

This protocol is an update of the protocol “Case-control study to assess potential risk factors related to human illness caused by Middle East respiratory syndrome coronavirus (MERS-CoV)” published on the WHO coronavirus website on 3 July 2013. It represents a significant revision resulting from multiple consultations with countries in the region that are experiencing indigenous transmission of the virus.

## **Case-control study to assess potential risk factors related to human illness caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

Version 5

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## Acknowledgement

This document was adapted from a protocol developed by the Consortium for the Standardization for Influenza Seroepidemiology (CONSISE), a global partnership aiming to develop influenza investigation protocols and standardize 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 (standardized, validated) seroepidemiological data to estimate infection attack rates and severity of the pandemic virus and to inform policy decisions. More information on the CONSISE network can be found on their website: [www.CONSISE.tghn.org](http://www.CONSISE.tghn.org).

## PROTOCOL SUMMARY

This investigation will provide data to evaluate exposures and risk factors for human cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV). This protocol outlines a case-control study and the epidemiological methods to guide data collection to assess risk factors for illness caused by MERS coronavirus (MERS-CoV) infection. Health care personnel and the evaluation of other contacts are addressed in a separate protocol.

Comments for the user's consideration are provided in purple text throughout the document.

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## 1.0 SCIENTIFIC BACKGROUND AND RATIONALE

The novel Coronavirus now known as Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first detected in a patient living in Saudi Arabia in September of 2012. Since that time, sporadic cases, small clusters, and large outbreaks have been reported in several countries. Recent investigations have suggested that camels and bats may harbor the virus. Although finding the animal reservoir is an important step in controlling spread of the virus, a more immediate need is to understand the route and mode of transmission to humans from animal sources, and the types of exposures that result in infection. Several possibilities exist, including direct contact with an infected animal, which could be either the reservoir species or an intermediate host species; contact with or consumption of unprocessed animal products; contact with the environment where an infected animal has recently been; or consumption of a food or beverage which has been contaminated by animal excreta. All of these have been implicated in other zoonotic infections. Learning the exposures that result in transmission to humans will allow measures to be taken to interrupt transmission. This investigation will provide data to evaluate risk factors for infection by reviewing exposures of known cases and comparing them to rates of exposure in similar uninfected individuals in the general population. For the purpose of this investigation, the cases under consideration will be those that are presumed NOT to have acquired their infection from another infected human.

### 1.1 OBJECTIVES

The data collected from this study will be used to refine/update recommendations for surveillance and case definitions, to characterize the key epidemiological transmission features of MERS-CoV virus, help understand spread, severity, spectrum of disease, impact on the community and to inform operational models for implementation of countermeasures such as case isolation, contact tracing and quarantine.

The primary objectives of this study are to:

- Identify modifiable non-human exposures that lead to human MERS-CoV infection
- Describe other risk factors for infection, such as pre-existing medical conditions.

## 2.0 STUDY PROCEDURES

### 2.1 METHODOLOGY

The study uses a case-control design that examines the differences in types of exposures between index and sporadic cases, also called *primary* cases, with laboratory-confirmed MERS-CoV infection and healthy controls in order to determine the risk associated with that exposure. A standard questionnaire has been provided in this protocol (Appendix A).

Because exposures vary greatly from season to season, and memory of exposures and activities can be lost over time, the study will focus on recent cases. It will be critical that the same timeframe for exposures is used for both cases and controls. The period of interest is the 14 days before the onset of illness in confirmed cases; however, as the controls have not been sick, the same-14 day period should be used. Controls should be chosen at random from the area of residence of the cases and be of the same age and sex as the cases.

The study should be a multinational effort combining standardized data from all participating countries. Implementation will be supported by an international team of experts and national focal points that will jointly resolve issues and questions regarding implementation by consensus.

If the case is deceased or too sick to be interviewed (e.g. is on mechanical ventilation), a proxy can be interviewed instead. The proxy should be a family member or close friend who knows about the activities of the case in the time before his/her illness and his/her usual habits. It may be that more than one proxy will be used for each case, though conflicting information will have to be resolved with further discussion with the proxies.

## 2.2 STUDY POPULATION

While there are many questions about the mode of transmission and risk factors for human-to-human transmission, the primary purpose of this study is to determine the *non-human* source of infection, such as exposures to animals or contaminated food products. Therefore, study subjects will include only primary cases, that is, sporadic cases with presumed non-human exposures that resulted in infection or index cases from clusters. These are cases that do not have a history of recent exposure to a confirmed or probable MERS-CoV infected case in the 14 days before onset of their illness, to exclude cases for whom the transmission may have occurred through human-to-human transmission. Cases should include only those confirmed according to the current WHO case definitions (see section 2.4.2 below). As many of the known cases have occurred as part of clusters in which human-to-human transmission is suspected to have occurred, it will be important to identify the *index* case in the cluster to include in the study. If there is uncertainty as to whether or not the case might have had significant exposure to another infected human in the 14 days before the case's illness, the case should not be enrolled as a study subject.

