Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Version: 1.1
Date: 25 January 2020

World Health Organization

Household transmission investigation protocol for 2019-novel coronavirus infection

Protocol summary

Household transmission investigation protocol for 2019-novel coronavirus infection	
Study population	All household contacts of a confirmed 2019-nCoV case
Potential output and analysis	Transmissibility in household settings Estimates of: • Secondary Infection rate (SIR) among close contacts and factors associated with secondary infection • Range of clinical presentation, risk factors for infection, and the extent and fraction of asymptomatic infections • Serologic response following confirmed 2019-nCoV infection Epidemiological modeling parameters: • Reproduction numbers: R_0 and R • Serial intervals specific to household setting • Incubation period • Infection attack rates
Study design	Prospective study of household contacts of confirmed 2019-nCoV cases, ideally before widespread community transmission occurs
Study duration	At a minimum, enrolled household contacts will complete four home visits within 28 days of enrolment/follow-up
Minimum information and specimens to be obtained from participants	Data collection: Epidemiological data including: clinical symptoms, exposures, including contact with confirmed case. Specimens: Respiratory (and other) to diagnose current 2019-nCoV infection, serum to inform seroepidemiological inferences

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 case for the novel coronavirus (2019-nCoV), first detected in Wuhan city, China in December 2019 (1).

Closed settings, such as the household, have a defined population that do not mix readily with the larger surrounding community, and therefore such settings provide a strategic way to track emerging respiratory infections and characterize virus transmission patterns because the denominator can be well defined. Also, exposure is within the setting, and follow-up of household contacts is generally more feasible in this well-defined setting as compared to an undefined one. Household setting studies allow us to determine transmission dynamics (reproduction number and serial interval) of the virus as well as to understand the clinical spectrum of illness in secondary cases (2). Closed settings are also useful to observe chains of transmission in an epidemic as the pool of susceptible, exposed individuals is larger. Therefore, in the case of multiple waves of infection through the closed setting, unique insight into transmission dynamics can be derived in the early epidemic stages.

To date initial surveillance has focused primarily on patients with severe disease, and, as such, the full spectrum of the disease, including the extent and fraction of mild or asymptomatic infection that do not require medical attention are not clear. Infections identified in close contacts may potentially be generalizable to naturally-acquired infections (in contrast to cases presenting for emergency care among which there would be fewer mild cases). Following close contacts with similar levels of exposure to infection from primary cases can also permit identification of the asymptomatic fraction. Principally, follow-up and testing of respiratory specimens and serum of close contacts can provide useful information about newly identified cases, as well as the spectrum of illness and frequency (by for example age) of asymptomatic and symptomatic infection.

With the emergency of a novel coronavirus, initial seroprevalence in the population will be low due to the virus being new in origin. Therefore, surveillance of antibody seroprevalence in a population can allow inferences to be made about the cumulative incidence of infection in the population. Household transmission studies also can provide the opportunity to follow-up confirmed cases to understand antibody kinetics.

The following protocol has been designed to investigate household transmission of 2019-nCoV in any country in which 2019-nCoV infection has been reported and households are exposed. Each country may need to tailor some aspects of this protocol to align with public health, laboratory and clinical systems, according to capacity, availability of resources and cultural appropriateness. However, using a standardized protocol such as the protocol described below, epidemiological exposure data and biological samples can be systematically collected and shared rapidly in a format that can be easily aggregated, tabulated and analyzed across many different settings globally for timely estimates of 2019-nCoV infection severity and attack rates, as well as to inform public health responses and policy decisions. This is particularly important in the context of a novel respiratory pathogen, such as 2019-nCoV.

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 study will be carried out.

1.1 Objectives

There are three primary objectives of this household transmission study:

1. To better understand the extent of transmission within a household by estimating the secondary infection rate[1] for household contacts at an individual level, and factors associated with any variation in the secondary infection risk.
2. To characterize secondary cases including the range of clinical presentation, risk factors for infection, and the extent and fraction of asymptomatic infections.
3. To characterize serologic response following confirmed 2019-nCoV infection (highly encouraged, but optional depending on laboratory capacity and resources)

Household transmission studies provide rich data that can permit evaluation of secondary objectives such as, but not limited to:

1. To estimate the serial interval[2] in a household setting.
2. To estimate incubation period[3], duration of infectiousness[4] and duration of detected shedding[5]
3. To characterize duration and severity of 2019-nCoV-associated disease.
4. Others (context specific/ optional)

[1] In this context the **secondary infection rate (SIR)** is a measure of the frequency of new cases of 2019-nCoV infection among the household contacts of a primary confirmed case in a defined period of time, as determined by a confirmed 2019-nCoV positive lab result. In simple terms: the proportion of household contacts of a primary case who subsequently become infected with 2019-nCoV

[2] 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.

[3] **Incubation period** is defined as the period of time between an exposure resulting in infection and the onset of clinical symptoms of disease.

[4] The **duration of infectiousness** is the time which virus is shed and able to be transmitted regardless of clinical symptoms

[5] It is currently not known how long **detectable 2019-nCoV virus shedding** lasts; information from this study would help to clarify the duration of shedding among individuals with confirmed infection.

