/no). If yes, please specify.
    - Lopinavir
    - Ritonavir
    - Tenofovir
    - Nelfinavir
    - Other antiretrovirals
- Antivirals (yes/no). If yes, please specify.
    - Oseltamivir
    - Favipiravir
    - Arbidol
    - Anti-hepatitis C treatments
    - Remdesevir
    - Other antivirals
- Medication for high blood pressure and cardiovascular disease (yes/no). If yes, please specify.
    - Angiotensin-converting enzyme (ACE) inhibitor (e.g. lisinopril, enalapril)
    - Angiotensin II receptor blockers (ARB) inhibitor (e.g. losartan, irbersarten)
    - Other anti-hypertensive for high blood pressure
    - Other medicine for high blood pressure and cardiovascular disease (E.g. antiarrhythmics, inotropes, chronotropes)
- Nonsteroidal Anti-inflammatory Drugs (NSAIDs) E.g. Aspirin, Ibuprofen, Indomethacin, Celecoxib, Diclofenac (yes/no).
- Botanicals-- Artemisia teas (COVID Organics) (yes/no)
- Immunocompromising drugs such as corticosteroids, cancer chemotherapy, cyclosporine, colchicine, drugs for autoimmune conditions such as lupus, rheumatoid arthritis or Crohn's disease (yes/no)
- Changes in concomitant medications

Any prophylactic medications that are indicated as concomitant medications being taken by HCWs will be considered during analysis as part of a prophylactic treatment. This will apply to the following prophylactic medications:

- Hydroxychloroquine
- Chloroquine
- Azithromycin
- Lopinavir/ritonavir
- Ivermectin

4 Data security/privacy

- The Application has received a full penetration test from an accredited third party to cover cyber security threats.
- Data is segregated between the collection nodes and analysis nodes. Only information technology support staff have access to the data in the nodes for the express purposes of server support.
- All data on the analysis platform is tokenized with a unique patient token generated on the node. This tokenization uses a powerful salted hash algorithm (a document explaining this process may be reviewed if necessary but cannot be released for security reasons).
- Access to the data platform is controlled by Azure Active Directory accounts managed by the Parexel Support team.
- Access to the Application can only be achieved by end user registration using a set of industry leading authentication providers.
- The application has a unidirectional data flow from the node to the analysis platform so there is no risk of horizontal escalation issues.

5 Determination of Sample Size

The targeted sample size of approximately 10,000 HCWs assumes that 20% of the study population are non-exposed to potential prophylactic treatments, with a baseline risk of SARS-CoV-2 infection in the study period of 10% (for unexposed: not treated with potential prophylactic treatment). A total of N=10,000 allows for 80% power to identify an effect size of Relative Risk = 0.78.

If these sample sizes are not reached with respect the study population being exposed/non-exposed to potential prophylactic treatments, the relative risk may be detected with lower power or it may not be statistically significant. However, the secondary objectives can still be examined.

6 Statistical analysis

6.1 Overview

All statistical analyses will be conducted using R (version 1.3.1093), unless otherwise specified.

For all descriptive analyses, categorical variables will be summarized by number of observations and percentage (%). Percentages will be rounded to one decimal place and will be based on available observations (known values), unless otherwise specified. Continuous variables will be summarized using descriptive statistics (n, mean, with standard deviation; minimum, first quartile, median, third quartile,

and maximum). Outliers will be included in descriptions as part of presenting ranges and percentiles (25^{th} and 75^{th}). The mean and SD will be rounded to one decimal place.

All statistical tests will be two-sided and at 5% level of significance.

6.2 Missing values

6.2.1 Missing values for non-outcome variables

For descriptive analyses, each variable will be described with frequencies of missing and "Not Known" values. Outliers will be included in description as part of presenting ranges and percentiles (25^{th} and 75^{th}).

In case of partial dates, the following transformations will be made to estimate time frames and durations:

- If only month and year are indicated, "15" will be added for day
- If only year is indicated, "01" will be added for day and "07" for month

If this decision implies negative duration or inconsistencies, it will be reviewed case by case. Otherwise, the date will be considered missing. The possibility of using multiple imputation will be explored, if required during analysis, to address missing data, and subsequently evaluated with sensitivity analyses.

6.2.2 Missing values for outcomes

Specific imputation methods will not be used for outcome variables. However, for descriptive analyses, each variable will be described with frequencies of missing and "Not Known" values, where applicable.