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### 2.2.1 CASE DEFINITIONS

Case definitions for reporting are provided by WHO and are subject to change as more information becomes available.<sup>1</sup>

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#### CONFIRMED CASE

A confirmed case of MERS-CoV is a person with laboratory confirmation of infection with MERS-CoV.

Currently, confirmatory testing requires molecular diagnostics including either a positive PCR result on at least two specific genomic targets or a single positive target with sequencing on a second. However, the Interim recommendations for laboratory testing for MERS-CoV should be consulted for the most recent standard for laboratory confirmation ([http://www.who.int/csr/disease/coronavirus\\_infections/en/](http://www.who.int/csr/disease/coronavirus_infections/en/)).

## 2.3 SUBJECT RECRUITMENT

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### 2.3.1 SUBJECT RECRUITMENT AND DATA COLLECTION

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<sup>1</sup> WHO Case Definitions for nCoV:

[http://www.who.int/csr/disease/coronavirus\\_infections/case\\_definition/en/index.html](http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/index.html)

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## RECRUITMENT OF CASES

Primary study subjects are laboratory-confirmed cases of MERS-CoV infection as described above. If cases are part of a cluster, only the index case – that is, the case with the earliest date of onset of illness and believed to have acquired infection from a non-human source – should be included in the study.

Care must be taken in the inclusion of cases *not* to bias the selection in favor of having had animal contact. That is, cases should be excluded only on the basis of whether or not they have had contact with another human case before their illness and not whether they have had contact with animals.

COMMENT: In some clusters, more than one index case may appear simultaneously (co-primary/co-index cases) and it is possible to tease out the transmission dynamics and identify the index case; another option for preliminary analysis is to exclude these cases from this case-control study.

COMMENT: This study will enroll only adults. The age of adulthood may vary by country, but should be specified in the protocol and standardized across countries. The age used in this protocol is 18 years.

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## INCLUSION AND EXCLUSION CRITERIA FOR CASES

### Inclusion criteria:

- Adult 18 years old and over.
- Has given consent either personally or by proxy, if the patient is too ill to give consent personally.
- Laboratory confirmation according to current WHO guidelines.

### Exclusion criteria:

- Has been admitted to hospital within 14 days prior to the onset of their MERS illness.
- Works in a health care facility.
- Has an epidemiological link<sup>2</sup> in the 14 days prior to onset of his/her MERS illness with either another documented case of MERS infection or someone admitted to hospital with a respiratory illness of unknown cause.

Note that cases should be included in the study even if they have died or are too sick to be interviewed. In each of these situations, family members and close friends can be interviewed as proxies.

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## RECRUITMENT OF CONTROLS

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<sup>2</sup> An epidemiological link includes:

- Close physical contact.
- Health care associated exposure, including providing direct care or working or staying in the same close environment.
- Working together in close proximity or sharing the same classroom environment
- Traveling together in any kind of conveyance
- Living in the same household.

To understand how rates of exposures to potential sources of infection differ between cases and uninfected individuals, it is necessary to recruit age- and sex-matched control subjects will be randomly selected as described below and asked for their consent to participate in the study.

To maximize the power to show differences in exposures, four controls should be recruited for each case.

Age matching can be done within a range that depends on the age of the case for which the control is being selected, as outlined below:

Age of case	Age range of control
18 to <25y.o.	Within $\pm$ 5 years of age
$\geq$ 25 y.o.	Within $\pm$ 10 years of age

## INCLUSION AND EXCLUSION CRITERIA FOR CONTROLS

### Inclusion criteria:

- Adult 18 years old or over.
- Has given consent.

### Exclusion criteria:

- Has been admitted to hospital within 14 days prior to the onset of their MERS illness.
- Works in a health care facility.
- Control has an epidemiological link<sup>2</sup> in the 14 days prior to onset of his/her MERS illness with either another documented case of MERS infection or someone admitted to hospital with a respiratory illness of unknown cause.

## RANDOM SELECTION OF CONTROLS

Two types of randomly selected controls can be included in this study 1) randomly selected neighborhood controls matched on age and sex and 2) randomly selected hospital controls matched on date of admission, age and sex. Each will yield a different perspective on the factors that influence risk of severe MERS infection. For example, neighborhood controls are also likely to be similar to cases in terms of socio-economic status and ethnicity, but will be very useful for looking at specific types of activities that were done in the time frame immediately before the case's illness. However, because of their similarity to cases, it will not likely be possible to see the influence of socio-economic status and ethnicity on risk. Hospital controls, on the other hand, are more likely to be different from cases in terms of these two issues, and so will facilitate evaluating the risk associated with them. However, specific activities and behaviors are likely to be heavily confounded by their association with certain socio-economic strata and ethnicities and so these controls will be less able to credibly demonstrate differences where those factors are concerned.

