Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study

Version: 1.0
Date: 26 May 2020
Contact: earlyinvestigations-2019-nCoV@who.int

World Health Organization

The emergence of a new virus means that understanding transmission patterns, severity, clinical features and risk factors for infection will be limited at the start of an outbreak. To address these unknowns, WHO has provided a range of early seroepidemiological investigation protocols (rebranded as the WHO Unity Studies). One additional study protocol to evaluate environmental contamination with the COVID-19 virus has also been provided.

These protocols are designed to allow for the rapid and systematic collection and sharing of data in a format that facilitates aggregation, tabulation and analysis across different settings.

Data collected using these investigation protocols will be crucial for refining recommendations for case definitions and surveillance, characterizing the key epidemiological features of COVID-19, helping to understand the spread, severity, spectrum of disease and impact on the community, and informing guidance on the use of countermeasures such as case isolation and contact tracing.

All of the WHO protocols for COVID-19 are available on the WHO website at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

COVID-19 investigation and study protocols currently available include:

- **The First Few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19)**
- **Household transmission investigation protocol for coronavirus disease 2019 (COVID-19)**
- **Protocol for assessment of potential risk factors for COVID-19 infection among health care workers in a health care setting**
- **Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study**
- **Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection**
- **Surface sampling of coronavirus disease (COVID-19): A practical "how to" protocol for health care and public health professionals**

For any questions, please contact: earlyinvestigations-2019-nCoV@who.int – attention: Alessandro Cassini and Isabel Bergeri.

Contents

Summary

The spread of an emerging novel respiratory pathogen such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is accompanied by uncertainty concerning its key epidemiological, clinical and virological characteristics, particularly its ability to spread in the human population and its virulence. Understanding SARS-CoV-2 infection among health workers and identifying the risk factors for adverse outcomes are important not only for characterizing virus transmission patterns and risk factors for infection, but also for preventing the future infection of health workers and patients, for informing and updating infection prevention and control (IPC) measures at health care facility and national levels, and for reducing secondary SARS-CoV-2 transmission within health care settings.

Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study	
Study population	Health workers exposed to COVID-19 patients
Study design	Nested case-control study of health workers exposed to confirmed COVID-19 patients Health workers with confirmed COVID-19 will be recruited as cases and other health workers in the same health care setting without infection will be recruited as controls (incidence density sampling).
Potential outputs and analysis	Risk factors for COVID-19 in health workers; effectiveness of current COVID-19 IPC measures among health workers; clinical presentation of COVID-19 patients; serological response following SARS-CoV-2 infection
Minimum information and specimens to be obtained from participants	**Data collection** Demographic and epidemiological information, along with information on risk factors related to IPC **Specimens** • Paired serology samples from cases and controls for serology testing – comprising one baseline serum sample taken during week 1 and another taken 21–28 days later • Optional – respiratory (and other) to diagnose current COVID-19 infection

1 Background

1.1 Introduction

The spread of an emerging novel respiratory pathogen is accompanied by uncertainty concerning its key epidemiological, clinical and virological characteristics, particularly its ability to spread in the human population and its virulence (case severity). This is the case for the novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first detected in Wuhan, China as a cluster of atypical pneumonia cases in December 2019. This novel coronavirus may have been circulating for several months before the detection of sustained human-to-human transmission in December 2019, with incidence rates of infection doubling in size every 7.4 days in the early stages and an estimated basic reproductive number of 2.2 *(1)*.

Other coronaviruses, such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), have been characterized by amplification events in health care settings, occasionally resulting in large nosocomial outbreaks. Overcrowding in emergency rooms, non-adherence to IPC measures and possible environmental contamination are thought to be implicated in such amplification events during MERS-CoV outbreaks. Health workers play a critical role, not only in the clinical management of patients but also in ensuring that adequate IPC measures are implemented in health care facilities. In addition, initial surveillance often focuses primarily on patients with severe disease. As a result, the full spectrum of disease may not be clear, including the extent and proportion of mild or asymptomatic infections that do not require medical attention and the role such infections may play in secondary transmission.

SARS-CoV-2 infection is thought to spread via respiratory droplets, contact with bodily fluids and with contaminated surfaces *(2)* and transmission to health workers is known to have occurred *(3)*. Individuals who are asymptomatic may be able to transmit infection, while individuals who have not reported close proximity to any known case have also been infected *(4)*. During the SARS-CoV outbreak, health workers accounted for 21% of cases *(5)*. Assessing the potential risk factors for SARS-CoV-2 infection among health workers will be essential for characterizing virus transmission patterns, preventing future infections of health workers and preventing the health-care-associated spread of COVID-19.

1.2 Objectives

The **primary objective** of this case-control study among health workers is:

- to characterize and assess the **risk factors for SARS-CoV-2 infection** in health workers exposed to COVID-19 patients.

The **secondary objectives** of the study are:

- to evaluate the **effectiveness of current COVID-19 IPC measures** among health workers;
- to describe the **range of clinical presentation** for SARS-CoV-2 infection in health workers, including disease duration and outcome; and
- to determine **serological responses** in health workers with confirmed SARS-CoV-2 infection following exposure to COVID-19 patients, and in those exposed to COVID-19 patients but without SARS-CoV-2 infection.

2 Methods

2.1 Design and duration

The current protocol for assessing COVID-19 risk factors consists of a **nested case-control study** of health workers involved in the care of any confirmed COVID-19 cases. The study is based upon the use of incidence density sampling (see section 2.3 Recruitment).

The study is to be initiated as soon as a case of SARS-CoV-2 infection is confirmed among health workers in a health care setting. Health workers with confirmed COVID-19 will be recruited as **cases**. Health workers exposed to COVID-19 patients in the same setting but without infection will be recruited as **controls** with a target of at least 2–4 controls for every case.

For countries or health care facilities willing and able to participate, WHO is proposing to conduct an **international multi-centre case-control study** in health care settings. Starting in May 2020 and running for 1 year, this proposed study will be coordinated by WHO and will be based upon the current protocol and its associated tools. Interested parties (facility or institution) are asked to send an email to: earlyinvestigations-2019-nCoV@who.int for the attention of Alessandro Cassini. Please note that in order to ensure data quality and completeness all health care facilities participating in the multi-centre study will need to meet the criteria set out in section 2.2.3 below.

Countries or health care facilities that are either unwilling or unable to participate in the international multi-centre nested case-control study can still apply the same study methods to conduct a case-control study among health workers in one or several health facilities. In this case, the individual level data will not be pooled across sites and will be managed and analysed only by local investigators and according to local agreements.

2.2 Population

For the purpose of this study, the definition of a "health worker" should not be too restrictive so that a large number of potentially exposed personnel can be included. For this reason, a **health worker** should be defined as any member of staff in the health care facility involved in the provision of care for a COVID-19 patient, including those who have been present in the same area as the patient as well as those who may not have provided direct care to the patient but who have had contact with the patient's body fluids, potentially contaminated items or environmental surfaces. This will include health care professionals, allied health workers and auxiliary health workers such as cleaning and laundry personnel, x-ray physicians and technicians, clerks, phlebotomists, respiratory therapists, nutritionists, social workers, physical therapists, laboratory personnel, cleaners, admission/reception clerks, patient transporters, catering staff and so on.

Exposure to COVID-19 patients is then defined as:

- close contact (within 1 metre and for more than 15 minutes) with a suspected/probable/confirmed COVID-19 patient(s);

OR

- indirect contact with fomites (for example, clothes, linen, utensils, furniture and so on) or with materials, devices or equipment linked to a suspected/probable/confirmed COVID-19 patient(s).

2.2.1 Case definition

A **case** is defined as a health worker:

- exposed in a health care setting to a COVID-19 patient in the 14 days prior to the health worker's confirmation test;

AND

- who is a confirmed COVID-19 case.*

Exclusion criterion**

- having a confirmed COVID-19 case among their close contacts, including in their household, within the previous 14 days (with the exception of the COVID-19 patient(s) to which they were exposed).**

* For the latest COVID-19 suspected, probable and confirmed case definitions refer to: Global surveillance for COVID-19 caused by human infection with COVID-19 virus. Interim guidance. Geneva: World Health Organization; 2020. Available at: https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov). Depending upon the feasibility of practice, local case definitions may be applied. If local case definitions are not available, the WHO definitions should be used.

** Please note that the above exclusion criterion is only applicable to the analysis of risk factors and not to the general descriptive analysis. Where a COVID-19 case answers yes to having been in close contact with confirmed cases outside their professional duties (in the community, household and so on), the record of this case will not be deleted and will be used for the descriptive analysis on exposure risks leading to infection (see section 3.2 below).

2.2.2 Control definition

A control is defined as a health worker:

- exposed in a health care setting to a COVID-19 patient in the 14 days prior to recruitment;

AND

- who is not being classified as a suspected* OR probable* OR confirmed *COVID-19 case.

Exclusion criterion

- having a positive serology test to SARS-CoV-2.

* For the latest COVID-19 suspected, probable and confirmed case definitions refer to: Global surveillance for COVID-19 caused by human infection with COVID-19 virus. Interim guidance. Geneva: World Health Organization; 2020. Available at: https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov). Depending upon the feasibility of practice, local case definitions may be applied. If local case definitions are not available the WHO definitions should be used.

2.2.3 Eligibility criteria for participation in the global multi-centre study

The criteria for participation in the international multi-centre case-control study to be coordinated by WHO are based upon the need to ensure acceptable data quality and completeness. The criteria to consider include:

- the capacity to perform follow-up of individuals (including collecting data with a standardized questionnaire), to perform data entry into a database coordinated by local investigators and to keep personal data confidential, noting that:
    - a member of staff will be needed who can dedicate time to study implementation and data-quality management,
    - previous experience in implementing a case-control study would be an advantage, and
    - leadership willingness to participate will be required;
- Capacity to perform testing for COVID-19 and to perform appropriate blood-collection procedures, specimen packaging, transport (for example, cold chain logistics) and storage, requiring:
    - access to a laboratory with adequate infrastructure for performing serological testing for SARS-CoV-2 infection (for example, using enzyme-linked immunosorbent assay),
    - blood culture diagnostics with internal quality control demonstrating quality results and laboratory accreditation, and
    - informatics capacity, including the use of data-collection tools, standardized patient records (for example, electronic medical records) and patient identifiers for linking.

2.3 Recruitment

Case enrolment
Once a health worker has been identified as a case of COVID-19 in a health care setting (regardless of the type, location and size of the health care facility) the research team will approach the administrator of the facility and invite them to participate in this study.

Control enrolment
This will be determined by considering the facility as a whole attending to COVID-19 patients then determining those health workers that have been exposed to COVID-19 patients based on the start and end dates of exposure according to the duty roster. Enrolling controls in parallel with cases in this way is known as “incidence density sampling” (see Fig. 1) and is a recommended approach for nested case-control studies. Incidence density sampling aims to produce a set of controls for epidemiological case-control studies which mimics the underlying pool of eligible cohort members. This approach can be distinguished from “traditional” case-control designs in which individuals are selected based on the criterion of remaining at risk at the end of the study.