Other methods, including complete case analysis, will be considered when appropriate. For 'time-to-event' outcomes, patients who are lost to follow-up prior to the time point of interest will be censored.

6.3 Descriptive analyses

Prior to implementing the analysis to address the primary objectives of the study, descriptive analyses will be carried out to understand the main features and patterns in the population and in the data collected. Study population characteristics will be tabulated at index date.

WHO Ordinal Scale for Clinical Improvement (see Appendix 1) scores distribution over time will be displayed. Kaplan-Meier estimates will be calculated, and curves plotted for each time-to-event outcome.

The observed incidence weekly rates of PCR-confirmed or symptomatic COVID-19 and of COVID-19-related hospitalizations and deaths will be tabulated over weeks by facilities and compared according to

prophylactic treatment use (yes/no; by treatment, subject to sufficient sample size; and by pre- and post-exposure (to COVID-19 patients) use, subject to sufficient sample size).

Applications of estimated propensity scores will be employed to explore differences between HCWs' profiles exposed versus non-exposed to potential prophylactic treatments. Propensity scores will be estimated for receipt of potential prophylactic treatments based on key covariates of interest for the HCWs' profiles (age, gender, race, type of HCW, BMI, smoking status, medical history). Estimated propensity score distributions will be displayed over weeks and a concordance analysis performed to detect any trend over time.

Stratified pooled analyses at country level will also be displayed.

6.3.1 Facility characteristics

Each facility will be descriptively summarized using data from separately completed facility level questionnaires; these questionnaires will be administered twice - at the start and end of the HCW level survey at each facility. This data will then be linked to HCW level data from the same facility to provide a broader context for the survey data, as well as to compare the results from HCW level survey with what could have been expected from the facility level data. Subsequently, an assessment of potential biases and limitations in this regard will be discussed in a study report.

In particular, a description of facilities will be provided in terms of type (public/private/community; teaching status) and size (number of beds), as well as existence of policies for prophylactic treatment and PPE use to prevent COVID-19 among HCWs. In addition, existence of BCG vaccination policy for HCWs and shortage of COVID-19 tests experienced by the facility will be described, as recorded in the facility level survey.

Also, the number of HCWs exposed to COVID-19 patients at each facility, the number of HCWs tested for, diagnosed with and died due to COVID-19 at each facility will be described, both since the start of pandemic (including within the last 30 days) and at the end of the survey in the facility.

The number of patients tested and treated for CODIV-19 at each facility will be described too.

6.3.2 Demographic characteristics

The following demographic characteristics of subjects included in the study will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.3 in the appendix):

- Age (Years)
- Biological Gender (Male; Female)
- Race (White; Black; Mixed race; Asian Indian; Asian Bangladeshi; Asian Pakistani; Other Asian; Other)

- Blood Type (A positive; A negative; B positive; B negative; O positive; O negative; AB positive; AB negative; Unknown)
- BMI in kg/m^2(derived from height (cm) and weight (kg) and grouped into the following categories: Normal weight (BMI of 18.5 to less than 25); Overweight (BMI of 25 to less than 30); Obese (BMI of 30 or greater); Underweight (BMI of less than 18.5); Missing)
- Smoking Status (Current Smoker; Past Smoker; Never Smoked)

6.3.3 Household characteristics

The following household characteristics of subjects included in the study will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.4 in the appendix):

- Others in household exposed to COVID-19 infected individuals (Yes; No; Unknown)
- Number of household members exposed to COVID-19 infected individuals
- Others in household showing symptoms of COVID-19 (Yes; No)
- Number of household members showing symptoms of COVID-19
- Others in household diagnosed with COVID-19 (Yes; No)
- Number of household members diagnosed with COVID-19
- Number of people living in household

For HCWs with COVID-19 at entry: responses to the baseline survey will be used.

For HCWs with COVID-19 at follow-up: maximum responses over the entire follow-up time available in the data cut. In addition, maximum responses in the 2 or 4 weeks (TBD) prior to COVID-19 infection date will be described.

For HCWs with no COVID-19 infection at any time: maximum responses over the entire follow-up time available in the data cut. In addition, maximum responses in the 2 or 4 weeks (TBD) prior to the data cut date will be described.