If resources are limited, neighborhood controls should be used for this study. Hospital controls are an optional additional group that can yield other information on risk.

**Neighborhood Controls:** The method to be used for this study will be to first identify the neighborhood of the case. Investigators will then go to the neighborhood and select controls directly through a random selection process on site.

**Procedure for control subject selection:** Once arriving at the home of the case, chose a random number between 1 and 10 (this can be done in advance using a random number generator or done simply by choosing a number written on a piece of paper drawn from a pile). Chose a direction to go from the residence of the case either by a coin toss, if there are only two directions possible, or by spinning a pencil on a sheet of paper if multiple possibilities. Proceed in that direction for the number of residences equal to the random number chosen in the beginning. This will be the first residence to seek a matched control for the case.

For example, if a 5 was drawn in the random number selection and the case's home is on a street in a residential neighborhood, toss a coin to decide whether to go to the right or left from the case home. If right is selected, go to the 5<sup>th</sup> house to the right and attempt to recruit a control of the same age and gender as the case. If the residence is an apartment building or other multifamily type dwelling, use similar random selection methods to choose the floor to start with, the direction to go from the elevator, and the first apartment to interview.

To choose subsequent controls, continue in the same direction selecting residences at the same random number interval as the initial one was selected (5 in this example). When faced with a choice of directions, use a random selection method such as a coin toss to decide which direction to go.

See inclusion/exclusion criteria above, and guidelines on age matching for control selection.

**Hospital Controls:** Patients who were admitted to the same health care facility on the same date as the index MERS-CoV patient will be identified from hospital/health care facility records. Four controls matched on date of admission, age and sex will be chosen at random from the hospital/ health care facility records. Contact information will be given to investigators by the records department of the participating health care facility from the admission record; however, no patient medical information will be made available to investigators. Initial contact with the identified controls will be made by telephone and/or in person interview(s) and asked to participate in the study. If the identified control refuses to participate, the investigation team will identify another randomly selected control matched on date of admission, age and sex until four controls per case are enrolled in the study.

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## INFORMED CONSENT

During the visits to both cases and controls, the purpose of the study will be explained to all eligible subjects and their consent obtained by a trained member of the investigation team.

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## DATA COLLECTION

After enrollment and informed consent is obtained, a standardized questionnaire will be administered. The study questionnaire for the use of all cases and controls can be found in Appendix A.



Data include some identifying information, demographic information, date of onset, and a series of detailed questions about behaviors, practices, exposures, and underlying medical conditions.

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### 2.3.2 PREVENTION OF MERS-COV TRANSMISSION IN FRONT-LINE STAFF

Prior to study implementation, front-line staff including all study personnel will be trained in infection control procedures (standard, contact, droplet or airborne precautions) including 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 patients during home visits and elsewhere, but also to minimize the risk of the personnel acting as a vector of MERS-CoV transmission between subjects members or between households. If N-95 respirators are to be used, they should be fit tested in advance.

## 2.4 ETHICAL CONSIDERATIONS

Ethical approval will be sought in accordance with local, regional and national authorities.

## 3.0 STUDY ENDPOINTS & STATISTICAL ANALYSES

The following section discusses the endpoints – that is, what will be measured and calculated using the data that are collected in this study – for the primary objectives, including statistical advice.

### 3.1 STUDY OUTCOME MEASURES

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#### 3.1.1 PRIMARY OUTCOME

The following will be assessed as study endpoint corresponding to the study’s primary objective:

- The ratio of the odds of exposure vs. odds of no exposure to a variety of potential sources of infection in cases vs. controls.
- The exposure or combination of exposures that best explain the resulting infection based on a regression model of all exposures.

### 3.2 STATISTICAL ANALYSES

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#### 3.2.1 FOR PRIMARY OBJECTIVE

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#### RISK FACTORS FOR HUMAN INFECTION

The reported practices among cases and matched controls should be compared using appropriate statistical tests, e.g., Bivariate associations between risk factors and infection will be determined by statistical tests and expressed as odds ratios with 95% confidence intervals. Logistic regression will be used to further analyze the associations to determine which best explains the resulting infection.

## 4.0 DATA MANAGEMENT

Data will be stored in a secure, password-protected database in the country where it is collected. Patient identity will be protected and only aggregate summary data released publically. Original data collection forms will be kept in locked storage.

