The First Few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19)

Version: 2.2
Date: 23 February 2020
Contact: EarlyInvestigations-2019-nCoV@who.int

World Health Organization

Reference:

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 Four Early sero-epidemiological Investigation Protocols (rebranded the WHO Unity Studies). One additional study to evaluate environmental contamination of COVID-19 is also provided.

These protocols are designed to rapidly and systematically collect and share data in a format that facilitates aggregation, tabulation and analysis across different settings globally.

Data collected using these investigation protocols will be critical to refine recommendations for case definitions and surveillance, characterize key epidemiological features of COVID-19, help understand spread, severity, spectrum of disease, and impact on the community and to inform guidance for application of countermeasures such as case isolation and contact tracing.

They are available on WHO website here: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations)

COVID-19 investigations and studies protocols currently available include:

1. The First Few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19).

2. Household transmission investigation protocol for coronavirus disease 2019 (COVID-19)

3. Protocol for assessment of potential risk factors for coronavirus disease 2019 (COVID-19) among health workers in a health-care setting.

4. Population-based age-stratified seroepidemiological investigation protocol for coronavirus 2019 (COVID-19) infection

5. Surface sampling of COVID-19 virus: a practical "how to" protocol for health care and public health professionals

Please contact earlyinvestigations-2019-nCoV@who.int

All WHO protocols for COVID-19 are available on the WHO website together with the technical guidance documents.

Version Control

Main updates for version 2:

- Update of the **"close contact" definition**: from 1 day before symptom onset to 4 days before symptom onset. The new definition for the purpose of this investigation protocol is: "Any person who had contact (within 1 metre) with a confirmed case during their symptomatic period, including 4 days before symptom onset".
- Capture **exposure also during the asymptomatic period of the confirmed case**.
- Expansion of symptoms questions **for suspected or probable cases to gastrointestinal symptoms** (same as for confirmed cases).
- For close contacts who health workers are, addition of risk-categorization questions to better estimate the level of the risk (high or low risk).
- Addition of a **symptom diary template** for close contacts to self-record and notify the presence or absence of various symptoms.
- Update of the **Go.Data** section, as now all FFX questionnaires are available as templates in Go.Data for country use.
- Addition of an appendix describing the key features of Go.Data and several hosting options for Go.Data (Appendix C).
- Updated references, to align with the latest WHO guidance.
- Technically edited version. Update of Appendix B, "Comparison between the features and complementarity of the main coronavirus disease 2019 (COVID-19) early investigation protocols", now that the risk assessment for health workers has been published.
- Update of the numbering of the FFX form and questions on where to get the data to calculate the epi parameters concerned (Table 3 of Section 3.3).
- Addition of the new generic WHO email address as a point of contact, to streamline all queries relating to protocols for early investigations.
- Change wording from "health-care workers" to "health workers" to account for non-medical health workers (ex. cleaners, etc.).

Main update version 2.2:

- Addition of loss of small or loss of taste symptom is questionnaire
- Clarification of close contact definition in relation to contact with a confirmed asymptomatic case
- Update of close contact definition in relation to contact with a confirmed symptomatic case : changed from 4 days to 2 days before symptom onset, and addition of "and the 14 days after the onset of symptoms"
- Update of HW contact definition to put back "AND who were not wearing proper personal protective equipment" (Note: was in original version 1.1)

.

Contents

Summary

The First Few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19).	
Population	The First Few X number of confirmed cases of COVID-19 infection and their close contacts.
Potential output and analysis	Transmission dynamics, severity and clinical spectrum, through estimates of, primarily: • the clinical presentation of COVID-19 infection and course of associated disease. • the secondary infection rate (SIR) and secondary clinical attack rate of COVID-19 infection among close contacts • the serial interval of COVID-19 infection. • the symptomatic proportion of COVID-19 cases (through contact tracing and laboratory testing). • identification of possible routes of transmission and secondarily: • the basic reproduction number (R_0) of COVID-19 • the incubation period of COVID-19 • the preliminary COVID-19 infection and disease-severity ratios (e.g. case-hospitalization and case-fatality ratios).
Design	Prospective case-ascertained study of all identified close contacts of laboratory-confirmed COVID-19 infections.
Start of the investigation	To be initiated in the first days after the arrival in Country X of a confirmed case of COVID-19 FFX is the primary protocol to be initiated in the case of a COVID-19 outbreak, upon identification of the initial laboratory-confirmed cases of COVID-19 virus in Country X in the early epidemic/pandemic phases.
Duration	At a minimum, enrolled cases and close contacts will complete data and specimen collection at enrolment (Day 1) and 14–21 days later, with two home visits.
Minimum data and specimens to be obtained from participants	• Data collection: epidemiological data, including clinical symptoms; exposures, including contact with confirmed case(s); and pre-existing conditions. • Specimens: respiratory (and other) to diagnose current COVID-19 infection; and serum to inform seroepidemiological inferences

This document sets out the methods to guide data collection and the public health investigation for the comprehensive assessment of confirmed COVID-19 cases and their close contacts.

The World Health Organization (WHO), in collaboration with technical partners, has developed a series of enhanced surveillance protocols that are harmonized to help provide detailed insight into the epidemiological characteristics of COVID-19. Other COVID-19 investigations protocols currently available include:

- *Household transmission investigation protocol for coronavirus disease 2019 (COVID-19) (1);*
- *Protocol for assessment of potential risk factors for coronavirus disease 2019 (COVID-19) among health workers in a health-care setting (2)*; and
- *Surface sampling of COVID-19 virus: a practical "how to" protocol for health-care and public health professionals (3).*

The scope and focus of this document and the first two listed above are compared in Appendix B.