Maximum responses will be defined as:

- For a yes/no question, “yes” will be considered
- For number of household members, the maximum number will be considered

6.3.4 Exposure to COVID-19 patients

The following household characteristics of subjects included in the study will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.5 in the appendix):

- Contact with confirmed COVID-19 patients (Yes; No)
- Direct care to COVID-19 patients (Yes; No)
- Face-to-face contact (within 1 metre) of COVID-19 patients (Yes; No)

- Present when aerosol generating procedures performed (Yes; No)
- Average number of COVID-19 patients in contact each week for past month
- Number of days spent at work in last week
- Number of hours worked directly with COVID-19 patients in last week

For HCWs with COVID-19 at entry: responses to the baseline survey will be used.

For HCWs with COVID-19 at follow-up: maximum responses over the entire follow-up time available in the data cut. In addition, maximum responses in the 2 or 4 weeks (TBD) prior to COVID-19 infection date will be described.

For HCWs with no COVID-19 infection at any time: maximum responses over the entire follow-up time available in the data cut. In addition, maximum responses in the 2 or 4 weeks (TBD) prior to the data cut date will be described.

Maximum responses will be defined as:

- For a yes/no question, "yes" will be considered
- For number of days spent at work and number of hours worked directly with the COVID-19 patients, a summation will be done
- For average number of COVID-19 patients in contact each week for past month, an average will be calculated

Using the follow-up survey data for questions with yes/no responses, the following plot will be generated to display exposure over time:

For,

i = question #

n_{it}= # of yes answers to question *i* at time t

n_t= # of responders at time t

$$r_t = \sum_i {}^{n_{it}}/_{n_t}$$

A line plot of r over time will then be displayed. Two separate lines will be generated, one for HCWs infected with COVID-19 and another for HCWs that were never infected with COVID-19.

6.3.5 Medical history

The following medical conditions of subjects included in the study will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.6 in the appendix):

- Any of the following conditions (Chronic lung disease; Diabetes; Cardiovascular (heart) disease); Chronic renal (kidney) disease; Chronic liver disease; Immunocompromised condition; Cancer, Obesity; Tuberculosis; Neurologic/neurodevelopmental; History of stroke; Hypertension (high blood pressure); Other chronic diseases; None of the above)

  To note, for HCWs who entered the survey with already confirmed or symptomatic COVID-19 disease (whether at entry or prior to entry), it will not be possible to attribute conditions listed under medical history section to the timeframe prior to or following COVID-19 disease, as these conditions are collected at entry with no recorded date of diagnosis. This is unlikely to be an issue for the chronic conditions listed, however this could pose a problem for including cardiovascular disease and history of stroke in the causal inference models outlined in the primary analysis. This issue will be assessed during the subgroup analysis of HCWs by COVID-19 status at study entry.

6.3.6 Medications for non-COVID-19 related purposes

The following medications for non-COVID related purposes will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.7 in the appendix):

- Antibiotics (yes/no). If yes, please specify.
  - Azithromycin
  - Trimethoprim/sulphamethoxazole
  - Macrolide antibiotics (roxithromycin, clarithromycin, erythromycin)
  - Other antibiotics
- Antimalarials (yes/no). If yes, please specify.
  - Hydroxychloroquine
  - Chloroquine
  - Sulfadoxine-pyrimethamine (SP)
  - Other antimalarials
- Antiparasitics (yes/no). If yes, please specify.
  - Ivermectin(yes/no)
  - Other antiparasitics
- Antiretrovirals for Human Immunodeficiency Virus (HIV) (yes/no). If yes, please specify.
  - Lopinavir
  - Ritonavir
  - Tenofovir
  - Nelfinavir
  - Other antiretrovirals
- Antivirals (yes/no). If yes, please specify.

  - Oseltamivir
  - Favipiravir
  - Arbidol
  - Anti-hepatitis C treatments
  - Remdesevir
  - Other antivirals
- Medication for high blood pressure and cardiovascular disease (yes/no). If yes, please specify.
  - Angiotensin-converting enzyme (ACE) inhibitor (e.g. lisinopril, enalapril)
  - Angiotensin II receptor blockers (ARB) inhibitor (e.g. losartan, irbersarten)
  - Other anti-hypertensive for high blood pressure
  - Other medicine for high blood pressure and cardiovascular disease (E.g. antiarrhythmics, inotropes, chronotropes)
- Nonsteroidal Anti-inflammatory Drugs (NSAIDs) E.g. Aspirin, Ibuprofen, Indomethacin, Celecoxib, Diclofenac(yes/no). If yes, please specify.
- Botanicals (yes/no)
  - Artemisia teas (COVID Organics)
- Immunocompromising drugs (yes/no). If yes, please specify.
  - Corticosteroids
  - Cancer chemotherapy
  - Cyclosporine
  - Drugs for autoimmune conditions such as lupus or rheumatoid arthritis, Crohn's disease

For HCWs with COVID-19 at entry: responses to the baseline survey will be used.