## REFERENCES

### Papers related to MERS-CoV:

- The WHO MERS-CoV Research Group. State of Knowledge and Data Gaps of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Humans. PLoS Currents Outbreaks 2013; Published, 2013 Nov 12. Edition 1. doi: 10.1371/currents.outbreaks.0bf719e352e7478f8ad85fa30127ddb8. Available here: <http://currents.plos.org/outbreaks/article/state-of-knowledge-and-data-gaps-of-middle-east-respiratory-syndrome-coronavirus-mers-cov-in-humans-2/>
- Buchholz U, Müller MA, Nitsche A, et al. Contact investigation of a case of human novel coronavirus infection treated in a German hospital, October-November 2012. Euro Surveill. 2013;18(8):pii=20406. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20406>
- WHO. Novel coronavirus infection in the United Kingdom, 23 September 2012; Available at: [http://www.who.int/csr/don/2012\\_09\\_23/en/index.html](http://www.who.int/csr/don/2012_09_23/en/index.html)
- Albarrak AM, Stephens GM, Hewson R, et al. Recovery from severe novel coronavirus infection. Saudi Med J 2012;33(12):1265-9.
- Corman VM, Müller MA, Costabel U, et al. Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. Euro Surveill. 2012;17(49):pii=20334. Available at <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20334>

### Risk factor investigations of other novel viruses:

- Dinh P, Long H, Tien N, et al. Risk factors for human infection with avian influenza A H5N1, Vietnam, 2004. Emerg Infect Dis 2006;12(12):1841-7.
- Reynolds MG, Anh BH, Thu VH, et al. Factors associated with nosocomial SARS-CoV transmission among healthcare workers in Hanoi, Vietnam, 2003. BMC Public Health 2006;6(207):207 doi:10.1186/1471-2458-6-207.
- Zhou L, Liao Q, Dong L, et al. Risk Factors for Human Illness with Avian InfluenzaA (H5N1) Virus Infection in China. JID 2009;199 (15 June): 1726-34
- Areechokchai D, Jiraphongsa C, Laosiritaworn Y, et al. Investigation of Avian Influenza (H5N1) Outbreak in Humans — Thailand, 2004. MMWR vol. 5 suppl. April 28 2006.
- Mounts A, Kwong H, Izurieta HS, et al. Case-Control Study of Risk Factors for Avian Influenza A (H5N1) Disease, Hong Kong, 1997. JID 1999;180:505-8
- Ai J, Huang Y, Xu K, Ren D, Qi X, Ji H, Ge A, Dai Q, Li J, Bao C, Tang F, Shi G, Shen T, Zhu Y, Zhou M, Wang H. Case-control study of risk factors for human infection with influenza A(H7N9) virus in Jiangsu Province, China, 2013. Euro Surveill. 2013 Jun 27;18(26):20510.

**APPENDIX A DATA COLLECTION FORM**

## Questionnaire for Case Control Study of Patients with MERS-CoV infection

The following questionnaire should be used for all cases and controls included in the investigation. **The timeframe for the questions to cases is the 14 day period before the onset of their illness.** For cases that happened in the past, it is useful to use memory prompts such as holidays or other memorable events that occurred around the same time to help the interviewee recall the specific time frame of interest. For controls, the same time frame should be asked about as for the case to which the control is matched (that is, the same calendar dates).

If the case has died or is otherwise unable to answer questions, a proxy such as person (e.g., family member, friend or co-worker) who knows the person well can answer the questions for him or her.

Each subject should be allocated a unique identification number.

**SECTION 1 GENERAL QUESTIONS**

**Contact Information of Subject**

1.1 Patient Name:

First name \_\_\_\_\_ Middle \_\_\_\_\_  
 Name(s) \_\_\_\_\_ Surname \_\_\_\_\_

1.2 National ID number: \_\_\_\_\_

1.3 Study ID Number |\_\_| |\_\_| |\_\_| |\_\_| |\_\_| |\_\_| |  
Country ID Study ID Number

1.4 Residence (City, Province): \_\_\_\_\_

1.5 Telephone number of subject: \_\_\_\_\_

1.5.1 May we contact you again with follow up questions or clarifications? 1 yes 0 no

1.6 Subject is a (circle one): 1 case 0 control

1.6.1 If case, when was the first symptom onset (dd/mm/yyyy): \_\_\_\_/\_\_\_\_/\_\_\_\_

1.6.2 If control, for which case is the subject a control (provide identification number of case):

Case Study ID Number |\_\_| |\_\_| |\_\_| |\_\_| |\_\_| |\_\_| |  
Country ID Study ID Number