All WHO protocols for COVID-19 are available on the WHO website *(4)*, together with the technical guidance documents *(5)*, including surveillance and case definitions *(6)*; patient management *(7)*; laboratory guidance *(8)*; infection prevention and control *(9)*; risk communication and community engagement *(10)*; travel advice *(11)*, and more *(12, 13)*.

Comments for the user's consideration are provided in purple text throughout the document, as the user may need to modify methods slightly because of the local context in which this investigation will be carried out.

1. Background

The detection and spread of an emerging respiratory pathogen are 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 (case-severity). This is the situation for coronavirus disease 2019 (COVID-19), first detected in Wuhan city, China in December 2019 *(14)*.

As with many novel respiratory pathogens, key epidemiological, clinical and virological parameters of the virus and the outbreak dynamics are unknown at the beginning. At this stage, the extent of infection, the route of transmission, the full range of disease presentation and the viral dynamics remain unknown for COVID-19. As a result, it is essential to understand the epidemiological, clinical and virological characteristics of the First Few X cases (FFX) of COVID-19 and their close contacts, in order to inform targeted guidance and measures for the Country X public health response.

The following protocol has been designed to investigate the FFX and their close contacts. It is an adaptation of generic protocols already in place in some countries, such as *"The First Few Hundred (FF100)" enhanced case and contact protocol* for pandemic influenza in the United Kingdom of Great Britain and Northern Ireland (United Kingdom) *(15)*. A harmonized global approach will facilitate rapid aggregation of data across countries.

It is envisioned that the FFX COVID-19 investigation will be conducted across several countries or sites with geographic and demographic diversity. Each country may need to tailor some aspects of this protocol to align with public health, laboratory and clinical systems, according to their country capacity and availability of resources, as well as the cultural appropriateness of the protocol. However, by using a standard protocol such as the one described here, epidemiological exposure data and biological samples can be systematically collected and shared rapidly in a format that can be easily aggregated, tabulated and analysed across many different settings globally. This will facilitate timely estimates of the severity and transmissibility of COVID-19 infection, as well as informing public health responses and policy decisions. This is particularly important in the context of a novel respiratory pathogen, such as the virus responsible for COVID-19.

1.1 Objectives

The overall aim of this protocol is to gain an early understanding of key clinical, epidemiological and virological characteristics of the first cases of COVID-19 infection detected in Country X, to inform the development and updating of public health guidance and to manage cases and reduce the potential spread and impact of infection in Country X. It is important to note that the first cases likely to be identified in this investigation may present with more severe infection, and the ability to detect a greater range of cases in terms of severity will be dependent on resources.

The **primary objectives** of this FFX investigation among cases and close contacts are to provide descriptions or estimates of:

- the clinical presentation of COVID-19 infection and course of associated disease;
- the secondary infection rate (SIR) and secondary clinical attack rate of COVID-19 infection among close contacts (overall, and by key factors such as setting, age and sex, for various end-points);
- the serial interval of COVID-19 infection;
- the symptomatic proportion of COVID-19 cases (through contact tracing and laboratory testing); and
- identification of possible routes of transmission.

The **secondary objectives** are to provide data to support the estimation of:

- the basic reproduction number (R_0) of COVID-19 virus;
- the incubation period of COVID-19; and
- the preliminary COVID-19 infection and disease-severity ratios (for example, case-hospitalization ratio [CHR] and case-fatality ratio [CFR]).

A reminder of some definitions of epidemiological terms:

- In this context, the **secondary infection rate** is a measure of the frequency of new **infections** of COVID-19 among contacts of confirmed cases in a defined period of time, as determined by a positive COVID-19 result. *In other words, it is the rate of contacts being infected, assessed through polymerase chain reaction (PCR)/serological assays on paired samples*.
- The **secondary clinical attack rate** is a measure of the frequency of new symptomatic **cases** of COVID-19 infection among the contacts of confirmed cases in a defined period of time, as determined by a positive COVID-19 result. *In other words, it* is *the rate of clinical manifestation of the infection in contacts.*
- The **serial interval** is defined as the period of time from the onset of symptoms in the primary case to the onset of symptoms in a contact case.
- The **basic reproduction number R_0** is defined as the number of infections produced, on average, by an infected individual in the early stages of the epidemic, when virtually all contacts are susceptible. Note that it can be assumed that there will be very little to no immunity to COVID-19.
- The **incubation period** is defined as the period of time between an exposure resulting in COVID-19 infection and the onset of the first clinical symptoms of the disease (*from infection or exposure to disease*).
- The **case-hospitalization ratio** is defined as the proportion of those infected with COVID-19 (that is, with a positive test result) who are admitted to hospital.
- The **case-fatality ratio** is defined as the proportion of people with COVID-19 (that is, with a positive test result) who die as a direct or indirect consequence of their infection.

This information will be used to refine/update recommendations for surveillance (for example, case definitions); to characterize the key epidemiological transmission features of the virus; to help understand the geographic spread, severity and impact on the community; and to inform operational models for implementation of countermeasures such non-pharmaceutical interventions *(16)* (for example, case isolation, contact tracing, etc.) and medical interventions, if possible.

1.2 Coordination of FFX investigation

Coordination of investigations and sharing of information in real-time will be needed at both country