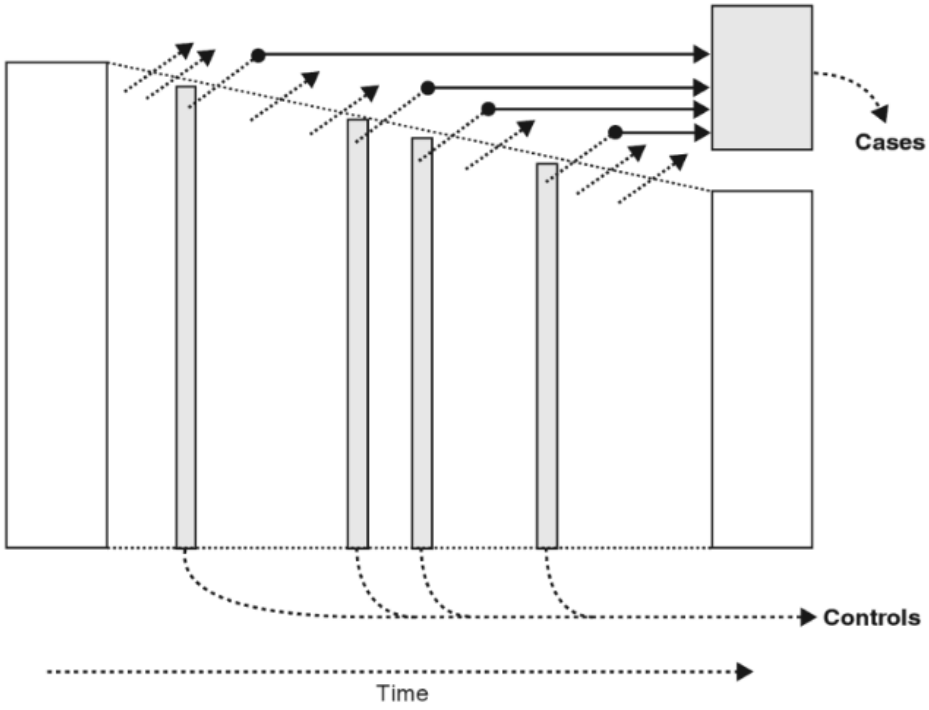
A list of all health workers in the same health care setting with any exposure to COVID-19 patients will need to be drawn up. This will be done in consultation with infection-control nurses in the health care settings. Duty rosters will be examined to ensure all exposed health workers can be identified and recruited into the study. After the potential participants list has been confirmed, the infection-control nurse (or occupational health nurse) will be asked to screen it against the control eligibility criteria and to send out study invitations to the eligible potential controls.

Local investigators should aim to identify **at least 2–4 controls for each case**.

Other considerations
Potential participants can finalize the informed consent process (see Appendix B) and complete the study questionnaire online. If there is more than one COVID-19 case among health workers in the same health care setting, then additional recruitment rounds will be conducted.

Questions on testing history (see laboratory form), specifically during the last 14 days, will allow for stratification during the subsequent analysis of results with the aim of reducing recall bias.

Fig. 1. Incidence density case-control study design for the health workers risk assessment protocol[1]



2.4 Data collection

At the same time as the **first serum sample** is collected, an **initial reporting form** (Form 1, Appendix A) will be used to collect relevant information. This form covers demographic information, symptom severity, medical history, use of medication, availability and adherence to IPC measures, and contact with and exposure to COVID-19 patients following their admission to the health care facility.

An administrator from the health care facility involved in this study will be asked to fill in a **health care facility form** (Form 3, Appendix A).

During the **second serum sample** collection, a **follow-up completion form** (Form 2, Appendix A) will be used to collect information from the participating health workers on their health status and symptom severity.

Information on the laboratory testing conducted is also included in both Forms 1 and 2.

A summary of the completion schedule for all of the above data-collection forms is shown in Table 1.

[1] Source: Szklo M and Nieto J. Epidemiology: Beyond the basics. Aspen Publishers, 2000.

Table 1. Completion schedule of data-collection forms

Form number	Purpose of form	Collecting from whom?	When should it be collected?
HEALTH WORKERS			
Form 1	**Initial** reporting form	For health workers whether they are case or control	As soon as possible after laboratory confirmation of COVID-19 in a health worker in a health care facility (**Day 1**)
Form 2	**Follow-up completion** reporting form	For health workers; final outcome	At least 21 days after completion of Form 1 (**Day 21–28**) Updates should be sought regularly if all of the required information is not available at the time of completing this form
LABORATORY			
Forms 1 & 2	**Laboratory form** (part of the initial and completion forms)	For health workers whether they are case or control	First sample: as soon as possible after confirmation of COVID-19 in a health worker in a health care facility, and after controls are selected Second sample: at least 21 days after completion of Form 1 Updates should be sought regularly if all the required information is not available at the time of completing this form
HEATH CARE FACILITY			
Form 3	Health care facility IPC assessment	For health care facility administrator	Needs to be filled out once for every health care facility involved in the study

2.5 Laboratory evaluations

Laboratory and biosafety guidance for COVID-19 can be found on the WHO website.

2.5.1 Sample collection

Paired serology samples will be collected from all participants (cases and controls) according to the timeline shown in Table 2. The first sample will be collected in week 1 of confirmation of the COVID-19 case and the second 21–28 days later. Controls whose samples test positive will be included as cases in the study, if they fulfil the criteria for a confirmed case.

Two serum samples will be collected from each participant upon recruitment into the investigation.

All those involved in the collection and transportation of specimens should be trained in safe handling practices and spill-decontamination procedures. For details regarding the transport of samples collected and infection control advice, please refer to the case management algorithm and laboratory guidance for the country or to the WHO laboratory guidance available on the WHO website.

As shown in Table 2, **respiratory samples** (for example, nasopharyngeal) and other specimens may also be collected to determine acute COVID-19 infection, as determined by the objectives of the investigation and the available resources and capacity.

2.5.2 Specimen transport

For each biological specimen collected, the time of collection, the conditions for transportation and the time of arrival at the study laboratory will be recorded. Specimens should reach the laboratory as soon as possible after collection. Serum should be separated from whole blood and can be shipped at 4 °C or frozen to −20 °C or lower (−80 °C) and shipped on dry ice. If the specimen is not likely to reach the laboratory within 72 hours, it should be frozen, preferably at −80 °C, and shipped on dry ice.

It is important to avoid the repeated freezing and thawing of specimens. To minimize the number of freeze-thaw cycles it is recommended to aliquot samples prior to freezing.

The transport of specimens within national borders should comply with applicable national regulations. The international transport of specimens should follow applicable international regulations as described in the WHO Guidance on regulations for the transport of infectious substances 2019–2020 *(6)*.

2.5.3 Laboratory analysis

Several assays for detecting the novel coronavirus have now been developed and their protocols or standard operating procedures (SOPs) can be found on the WHO website.

Serological assays specific to COVID-19 are currently under development or are in the process of evaluation. The protocols or SOPs will be published on the WHO website once they become available. Cross-reactivity to other coronaviruses may be an issue and should be considered in the interpretation of data. Multiple assays may be required to confirm seropositivity for COVID-19 virus. Serum samples could be stored at −80 °C until more information on the performance of the serological assays becomes available.

Table 2. Timeline of data and sample collection

Day since recruitment	1	…	…	**21–28**
Visit to health care facility and data collection				
Serum sample				
Respiratory samples	Optional and dependent upon situation and resource availability			Optional and dependent upon situation and resource availability
Other specimens (if relevant)	Optional and dependent upon situation and resource availability			

Blue boxes indicate activities which are needed for the study.
Green boxes indicate when additional specimens could be collected above the minimum specimen requirements of the study to increase the information available. These could include respiratory samples for molecular testing to detect acute COVID-19 infection, regardless of symptoms.

2.6 Ethical considerations

2.6.1 Informed consent

Informed consent will need to be obtained from all study participants. Participants will be informed of the purpose of the study and that participation is voluntary. Approval will be sought from participants for the collection of blood samples and epidemiological data. Participants are free to withdraw at any time, without reason and without any effect on their professional responsibilities. This study poses minimal risks to the participants, involving the collection of a small amount of blood. Blood taking may cause mild and transient physical and/or psychological discomfort to the participants but not any significant long-term risk. Participants will indirectly benefit from the data collected as this will lead to better understanding of the transmission of SARS-Cov-2 and therefore to improved infection prevention. The study will be conducted in compliance with this protocol, the Declaration of Helsinki *(7)*, good clinical practice and the applicable regulatory requirements. Ethical approval will be sought in accordance with national requirements.

Participant confidentiality must be maintained throughout the study, especially in the case of health workers exposed to COVID-19. All study participants must be assigned a study identification number by the investigation team for the labelling of questionnaires and clinical specimens. The linking of this identification number to individuals will be managed by the investigation team and the Ministry of Health (or equivalent) if required and will not be disclosed elsewhere.

To reduce bias, it is highly recommended that the interviewer is blind to the classification of the interviewee as a case or control. This also helps to preserve participant confidentiality.

If data are to be shared with WHO or any agency or institution providing support for data analysis, then only the study identification number and no personal information should be included.

2.6.2 Treatment of subjects

This is a case-control study and the investigators are not necessarily involved in the clinical management of patients.

2.6.3 Direct access to source data/documents

WHO will permit trial-related monitoring, audits, Institutional Review Board/Independent Ethics Committee (IRB/IEC) review, and regulatory inspection(s) and will provide direct access to anonymized source data/documents.

2.6.4 Data handling and record keeping

Upon request, WHO will provide a Go.Data template for data collection to local investigators. Investigators participating in the international multi-centre study coordinated by WHO will provide anonymized data through the Go.Data data-collection tool provided by WHO.

Go.Data is an electronic data-collection tool that has been designed to be used by WHO, the Global Outbreak Alert and Response Network (GOARN), Member States and partners to support and facilitate outbreak investigations. The tool includes functionality for case and contact field data collection, contact follow-up and visualization of chains of transmission. The tool comprises a web application and an optional mobile app, and is intended for use by any outbreak responders, including WHO staff, and staff from ministries of health and partner institutions.

Questionnaire data (except identifying data) will be entered by the participants or research staff directly into the electronic data-capture system at the time of contact with the participants. The information on participants collected during the research study will be encrypted. Any information on participants will have a number assigned to it instead of their name. Only the researchers will know what these numbers are. Quality control checking, tracking and cleaning of the data will be conducted every week. All original paper documents containing identifying data (for example, the Informed Consent Form) will be stored in a locked cabinet. All personal data will be kept confidential.

Original paper documents will be destroyed 3 years after the end of the study. None of the subjects' personal information will be revealed in any subsequent research output.

2.6.5 Publication policy

The data are owned by the participating investigators. Anonymized data will be shared with WHO if participation in the multi-centre study coordinated by WHO is taking place (see Appendix D, Data-Sharing Agreement). The results of the multi-centre international study will be published in international peer-reviewed journals and conference presentations and will be shared globally by WHO in order to inform public health responses and policy decisions.