1.7 Gender (circle one): 1 Male 0 Female

1.8 Date of interview (dd/mm/yyyy): \_\_\_\_/\_\_\_\_/\_\_\_\_

1.9 Place of interview (city, province): \_\_\_\_\_

1.9.1 Location of interview? 1 Barn 2 Market 3 Household 4 Hospital 5 Other \_\_\_\_\_

1.10 Person answering questions is:

1 subject 2 relative (specify relationship: \_\_\_\_\_) 3 friend 4 coworker

1.11 Language used for interview: 1 English 2 Arabic 3 Other, please specify \_\_\_\_\_

1.12 Name of interviewer: \_\_\_\_\_

1.13 Contact information of interviewer (including Institution and phone number):  
\_\_\_\_\_

### General questions

1.14. Place of primary residence of subject (address): \_\_\_\_\_

1.14.1. GPS coordinates of residence  
\_\_\_\_\_

1.14.2. Do you have home(s) elsewhere? 1 yes 0 no 9 unknown

1.14.3. If yes, please specify where (address): \_\_\_\_\_

1.15. Date of birth: \_\_\_/\_\_\_/\_\_\_ (mm/dd/yyyy)

1.16. Occupation(s): \_\_\_\_\_

1.16.1. Where is the work done (address): \_\_\_\_\_

## SECTION 2 EXPOSURE QUESTIONS

Exposure history should be focused on a specified time period before the symptom onset of the MERS-CoV case. If the subject being questioned is a case, then exposure should be for the 14 days prior to the date of the first symptom onset (See question 1.5.1). For controls, the same time frame would be asked about as for the case to which the control is matched (see question 1.5.2). When actually asking questions, the interviewer should specify the exact dates on the calendar based on the individual case/control rather than referring to the 2 weeks prior to illness. Use of an actual calendar and other memory prompts may help in eliciting accurate responses.

COMMENT: To the Interviewer: Enter exposure dates of interest here: \_\_\_\_\_

## RECENT TRAVEL HISTORY

**The following questions relate to travel within the 14 days prior to illness** (or the same dates as the 14 days before onset in the matched case, if interviewee is a control) **and the animals you encountered during these travels.**

### Recent Travel History OUTSIDE the country of residence

2.1. Did you travel OUTSIDE of your country of residence in the 14 days before symptom onset (COMMENT: the interviewer should state the time period here based on the answer in question 1.6.1)?  
1 yes 0 no 9 unknown *if no, go to question 2.3*

2.2. If yes, list the areas to which you have travelled in the last 14 days before onset of illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control).

2.2.1. Place name and country: \_\_\_\_\_

2.2.1.1. Dates Travelled: \_\_\_\_\_ to \_\_\_\_\_

2.2.2. Place name and country: \_\_\_\_\_

2.2.2.1. Dates Travelled: \_\_\_\_\_ to \_\_\_\_\_

2.2.3. Place name and country: \_\_\_\_\_

2.2.3.1. Dates Travelled: \_\_\_\_\_ to \_\_\_\_\_

2.3. Have you attended any recent mass gatherings (e.g., weddings, festivals or religious pilgrimages) outside of your country where there were large numbers of people together?

1 yes 0 no 9 unknown

2.3.1. Specify event and location: \_\_\_\_\_

**Recent Travel History WITHIN the country of residence**

2.4. Did you travel to areas INSIDE of your country other than your governorate of residence in the 14 days before symptom onset (COMMENT: the interviewer should state the time period here based on the answer in question 1.5.1)?

1 yes 0 no 9 unknown *if no, go to question 2.6*

2.5. If yes, list the areas to which you have travelled in the last 14 days before onset of illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control).

2.5.1. Place name and country: \_\_\_\_\_

2.5.1.1. Dates Travelled: \_\_\_\_\_ to \_\_\_\_\_

2.5.2. Place name and country: \_\_\_\_\_

2.5.2.1. Dates Travelled: \_\_\_\_\_ to \_\_\_\_\_

2.5.3. Place name and country: \_\_\_\_\_

2.5.3.1. Dates Travelled: \_\_\_\_\_ to \_\_\_\_\_

2.6. Have you attended any recent mass gatherings (e.g., weddings, festivals or religious pilgrimages) in areas inside your country other than in your governorate of residence where there were large numbers of people together?

1 yes 0 no 9 unknown *if no, go to question 2.7*

2.6.1. Specify event and location: \_\_\_\_\_

**HUMAN EXPOSURES**

2.7. Have you had direct contact (e.g., touch, share a bed) within the 14 days before your illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control) with a person who had a respiratory illness with cough and fever during the time in which the person was sick? 1 yes 0 no 9 unknown

2.8. Have you in the 14 days before your illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control) visited a hospital/medical clinic/doctor's office/health station for treatment for any reason?