For HCWs with COVID-19 at follow-up: medications used at any time over the entire follow-up time available in the data cut. In addition, medications used at any time in the 2 or 4 weeks (TBD) prior to COVID-19 infection date will be described.

For HCWs with no COVID-19 infection at any time: medications used at any time over the entire follow-up time available in the data cut. In addition, medications used at any time in the 2 or 4 weeks (TBD) prior to the data cut date will be described.

6.3.7 Prophylactic medications

Prophylaxis usage of subjects included in the study will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.8 in the appendix):

A stacked bar chart will be used to display the prophylaxis usage during the follow-up period. The x-axis will be dates of survey responses and the stacked bars will be grouped by yes/no (corresponding to prophylaxis use at specific dates). This will be done separately for HCWs infected with COVID-19 and those uninfected. The stacked bar charts can be used to compare prophylaxis use among infected/uninfected HCWs over time. This will be done for “any prophylaxis use” and if sample if sample sizes permit they will

be presented for the major individual prophylaxis treatments (ie. azithromycin, chloroquine/hydroxychloroquine, ivermectin, lopanavir).

Prophylaxis usage pre- and post- first date of COVID-19 exposure will also be described, stratified further by COVID-19 infection status.

- Types, intake frequency, and doses of prophylactic treatments
    - Treatment name
    - Date started
    - Date stopped
    - Dose (intake)
    - Duration of treatment
    - Dose frequency and dosing interval
    - Status (stopped/ongoing)
    - Reason for stopping (not available/side effects/expense/other)
    - Number of missed doses and reason (not available/side effects/expense/other)

For HCWs with COVID-19 at entry: prophylaxis treatments used before the COVID-19 infection date will be described.

For HCWs with COVID-19 at follow-up: prophylaxis treatments used over the entire follow-up time available in the data cut. In addition, prophylaxis treatments used within 2 or 4 weeks (TBD) before COVID-19 infection date will be described.

For HCWs with no COVID-19 infection at any time: prophylaxis treatments used over the entire follow-up time available in the data cut. In addition, prophylaxis treatments used within 2 or 4 weeks (TBD) prior to the data cut date will be described.

6.3.8 PPE usage

The following PPE usage of subjects included in the study will be descriptively summarized for HCWs with and without COVID-19 infection (see Table 8.2.9 in the appendix):

A stacked bar chart will be used to display PPE usage during the follow-up period. The x-axis will be dates of survey responses and the stacked bars will be grouped by yes/no (corresponding to PPE use at specific dates). This will be done separately for HCWs infected with COVID-19 and those uninfected. The stacked bar charts can be used to compare PPE use among infected/uninfected HCWs over time. This will be done for the four types of PPE (eg. masks, eye protection, gowns, gloves).

- PPE used in workplace since first known contact with COVID-19 patients
    - Mask (Yes always; Yes not always; No)
    - Type of Mask (N95 Respirator Mask; Other)
    - Eye Protection (Yes always; Yes not always; No)

  - Gown (Yes always; Yes not always; No)
  - Gloves (Yes always; Yes not always; No)
- The number of PPEs used as "yes always" among mask, eye protection, gown, gloves will also be summarized: none, one, two, three, all four

For HCWs with COVID-19 at entry: responses to the baseline survey will be used

For HCWs with COVID-19 at follow-up: overall PPE usage over the entire follow-up time available in the data cut. In addition, overall PPE usage in the 2 or 4 weeks (TBD) prior to COVID-19 infection date will be described.

For HCWs with no COVID-19 infection at any time: overall PPE usage over the entire follow-up time available in the data cut. In addition, overall PPE usage in the 2 or 4 weeks (TBD) prior to the data cut date will be described.