2.6.7 Prevention of infection in investigation personnel

All personnel involved in the investigation need to be trained in IPC procedures (standard contact, droplet, contact and airborne precautions, as determined by national or local guidelines). These procedures should include proper hand hygiene and the correct use of medical or respiratory face masks, if necessary, not only to minimize the investigator's own risk of infection when in close contact with health workers who have had potential exposure to a COVID-19 patient, but also to minimize the risk of spread among the health worker contacts of a COVID-19 patient. Investigators will be expected to complete the WHO online training course on Infection Prevention and Control (IPC) for Novel Coronavirus (COVID-19) available at: https://openwho.org/courses/COVID-19-IPC-EN

2.7 Summary of study processes

A summary of the study processes is provided below in Box 1.

Box 1. Summary of study processes

Study appraisal

Who, Where and Why: local investigators or researchers from a national/regional institution or from a health care facility interested in implementing the protocol should read the protocol and related documents. If required, a data-collection tool template for this study is available on the Go.Data application. For any questions, please email earlyinvestigations-2019-nCoV@who.int

- ☐ Read the protocol
- ☐ Identified collaborators, received approval for implementing the study and signed Confidentiality Agreement
- ☐ Identified laboratory with serological testing capacity
- ☐ Identified a data-collection tool
- ☐ Checked the ethical committee requirements

Enrolment in the WHO international multi-centre study

Who: local investigators interested in participating in the WHO international multi-centre study can email earlyinvestigations-2019-nCoV@who.int. Participation will be assessed according to the criteria outlined in the study protocol.

Participation in the multi-centre study will require a local investigator signature on the Confidentiality Agreement and on the Data-Sharing Agreement (see protocol Appendices C and D respectively). Data collection should be complete and shared through the Go.Data template available on the WHO secure server accessible through a web browser.

- ☐ Emailed WHO with information on the criteria outlined in the protocol
- ☐ Signed the WHO Data-Sharing Agreement

Data collection starts

When a health worker becomes a confirmed COVID-19 case.

For each health worker, up to 4 controls (2 minimum), also exposed to COVID-19 patients, are selected (in collaboration with the health care facility administration). Refer to the eligibility criteria for cases and controls. Cases and controls sign the Informed Consent Form (Appendix B) and are administered the "Case and control initial reporting form" questionnaire (**Form 1**). This should be done each time a health worker is confirmed to be a COVID-19 case.

A hospital administrator or similar is administered the "Health care facility reporting form" questionnaire (**Form 3**).

Serological samples are taken from cases and controls, and the laboratory forms are filled in.

- ☐ Draw up to 4 controls per case identified
- ☐ Submit for signature the Informed Consent Form to case, controls and hospital administrator
- ☐ Administer the Case and control initial reporting form to cases and controls, and the Health care facility reporting form to the hospital administrator or equivalent
- ☐ Collect first serological samples from cases and controls and send to laboratory. Follow-up for results.

After 21–28 days

- ☐ Administer the "Follow-up completion form for case and control" (**Form 2**)
- ☐ Collect second serological samples from cases and controls

3 Statistical analysis

3.1 Sample size and pooling of data

WHO will consider pooling anonymized data from countries willing and able to participate in the international multi-centre study in order to increase the statistical power to detect risk factors with moderate effect sizes. This larger study will undoubtedly lead to a more robust analysis of potential factors affecting the secondary infection risk, and to a more detailed characterization of serological responses following infection. It is intended that as many as possible confirmed cases of COVID-19 in health workers will be included, with at least two controls for every case (up to a maximum of four). Considering the implementation capacity, infection situation among health workers and the cumulative sample size of similar WHO multi-country studies, the proposed upper limit of cumulative sample size of cases for the international multi-centre study is 50 000.

For those countries/sites participating in the WHO international multi-centre study with only a small number of cases (≤ 20 cases from one study site/facility) the individual study results will not be published. Instead, data will be aggregated from different study sites/facilities and analysed collectively to enlarge the sample size and to minimize the risk of stigma and/or disciplinary action.

For those countries not participating in the WHO international multi-centre study and willing to calculate their own estimates, the sample size will need to be determined by statistical methods according to the chosen study design (case-control study), study population and the specific objectives of the study. Sample sizes can be calculated using statistical formulas or tools available online (for example, at: http://www.openepi.com/Menu/OE_Menu.htm) or in standard statistical packages. It is important to note that a larger sample size would be required if study sites wanted to stratify by effect modifier or to adjust for confounding factors.

3.2 Statistical considerations

The combination of epidemiological, virological (genomic, antigenic) and serological data can provide an unparalleled early situational awareness of the pandemic and promote a proportionate and targeted public health response.

A descriptive analysis (time, place and person) should provide preliminary insight into the clinical spectrum and course of disease due to SARS-CoV-2 infection among health workers. Moreover, a descriptive analysis of the number of health workers found to be positive over the total number of health workers at occupational risk of COVID-19 may provide useful information for estimating the incidence of COVID-19 among health workers. Finally, the inclusion of health workers that were exposed to close contact with COVID-19 confirmed cases outside of their occupational setting (in the household, community or through colleagues) in the initial descriptive analysis (but excluded from the advanced analysis) will allow for identification of the possible setting in which the infection occurred.

Advanced analysis – this incidence density case-control study will allow for matching by time and health facility. In addition to the descriptive analysis, univariate logistic regression analysis will be used to calculate the odds ratios (ORs) and their 95% confidence intervals (95% CIs) for each risk factor and IPC measure. Multivariate logistic regression analysis will be completed to generate adjusted ORs and 95% CIs.

A detailed statistical analysis plan will be developed for the WHO international multi-centre study and will be shared with study sites.

Table 3 provides an overview of the epidemiological parameters that can be measured to meet each of the objectives of this investigation.

Table 3. Epidemiological parameters to be measured for each study objective

Objective	Parameter
1. To characterize and assess the **risk factors** for COVID-19 in health workers with exposure to COVID-19 patients	To characterize: • description of cases by potential risk factors (frequencies, proportion, etc.). To assess: • adjusted ORs and their 95% CI
2. To evaluate the **effectiveness of current IPC measures** among health workers	• Adjusted ORs and their 95% CI for current IPC measures
3. To describe the range of **clinical presentation** for SARS-CoV-2 infection in health workers, including the duration and outcome of the disease	• Frequencies, proportion of clinical symptoms, duration and outcome of the disease • Proportion of asymptomatic and symptomatic fractions
4. To determine **serological responses** in health workers with confirmed SARS-CoV-2 infection exposed to COVID-19 patients	• Antibody titre of both baseline and convalescent serum samples • Change in serum level of specific antibodies to COVID-19 virus (IgM, IgG, IgA) between baseline and convalescent serum samples, calculated using geometric mean titres (increase in titre) • Proportion of asymptomatic or pre-symptomatic/subclinical infections (the proportion of individuals seropositive for COVID-19 who reported no symptoms of COVID-19 infection)

4 Financing

Resources incurred in data collection, sample collection and laboratory testing would be funded by [***Insert here the national or international funding source identified by the investigators***].

5 References

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med. 2020;382:1199–207.
2. Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020;395(10223):514–23.
3. Coronavirus disease 2019 (COVID-19). Situation Report – 82. Geneva: World Health Organization; 2020 (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200411-sitrep-82-covid-19.pdf?sfvrsn=74a5d15_2, accessed 25 May 2020).
4. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med. 2020;382:970–1.
5. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 [webpage]. As of 31 December 2003. Geneva: World Health Organization (https://www.who.int/csr/sars/country/table2004_04_21/en/, accessed 25 May 2020).
6. Guidance on regulations for the transport of infectious substances 2019–2020. Applicable as from 1 January 2019. Geneva: World Health Organization; 2019 (https://www.who.int/ihr/publications/WHO-WHE-CPI-2019.20/en/, accessed 25 May 2020).
7. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bull World Health Organ. 2001;79(4):373–4.

6 Acknowledgments

This generic protocol was adapted from the WHO protocol entitled “Assessment of potential risk factors of Middle East respiratory syndrome coronavirus (MERS-CoV) infection among health care personnel in a health care setting”, the household and first few X cases and close contacts (FFX) investigation protocols for pandemic influenza and from the “Prospective study of household transmission of influenza” developed by the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE).

This document was developed by: Alessandro Cassini, Isabel Bergeri, Maria Van Kerkhove, Benedetta Allegranzi and April Baller (World Health Organization), and Ben Cowling, Jingyi Xiao, Greta Chun-huen Tam (Hong Kong University) with contributions from the following staff and partners: Armand Bejtullahu, Maria Clara Padoveze, Alice Simniceanu, Rebecca Grant (World Health Organization), Marta Valenciano and Anthony Nardone (Epiconcept).

The members of the WHO Expert Working Group on Pandemic Influenza Special Investigations and Studies substantively supported the development of the pandemic influenza version of the early investigation protocols by providing strategic direction and direct inputs into the drafts. These include (in alphabetical order): Silke Buda (RK Institute, Germany), Cheryl Cohen (Ministry of Health, South Africa), Ben Cowling (Hong Kong University), Jeffery Cutter (Ministry of Health, Singapore), Rodrigo Fasce (NIC, Chile), Gail Garson (GOARN Operational Support Team – Chair of Research Subgroup, United Kingdom), Arunkumar Govindakarnavar (Manipal Institute of Virology, Manipal Academy of Higher Education, India), Jean-Michel Heraud (Institut Pasteur de Madagascar, Madagascar), Peter Horby (ISARIC, United Kingdom), Sue Huang (Institute of Environmental Science and Research, New Zealand), Bryan Kim (GOARN Operational Support Team, Switzerland), Vernon Lee (Ministry of Health, Singapore), Adrian Marcato (University of Melbourne, Australia), Jodie McVernon (Peter Doherty Institute, Australia), Richard Pebody (Public Health England, United Kingdom), Melissa Rolf (US Centers for Disease Control and Prevention, United States of America), Hassan Zaraket (American University of Beirut, Lebanon) and Lei Zhou (Chinese Center for Disease Control and Prevention, China).

Appendix A: Questionnaires and guidance

Form 1: Case and control initial reporting form (Day 1)

Automatically generated by Go.Data or entered by interviewer

1. Administration	
Unique health worker ID	
Case/control status[1]	☐ Case ☐ Control
Name of health care facility	
Form completion date (dd/mm/yyyy)	___/___/___
Was the interviewer blind to the case/control status of the interviewee?	☐ Yes ☐ No ☐ Unknown

***Instruction 1**: personal information will be kept confidential by the local investigators according to their procedure. No personal information will be sent or shared in any way with WHO. No personal information will be published. When we publish the results of this study, your confidential personal information will not be shown.*

2. Identifier and basic information	
First name[2]	
Surname[2]	
Sex	☐ Male ☐ Female ☐ Not known
Date of birth (dd/mm/yyyy)[2]	___/___/___
Telephone (mobile) number[2]	
Age (years, months)	
Email address[2]	
National social number/identifier (if applicable)[2]	
Country of residence	
Nationality	
Occupation in health care facility	☐ Medical doctor ☐ Registered nurse (or equivalent) ☐ Assistant nurse, nurse technician (or equivalent) ☐ Radiology/x-ray technician ☐ Phlebotomist ☐ Physical therapist ☐ Nutritionist/dietician ***Other health provider***: ☐ Laboratory personnel ☐ Admission/reception clerk ☐ Patient transporter ☐ Catering staff ☐ Cleaner

[1] To be filled in by the lead investigator after the interview to ensure that the interviewer is blind to the case/control status of the interviewee.

[2] All of these variables will be anonymized.