1 yes 0 no 9 unknown *if no, go to question 2.9*

2.8.1. Name and address of medical facility: \_\_\_\_\_

2.8.2. Dates of visit/admission? (dd/mm/yyyy)? \_\_\_/\_\_\_/\_\_\_

2.8.3. Reason for visit? \_\_\_\_\_

2.9. Did you visit or care for a sick person in the hospital with a respiratory illness such as pneumonia in the 14 days before your illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control)? 1 yes 0 no 9 unknown *if no, go to question 2.10*

2.9.1. Did you come in direct contact (e.g., touch) with the person who was in the hospital? 1 yes 0 no 9 unknown

**ANIMAL EXPOSURES**

The following questions address **animal exposures** during the 14 day period before the patient’s illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control).

**Animal contact**

2.10 Do you own a farm or barn with animals? 1 yes 0 no *if no, go to question 2.11*

2.10.1 Where is the location of the farm (address)?  
\_\_\_\_\_

2.11 Do others living in your household (e.g., domestic help or relative) frequently visit or work on a farm or market where camels are kept or sold? 1 yes 0 no 9 unknown

2.12 Have others living in your household (e.g., domestic help or relative) visited or worked in the in the past 2 weeks at a farm or market where camels are kept or sold? 1 yes 0 no 9 unknown

2.13 Have others living in your household (e.g., domestic help or relative) had direct contact with camels in the past 2 weeks? 1 yes 0 no 9 unknown

2.13.1 If yes, please circle all that apply. Person in household is:

- 1 spouse
- 2 other relative
- 3 domestic help
- 4 other resident of household (e.g. temporary visitor)

2.14 Were any livestock (e.g. camels, sheep, goats, cattle, horses), kept in or around your home during this period? 1 yes 0 no 9 unknown *if no, go to question 2.15*

2.14.1 Name the species, the number of animals and what they are used for?

<b>Species</b>	<b>Number of animals</b>	<b>What they are used for? (circle one)</b>	<b>Any ill during 14 days prior to case symptom onset? (circle one)</b>
	< 10 animals ≥ 10 animals	Food racing work pets	Yes no unknown
	< 10 animals ≥ 10 animals	Food racing work pets	Yes no unknown

	< 10 animals ≥ 10 animals	Food racing work pets	Yes no unknown
	< 10 animals ≥ 10 animals	Food racing work pets	Yes no unknown

- 2.15 Were you aware of any bats present in or outside around your house during this time?  
1 yes 0 no 9 unknown
- 2.16 Did you visit a farm where livestock (camels, sheep, goats, cattle, horses) are kept during the study period (14 days prior to symptom onset for the case and same time period for control)?  
1 yes 0 no 9 unknown *If no, go to question 2.17*
- 2.16.1 Where is the location of this farm (address): \_\_\_\_\_
- 2.16.2 Which kinds of animals (circle all that apply)  
Camel Goat Sheep Horse Cattle
- 2.16.3 Did you have physical contact (touch) with livestock animals (camels, sheep, goats, cattle, horses) while there? 1 yes 0 no 9 unknown *If no, go to question 2.16.6*
- 2.16.4 Were any of these animals sick?  
1 yes 0 no 9 unknown *If no, go to question 2.16.6*
- 2.16.5 Which species of animals were sick?  
Camel Goat Sheep Horse Cattle
- 2.16.6 Did you eat or drink anything while on the farm?  
1 yes 0 no 9 unknown *if no, go to question 2.16.7*
- 2.14.6.1 Please specify what you ate or drank at the farm  
\_\_\_\_\_
- 2.16.7 Did you touch any items such as fences, textiles, machinery, clothing, or other physical objects that may have had contact with animals on the farm?  
1 yes 0 no 9 unknown
- 2.16.8 Did you have contact with any carcasses, body fluids, secretions, urine or excrement of animals on the farm while there? 1 yes 0 no 9 unknown
- 2.16.9 Did you have contact with any animal bedding, straw or feed on the farm while there?  
1 yes 0 no 9 unknown
- 2.16.10 Did you do any of the following activities while on the farm:  
Feed animals? 1 yes 0 no 9 unknown  
Clean animal housing? 1 yes 0 no 9 unknown

Clean farm equipment? 1 yes 0 no 9 unknown

Slaughter animals? 1 yes 0 no 9 unknown

Assist with the birth of animals? 1 yes 0 no 9 unknown

Milk camels? 1 yes 0 no 9 unknown

Kiss/hug camels? 1 yes 0 no 9 unknown

Other tasks? 1 yes 0 no 9 unknown (please specify):  
\_\_\_\_\_

2.16.11 Were you aware of any bats present in or outside around the farm during this time?  
1 yes 0 no 9 unknown

2.17 Did you visit a market selling livestock animals during the study period (14 days prior to symptom onset for the case and same time period for control)?  
1 yes 0 no 9 unknown *if no, go to question 2.18*

2.17.1 What kinds of animals were sold/slaughtered there (circle all that apply)?

Camel Goat Sheep Horse Cattle

2.17.2 Did you have direct physical contact with any of these animals?  
1 yes 0 no 9 unknown *if no, go to question 2.17.4*