2 Study procedures

2.1 Study design

The household transmission investigation is a case-ascertained prospective study of all identified household contacts of a laboratory confirmed 2019-nCoV infection (see 2.2 Study population). It is intended to provide rapid and early information on the clinical, epidemiological and virological characteristics of 2019-nCoV.

This investigation should be conducted following the identification of a laboratory-confirmed 2019-nCoV infection in any country. It should also ideally be conducted before widespread community transmission occurs. That is, within the early phases of an epidemic following the identification of a laboratory confirmed 2019-nCoV infection.

2.2 Study population

The study population is derived from the identification of any laboratory confirmed 2019-nCoV infection. This is distinct from a household cohort study in which a group of disease-free households are recruited and then followed over time. Every effort should be made to include all identified household contacts of cases of a laboratory confirmed 2019-nCoV infection.

For the purpose of this investigation, primary cases will be identified through surveillance of individuals who are diagnosed with laboratory confirmed 2019-nCoV infection. 2019-nCoV case definitions for reporting are available on the WHO website, although they are subject to further updates as more information becomes available.

COMMENT: All WHO guidance material for 2019-nCoV is available on the WHO website. This currently includes case definitions, laboratory guidance, infection prevention and control and travel guidance.

For the purpose of this investigation, a **household** is defined as a group of people (2 or more) living in the same residence. In practice, the technical definition may vary due to social, political and cultural practices.
Definitions of a household which may be used (but are not limited to):

- Two or more people living together in a domestic residence (residential institutions, such as boarding schools, dormitories, hostels or prisons will be excluded).
- A dwelling or group of dwellings with a shared kitchen or common opening onto a shared household space.

For the purpose of this investigation, **a household contact** is defined as a person who has resided in the same household as the primary 2019-nCoV case while the case was symptomatic.

COMMENT: For the purposes of comparability between investigations, it is important that whichever definition of a household contact is well detailed in any reporting on the investigation.

2.3 Exclusion criteria

Households may need to be excluded (or not, if it is possible to tease out the transmission dynamics) if:

- Date of onset is the same for more than one family member

2.4 Study duration

The investigation can continue for as long as is determined feasible by the country implementing the investigation. However, ideally, enrolled household contacts will complete **four home visits within 28 days of enrolment/follow-up**. Specimens, and information on risk factors and symptoms will be collected from primary cases and from each of his/her household contacts. The duration of follow-up may vary depending on further secondary objectives.

Study enrolment **could be extended as far as desired, however** the most valuable period in order to use data for targeted public health action is in the early phases of the epidemic.

2.5 Data collection

Information on primary cases and their close contacts should be sought through a combination of face-to-face or telephone interview of the case (or family members if the case is too ill to be interviewed), household members, self-reporting, interview of health care providers and/or review of medical records where required.

An investigation questionnaire can be found in Appendix 1 of this document. These forms are not exhaustive, but outline the data collection required for insight into the epidemiology of 2019-nCoV and may be updated further. This will still need to be adapted based on the local setting, and outbreak characteristics.

Once a case of 2019-nCoV infection has been identified and recruited into the investigation, a home visit will need to be conducted to identify all eligible household contacts, to collect relevant socio-demographic and clinical information and to allow molecular confirmation of secondary infections and establish baseline antibody status, (or at a minimum to collect serum to test seroprevalence once serology capacity is available).

2.6 Follow up of cases and contacts

For the purposes of this investigation, data and specimens will be collected through home visits from cases and contacts on the day of recruitment (Day 1), followed by home visits on day 7, day 14, and day 28 if possible.

COMMENT: For surveillance, follow up needs to be more frequent. The specimen collection schedule for the household transmission investigation described here, is added on top of normal follow up of contacts.

For cases, data will be collected using **Form 1a** for the first visit, followed by **Forms 2, 3 and 4**. For contacts, data will be collected using **Form 1b** for the first visit, followed by **Forms 2, 3 and 4**.

Symptom diaries (template available in Appendix 1 of this protocol) will be provided for all household contacts to complete for up to 28 days after the administration of the baseline questionnaire, with a minimum of 14 days, to record presence or absence of various signs or symptoms. A proxy may fill out the symptom diaries on behalf of those unable to complete the form themselves.

Any household contact with clinical symptoms within 14 days of the last exposure/contact with the primary case should be considered as a symptomatic contact and so a possible/suspected case, and therefore managed as such.

The table below provides an overview of the follow-up procedures

	Purpose of form	**Collecting from whom?**	**When should it be collected?**
Confirmed cases			
Form 1a	Minimum data reporting form	For **confirmed** cases	As soon as possible after laboratory confirmation of a case **(Day 1)**
Forms 2, 3 and 4	Case **follow-up** forms	For **confirmed** cases (outcomes)	At home visits (**Days 7, 14 and 28**) respectively
Household contacts			
Form 1b	Contact data reporting form	For households contacts	As soon as possible, ideally within 24 hours after laboratory confirmation of the primary case (**Day 1**)
Forms 2, 3 and 4	Contact **follow-up** forms	For households contacts (outcomes)	At home visits (**Days 7, 14 and 28**) respectively
Symptom diaries	Record presence or absence of various signs or symptoms.	For confirmed cases (if possible) and households contacts	For up to 28 days after the administration of the baseline questionnaire (Form 1b), with a **minimum of 14 days**
Confirmed cases and household contacts			
Laboratory results report	Track and summarize all laboratory results (and methods used)	For confirmed cases and households contacts	This table will need to be filled/ updates to at each specimen collection time point above

2.7 Specimen collection

COMMENT: The following is intended to guide minimum specimen collection from confirmed cases and their household contacts. It may be more useful to collect respiratory specimens from study participants at a more frequent interval to provide more detailed insight into the duration of shedding and the serial interval (not just the symptomatic serial interval).