	☐ Administration/clerk ☐ Other [***specify***]:
Educational level	☐ None ☐ Primary ☐ Secondary ☐ Tertiary/University ☐ Prefer not to answer

Instruction 2*: The information collected below will not be linked to your confidential personal information. Please answer the questions below honestly. Your data will help us to understand the potential risk factors for SARS-CoV-2 infection among health workers and to prevent future infections of health workers.*

3. Context	
Are you a health worker specifically dedicated to caring for COVID-19 patients?	☐ Yes If yes, please specify the number of days dedicated to COVID-19 patients only during previous 14 days: _____ ☐ No ☐ There are no COVID-19 dedicated staff in my facility
Did you receive specific training in the care of COVID-19 patients?	☐ Yes ☐ No ☐ Not sure
In the past 14 days, outside of your occupational duties have you been in contact with a person or persons known to have been diagnosed with Covid-19?	☐ Yes If yes, was this ☐ household ☐ professional colleagues ☐ Most days (≥ 8 days) ☐ Some days (4–7 days) ☐ Few days (≤ 3 days) ☐ everyday social interactions (e.g. public transport, market) ☐ No ☐ Not sure
In the past 14 days, how often have you used public transport?	☐ Most days (≥ 8 days) ☐ Some days (4–7 days) ☐ Few days (≤ 3 days) ☐ Not used public transport
In the past 14 days, how often have you had social interaction with individuals outside of work, home or transport (e.g. in markets, shops etc.)	☐ Most days (≥ 8 days) ☐ Some days (4–7 days) ☐ Few days (≤ 3 days) ☐ Not had any other social interaction

4. Adherence to infection prevention and control (IPC) measures	
What was the date of your most recent IPC training within the health care facility (dd/mm/yyyy)?	___/___/___ ☐ Forgotten/not sure ☐ I don't know what IPC standard precautions are
How much cumulative IPC training (standard precautions, additional precautions) have you received at this health care facility?	☐ Less than 2 hours ☐ More than 2 hours ☐ I don't know what IPC standard precautions are
Was the IPC training on personal protective equipment (PPE) carried out remotely (e.g. presentations only, e-learning) or were practical sessions on standard precautions/additional precautions conducted?	☐ Only remotely/theoretical ☐ Only practical ☐ Both ☐ I don't know what IPC standard precautions are
Do you know the recommended moments for hand hygiene in health care?	☐ I don't know them ☐ Yes, all 3 ☐ Yes, all 4 ☐ Yes, all 5 ☐ Yes, all 6
Do you follow recommended hand hygiene practices?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never
Do you use alcohol-based hand rub or soap and water before touching a patient?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never
Do you use alcohol-based hand rub or soap and water before cleaning/aseptic procedures?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never
Do you use alcohol-based hand rub or soap and water after (risk of) body fluid exposure?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never
Do you use alcohol-based hand rub or soap and water after touching a patient?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never
Do you use alcohol-based hand rub or soap and water after touching a patient's surroundings?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely
Is alcohol-based hand rub available at point of care	☐ Yes ☐ No ☐ Occasionally ☐ Not sure

Do you follow IPC standard precautions when in contact with any patient?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never ☐ I don't know what IPC standard precautions are
Do you wear PPE when indicated? (PPE includes: medical/surgical mask, face shield, gloves, goggles/glasses, gown, coverall, head cover, respirator (e.g. N95 or equivalent) and shoe covers)	☐ Always, according to the risk assessment ☐ Most of the time, according to the risk assessment ☐ Occasionally ☐ Rarely ☐ Never
Is PPE available in sufficient quantity in the health care facility?	☐ Yes ☐ No ☐ Unknown
If no, which PPE is missing?	☐ Medical/surgical masks ☐ Face shield or goggles/glasses ☐ Gloves ☐ Gown and coverall ☐ Head cover ☐ Respirator (e.g. N95, FFP2 or equivalent) used when exposed to aerosol-generating procedures ☐ Shoe covers

5. Exposures to COVID-19 infected patient(s)	
Date of admission of COVID-19 confirmed patient (dd/mm/yyyy) (If you were exposed to more than one COVID-19 patient, please provide the earliest admission date among them)	___/___/___ ☐ Unknown
How many COVID-19 patients have you been exposed to during your occupational duties?	_____ (a range is also permissible)
Have you had close contact (within 1 metre) with the patient(s) since their admission?	☐ Yes ☐ No ☐ Unknown
• If yes, how many times (total)?	☐ < 10 times ☐ 10–50 times ☐ > 50 times Please specify exactly how many times (if you can recall, optional): _____
• If yes, what was the maximum amount of time you spent with a COVID-19 patient?	☐ < 5 minutes ☐ 5–15 minutes ☐ > 15 minutes
• If yes, did you have prolonged face-to-face exposure (> 15 minutes)?	☐ Yes ☐ No ☐ Unknown If yes, did you wear PPE? ☐ Yes ☐ No ☐ Unknown

	If yes, what type? Tick all that apply: ☐ Medical/surgical mask ☐ Face shield ☐ Gloves ☐ Goggles/glasses ☐ Gown ☐ Coverall ☐ Head cover ☐ Respirator (e.g. N95, FFP2 or equivalent) ☐ Shoe covers
- If you were wearing a medical/surgical mask, what type?	
- If you were wearing a respirator, was it test fitted?	☐ Yes ☐ No ☐ Unknown
- If you were wearing gloves, did you remove them after contact with the patient?	☐ Yes ☐ No ☐ Unknown
• If yes, did you perform hand hygiene before contact with the patient?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never If yes: ☐ Alcohol-based hand rub ☐ Soap and water ☐ Water
• If yes, did you perform hand hygiene after contact with the patient?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never If yes: ☐ Alcohol-based hand rub ☐ Soap and water ☐ Water
• If yes, were you present for any aerosolizing procedures performed on the patient?	☐ Yes ☐ No ☐ Unknown If yes, describe the procedure: If yes, did you wear PPE? ☐ Yes ☐ No ☐ Unknown If yes, what type? Tick all that apply: ☐ Medical/surgical mask ☐ Face shield ☐ Gloves ☐ Goggles/glasses

	☐ Gown ☐ Coverall ☐ Head cover ☐ Respirator (e.g. N95, FFP2 or equivalent) ☐ Shoe covers
• If yes, did you come into contact with the patient's body fluids?	☐ Yes ☐ No ☐ Unknown If yes, which body fluids:_____ If yes, were you wearing PPE? ☐ Yes ☐ No ☐ Unknown If yes, what type? Tick all that apply: ☐ Medical/surgical mask ☐ Face shield ☐ Gloves ☐ Goggles/glasses ☐ Gown ☐ Coverall ☐ Head cover ☐ Respirator (e.g. N95, FFP2 or equivalent) ☐ Shoe covers
Have you had direct contact with the patient's materials since their admission? (Patient's materials include personal belongings, linen and medical equipment that the patient may have come into contact with)	☐ Yes ☐ No ☐ Unknown
• If yes, which materials?	Tick all that apply: ☐ Clothes ☐ Personal items ☐ Linen ☐ Medical devices used on the patient ☐ Medical equipment connected to the patient (e.g. ventilator, infusion pump etc.) ☐ Other: _____
• If yes, how many times since their admission (total)?	☐ < 10 times ☐ 10–50 times ☐ > 50 times Please specify exactly how many times (if you can recall, optional): _____
• If yes, did you come into contact with the patient's body fluids via the patient's materials?	☐ Yes ☐ No ☐ Unknown If yes, which body fluids: _____ If yes, were you wearing PPE?

	☐ Yes ☐ No ☐ Unknown If yes, what type? Tick all that apply: ☐ Medical/surgical mask ☐ Face shield ☐ Gloves ☐ Goggles/glasses ☐ Gown ☐ Coverall ☐ Head cover ☐ Respirator (e.g. N95, FFP2 or equivalent) ☐ Shoe covers
• If yes, did you perform hand hygiene before coming into contact with the patient's materials?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never If yes: ☐ Alcohol-based hand rub ☐ Soap and water ☐ Water
• If you were wearing gloves, did you remove them after contact with the patient?	☐ Yes ☐ No ☐ Unknown
• If yes, did you perform hand hygiene after contact with the patient's materials?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never If yes: ☐ Alcohol-based hand rub ☐ Soap and water ☐ Water
Have you had direct contact with the surfaces around the patient?	☐ Yes ☐ No ☐ Unknown
• If yes, which surfaces?	Tick all that apply: ☐ Bed ☐ Bathroom ☐ Ward corridor ☐ Patient table ☐ Bedside table ☐ Dining table ☐ Medical gas panel ☐ Other: _____
• How many times since their admission (total)?	☐ < 10 times ☐ 10–50 times ☐ > 50 times Please specify exactly how many times (if

	you can recall, optional): _____
• If yes, did you come into contact with the patient's body fluids via the surfaces around the patient?	☐ Yes ☐ No ☐ Unknown If yes, which body fluids: _____ If yes, were you wearing PPE? ☐ Yes ☐ No ☐ Unknown If yes, what type? Tick all that apply: ☐ Medical/surgical mask ☐ Face shield ☐ Gloves ☐ Goggles/glasses ☐ Gown ☐ Coverall ☐ Head cover ☐ Respirator (e.g. N95, FFP2 or equivalent) ☐ Shoe covers
• If yes, did you perform hand hygiene after contact with these surfaces?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never If yes: ☐ Alcohol-based hand rub ☐ Soap and water ☐ Water

6a. Health worker symptoms	
Date of first symptom onset (dd/mm/yyyy)	___/___/___ ☐ Forgotten/not sure
Fever (≥ 38 °C) or history of fever	☐ Yes ☐ No ☐ Unknown If yes, specify maximum temperature:_____
Respiratory symptoms:	
Sore throat	☐ Yes ☐ No ☐ Unknown
Cough	☐ Yes ☐ No ☐ Unknown
Runny nose	☐ Yes ☐ No ☐ Unknown
Shortness of breath	☐ Yes ☐ No ☐ Unknown
Other symptoms:	
Chills	☐ Yes ☐ No ☐ Unknown
Vomiting	☐ Yes ☐ No ☐ Unknown
Nausea	☐ Yes ☐ No ☐ Unknown
Diarrhoea	☐ Yes ☐ No ☐ Unknown
Headache	☐ Yes ☐ No ☐ Unknown
Rash	☐ Yes ☐ No ☐ Unknown
Conjunctivitis	☐ Yes ☐ No ☐ Unknown
Muscle ache	☐ Yes ☐ No ☐ Unknown

Joint ache	☐ Yes ☐ No ☐ Unknown
Loss of appetite	☐ Yes ☐ No ☐ Unknown
Loss of smell (anosmia) or taste	☐ Yes ☐ No ☐ Unknown
Nosebleed	☐ Yes ☐ No ☐ Unknown
Fatigue	☐ Yes ☐ No ☐ Unknown
Seizures	☐ Yes ☐ No ☐ Unknown
Altered consciousness	☐ Yes ☐ No ☐ Unknown
Other neurological signs	☐ Yes ☐ No ☐ Unknown If yes, specify: _____
Other symptoms	☐ Yes ☐ No ☐ Unknown If yes, specify: _____