2.17.3 Which animals did you have direct physical contact (circle all that apply)?

Camel Goat Sheep Horse Cattle

2.17.4 Did you consume any food at the animal market? 1 yes 0 no 9 unknown

2.18 Did you visit a slaughter house during the study period (14 days prior to symptom onset for the case and same time period for control)?  
1 yes 0 no 9 unknown *if no, go to question 2.19*

2.18.1 What kinds of animals were slaughtered there (circle all that apply)?

Camel Goat Sheep Horse Cattle

2.18.2 Did you have direct physical contact with any of these animals?  
1 yes 0 no 9 unknown *if no, go to question 2.19*

2.18.3 Which animals did you have direct physical contact (circle all that apply)?

Camel Goat Sheep Horse Cattle

2.18.4 Did you consume any food at the slaughter house? 1 yes 0 no 9 unknown

2.19 Did you visit a racetrack or stable where camels are stabled, trained or raced during the study period (14 days prior to symptom onset for the case and same time period for control)?  
1 yes 0 no 9 unknown *if no, go to question 2.20*

2.19.1 Location of these venues (addresses): \_\_\_\_\_



2.19.2 Did you have physical contact with a camel while there? 1 yes 0 no 9 unknown

2.20 Did you visit any other venue at which livestock animals were present during the study period (14 days prior to symptom onset for the case and same time period for control)?  
1 yes 0 no 9 unknown *if no, go to question 2.21*

2.20.1 Please give the address of the venue? \_\_\_\_\_

2.20.2 Did you have direct contact with animals while there? 1 yes 0 no 9 unknown  
*if no, go to question 2.21*

2.20.3 Which animals did you have direct physical contact (circle all that apply)?

Camel Goat Sheep Horse Cattle

2.21 Did you personally participate in the slaughtering of an animal during the study period (14 days prior to symptom onset for the case and same time period for control)?  
1 yes 0 no 9 unknown *if no, go to question 2.22*

2.21.1 If yes, what species of animals? (circle all that apply)

Camel Goat Sheep Horse Cattle

**The next 4 questions are about what you have generally done over the last six months.**

2.22 During the last six months, how often on average have you been on a farm that housed livestock such as camels, sheep, goats, cattle, horses?

Daily

At least once per week

At least once per month but less than once per week

At least several times in the six months but less than once per month

Never

Unknown

2.23 During last six months, how often on average have you been in a live animal market that sold livestock such as camels, sheep, goats, cattle, horses?

Daily

At least once per week

At least once per month but less than once per week

At least several times in the six months but less than once per month

Never

Unknown

2.24 During last six months, how often on average have you had direct physical contact with livestock such as camels, sheep, goats, cattle, horses?

Daily

At least once per week

At least once per month but less than once per week

At least several times in the six months but less than once per month

Never *if never, go to question 2.26*

Unknown

2.25 If you have had direct physical contact with livestock such as camels, sheep, goats, cattle, horses in the last six months, which animal did you have contact with (mark all that apply)?

Camel      Goat      Sheep      Horse      Cattle

**FOOD EXPOSURES**

**The following series of questions are focused on food exposures in the 14 days prior to the case-patient's symptom onset** (or the same dates as the 14 days before onset in the matched case, if interviewee is a control).

2.26 In the 14 days prior to your illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control) did you eat any of the following food items uncooked:

2.26.1 Fresh fruits? 1 yes    0 no    9 unknown if yes, list fruits: \_\_\_\_\_

\_\_\_\_\_

2.26.2 Dried fruits? 1 yes    0 no    9 unknown if yes, list fruits: \_\_\_\_\_

\_\_\_\_\_

2.26.3 Raw dates? 1 yes    0 no    9 unknown

2.26.4 Vegetables? 1 yes    0 no    9 unknown if yes, list vegetables: \_\_\_\_\_

\_\_\_\_\_

2.27 In the 14 days prior to your illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control) did you drink fresh (i.e. not canned or processed) fruit or vegetable juices? 1 yes    0 no    9 unknown *if no, go to question 2.28*

2.27.1 Please specify type: \_\_\_\_\_

2.28 In the 14 days prior to your illness (or the same dates as the 14 days before onset in the matched case, if interviewee is a control) did you eat any uncooked or partially cooked meat?