2.7.1 Confirmed cases

All baseline respiratory and serum samples (as directed by specimen collection guidance in the country) should be collected from confirmed cases, as soon as possible after laboratory confirmation. Liaise with the relevant local public health laboratory or the nearest relevant laboratory to determine which specimens have already been collected for confirmed cases and if they are of sufficient quality and quantity for this investigation.

Follow-up samples (and other samples) may include upper respiratory tract samples, clotted blood, but also oral fluid, urine, feces and should be collected at a frequency described in Figure 1. Lower respiratory tract samples can also be collected, if feasible but recommended infection prevention and control precautions should be in place prior to collection (see 2.9.3 Prevention of 2019-nCoV infection in investigation personnel). Appropriate PPE should be worn when specimens are being collected from confirmed cases.[6]

2.7.2 Household contacts

All baseline upper respiratory specimens (nasopharyngeal/oropharyngeal swab) and serum samples should be collected at the initial home visit. Respiratory specimens should be collected for molecular testing, as well as serum samples for serology, from all members of the household, regardless of symptoms, together with the administration of the baseline questionnaire. At the day 7 and day 14 visits, respiratory samples (and other relevant specimens) will be collected from all members of the household for virologic testing, regardless of symptoms, and at the day 28 visit, serum sample, (and other potentially relevant specimens) could be collected from all household contacts – see Figure 1

Paired serological samples from all household contacts allow for confirmation of seroconversion, and are useful to confirm the secondary-infection attack rate and the proportion of infections that are asymptomatic. They can be taken regardless of symptoms.

Other specimens (as described for confirmed cases) may be collected according to clinical presentation, resources and observed patterns of viral shedding (described earlier) and may be collected by research staff depending on resources, logistics and training.

2.7.3 Note on serology

Paired clotted blood samples should be taken for serology and handled and separated correctly by the laboratory. Paired serological samples from confirmed cases are needed to aid the development of serological testing, to determine an accurate secondary-infection attack rate.

Serum samples should be taken on all 2019-nCoV confirmed cases.

- An acute baseline clotted blood sample should be taken as soon as possible, and ideally no later than 7 days after symptom onset.
- A follow up (or convalescent) clotted blood sample should be taken:
    - at least 14 days after the baseline sample,

[6] Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care - WHO Guidelines. Geneva, World Health Organization, 2014. Available at http://apps.who.int/iris/bitstream/10665/112656/1/97892 41507134_eng.pdf

- OR 28 days after symptom onset if an acute sample couldn't be taken when the case was symptomatic.

Figure 1: Timeline of data and specimen collection in the household transmission study

Day since recruitment	**0** (±1)	…	**7**	…	**14**	…	**28**
Home visit and data collection							
Respiratory sample		(optional)		(optional)		(optional)	(optional)
Serum sample (dependent on country)			(optional)		Highly encouraged		
Other specimens (if relevant)	(optional- situation dependent)						
Symptom diaries						Highly encouraged	

Legend:
Blue boxes indicate activities which are needed for the study
Light blue boxes indicate when serum collection (or symptom diaries) is highly encouraged, but not essential according to resources and capacity.
Green boxes indicate where additional specimens could be collected above the minimum specimen requirements of this study to increase information available. Please note that this could also include collecting specimens from household contacts when they first become symptomatic.

2.8 Specimen transport

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

For each biological sample 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. If the specimen is not likely to reach the laboratory within 72 hours, specimens should be frozen, preferably at -80°C, and shipped on dry ice. It is, however, important to avoid repeated freezing and thawing of specimens. The storage of respiratory and serum specimens in domestic frost-free freezers should be avoided, owing to their wide temperature fluctuations. Serum should be separated from whole blood and can be stored and shipped at 4°C or frozen to -20°C or lower and shipped on dry ice.

Transport of specimens within national borders should comply with applicable national regulations. International transport of specimens should follow applicable international regulations as described in the WHO Guidance on Regulations for the Transport of Infectious Substances 2013- 2014.

2.9 Ethical considerations

Ethical requirements will vary by country. In some countries, this investigation may fall under public health surveillance (emergency response) acts and may not require ethical approval from an Institutional Review Board.

2.9.1 Informed consent

The purpose of the investigation will be explained to all known contacts of a confirmed 2019-nCoV infected patient. Informed consent will be obtained from all cases and contacts willing to participate in the investigation before any procedure is performed as part of the investigation by a trained member of the investigation team. Consent for children under the legal age of consent will be obtained from a parent or legal guardian. Each participant must be informed that participation in the investigation is voluntary and that s/he is free to withdraw, without justification, from the investigation at any time without consequences and without affecting professional responsibilities.