6.b Radiology report	
Have you had radiological evidence of pneumonia (e.g. by chest X-ray or computed tomography scan) since the patient was admitted?	☐ Yes ☐ No ☐ Unknown

7. Health worker pre-existing condition(s)	
Do you have any underlying disease or pre-existing condition(s)?	☐ Pregnancy If yes, specify trimester: ☐ First ☐ Second ☐ Third ☐ Unknown ☐ Obesity If yes, BMI: _____ ☐ Cancer ☐ Diabetes ☐ HIV/other immune deficiency ☐ Heart disease ☐ Asthma (requiring medication) ☐ Chronic lung disease (non-asthma) ☐ Chronic liver disease ☐ Chronic haematological disorder ☐ Chronic kidney disease ☐ Chronic neurological impairment/disease ☐ Organ/bone marrow recipient ☐ No ☐ Unknown ☐ Others, please specify: _____

8. Treatment/medications(s)	
Are you taking any medication(s) regularly (apart from those for COVID-19)?	☐ Statin medication ☐ Steroid medication ☐ Antidiabetic medication ☐ Immunosuppressive medication ☐ No ☐ Unknown ☐ Other(s), please specify: _____

Did you receive a prophylactic treatment for COVID-19 in the last 14 days?	☐ Yes ☐ No ☐ Unknown If yes, which drug was received: _____ Date started (dd/mm/yyyy) ___/___/___ Date stopped (dd/mm/yyyy) ___/___/___ Dosage: _____

The following parts 9a and 9b are to be filled out by the lead investigator[1] during the health worker interview, and after contacting clinicians and laboratory staff to obtain the retrospective laboratory data

9a. Laboratory: serology testing methods and results							
Complete a new line for each specimen collected and each type of test done							
Laboratory identification number	**Date sample collected (dd/mm/yyyy)**	**Date sample received (dd/mm/yyyy)**	**Type of sample**	**Type of test**	**Result**	**Result date (dd/mm/yyyy)**	**Specimens shipped to other laboratory for confirmation?**
	___/___/___	___/___/___	□ Serum □ Other, specify:	Specify type: (e.g. ELISA/IFA IgM/IgG/IgA, neutralization assay, RDT etc.)	□ POSITIVE If positive, COVID-19 antibody titre: _____ □ NEGATIVE □ INCONCLUSIVE	___/___/___	□ Yes If yes, specify date shipped: ___/___/___ If yes, name of the laboratory: □ No

9b. Laboratory: virology testing methods and results									
Complete a new line for each specimen collected and each type of test done									
Laboratory identification number	**Date sample collected (dd/mm/yyyy)**	**Date sample received (dd/mm/yyyy)**	**Reason for testing**	**Times tested for COVID-19 in the 15 days prior**	**Type of sample**	**Type of test**	**Result**	**Result date (dd/mm/yyyy)**	**Specimens shipped to other laboratory for confirmation?**
	__/___/___	__/___/___	□ Onset of symptoms □ Close contact (within 1 metre) with a confirmed COVID-19 patient	Number:_____ Date that this person was last tested for COVID-19 ___/___/___	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Other, specify:	□ PCR □ Whole genome sequencing □ Partial genome sequencing □ Other, specify:	□ POSITIVE for COVID-19 □ NEGATIVE for COVID-19 □ POSITIVE	___/___/___	□ Yes If yes, specify date shipped: ___/___/___ If yes, name of the laboratory: □ No

[1] To be filled in by lead investigator to ensure that the interviewer remains blind to the case/control status of the interviewee.

			without appropriate PPE □ Routine test □ Control □ Other, specify: _____	Result of previous test: □ POSITIVE for COVID-19 □ NEGATIVE for COVID-19 □ POSITIVE for other pathogens Please specify which pathogens:			for other pathogens Please specify which pathogens:		

10. Status of form completion	
Form completed	☐ Yes ☐ No or partially If No or partially, reason: ☐ Missed ☐ Not attempted ☐ Not performed ☐ Refusal ☐ Other, specify:

Form 2. Follow-up completion form for case and control (Day 21–28)

The following form is to be filled out at the time the second serology samples are being taken (21–28 days after enrolment)

Automatically generated by Go.Data or entered by interviewer

1. Administration	
Unique health worker ID	
Case/control status[1]	☐ Case ☐ Control
Name of health care facility	
Form completion date (dd/mm/yyyy)	___/___/___
Was the interviewer blind to the case/control status of the interviewee?	☐ Yes ☐ No ☐ Unknown

2. Outcome	
Outcome	☐ Alive ☐ Dead ☐ NA ☐ Unknown If dead, cause:
Outcome current as of (dd/mm/yyyy)	___/___/___ ☐ Unknown ☐ NA
Hospitalization	☐ Yes ☐ No ☐ Unknown If yes, date of first hospitalization: ___/___/___ ☐ Unknown If yes, reason for hospitalization:

3. Health worker status	
Have you been classified as a suspected OR probable OR confirmed COVID-19 case since participating in this study?	☐ Yes ☐ No ☐ Unknown

4a. Symptoms		
Date of first symptom onset (dd/mm/yyyy)		___/___/___ ☐ Forgotten/not sure
Fever (≥ 38 °C) or history of fever		☐ Yes ☐ No ☐ Unknown If yes, specify maximum temperature: _____
Respiratory symptoms:		
Sore throat	☐ Yes ☐ No ☐ Unknown	
Cough	☐ Yes ☐ No ☐ Unknown	

[1] To be filled in by the lead investigator after the interview to ensure that the interviewer is blind to the case/control status of the interviewee.

Runny nose	☐ Yes ☐ No ☐ Unknown
Shortness of breath	☐ Yes ☐ No ☐ Unknown
Other symptoms:	
Chills	☐ Yes ☐ No ☐ Unknown
Vomiting	☐ Yes ☐ No ☐ Unknown
Nausea	☐ Yes ☐ No ☐ Unknown
Diarrhoea	☐ Yes ☐ No ☐ Unknown
Headache	☐ Yes ☐ No ☐ Unknown
Rash	☐ Yes ☐ No ☐ Unknown
Conjunctivitis	☐ Yes ☐ No ☐ Unknown
Muscle ache	☐ Yes ☐ No ☐ Unknown
Joint ache	☐ Yes ☐ No ☐ Unknown
Loss of appetite	☐ Yes ☐ No ☐ Unknown
Loss of smell (anosmia) or taste	☐ Yes ☐ No ☐ Unknown
Nosebleed	☐ Yes ☐ No ☐ Unknown
Fatigue	☐ Yes ☐ No ☐ Unknown
Seizures	☐ Yes ☐ No ☐ Unknown
Altered consciousness	☐ Yes ☐ No ☐ Unknown
Other neurological signs	☐ Yes ☐ No ☐ Unknown If yes, specify:
Other symptoms	☐ Yes ☐ No ☐ Unknown If yes, specify:

4b. Radiology report	
Have you had radiological evidence of pneumonia (e.g. by chest X-ray or computed tomography scan) since the patient was admitted?	☐ Yes ☐ No ☐ Unknown

The following parts 5a and 5b are to be filled out retrospectively by the lead investigator

5a. Laboratory: serology testing methods and results							
Complete a new line for each specimen collected and each type of test done							
Laboratory identification number	**Date sample collected (dd/mm/yyyy)**	**Date sample received (dd/mm/yyyy)**	**Type of sample**	**Type of test**	**Result**	**Result date (dd/mm/yyyy)**	**Specimens shipped to other laboratory for confirmation?**
	___/___/___	___/___/___	□ Serum □ Other, specify:	Specify type (e.g. ELISA/IFA IgM/IgG, neutralization assay, etc.)	□ POSITIVE If positive, COVID-19 antibody titre: □ NEGATIVE □ INCONCLUSIVE	___/___/___	□ Yes If Yes, specify date shipped: ___/___/___ If yes, name of the laboratory: □ No

5b. Laboratory: virology testing methods and results (OPTIONAL)							
Complete a new line for each specimen collected and each type of test done							
Laboratory identification number	**Date sample collected (dd/mm/yyyy)**	**Date sample received (dd/mm/yyyy)**	**Type of sample**	**Type of test**	**Result**	**Result date (dd/mm/yyyy)**	**Specimens shipped to other laboratory for confirmation?**
	___/___/___	___/___/___	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Other, specify:	□ PCR □ Whole genome sequencing □ Partial genome sequencing □ Other, specify:	□ POSITIVE for COVID-19 □ NEGATIVE for COVID-19 □ POSITIVE for other pathogens Please specify which pathogens:	___/___/___	□ Yes If yes, specify date shipped ___/___/___ If yes, name of the laboratory: □ No

6. Status of form completion	
Form completed	☐ Yes ☐ No or partially If No or partially, reason: ☐ Missed ☐ Not attempted ☐ Not performed ☐ Refusal ☐ Other, specify:

Form 3: Health care facility reporting form

The following form will need to be filled out by a health care facility administrator once for every health care facility involved in the investigation.

Health care facility information	
Name of the health care facility in which the COVID-19-confirmed patient is being cared for	
Type of health care facility[1]	☐ Tertiary care hospital ☐ Secondary care hospital ☐ Primary care facility ☐ Long-term care facility/rehabilitation centre ☐ Other, please specify: _____
Location of health care facility	Please state city, country: _____
Size of health care facility	**Clinic** ☐ Solo practice ☐ Group practice **Hospital** ☐ Fewer than 100 beds ☐ 100–499 beds ☐ 500 or more beds
Does the facility have COVID-19 patients admitted?	☐ Yes ☐ No ☐ Unknown
How many beds are dedicated to COVID-19 patients?	
Does the facility have a dedicated area for triage and care for COVID-19 patients?	☐ Yes ☐ No ☐ Unknown
Are there staff dedicated to the care of COVID-19 patients?	☐ Yes ☐ No ☐ Unknown
How many health workers are dedicated to the care of COVID-19 patients? [Insert total number of health workers if there are no dedicated staff]	
Does the facility implement a screening strategy for health workers?	☐ Yes, based on staff self-reporting ☐ Yes, based on active monitoring of symptoms ☐ No If yes, frequency of screening (e.g. daily): _____

[1] As a guide to the definition of health care facilities, particularly in terms of the services available, please refer to the Definitions and Terms for Different Levels of Hospital available at: https://www.who.int/management/facility/ReferralDefinitions.pdf. In general, however, do not refer to the number of beds indicated in this guide.