Overall PPE usage will be defined as the following from multiple weekly surveys being considered as above:

Responses seen in all weekly surveys being considered	Overall PPE usage
Yes always	Yes always
Yes always Yes not always	Yes not always
Yes always No	Yes not always
Yes always Yes not always No	Yes not always
Yes not always	Yes not always
Yes not always No	Yes not always
No	No

6.3.9 COVID-19 symptoms

The distribution of COVID-19 symptoms will be displayed for the following time periods after first indication of symptoms:

- Symptoms at any time on or after first symptoms seen for the HCW
- Symptoms within 1 week after first symptoms seen for the HCW
- Symptoms within 1-2 weeks after first symptoms seen for the HCW
- Symptoms within 2-4 weeks after first symptoms seen for the HCW
- Symptoms >4 weeks after first symptoms seen for the HCW

A summary of the proportion of HCWs that had at least one symptom, at least two symptoms, at least three symptoms will also be displayed within these time periods. A histogram will be produced where the bins along the x-axis are the number of unique symptoms each HCW reports on their survey. This descriptive analysis will aid in determining which symptoms or group of symptoms will be considered for diagnosing HCWs as being COVID-19 infected.

6.4 Primary analysis

6.4.1 Frailty model: mixed effect Cox regression

For the time to COVID-19 infection outcome, both crude and adjusted hazards ratios will be estimated for time to COVID-19 infection with respect to prophylaxis use. The primary objective of this analysis is to assess the association between prophylactic treatments and the reduced risk of SARS-CoV-2 infection in HCWs caring for COVID-19 patients. A mixed effect Cox regression model (ie. frailty model) will be used to estimate adjusted hazard ratios. This method will allow the utilization of both the repeated measures gathered from each HCWs surveys, as well as the incorporation of time-varying covariates of interest such as PPE usage and COVID-19 exposure. Each subject will be included as a random effect. Both time-fixed and time-varying covariates will be included in the model. Covariates will be assessed using a univariate model, any covariates with a p-value less than 0.20 will be included in a multivariate model. A backward stepwise process will then be completed, where the covariates with largest p-value are removed one at a time until all covariates that remain are significant at the 0.10 level. The time-fixed covariates, healthcare facility and country will be included in the model regardless of their significance level. Including the healthcare facility and country covariates will make each healthcare worker's COVID-19 outcome conditionally independent on the background COVID-19 incidence occurring within each subject's healthcare facility and country. A list of additional covariates to be considered can be found in Table 5.4.1. For each subject in the control group, the index date (ie. time of first known exposure to COVID-19 patients) will be used as time zero. For HCWs that are treated with prophylaxis at any time their index date will be 7 days after initiation of treatment. Having an index date near treatment initiation will prevent the introduction of survivorship bias into the analysis.

Table 5.4.1 Model Covariates

Time-fixed/Time-varying Covariate	Covariate Name
Time-fixed Covariates	Healthcare facility, Country, Age, Biological Gender, BMI, Smoking status, Ethnicity, Blood type, Primary work location, Type of healthcare worker, Medical history

Time-varying Covariates	Others in household exposed to COVID-19 infected individuals, Others in household showing symptoms of COVID-19, Others in household diagnosed with COVID-19, Number of COVID-19 infected patients exposed to, Direct care to COVID-19 patients, Face-to-face contact of COVID-19 patients, Present when aerosol generating procedures performed, Mask usage, Gown usage, Eye protection usage, Glove usage

Note: The necessity to create composite variables or collapse categories within variables will be determined upon the completion of the descriptive analyses. A correlation analysis will be completed to assess the level of correlation between variables, if a high level of correlation is found only one of the variables will be included as a covariate in the models.

A Cox model with mixed effects can be formulated as $h_i(t) = h_o(t)\exp(\boldsymbol{X}_i B + \alpha_j)$, where α_j denotes the random effect associated with the j-th cluster. The random effect can be thought of as a random intercept that modifies the linear predictor, while the shared frailty term has a multiplicative effect on the baseline hazard function: $h_i(t) = h_o(t)\exp(\alpha_j)\exp(\boldsymbol{X}_j B)$[3].

6.5 Secondary analysis

All time-to-event secondary analyses will be conducted similarly as for the primary analysis. They include:

- Time to clinical events (each defined by the WHO severity score or proxies to be defined)
  - Ambulatory status with no limitation of activities (WHO Ordinal Scale classification 1). This will be defined as subjects reporting COVID-19 related symptoms, clinical diagnosis of COVID-19 or positive test results, but reporting “No” limitation of activities due to their symptoms and no hospitalisation.
  - Ambulatory status with limitation of activities (WHO Ordinal Scale classification 2). This will be defined as subjects reporting COVID-19 symptoms, clinical diagnosis of COVID-19 or positive test results and reporting “Yes” to having their usual activities limited being limited due to their symptoms, but no hospitalisation.
  - Hospitalised mild disease (WHO Ordinal Scale classifications 3 and 4). This is defined as being hospitalised without being admitted to the ICU or without ventilation.
  - Hospitalised severe disease (WHO Ordinal Scale classifications 5 to 7). This is defined as being hospitalised with either admittance to the ICU and/or receiving ventilation.
  - Death (WHO Ordinal Scale classification 8)