COMMENT: The age of consent may vary by country. Check the requirements of local, regional or national authorities.

Informed consent will seek approval to collect blood, respiratory samples and epidemiological data for the intended purpose of this investigation, that samples may be shipped outside of the country for additional testing and that samples may be used for future research purposes.

2.9.2 Risks and benefits for subjects

This investigation poses minimal risk to participants, involving the collection of a small amount of blood and respiratory specimens. The direct benefit to the participant is the possibility for early detection of 2019-nCoV infection which would allow for appropriate monitoring and treatment. The primary benefit of the study is indirect in that data collected will help improve and guide efforts to understand transmission of 2019-nCoV and prevent further spread of 2019-nCoV.

2.9.3 Prevention of 2019-nCoV infection in investigation personnel

All personnel involved in the investigation need to be trained in infection prevention and control procedures (standard contact, droplet or airborne precautions, as determined by national or local guidelines). These procedures should include proper hand hygiene and the correct use of surgical or respiratory face masks, if necessary, not only to minimize their own risk of infection when in close contact with 2019-nCoV infected patients, but also to minimize the risk of spread among contacts of 2019-nCoV infected patients.

WHO technical guidance on infection prevention and control specific to 2019-nCoV can be found on the WHO website.

3 Laboratory testing

Laboratory guidance for 2019-nCoV can be found on the WHO website.

Several assays that detect the novel coronaviruses detected in Wuhan, China have been recently developed and the protocols or SOPs can also be found on the WHO website.

4 Statistical analyses

4.1 Sample size

This investigation is intended to be implemented to provide rapid and early information on the clinical, epidemiological and virological characteristics of 2019-nCoV. Larger studies will undoubtedly permit more robust analysis of potential factors affecting the secondary infection risk, more precise estimation of the asymptomatic fraction, and more detailed characterization of serologic responses following infection

4.2 Epidemiological parameters

The table below provides an overview of the epidemiological parameters that can be measured as part of this investigation

Parameter	**Definition** (*in bracket*: "simplified" expression of it)	**Form and questions where to get the data to calculate the parameters concerned**	**Comments, limitations**
Course of disease	A description of the distribution of cases by time, person and place	Form 1: Q3, Q4, Q5 Form 2: Q3 Form 3,4,5	*Location will need to be supplemented by notification data to recognize geospatial trends
Symptomatic proportion of cases (asymptomatic fraction)	The proportion of cases who show symptoms or signs of 2019-nCoV infection	Form 1: Q6 Form 2: Q5 Form 3,4,5 Form 6	*The numerators of interest are the numbers of those contacts reporting various signs and symptoms of infection (e.g. fever, cough) and the number/proportion of those contacts reporting no signs or symptoms (i.e. the asymptomatic fraction); the denominator is the total number of cases.
Secondary infection rate (also called secondary infection incidence)	A measure of the frequency of new cases of 2019-nCoV infection among the close contacts of confirmed cases in a defined period of time *(The rate of contacts being infected. Assessed through serological assays on paired samples)*	Form 3,4,5	*The numerator will be determined as the number of household contacts with confirmed 2019-nCoV infection, while the denominator will be determined as the total number of household contacts. *represents an overall risk of infection among household contacts for a defined time period.
Clinical presentation	The range of clinical symptoms in cases and contacts. (*Severity*)	Form 1: Q6 Form 2: Q5	*In-hospital clinical studies will enhance understanding of clinical course, severity and risk determinants, as well as case fatality.
Serological response to infection	Change in serum level of specific antibodies to 2019-nCoV (*Increase in titre*)	Form 3,4,5	*This will only be able to be calculated with the addition of laboratory data *Will be supplemented by findings of clinical studies and first few outbreak studies to confirm that seroconversion

			following an infection is anticipated
Incubation period	The time period between 2019-nCoV exposure and the appearance of the first sign or symptom of the disease (from infection to disease)	Form 6	
Serial interval distribution	The time between onset of symptoms in the case to onset of symptoms in the close contact	Form 1: Q6 Form 2: Q5 Form 3,4,5 Form 6	*Will be greatly enhanced by information from first few outbreaks where transmission chains may be more identifiable and prolonged
Generation time distribution	Time between infection in the case and infection in the close contact	Form 3,4,5	*Will be greatly enhanced by information from first few outbreaks where transmission chains may be more identifiable and prolonged
Population groups most at risk	Determining the groups who are most vulnerable to 2019-nCoV infection (e.g. age groups, gender, occupation)	Form 1: Q4, Q5 Form 2: Q3, Q4	*May only be an early signal, other sources of information will need to be used to inform decision making (line listing of cases and other clinical case series) *This may be biased from this study, as we are recruiting on the basis of being detected and confirmed to have 2019-nCoV and healthcare seeking behaviour may vary between population groups
Genomic data		Form 3,4,5	*An alternate means to estimate the reproduction number *May supplement other transmission data to inform transmission parameter estimates, although likely to be delayed beyond the initial public health response phase.
Basic reproduction number R_0	A measure of the number of infections produced, on average, by an infected individual in the early stages of the epidemic, when	Form 2: Q5 Form 3,4,5 Form 6	*Can be calculated using different approaches; identifying clusters and cluster size (using epi methods and