Does the health care facility adopt a universal masking policy for all health workers?	☐ Yes, including all patients and visitors ☐ Yes, extended to patients only ☐ Yes, only for health workers ☐ No
Does the health care facility have appropriate WASH services and materials?[1]	☐ Yes ☐ No ☐ Unknown
Does the health care facility have an IPC programme and team or at least a dedicated and trained focal point?	Tick all that apply: ☐ IPC programme ☐ IPC team/service ☐ IPC focal point ☐ IPC training ☐ I don't know what an IPC programme is
Does the health care facility have IPC guidelines for health workers?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what IPC guidelines are
Does the health care facility have IPC guidelines for standard and additional transmission-based precautions?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what IPC standard and additional precautions are
Does the health care facility have regular IPC training for health workers (at least once a year)?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what IPC training is
Does the health care facility have PPE available?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what PPE is
Is PPE available in sufficient quantity in the health care facility?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what PPE is
Is the PPE available of good quality and fit for purpose?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what PPE is
Is alcohol-based hand rub easily available (i.e. at the point of care) for hand hygiene within the health care facility?	☐ Yes ☐ No ☐ Unknown If yes: ☐ In every ward (corridor) ☐ In every room ☐ Next to each bed
Are soap and water available for hand hygiene within the health care facility?	☐ Yes ☐ No ☐ Unknown
Does the health care facility conduct regular (at least once a year) hand hygiene audits and provide feedback to health workers?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what hand hygiene audits are If yes, date of last hand hygiene audit (dd/mm/yyyy): ___/___/___
Does the health care facility conduct other IPC audits?	☐ Yes ☐ No ☐ Unknown ☐ I don't know what other IPC audits are If yes, date of last IPC audit (dd/mm/yyyy): ___/___/___

[1] As set out in the 2016 WHO Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level, Core component 8; available at: http://www.who.int/infection-prevention/publications/core-components/en/. An assessment of Core component 8 can be conducted using the WHO Infection prevention and control assessment framework at the facility level; available at: https://www.who.int/infection-prevention/tools/core-components/IPCAF-facility.PDF.

Does the health care facility have a surveillance system for health-care-associated infections in patients?	☐ Yes ☐ No ☐ Unknown
Does the health care facility have a surveillance system for health-care-associated infections in health workers?	☐ Yes ☐ No ☐ Unknown
Does the health care facility screen staff on arrival for symptoms of infection?	☐ Yes ☐ No ☐ Unknown
Does the health care facility alert all health workers if a SARS-CoV-2-infected patient is being cared for within the health care facility?	☐ Always ☐ In most situations ☐ Sometimes we are not alerted in time ☐ Rarely alerted on time ☐ Never ☐ Unknown
Does the health care facility have a well-equipped triage station at the entrance, supported by trained staff?	☐ Yes ☐ No ☐ Unknown
Are patients with suspected SARS-CoV-2 infection isolated upon arrival at the health care facility?	☐ Always ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never ☐ Unknown
Is a medical mask fitted to patients with suspected SARS-CoV-2 infection upon arrival at the health care facility?	☐ Always ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never ☐ Unknown
Are health worker staffing levels adequate for patient workload?	☐ Always, as recommended ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never ☐ Unknown
Does bed occupancy exceed the standard capacity of the health care facility?	☐ Always ☐ Most of the time ☐ Occasionally ☐ Rarely ☐ Never ☐ Unknown

Appendix B: Informed consent

The Informed Consent Form below should be adapted with the institutional letterhead

Informed Consent Form Version 1.0

This Informed Consent Form is for health workers with exposure to COVID-19 patients. The title of our research protocol is **Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study**.

[Name of Principal Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Protocol and version]

This Informed Consent Form consists of two parts:

- Participant Information Sheet (to share information about the research with you)
- Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form.

PART I: Participant Information Sheet

Introduction
You are being invited to take part in the above research study. Before you decide to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and do not hesitate to ask our staff if there is anything that is not clear or if you would like more information. Please take the time to decide whether or not you wish to take part. Further details of our research study are given below.

Purpose of the research
The global risk of the spread of novel coronavirus disease 2019 (COVID-19) is very high according to WHO (as of early March 2020) and transmission of the causative SARS-CoV-2 virus to health workers has occurred. Assessing the potential risk factors for SARS-CoV-2 infection among health workers is essential for characterizing virus transmission patterns, preventing future infections of health workers and preventing health-care-associated infection with SARS-CoV-2.

Type of research intervention
This research will involve taking paired blood samples from you; one during week 1 and then another 21–28 days later. You will be invited to complete a questionnaire before your blood sample is taken.

Participant selection
We are inviting health workers who work in health care settings in which COVID-19 patients are being cared for.

If you are a health worker in a health care facility and were exposed to SARS-CoV-2-infected patients in the facility within the last 14 days, you are eligible to participate if:

- you are a confirmed case of SARS-CoV-2 and you do not have a confirmed SARS-CoV-2 case among your household/close contacts within the previous 14 days (except for the SARS-CoV-2-infected patient(s) you were exposed to);

OR

- at least one of your colleagues in your health care facility is a confirmed case and you have not been classified as a suspected/probable case.

Voluntary participation
Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, there will be no penalty or loss of benefits to which you are otherwise entitled. You may change your mind later and stop participating even if you agreed earlier.

Procedures and protocol
During the research study you will make two visits to the clinic.

- In the first visit, a small amount of blood (equal to about a teaspoon) will be taken from your arm. This blood will be tested for the presence and amount of antibody associated with your immune response to SARS-CoV-2 infection. You will be asked to complete a questionnaire on your demographics, adherence to infection prevention and control (IPC) measures, exposure to SARS-CoV-2-infected patients, symptoms, pre-existing conditions and use of medication.
- In the second visit, which will be 21–28 days later, you will again be asked some questions about your symptoms and another blood draw will be done. Paired blood samples taken at the beginning and end of your participation in this study will allow the investigator to measure the presence and amount of antibody associated with your immune response to SARS-CoV-2 infection.

Duration
The research study takes place over approximately 1 month. During that time, it will be necessary for you to come to the clinic on 2 separate days, for about 1 hour each time (although it may be possible to collect the samples during homecare and to obtain your answers to the questionnaire via telephone).

Risks
This study poses minimal risks to you. The visits will take up a small amount of time, but we will try to keep each visit as short as possible. There may be some minor issues while collecting the small amount of blood, such as discomfort, bruising, minor infection or bleeding during the procedure. To minimize the risk of stigma and/or retaliation for noncompliance with IPC measures, we will not publish the results of individual studies involving only a small number of cases (less than or equal to 20 cases from one study site/facility).

Benefits
All participants will indirectly benefit from the data collected as this will help us to better understand the transmission of SARS-CoV-2 and therefore better prevent future infections. If we have taken paired blood samples from you, the laboratory results will be made available to you.

Confidentiality
The information that we collect during this research study will be kept confidential. Information collected about you will be stored away and no one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is, and that information will be securely locked away. It will not be shared

with or given to anyone except ... [***insert here the names of all those who will have access to the information, such as research sponsors, the Data Safety Monitoring Board, study clinician, etc.***].

Sharing the results
We will publish the results of this research study in international peer-reviewed journals and conference presentations and will share some information globally via the World Health Organization in order to provide data for public health responses and policy decisions. Confidential information will not be shared. You will be able to obtain a copy of the published results by contacting our research team.

Right to refuse or withdraw
You do not have to take part in this research study if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected. Any data collected so far (responses and serum sample results) will be destroyed in the event of withdrawal from the study.

Who to contact?
If you have any questions, you may ask our staff now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [***insert here the relevant contact names, telephone numbers/emails***].

This proposal has been reviewed and approved by ... [***insert here the name of the local Institutional Review Board (IRB)***], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find out more about the IRB, please contact ... [***insert here the relevant contact name, telephone number/e-mail***].

PART II: Certificate of Consent

Statement by the Participant
I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a Participant in this research.

Print name of Participant_____

Signature of Participant _____

Date _____
Day/month/year

If illiterate
A literate Witness must sign (if possible, this person should be selected by the Participant and should have no connection to the research team). Participants who are illiterate should also provide their thumbprint in the box shown below.

I have witnessed the accurate reading of the consent form to the potential Participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of Witness_____ AND OBTAIN Thumbprint of Participant

Signature of Witness _____

Date _____
Day/month/year

Statement by the researcher/person taking the consent
I have accurately read out the Participant Information Sheet to the potential Participant, and to the best of my ability made sure that the Participant understands the study procedures that will be done.

I confirm that the Participant was given an opportunity to ask questions about the study, and that all of the questions asked by the Participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and that consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the Participant.

Print name of researcher/person taking the consent_____

Signature of researcher/person taking the consent_____

Date _____
Day/month/year

Appendix C: Confidentiality Agreement

WORLD HEALTH ORGANIZATION
CONFIDENTIALITY UNDERTAKING

1. The World Health Organization (WHO), through its Infection Prevention and Control (IPC) Technical and Clinical Hub, is promoting research and development protocols related to the COVID-19 outbreak, which it considers to be proprietary to itself and to parties collaborating with it. This agreement relates to the protocol "Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study".

2. The WHO IPC Technical and Clinical Hub, its recognized collaborators and the local investigators of the research protocols may gain access to confidential information relating to the abovementioned protocol disclosed by other participants and clearly stated to be confidential ("Confidential Information"). To safeguard the confidentiality of such Confidential Information, each participant is required to sign the Undertaking set forth in this document.

3. The Undersigned hereby undertakes to treat Confidential Information as confidential and proprietary, and agrees to take all reasonable measures to ensure that Confidential Information is not used, disclosed, copied or otherwise transmitted by or on behalf of the Undersigned, whether in whole or in part, other than for the Purpose; except that the Undersigned shall not be bound by any such obligations if and to the extent he/she is clearly able to demonstrate that any such Confidential Information: (a) was in the public domain at the time of disclosure at the Forum; or (b) becomes part of the public domain through no fault of the Undersigned.

4. The Undersigned's obligations shall survive the termination of the study period.

5. Any dispute relating to the interpretation or application of this Undertaking shall, unless amicably settled, be subject to a conciliation. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the parties or, in the absence of agreement, with the rules of arbitration of the International Chamber of Commerce. The parties shall accept the arbitral award as final.

6. Nothing contained in or relating to this Undertaking shall be construed as a waiver of any of the privileges and immunities enjoyed by WHO, and/or as submitting WHO to any national court jurisdiction.

   Agreed to and accepted by the Undersigned as of the date set forth below.

Name: _____

Signature: _____

Date: _____

Appendix D: Data-Sharing Agreement

DATA-SHARING AGREEMENT

Schedule of particulars

This Data-Sharing Agreement is comprised of: (i) this Schedule of Particulars; (ii) Annex I – General Conditions; and (iii) Annex II – Project Description (together, the "**Agreement**").

Pursuant to the terms of this Agreement, the Contributor hereby agrees to provide, and WHO hereby agrees to accept, the Data for the Purpose of Use and subject to the Restrictions on Use.

In this Agreement, the following expressions have the following meanings:

1. The " **Contributor**": [full legal name of your institution];
2. "**WHO**": the World Health Organization, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland;
3. The "**Data**": Any data, results and reports, unpublished or otherwise, collected during or resulting from the Project which are owned by the Contributor and provided by the Contributor to WHO during the term of this Agreement;
4. The "**Parties**": the Contributor and WHO;
5. The "**Project**" as further described in Annex II;
6. The "**Purpose of Use**": The Data are provided to WHO for WHO to implement the Project which is summarized in Annex II and for use in related materials and activities, including but not limited to WHO's internal research purposes;
7. The "**Restrictions on Use**": The Data shall not be used for any purpose other than the Purpose of Use;
8. The "**Term of Agreement**": [Unrestricted in time]; and
9. "**Data Charges**": The Data will be provided free of charge.

Acknowledged and agreed:

Signed for and on behalf of WHO		Signed for and on behalf of the Contributor
Name:	Benedetta Allegranzi	Name:
Title:	Technical Lead, IPC Hub and Task Force	Title:
Date:		Date:

Annex I – General Conditions

1. Use

1.1. The Data are supplied by the Contributor to WHO solely for the Purpose of Use and subject to the Restrictions on Use.