Furthermore, to explore key factors (eg. PPE, HCW and healthcare facility characteristics, underlying co-morbidities, household history and COVID-19 exposure) that potentially modify the risk of COVID-

19 among HCWs, the following analysis will be undertaken. For the covariates remaining in the final model of the primary analysis, one covariate will be removed at a time and will be tested using a liklihood ratio test to determine their association with the primary outcome.

Finally, as described in section 3.5.2, the type of prophylactic treatments (Chloroquine, Hydroxychloroquine, Azithromycin, Lopinavir/ritonavir, Ivermectin, others) will be characterized by dose, frequency and duration, overall and by country/region/site. To note, prophylactic treatment use will be defined by relevant indication from 'prophylactic treatment' section of the survey; in addition, if there is an indication of drugs in 'concomitant medications' section that are also listed but not selected under 'prophylactic treatment' section, those indications will be added too.

Other derived variables such as time in hospitalization will be analyzed via generalized mixed effect models.

6.6 Subgroup analyses

The adjusted analyses of the primary and secondary outcomes will be replicated:

- According to the subgroup of HCWs by COVID-19 status at entry, i.e. separately for those who already had COVID-19 at entry vs those without COVID-19 at entry
- According to the subgroup of HCWs for which PCR-confirmed absence of infection at index date is demonstrated
- According to the subgroup of HCWs for which serology results are available at entry and follow-up
- According to the time from index date to entry in the registry date. Depending on the distribution of the length of time from index date to study enrollment date in these two times, a subgroup analysis may be undertaken. Groups will be formed by binning time from index date to study enrollment date (eg. 0-1 month, 1-2 months, 2-3 months, greater than 3 months)

6.7 Sensitivity analyses

The following sensitivity analyses will be performed for the primary analysis:

- According to the four definitions of the primary outcome of COVID-19 infection (ie. positive test only, symptoms only, clinical diagnosis only, hospitalized only)
- Imputing unexplained drop-outs as events. Healthcare workers that are lost to follow-up will be treated as positive for COVID-19 infection.

In the event that the estimated hazard ratio of treated versus control in the primary analysis is 0.8 or less, but no statistical significance can be established due to a small sample size, an alternative approach such as empirical Bayesian meta-analysis will be employed to leverage published local data.

7 Minimization of study bias

As this is an observational study based on self-reported information from HCWs, there are several potential limitations and biases that will need to be considered, as follows:

7.1 Selection bias

- To minimize the impact of selection bias in the selection of participants, in each healthcare facility, the list of exposed HCWs will be obtained and all eligible HCWs will be offered enrollment. Furthermore, to assess the impact of selection bias, facility level data will be compared with HCW level data as outlined in section 5.3.1. Finally, an inverse probability weighting analysis (see section 5.4.2) will be undertaken. Incorporating data from relevant covariates will allow the reweighting of individuals to help achieve a more balanced analysis. This is achieved by increasing the weight of those individuals who were less likely to be enrolled in the study, and decreasing the weight of individuals who were more likely to be enrolled.

7.2 Survival bias

- To assess the impact of this bias, a metadata of healthcare facility level variables will be collected at time of the registry establishment and at the end of the study, including number of exposed to COVID-19 HCWs, number of HCWs who developed COVID-19 and who died from COVID-19 at each participating healthcare facility. This analysis is outlined in section 5.3.1.

7.3 Recall bias

- Similar to both selection and survival bias above, this potential source of bias will be assessed based on evaluations of facility-level data as outlined in section 5.3.1.

7.4 Information bias

- All information is self-reported, and there is no mechanism to verify the accuracy of information entered into the web-application. Relatedly, the reporting of hospitalization and death are dependent on the reliable participation of a secondary contact, who may be difficult to contact in the case of an HCW's death.

7.5 Indication bias

- Association of compared therapies may be confounded by non-random treatment selection/allocation that may have its provenance in unknown mechanisms associated with confounding by indication and channeling bias, among others. These may at least, in part, be addressed through the use of inverse probability weighting as outlined in section 5.4.2 by adjusting for relevant covariates (ie. confounders).