	virtually all contacts are susceptible. *(average number of infections/disease arising from one infection*) Reminder: Basic reproductive ratio (R_0) – everyone is susceptible and there is no control, maximum value that R can take is equal to the transmission potential.		potentially genetic information to identify how many secondary cases are occurring), and using the epidemic curve and how steep it is *R can be calculated using multiple sources of information incident case notifications, incident hospitalisation by age (as a potentially more stable alternative) or genomic data, all of which will be taken together as an estimate of transmissibility.
Reproductive ratio (R)	Ever-changing quantity of the amount of secondary cases produced by a primary case across time and space (i.e. context-specific)	Form 2: Q5 Form 3,4,5 Form 6	*Not the main aim of household transmission studies, but if the study is continued and transformed into a long-term "cohort" study we may be able to calculate it.

5 Reporting of findings

5.1 Reporting

Any investigation of this nature should include reporting on the following information:

(1) the number of households, the number of household contacts included;
(2) the number of PCR-confirmed 2019-nCoV cases among the household contacts;
(3) the number of symptomatic household contacts;
(4) the number of household contacts with serologic evidence of 2019-nCoV infection. If sample size permits, these numbers should be stratified by age.

It is also important to fully document the study design, including the definition of households and household contacts, the approach to ascertainment of primary cases and secondary cases, the duration of follow-up, and the laboratory methods used to ensure that data can be pooled to increase power in estimating epidemiological parameters.

Ideally, information would be collected in a standardized format according to the questionnaires and tools in this generic protocol to assist with data harmonization and comparison of results (see forms in Appendix A).

If the data is shared by the implementing organization to WHO or any agency or institution providing support for data analysis, data shared will include only the study identification number and not any personably identifiable information.

6 References

1. World Health Organization. Disease Outbreak News: Pneumonia of unknown cause – China https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/?fbclid=IwAR2v89e9lp70O6GTra13FIPHCLw4WJ8kL20Uylx5zZNtWAYvbR0sEATr_rg (Accessed 22 January 2020)

2. Lau LL, Nishiura H, Kelly H, Ip DK, Leung GM, Cowling BJ. Household transmission of 2009 pandemic influenza A(H1N1): a systematic review and meta-analysis. Epidemiology 2012 (in press)

6.1 References for 2019-nCoV

WHO Disease Outbreak News
https://www.who.int/csr/don/en/

Surveillance and case definitions
https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov)

Laboratory guidance
https://www.who.int/health-topics/coronavirus/laboratory-diagnostics-for-novel-coronavirus

Clinical management
https://www.who.int/internal-publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected

Infection prevention and control
https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected

Risk communications
https://www.who.int/publications-detail/risk-communication-and-community-engagement-readiness-and-initial-response-for-novel-coronaviruses-(-ncov)

7 Acknowledgments

This generic protocol was adapted from the protocol entitled “Household Transmission Investigation Protocol for pandemic influenza A(HxNy) in Country X” and “Prospective Study of household transmission of Influenza” by the Consortium for the Standardisation for Influenza Seroepidemiology (CONSISE). CONSISE is a global partnership aiming to develop influenza investigation protocols and standardise seroepidemiology to inform public health policy for pandemic, zoonotic and seasonal influenza. This international partnership was created out of a need, identified during the 2009 H1N1 pandemic, for better (standardised, validated) seroepidemiological data to estimate infection attack rates and severity of the pandemic virus and to inform policy decisions.

WHO staff: Isabel Bergeri, Kaat Vandemaele, Maria Van Kerkhove, Ann Moen, Wenqing Zhang, Aspen Hammond, Julia Fitzner, John Watson, Anne Perrocheau, Yuka Jinnai, Stéphane Huggonnet, Oliver Morgan, Sooyoung Kim, Rebecca Grant and John Watson (US CDC).

Outside WHO, a large number of extra non-WHO individuals were involved in the creation and revision of this protocol as part of the WHO expert working Group on Pandemic Influenza Special Investigation Studies (by alphabetical order). These include: Silke Buda (RK Institute, Germany), Cheryl Cohen (MoH South Africa), Ben Cowling (Hong Kong University, Jeffery Cutter (MoH Singapore), Vernon Lee (MoH Singapore), Rodrigo Fasce (NIC Chile), Gail Garson (GOARN operational support team- Research sub-group chair, United Kingdom), Jean-Michel Heraud (Institut Pasteur de Madagascar), Peter Horby (ISARIC, United Kingdom), Sue Huang (NIC, Institute of Environmental Science and Research, New Zealand), Arunkumar Govindakarnavar (Manipal Institute of Virology Manipal, Academy of Higher Education), Bryan Kim (WHO GOARN operational support team, Switzerland), Vernon Lee (MoH Singapore), Adrian Marcato (University of Melbourne, Australia), Jodie McVernon (Peter Doherty Institute, Australia), Richard Pebody (Public Health England, United Kingdom), Melissa Rolf (US CDC), Hassan Zaraket (American University of Beirut, Lebanon), Lei Zhou (China CDC).