1.2. Other than for and within the Purpose of Use, the Data shall not be transferred, sold, offered for sale or otherwise used, without the prior written agreement of the Contributor.

1.3. WHO shall only allow parties who have a need to know for the Purpose of Use and who are bound by similar obligations of confidentiality and restrictions on use as contained in this Agreement to have access to the Data.

1.4. In implementing the Purpose of Use, WHO will: not attempt to identify or contact research participants included in the Data; Respect the confidentiality of the Data; and maintain the Data in a secure location on a password-protected, WHO-internal network protected by standard encoding and the WHO firewall for the duration of the Purpose of Use.

2. Confidentiality

2.1. The Data may incorporate confidential information of the Contributor. Accordingly, if and to the extent any such Data are clearly marked by the Contributor as “confidential”, WHO shall during the term of this Agreement and for a period of five years following its termination, treat such Data confidential and only disclose them under like obligations of confidentiality and restrictions on use as those contained herein. WHO shall be deemed to have fulfilled its obligations, if it exercises at least the same degree of care in maintaining confidentiality as it would in protecting its own confidential information.

2.2. However, the above mentioned obligations of confidentiality shall not apply to Data which: (i) can be shown to have been known to WHO at the time of its acquisition from the Contributor; (ii) are acquired from a third party, not in breach of any obligation of confidentiality to the Contributor; (iii) are independently devised or arrived at by, on behalf of, or for WHO without access to the Information; or (iv) enter the public domain otherwise than by breach of the undertakings set out in this Agreement.

3. Rights

3.1. Except for the rights explicitly granted to WHO hereunder, nothing contained in this Agreement shall be construed as conveying any rights under any patents or other intellectual property which either party may have or may hereafter obtain.

3.2. Nothing contained in this Agreement shall restrict the Contributor's right to sell, transfer, assign or distribute the Data to any other person for commercial or non-commercial purposes.

4. Publications

4.1. Subject to the Contributor's proprietary rights, the results obtained through use of the Data within the Purpose of Use may be published by WHO and/or parties collaborating with WHO. In order to avoid prejudice to the Contributor's proprietary rights, WHO shall transmit any material intended to be published or relevant portions thereof, to the Contributor under confidential cover for review at least ten days prior to its submission to any editor, publisher, referee or meeting organizer. In absence of any objection by the Contributor within that thirty-day period concerning prejudice to its proprietary rights, the publication may proceed, provided, however, that the Contributor shall be duly acknowledged in such publication.

4.2. WHO will prepare manuscript(s) of the results of the Purpose of Use for publication, pursuant to the terms of the applicable protocol, and publish such manuscripts pursuant to WHO's rules and regulations, including its policy on open access, as contained at: http://www.who.int/about/policy/en/. WHO may further use the results of the Purpose of Use to update relevant WHO recommendations and develop any guidelines, including publication thereof, and may further publish those results.

4.3. If a manuscript of the Research Activities is submitted for publication, WHO will in all events retain the Data until the peer review process is completed, and then for one year after publication to ensure sufficient time to address any required responses to the findings (e.g., letters to the editor).

4.4. WHO will ensure that all publications relating to the Data will appropriately acknowledge WHO, the Contributor, and all other entities contributing data to the publication.

5. Undertakings of the Contributor

5.1. The Contributor represents and warrants that: It has obtained all rights and permissions necessary to transfer the Data to WHO and for WHO to implement the Purpose of Use and all other activities relating to the Data as described herein; The Data have been collected from clinical trials, observational studies, or surveillance systems that have been conducted in accordance with all applicable laws; and The individual(s) to whom the Data relate have provided their 'informed consent' to participate in the study wherein their data was collected if required by, and in accordance with, applicable laws.

5.2. Prior to transmitting the Data to WHO, the Contributor will: Verify whether approval from their local/relevant Ethics Review Committee is required for the use of the Data for the Purpose of Use, and if that approval is required, obtain it; and Anonymize all participant-level data in the Data, pursuant to agreed standards, to remove all information in the Data that could be used to identify research participants.

5.3. The Contributor will transmit the Data to WHO securely, using secure file transfer protocol.

5.4. The Contributor will avoid providing to WHO any information relating to the Data or the Research Activities that relates to a natural person, which, either directly or indirectly, in combination with other information available or likely to be available to WHO, can identify such natural person.

5.5. The Contributor makes no warranty of the fitness of the Data for any particular purpose or any other warranty, either express or implied. However, to the best of the Contributor's

knowledge, the use of the Data within the Purpose of Use shall not infringe on the proprietary rights of any third party.

5.6. WHO agrees that (except as may explicitly be provided in this Agreement) the Contributor has no control over the use that is made of the Data by WHO or parties collaborating with WHO in accordance with the terms of this Agreement. Consequently, WHO agrees that the Contributor shall not be liable for such use.

6. Other Matters

6.1. Nothing in this Agreement shall be interpreted as establishing a partnership between the parties or establishing one party as the agent of the other or conferring a right on one party to bind the other, except as may be specifically set out herein.

6.2. Without the prior written approval of the other Party, neither Party shall, in any statement or material of an advertising or promotional nature, refer to this Agreement or the relationship between the Parties, or use the name (or any abbreviation thereof) and/or emblem of the other Party.

6.3. Any dispute relating to the interpretation or application of this Agreement shall, unless amicably settled, be subject to conciliation. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the parties or, in the absence of agreement, with the rules of arbitration of the International Chamber of Commerce. The Parties shall accept the arbitral award as final.

6.4. Nothing contained herein shall be construed as a waiver of any of the privileges and immunities enjoyed by WHO under national or international law and/or as submitting WHO to any national court or jurisdiction.

6.5. This Agreement sets forth the entire understanding between the parties and supersedes any prior agreements, written or verbal related to the Data. It shall only be capable of change by written amendment executed by duly authorized officers of the Parties.

****

Annex II – Project Description

Assessment of risk factors for coronavirus disease 2019 (COVID-19) in health workers: protocol for a case-control study.

Background: The spread of an emerging respiratory pathogen such as SARS-CoV-2 is accompanied by uncertainty over the key epidemiological, clinical and virological characteristics of the novel pathogen and particularly its ability to spread in the human population and its virulence. Understanding SARS-CoV-2 infection among health workers and the risk factors for adverse outcomes is important not only for characterizing virus transmission patterns and risk factors for infection, but also for preventing future infection of health workers and patients, for informing and updating infection prevention and control measures at health care facility and national level and for reducing secondary SARS-CoV-2 transmission within health care settings.

Population studied: Health workers with exposure to COVID-19 patients.

Study design: We propose to conduct a case-control study of health workers involved in care of any confirmed COVID-19 cases. Health workers with confirmed SARS-CoV-2 infection will be recruited as cases and other health workers in the same health care setting without infection will be recruited as controls. Basic information and risk factor information will be collected from participants. Paired serology samples will be collected from cases and controls for serology testing; baseline serum during week 1 and another 21–28 days later.

Outcomes and analyses: Risk factors for SARS-CoV-2 infection in health workers, effectiveness of current SARS-CoV-2 infection prevention and control measures among health workers, clinical presentation of COVID-19 patients, serologic response following SARS-CoV-2 infection.

Please refer to the specific protocol and relevant documents (case/control questionnaire, health care facility questionnaire, laboratory reporting form, study completion form, Confidentiality agreement and Informed Consent Form. These are available upon request from the WHO IPC Technical and Clinical Hub (earlyinvestigations-2019-nCoV@who.int for the attention of Alessandro Cassini) and at https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

****

Appendix E: Go.Data software

Go.Data: what is it?

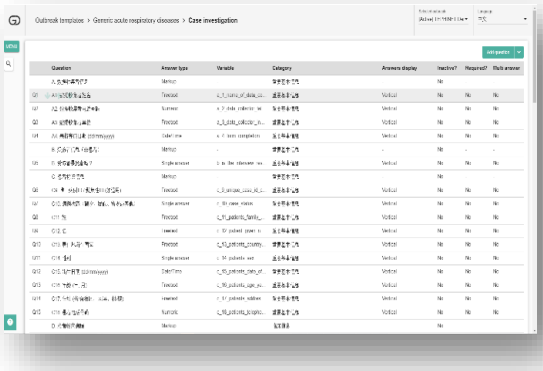
Go.Data is a field data-collection platform focusing on case data (including laboratory, hospitalization and other variables, through a case investigation form) and contact data (including contact follow-up). Main outputs from the Go.Data platform are contact follow-up lists and chains of transmission.

What are the key features of the Go.Data software?

Multiplatform
Go.Data offers different types of operation (online, offline) and different types of installation (server, stand-alone). It functions on a range of operating systems (Windows, Linux, Mac). In addition, Go.Data has an optional mobile app for Android and iOS. The mobile app is focused on case and contact data collection, and contact tracing and follow-up.

Multilingual
Go.Data is multilingual, with the possibility to add and manage additional languages through the user interface.

Configurable



It is highly configurable, with the possibility to manage:

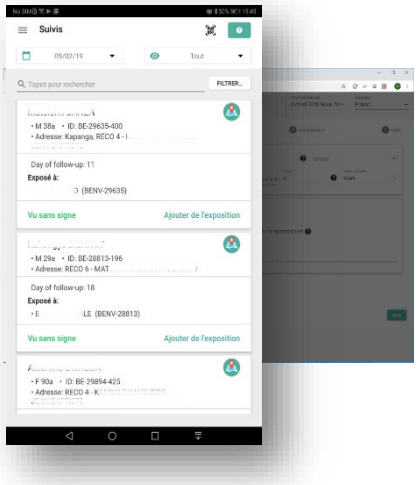
- reference data,
- location data, including coordinates,
- outbreak data, including variables on the case investigation form and the contact follow-up form.

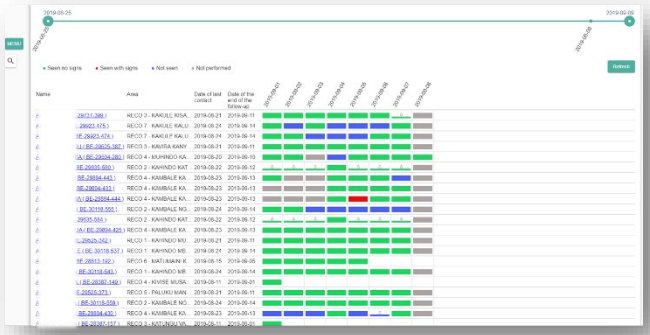
One Go.Data installation can be used to manage multiple outbreaks. Each outbreak can be configured in a different way to match the specifics of a pathogen or environment.

Case and contact data collection
The user can add cases, contacts and laboratory results. In addition, users also have an option to create events that may be relevant for outbreak investigation.

Contact follow-up lists are generated using outbreak parameters (that is, the number of days to follow up contacts, how many times per day should contacts be followed up).