7.6 Protopathic bias

- The study may also be affected by protopathic bias in which the timing of, for example, formal diagnosis with regard to when symptoms and treatment occurs can result in incorrect causal inference regarding the effect of the treatment exposure on the risk of the outcome. To assess the impact of this bias, as outlined in section 5.6, sensitivity analyses will be conducted among the subgroup of HCWs for which PCR-confirmed absence of infection at index date is demonstrated, and according to the subgroup of HCWs for which serology results are available.

8 References

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9 Appendix

WHO Ordinal Scale for Clinical Improvement[1]

Patient State	Descriptor	Score
Uninfected	No clinical or virological evidence of infection	0
Ambulatory	No limitation of activities	1
	Limitation of activities	2
Hospitalized Mild disease	Hospitalized, no oxygen therapy	3
	Oxygen by mask or nasal prongs	4
Hospitalized Severe Disease	Non-invasive ventilation or high-flow oxygen	5
	Intubation and mechanical ventilation	6
	Ventilation + additional organ support – pressors, RRT, ECMO	7
Dead	Death	8

9.1 Shell tables

Table 8.2.1 COVID-19 exposure status among all screened healthcare workers

Characteristic	Infected at baseline N = xxx	Infected during follow-up N = xxx	Uninfected N = xxx	Total
Exposed to COVID-19 infected patients prior to enrollment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Exposed to COVID-19 infected patients within 30 days of enrollment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Table 8.2.2 Primary and Secondary Outcomes at baseline and follow-up among the overall population

Outcomes	Total N=	Prophylaxis exposure		PPE usage	
		Yes N=	No N=	Yes N=	No N=
Primary Outcome					
SARS-CoV-2 infection among HCWs exposed to COVID-19 patients	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Secondary Outcomes					
SARS-CoV-2 uninfected HCWs	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SARS-CoV-2 infection with ambulatory status and no limitation of activities	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SARS-CoV-2 infection with ambulatory status and limitation of activities	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hospitalized due to COVID-19 illness with mild disease	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hospitalized due to COVID-19 illness with severe disease	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
All-cause mortality	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Table 8.2.3 Static Variables by COVID-19 indication

Characteristic	Parameter	Infected N=	Uninfected N=	Total N=
Age (years)	N	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx
Biological Gender	Female	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Male	xx (xx.x)	xx (xx.x)	xx (xx.x)
BMI	Normal Weight	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Overweight	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Obese	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Underweight	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Unknown	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Smoking status	Current Smoker	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Past Smoker	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Never Smoker	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race	White	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Black	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Mixed race	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Asian - Indian	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Asian - Bangladeshi	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Asian - Pakistani	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Asian - other	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unknown	xx (xx.x)	xx (xx.x)	xx (xx.x)
Blood Type	A positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
	A negative	xx (xx.x)	xx (xx.x)	xx (xx.x)
	B positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
	B negative	xx (xx.x)	xx (xx.x)	xx (xx.x)

Characteristic	Parameter	Infected N=	Uninfected N=	Total N=
	O positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
	O negative	xx (xx.x)	xx (xx.x)	xx (xx.x)
	AB positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
	AB negative	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unknown	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Work Location	Hospital Emergency Department (ED)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Intensive Care Unit (ICU)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Hospital medical floor	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other hospital department	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Community health clinic	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
Type of Healthcare Worker	Medical Doctor	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Clinical Officers	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Licensed Physician / Nurse Practitioner	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Registered Nurse or equivalent	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Assistant Nurse, Nurse technician (or equivalent)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Phlebotomist	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Clinical Pharmacist	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Clinical Physical therapist	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Respiratory therapist	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Community Health Worker	xx (xx.x)	xx (xx.x)	xx (xx.x)

Table 8.2.4 Household characteristics at baseline by COVID-19 indication

Characteristic	Parameter	Infected at baseline N = xxx	Infected at follow-up N = xxx	Not infected N = xxx	Total N = xxx
Others in household exposed to COVID-19 infected individuals	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unknown	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of household members exposed to COVID-19 infected individuals	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx
Others in household showing symptoms of COVID-19	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of household members showing symptoms of COVID-19	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx
Others in household diagnosed with COVID-19	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of household members diagnosed with COVID-19	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx
Number of people living in household	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)