A special mention to Ben Cowling for his guidance throughout the development of this protocol and to Adrian Marcato, who during his internship in WHO, supported the development of this protocol.

Appendices

Appendix A: Sample questionnaires - Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 1a : Report Form for cases - Day 1
Form 1b : Report Form for household contacts - Day 1

Form 2: Report Form for cases and household contacts – Day 7
Form 3: Report Form for cases and household contacts – Day 14
Form 4: Report Form for cases and household contacts – Day 28

Form 5: Laboratory results

Form 6: Symptom diary

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 1a : Report Form for cases - Day 1

Unique Primary Case ID / Household Number	

1. Current Status	□ Alive □ Dead

2. Data Collector Information	
Name of data collector	
Data collector Institution	
Data collector telephone number	
Mobile number	
Email	
Form completion date (DD/MM/YYYY)	___/___/___
Date of interview with informant (DD/MM/YYYY)	___/___/___

3. Interview respondent information (if the persons providing the information is not the primary case)	
First name	
Surname	
Sex	□ Male □ Female □ Not known
Date of Birth (DD/MM/YYYY)	___/___/___
Relationship to primary case	
Respondent address	
Telephone (mobile) number	

4. Primary case Identifier Information	
First name	
Surname	
Sex	□ Male □ Female □ Not known
Date of Birth (DD/MM/YYYY)	___/___/___
Telephone (mobile) number	
Age (years, months)	
Email	
National social number/ identifier (if applicable)	
Country of residence	
Nationality	
Ethnicity (optional)	
Responsible Health Centre	
Nursery/School/College if appropriate Work/ Stay home etc	

5. Household information	
Location of household / Address of primary case	
Household size (number of people who usually live in the house, this will be varied depending on culture)	
Number of rooms in house	

Number of bedrooms	
Age of each household member	_____ _____ _____ _____ _____

6a. Primary case symptoms from onset of illness	
Date of first symptom onset* (DD/MM/YYYY)	___/___/___ □ Asymptomatic □ Unknown
Fever (≥38 °C) or history of fever*	□ Yes □ No □ Unknown If yes, specify maximum temperature from onset of illness:
Date of first health facility visit (including traditional care)* (DD/MM/YYYY)	___/___/___ □ NA □ Unknown
Total number of visits to health facilities since onset of illness	
Total number of health facilities visited since onset of illness	□ NA □ Unknown Specify:
6b. Respiratory symptoms	
Sore throat*	□ Yes □ No □ Unknown If Yes, date (DD/MM/YYYY): ___/___/___
Cough*	□ Yes □ No □ Unknown If Yes, date (DD/MM/YYYY): ___/___/___
Runny nose*	□ Yes □ No □ Unknown
Shortness of breath*	□ Yes □ No □ Unknown If Yes, date (DD/MM/YYYY): ___/___/___
6c. Other symptoms	
Chills	□ Yes □ No □ Unknown
Vomiting	□ Yes □ No □ Unknown
Nausea	□ Yes □ No □ Unknown
Diarrhoea	□ Yes □ No □ Unknown
Headache	□ Yes □ No □ Unknown
Neurological signs If Yes, specify	□ 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
Nose bleed	□ Yes □ No □ Unknown
Fatigue	□ Yes □ No □ Unknown
General malaise	□ Yes □ No □ Unknown
Seizures	□ Yes □ No □ Unknown
Altered consciousness	□ Yes □ No □ Unknown

Other symptoms	□ Yes □ No □ Unknown If yes, specify:

7. Primary case pre-existing condition(s)	
Obesity	□ Yes □ No □ Unknown
Cancer	□ Yes □ No □ Unknown
Diabetes	□ Yes □ No □ Unknown
HIV/other immune deficiency	□ Yes □ No □ Unknown
Heart disease	□ Yes □ No □ Unknown
Asthma (requiring medication)	□ Yes □ No □ Unknown
Chronic lung disease (non-asthma)	□ Yes □ No □ Unknown
Chronic liver disease	□ Yes □ No □ Unknown
Chronic haematological disorder	□ Yes □ No □ Unknown
Pregnancy	□ Yes □ No □ Unknown If yes, specify trimester: □ First □ Second □ Third □ NA Estimated delivery date (DD/MM/YYYY) ___/___/___
Chronic kidney disease	□ Yes □ No □ Unknown
Chronic neurological impairment/disease	□ Yes □ No □ Unknown
Organ or bone marrow recipient	□ Yes □ No □ Unknown
Other pre-existing condition(s)	□ Yes □ No □ Unknown If yes, specify:
Primary case was vaccinated for influenza in the 12 months prior to onset of illness	□ Yes □ No □ Unknown If Yes, date of vaccination, (DD/MM/YYYY) ___/___/___ Country of vaccination:
Primary case was vaccinated with pneumococcal vaccine If Yes, date (DD/MM/YYYY)	□ Yes □ No □ Unknown (DD/MM/YYYY) ___/___/___

8. Case specimen collection (Day 1- baseline)	
Date baseline respiratory sample collected (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___ □ NA
What type of respiratory sample was collected?	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Others
Has baseline serum been taken?	□ Yes □ No □ Unknown If yes, specify date (DD/MM/YYYY):
Which laboratory was the specimen sent to?	
Date sent to other laboratory with coronavirus expertise (if applicable) (DD/MM/YYYY)	___/___/___
9. Laboratory results reporting	