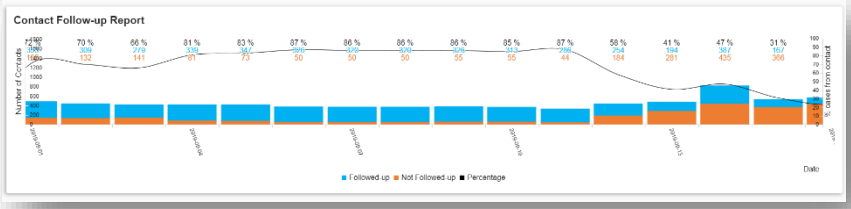
Extensive data export and import features are available to support the work of the data managers and data analysts.





Performing contact follow-up

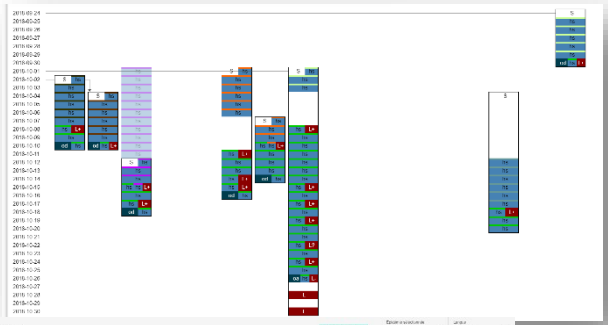
Go.Data has features to perform contact tracing using the web app or optional mobile app. Contact follow-up data are presented in the form of lists, graphs and operational dashboards. Contact tracing coordinators can review the workload of each contact tracing team.

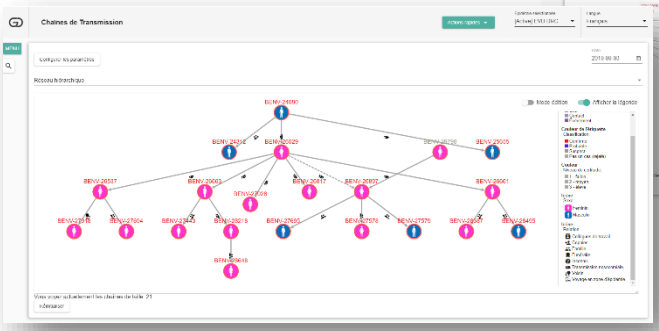


Extensive visualization features

Go.Data can be used to generate chains of transmission in the form of:

- networks, simple and hierarchical;
- timelines, using date of onset, date of reporting or date of last contact; and
- bar charts combining the date of onset, hospitalization data, laboratory testing data and outcome.





System administration

System administrators have access to an extensive set of features to manage users, assign roles and permissions and limit access to specific outbreak(s) only. In addition, they have access to usage logs, and can create and restore backups and manage the settings of one Go.Data instance.

Please visit www.who.int/godata or contact godata@who.int for more information.

Options for Go.Data hosting in countries

Option #1
Centrally Hosted server

One Go.Data installation for the entire region or for multiple countries. Separate outbreak is created for each country on the central server instance of Go.Data, and user access is provided at outbreak level (i.e. users from one country can only access case and contact data from their own country).

+

- Maintenance is easier.
- Installation of any updates is done centrally.
- Synchronization of the mobile phones can be done from anywhere.

–

- Countries may be reluctant to host detailed information that is required for contact tracing (e.g. names, addresses) on an external server.
- May require agreements between centralized server owner and Member States for this arrangement.
- Centralized server to manage user accounts and user access.

Option #2
Country hosted server

Separate Go.Data installation for each country. Countries install Go.Data on their infrastructure.

+

- Country has complete ownership and control of the server.
- Synchronization of the mobile phones can be done from anywhere.

–

- Likely to take more time to implement, as this option requires internal governmental approvals and provisioning infrastructure.
- Requires dedicated staff/team to manage the server.
- Not all countries may be in a position to host a Go.Data server.

Option #3
Standalone installation

Go.Data is installed on one or more computers in the country. These are typically personal computers or notebook/laptop computers. Data can be replicated across the computers.

+

- Fast to implement.
- User has complete ownership and control of the computer and data.

–

- In order to synchronize mobile phones, users have to be physically in the same location where the computer is.
- If there are multiple instances in a country it will be required to setup consolidation point.
- Personal data stored on multiple standalone computers.
- Limited availability of Go.Data to when laptop is running.
- Increased security risks through loss or damage of the standalone computer.

Go.Data terms of use and software license agreement

Please read these Terms of Use and Software License Agreement (the "**Agreement**") carefully before installing the Go.Data Software (the "**Software**").

By installing and/or using the Software, you (the "**Licensee**") enter into an agreement with the World Health Organization ("**WHO**") and you accept all terms, conditions, and requirements of the Agreement.

1. Components of the software
1.1. The Software is a product developed by WHO (the "**Software**") and enables you to input, upload and view your data (the "**Data**").

This Agreement governs your use of the Software you have downloaded.

2. Third-party software
2.1. *Third-party software embedded in the Software.* The Software utilizes third party open source software, issued under multiple license types (including Artistic 2.0, Apache 2.0, the "GNU Affero GPL version 3", BSD (3 clause), ISC, WTFPL and the "MIT license") (the "**Third Party Components**") which are embedded within the Software.

2.2. *WHO disclaimers for third-party software*. WHO makes no warranties whatsoever, and specifically disclaims any and all warranties, express or implied, that either of the Third Party Components are free of defects, virus free, able to operate on an uninterrupted basis, merchantable, fit for a particular purpose, accurate, non-infringing or appropriate for your technical system.

[2.3. *Other third-party software*. To the extent you are required to enter into a user license in order to use the Software, WHO is not a party to any such license, and WHO therefore disclaims all liability, responsibility, and/or involvement with any such license. WHO shall not be held liable or responsible for either any breach of any of the terms and conditions of such user licenses entered by you, or any damages arising from your use of such user licenses].

2.4. *No WHO endorsement of third-party software*. The use of the Third-Party Components or other third-party software does not imply that these products are endorsed or recommended by WHO in preference to others of a similar nature.

3. License and terms of use for the software
3.1. Copyright and license. The Software is copyright (©) World Health Organization, 2018, and is distributed under the terms of the GNU Affero General Public License (GPL), version 3. As stated in the source code for the Software, the Software incorporates or makes reference to the Third Party Components, and WHO issues the Software under GNU Affero GPL "version 3" in part to comply with the terms of those software. WHO disclaims any responsibility or liability with respect to the use or completeness of such license.

4. Copyright, disclaimer and terms of use for the maps
4.1. The boundaries and names shown, and the designations used on the maps [embedded in the Software] (the "**Maps**") do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

4.2. Unlike the Software, WHO is not publishing the Maps under the GNU Affero GPL. The Maps are not based on "R", they are an independent and separate work from the Software and are not distributed as "part of a whole" with the Software, as those terms and concepts are used in the GPL.

5. Retained rights and limitations on use

5.1. *Retained Rights*. Except as otherwise indicated herein, WHO owns and shall retain all right, title and interest in and to the Software, including all intellectual property rights embodied therein, including (i) all of the service marks, trademarks, trade names or any other designations associated with the Software; and (ii) all copyrights, patent rights, trade secret rights, and other proprietary rights relating to the Software. Nothing contained in this License shall be deemed to convey to the Licensee any title or ownership in the Software or the related documentation.

5.2. *Technical limitations of use*. You shall not remove any WHO identification or notices of any proprietary, patent or copyright restrictions from the Software, or any support material such as the related documentation.

6. Acknowledgment and use of WHO name and emblem

6.1. You shall not state or imply that results from the Software are WHO's products, opinion, or statements. Further, you shall not (i) in connection with your use of the Software, state or imply that WHO endorses or is affiliated with you or your use of the Software, the Software, the Maps, or that WHO endorses any entity, organization, company, or product, or (ii) use the name or emblem of WHO in any way. All requests to use the WHO name and/or emblem require advance written approval of WHO.

7. Disclaimers by WHO

7.1. *No WHO warranties*. WHO makes no warranty with respect to the Software, and disclaims all statutory or implied warranties, expressed or implied, as to the accuracy, completeness or usefulness of any information, apparatus, product, or process related to the Software, including, without limitation, to any warranty of design or fitness for a particular purpose, even if WHO has been informed of such purpose. WHO does not represent that the use of the Software would not infringe third parties' proprietary rights. WHO provides the Software "as is", and does not represent that the Software is operational, free of defects, virus free, able to operate on an uninterrupted basis, or appropriate for your technical system.

7.2. *Country or area designations*. The designations employed and the presentation of the material in the Software do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries.

7.3. *Mentions of companies or products*. Any mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

8. Limitation of WHO's Liability

8.1. WHO shall not be liable for any loss or damage arising directly or indirectly in connection with, or resulting from, your use of the Software.

8.2. WHO further expressly excludes liability for any indirect, special, incidental or consequential damages which may arise in respect of the Software and its use, and the results thereof.

8.3. WHO expressly excludes liability for any damages which may arise in respect of the use of the Data by the Licensee.

9. Your Indemnification of WHO
9.1. You shall indemnify, hold harmless, and defend at your own expense WHO, its officers, agents, and employees from and against any claims, demands, causes of action, and liability of any nature or kind resulting from or relating to your use of the Software.

10. Term and termination of this agreement
10.1. This Agreement shall remain in effect so long as you hold any copy of the Software on any of your computer systems or storage media. This Agreement, including the rights granted under it, shall terminate automatically upon any breach by you of any of its terms. Further, WHO may terminate this Agreement, including the rights granted under it, at any time, with immediate effect, for any reason, by written notice to you. This Agreement is the entire agreement between you and WHO with respect to its subject matter. This Agreement may only be amended by mutual written agreement of you and WHO.

10.2. Upon termination of this License for any reason whatsoever, you shall immediately cease all use of the Software and destroy and/or remove all copies of the Software from your computer systems and storage media.

11. General provisions
11.1. You may not assign this Agreement without the prior written agreement of WHO (such agreement not to be unreasonably withheld).

11.2. This Agreement may not be supplemented, modified, amended, released or discharged, unless approved in writing by WHO. WHO reserves the right to make changes and updates to this Agreement without prior notification. Such changes and updates shall be applied as of the date of their issuance. Any waiver by WHO of any default or breach hereunder shall not constitute a waiver of any provision of this Agreement or of any subsequent default or breach of the same or a different kind.

11.3. If any provision of this Agreement is invalid or unenforceable, it is to that extent to be deemed omitted. The remainder of the Agreement shall be valid and enforceable to the maximum extent possible.

11.4. Paragraph headings in this Agreement are for reference only.

11.5. Any matter relating to the interpretation or application of this Agreement which is not covered by its terms shall be resolved by reference to Swiss law. Any dispute relating to the interpretation or application of this Agreement shall, unless amicably settled, be subject to conciliation. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the parties or, in the absence of agreement, in accordance with the UNCITRAL Arbitration Rules. The parties shall accept the arbitral award as final.

12. Privileges and Immunities of WHO
12.1. Nothing contained herein or in any license or terms of use related to the subject matter herein (including, without limitation, the GNU General Public License discussed in paragraph 3.1 above) shall be construed as a waiver of any of the privileges and immunities enjoyed by the World Health Organization under national or international law, and/or as submitting the World Health Organization to any national jurisdiction.

WHO reference number: WHO/2019-nCoV/HCW_RF_CaseControlProtocol/2020.1