	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx

Table 8.2.5 COVID-19 exposure at baseline by COVID-19 indication

Characteristic	Parameter	Infected at baseline N = xxx	Infected at follow-up N = xxx	Not infected N = xxx	Total N = xxx
Contact with confirmed COVID-19 patients	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Direct care to COVID-19 patients	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Face-to-face contact (within 1 metre) of COVID-19 patients	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Present when aerosol generating procedures performed	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Average number of COVID-19 patients in contact each week for past month	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx
Number of days spent at work in last week	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx
Number of hours worked directly with COVID-19 patients in last week	N	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx	xx	xx	xx
	Min-Max	xx-xx	xx-xx	xx-xx	xx-xx
	IQR	xx	xx	xx	xx

Table 8.2.6 Comorbidities at baseline by COVID-19 indication

Comorbidities*	**Infected** N = xxx	**Not infected** N = xxx	**Total** N = xxx
Hypertension	xx (xx.x)	xx (xx.x)	xx (xx.x)
Diabetes	xx (xx.x)	xx (xx.x)	xx (xx.x)
Chronic lung disease	xx (xx.x)	xx (xx.x)	xx (xx.x)
Obesity	xx (xx.x)	xx (xx.x)	xx (xx.x)
Immunocompromised condition	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cardiovascular disease	xx (xx.x)	xx (xx.x)	xx (xx.x)
Chronic liver disease	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cancer	xx (xx.x)	xx (xx.x)	xx (xx.x)
History of stroke	xx (xx.x)	xx (xx.x)	xx (xx.x)
Tuberculosis	xx (xx.x)	xx (xx.x)	xx (xx.x)
Neurological/neurodevelopmental	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other chronic diseases	xx (xx.x)	xx (xx.x)	xx (xx.x)
None of the above	xx (xx.x)	xx (xx.x)	xx (xx.x)

**Non-exclusive categories*

Table 8.2.7 Concomitant medications at baseline by COVID-19 indication

Type*	Name	Infected at baseline N = xxx	Infected at follow-up N = xxx	Not infected N = xxx	Total N = xxx
Antibiotics					
	Azithromycin	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Trimethoprim/sulphamethoxazole	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Macrolide antibiotics (roxithromycin, clarithromycin, erythromycin)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Antimalarials					
	Hydroxychloroquine	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Chloroquine	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Sulfadoxine-pyrimethamine (SP)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Antiparasitics					
	Ivermectin	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Antiretrovirals for Human Immunodeficiency Virus (HIV)					
	Lopinavir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Ritonavir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Tenofovir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Nelfinavir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Antivirals					
	Oseltamivir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Favipiravir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Arbidol	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Anti-hepatitis C treatments	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Remdesivir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Medication for high blood pressure and cardiovascular disease					

Type*	Name	Infected at baseline N = xxx	Infected at follow-up N = xxx	Not infected N = xxx	Total N = xxx
	Angiotensin-converting enzyme (ACE) inhibitor (e.g. lisinopril, enalapril)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Angiotensin II receptor blockers (ARB) inhibitor (e.g. losartan, irbersarten)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other anti-hypertensive for high blood pressure	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other medicine for high blood pressure and cardiovascular disease (E.g. antiarrhythmics, inotropes, chronotropes)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Nonsteroidal Anti-inflammatory Drugs (NSAIDs) E.g. Aspirin, Ibuprofen, Indomethacin, Celecoxib, Diclofenac		xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Botanicals—Artemisia teas		xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Immunocompromising drugs					
	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
None of the above		xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

*Non-exclusive categories

Table 8.2.8 Prophylaxis use

Characteristic*	**Infected at baseline** N = xxx	**Infected at follow-up** N = xxx	**Not infected** N = xxx	**Total** N = xxx
Azithromycin	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Chloroquine	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Hydroxychloroquine	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Ivermectin	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Lopinavir/Ritonavir	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Other (will be specified further based on the data)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Unknown	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)

*Non-exclusive categories

Table 8.2.9 PPE usage at baseline

Characteristic	Infected at baseline N = xxx	Infected at follow-up N = xxx	Not infected N = xxx	Total N = xxx
Mask				
Yes - always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Yes – not always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Gown				
Yes - always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Yes – not always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Eye protection				
Yes - always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Yes – not always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Gloves				
Yes - always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
Yes – not always	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
PPE Yes - always used				
At least one type	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
At least two types	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
At least three types	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)
All four types	xx (xx.x)	xx (xx.x)	xx (xx.x)	xxx (xx.x)