Please impute laboratory results once they become available in the "Laboratory results report"

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 1b : Report Form for household contacts - Day 1

Unique Primary Case ID / Household Number	

1. Current Status	□ Alive □ Dead

2. Data Collector Information	
Name of data collector	
Data collector Institution	
Data collector telephone number	
Mobile number	
Email	
Form completion date (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___
Date of interview with informant (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___

3. Contact Identifier Information	
First name	
Surname	
Sex	□ Male □ Female □ Not known
Date of Birth (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___
Relation to confirmed case	
Telephone (mobile) number	
Age (years, months)	
Email	
National social number/ identifier (if applicable)	
Country of residence	
Nationality	
Ethnicity (optional)	
Responsible Health Centre	
Nursery/School/College if appropriate Work/ Stay home etc	

4. Household information	
Location of household / Address of contact if different to address of primary case	
Date of last contact with the confirmed case (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___
Does the contact share a room (or usually does) with the primary case?	□ Yes □ No □ Unknown
Number of days during the time the case was ill at home that were spent in contact with case (refer to household contact definition)	
Did the contact take care of the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact hug the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact kiss the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact shake hands with the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown

Did the contact share a meal with the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact eat from the same plate with hands with the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact share a drinking cup/glass with the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact share utensils with the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact sleep in the same room as the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown
Did the contact share a toilet with the case during the time he/she was ill at home before hospitalization?	□ Yes □ No □ Unknown

5a. Contact symptoms	
Has the contact experienced any respiratory symptoms (sore throat, cough, running nose, shortness of breath) in the period from 10 days before onset in the confirmed case until the present?	□ Yes □ No If no, please skip to next section 5c
Date of first symptom onset (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___ □ Asymptomatic □ Unknown
Fever (≥38 °C) or history of fever	□ Yes □ No □ Unknown If yes, specify maximum temperature:
5b. Respiratory symptoms	
Sore throat	□ Yes □ No □ Unknown If Yes, date (DD/MM/YYYY): ___/___/___
Cough	□ Yes □ No □ Unknown If Yes, date (DD/MM/YYYY): ___/___/___
Runny nose	□ Yes □ No □ Unknown
Shortness of breath	□ Yes □ No □ Unknown If Yes, date (DD/MM/YYYY): ___/___/___
5c. Other symptoms	
Chills	□ Yes □ No □ Unknown
Vomiting	□ Yes □ No □ Unknown
Nausea	□ Yes □ No □ Unknown
Diarrhoea*	□ Yes □ No □ Unknown
Headache*	□ Yes □ No □ Unknown
Neurological signs* If Yes, specify	□ Yes □ No □ Unknown
Rash*	□ Yes □ No □ Unknown
Conjunctivitis*	□ Yes □ No □ Unknown
Muscle aches*	□ Yes □ No □ Unknown
Joint ache	□ Yes □ No □ Unknown
Loss of appetite	□ Yes □ No □ Unknown

Nose bleed	□ Yes □ No □ Unknown
Fatigue	□ Yes □ No □ Unknown
General malaise	□ Yes □ No □ Unknown
Seizures	□ Yes □ No □ Unknown
Altered consciousness	□ Yes □ No □ Unknown
Other symptoms*	□ Yes □ No □ Unknown If yes, specify:

6. Contact pre-existing condition(s)	
Obesity	□ Yes □ No □ Unknown
Cancer	□ Yes □ No □ Unknown
Diabetes	□ Yes □ No □ Unknown
HIV/other immune deficiency	□ Yes □ No □ Unknown
Heart disease	□ Yes □ No □ Unknown
Asthma (requiring medication)	□ Yes □ No □ Unknown
Chronic lung disease (non-asthma)	□ Yes □ No □ Unknown
Chronic liver disease	□ Yes □ No □ Unknown
Chronic haematological disorder	□ Yes □ No □ Unknown
Pregnancy	□ Yes □ No □ Unknown If yes, specify trimester: □ First □ Second □ Third □ NA Estimated delivery date (DD/MM/YYYY) ___/___/___
Chronic kidney disease	□ Yes □ No □ Unknown
Chronic neurological impairment/disease	□ Yes □ No □ Unknown
Organ or bone narrow recipient	□ Yes □ No □ Unknown
Other pre-existing condition(s)	□ Yes □ No □ Unknown If yes, specify:
Contact was vaccinated for influenza in the 12 months prior to onset of illness in the case	□ Yes □ No □ Unknown If Yes, date of vaccination (DD/MM/YYYY) ___/___/___ Country of vaccination:
Contact was vaccinated with pneumococcal vaccine If Yes, date (DD/MM/YYYY)	□ Yes □ No □ Unknown (DD/MM/YYYY) ___/___/___

7. Contact specimen collection (Day 1- baseline)	
Date baseline respiratory sample collected* (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___ □ NA
What type of respiratory sample was collected?	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Others
Has baseline serum been taken?	□ Yes □ No □ Unknown If yes, specify date (DD/MM/YYYY):
Which laboratory was the specimen sent to?	
Date sent to other laboratory with coronavirus expertise (if applicable) (DD/MM/YYYY)	___/___/___
8. Laboratory results reporting	
Please impute laboratory results once they become available in the "Laboratory results report"	

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 2: Report Form for cases and household contacts – Day 7

10. Respiratory specimen collection (Day 7)	
Unique Primary Case ID / Household number	□ NA
Date of sample collection (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___ □ NA
What type of respiratory specimen was collected?	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Others
Who collected the respiratory specimen?	□ Study staff/ research nurse □ Self-collected
Which laboratory was the specimen sent to?	
Date sent to other laboratory with coronavirus expertise (if applicable) (DD/MM/YYYY)	___/___/___ Specify laboratory:
11. Laboratory results reporting	
Please impute laboratory results once they become available in the "Laboratory results report"	

12. Outcome (Day 7)	
Outcome	□ Alive □ Died □ NA □ Unknown If dead, cause:
Outcome current as of date (DD/MM/YYYY)	___/___/___ □ Unknown □ NA
Hospitalization	□ Yes □ No □ Unknown If yes, date of first hospitalization ___/___/___ □ Unknown If yes, specify reason for hospitalisation:

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 3: Report Form for cases and household contacts – Day 14

13. Respiratory specimen collection (Day 14)	
Unique Primary Case ID / Household number	□ NA
Date of sample collection (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___ □ NA
What type of respiratory specimen was collected?	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Others
Who collected the respiratory specimen?	□ Study staff/ research nurse □ Self-collected
Which laboratory was the specimen sent to?	
Date sent to other laboratory with coronavirus expertise (if applicable) (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___ Specify laboratory:
14. Laboratory results reporting	
Please impute laboratory results once they become available in the "Laboratory results report"	

15. Outcome (Day 14)	
Outcome	□ Alive □ Died □ NA □ Unknown If dead, cause:
Outcome current as of date (DD/MM/YYYY)	___/___/___ □ Unknown □ NA
Hospitalization	□ Yes □ No □ Unknown If yes, date of first hospitalization ___/___/___ □ Unknown If yes, specify reason for hospitalisation:

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 4: Report Form for cases and household contacts – Day 28

16. Respiratory specimen collection (Day 28)	
Unique Primary Case ID / Household number	□ NA
Date of sample collection (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___ □ NA
What type of respiratory specimen was collected?	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Others
Who collected the respiratory specimen?	□ Study staff/ research nurse □ Self-collected
Which laboratory was the specimen sent to?	
Date sent to other laboratory with coronavirus expertise (if applicable) (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___ Specify lab:
17. Laboratory results reporting	
Please impute laboratory results once they become available in the "Laboratory results report"	

18. Outcome (Day 28)	
Outcome	□ Alive □ Died □ NA □ Unknown If dead, cause:
Outcome current as of date (DD/MM/YYYY)	(DD/MM/YYYY) ___/___/___ □ Unknown □ NA
Hospitalization	□ Yes □ No □ Unknown If yes, date of first hospitalization ___/___/___ □ Unknown If yes, specify reason for hospitalisation:

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 5: Laboratory results

This table will need to be completed for every specimen collection at each point in the follow-up, depending on the chosen specimen collection schedule.

19a. Molecular testing methods and results:	
Lab identification number	
Date sample collected (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___
Date sample received (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___
Type of sample	□ Nasal swab □ Throat swab □ Nasopharyngeal swab □ Others, specify:
Type of test	□ PCR □ Whole genome sequencing □ Partial genome sequencing □ Other, specify
Result	□ 2019-nCoV □ Others, specify:
Date of result (DD/MM/YYYY)	___/___/___
Specimen shipped to other laboratory for confirmation - Date (DD/MM/YYYY)	□ Yes □ No (DD/MM/YYYY)___/___/___

19b. Serology testing methods and results:	
Lab identification number	
Date sample collected (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___
Date sample received (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___
Type of sample	□ Serum □ Others, specify:
Result (2019-nCoV antibody titres)	
Date of result (DD/MM/YYYY)	___/___/___
Specimen shipped to other laboratory for confirmation - Date (DD/MM/YYYY)	□ Yes □ No (DD/MM/YYYY)___/___/___

Household transmission investigation protocol for 2019-novel coronavirus (2019-nCoV) infection

Form 6: Symptom diary

Each household contact will be asked to record the presence or absence of various signs or symptoms each day for up to 28 days after the administration of the baseline questionnaire (minimum 14 days).

With 2019-nCoV, the extent of clinical presentation and spectrum remains unclear, so symptom diaries may be broadened to include vomiting, diarrhea, abdominal pain, etc., as relevant and may need to be altered to include symptom data for longer than 14 days.

If no symptoms are experienced, ensure that *None* is selected in the second column.

Day	**Symptoms**						
	No symptoms (check if none experienced)	**Fever ≥38°C**	**Sore throat**	**Cough**	**Runny nose**	**Shortness of breath**	**Other symptoms: specify**
0	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
1	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
2	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
3	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
4	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
6	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
7	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
8	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
9	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
10	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
11	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
12	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
13	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
14	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	
…							
28	□ None	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	□ Yes □ No	