1 yes    0 no    9 unknown *if no, go to question 2.29*

2.28.1 Specify type of animal consumed: \_\_\_\_\_

2.28.2 Specify body part consumed (e.g., flesh, blood, etc.): \_\_\_\_\_

2.28.3 Did you eat any uncooked animal liver? 1 yes    0 no    9 unknown

2.29 Did you personally cook or otherwise handle raw meat in the study period?  
1 yes 0 no 9 unknown *if no, go to question 2.30*

2.29.1 Specify type of meat: \_\_\_\_\_

2.30 Did you drink any unpasteurized milk or milk products (including yoghurt or cheese) during the study period? 1 yes 0 no 9 unknown *if no, go to question 2.31*

2.30.1 What products did you consume? \_\_\_\_\_

2.30.2 Specify from what kind of animal (cow, goat, camel, sheep, horse): \_\_\_\_\_

2.31 Did you drink any camel urine during the study period? 1 yes 0 no 9 unknown

2.32 Did you chew swack during the study period? 1 yes 0 no 9 unknown

**The next questions are collecting food consumption habits over a longer period of time.**

2.33 During the last six months, how often on average did you consume any of the following products:

	Daily	At least once per week	Less than once per week but more than once per month	Less than once per month but several times in the six months	Never	Unknown	Type
Fresh fruit							
Dried fruits							
Fresh salad							
Unpasteurized milk products							
Raw meat products							
Other animal products							

**SECTION 3 BACKGROUND SUBJECT INFORMATION AND MEDICAL HISTORY**

3.1. What is the highest education level you finished?

None or less than primary

Primary school (6 years or less)

High school graduate

University graduate

Graduate school degree

3.2. What is your approximate household income level?

Level 1 (enter here after consultation with coordinating committee)

Level 2 (enter here after consultation with coordinating committee)

Level 3 (enter here after consultation with coordinating committee)

### Personal living situation

3.3. What is your current marital status? (circle one)

Single Married

Divorced Widowed

3.4. How many people live in your household with you (one household is defined as sharing a single kitchen)?

3.4.1. Children aged less than 18 years old: \_\_\_\_\_

3.4.2. Adults aged 18 years and older: \_\_\_\_\_

3.5. What type of dwelling do you currently live in? (circle one)

apartment house villa other (please specify: \_\_\_\_\_)

3.6. Were you exposed to any sand storms during the study period? 1 yes 0 no 9 unknown

### BACKGROUND MEDICAL HISTORY

The following questions are addressing your background medical history and other background questions.

3.7. Smoking

3.7.1. Do you currently smoke tobacco (e.g., cigarettes, cigars, shisha)?

Daily -----> go to question 3.7.1.1

Less than daily -----> go to question 3.7.1.1

Not at all -----> go to question 3.7.3

Don't know -----> go to question 3.7.2

3.7.1.1 Do you share your tobacco (e.g., shisha)? 1 yes 0 no 9 unknown

3.7.2. Have you smoked tobacco daily in the past?

Yes-----> go to question 3.7.3

No-----> go to question 3.8

Don't know-----> go to question 3.8

3.7.3. In the past, have you smoked tobacco on a daily basis, less than daily, or not at all?

COMMENT: Interviewer, if respondent has done both "daily" and "less than daily" in the past check "daily"

Daily

Less than daily

Not at all

Don't know

3.8. Is there any hereditary disease running in your family?

1 yes 0 no 9 unknown *if no, go to question 3.9*

3.8.1. Please specify the disease(s): \_\_\_\_\_

3.9. Do you have any of the following pre-existing chronic conditions:

3.9.1. Diabetes? 1 yes 0 no 9 unknown *if no, go to question 3.9.2*

3.9.1.1. Do you use insulin: 1 yes 0 no 9 unknown

3.9.2. Asthma? 1 yes 0 no 9 unknown *if no, go to question 3.9.3*

3.9.2.1. Which of the following, if any, have been used for treatment in the last month

(circle all that apply):

Handheld Inhalers Oral medications to open airways

oral steroids Home nebulizer treatment to open airways

other (specify): \_\_\_\_\_

3.9.3. Emphysema, chronic bronchitis or other chronic lung disease besides asthma?

1 yes 0 no 9 unknown *if no, go to question 3.9.4*

3.9.3.1. Are medications used for treatment? 1 yes 0 no 9 unknown

*if no, go to question 3.9.4*

3.9.3.2. Name medications: \_\_\_\_\_

3.9.4. Kidney failure? 1 yes 0 no 9 unknown *if no go to question 3.9.5*

3.9.4.1. Are you currently receiving dialysis? 1 yes 0 no 9 unknown

3.9.5. Chronic liver disease such as hepatitis? 1 yes 0 no 9 unknown

3.9.6. Heart disease? 1 yes 0 no 9 unknown

*if no, go to question 3.9.7*

3.9.6.1. Please specify what heart disease you have \_\_\_\_\_

3.9.6.2. Describe your specific condition: \_\_\_\_\_

3.9.7. History of cancer treatment in the last year? 1 yes 0 no 9 unknown

*if no, go to question 3.10*

3.9.7.1. Please indicate the type of cancer: \_\_\_\_\_

3.9.7.2. Circle all treatments received:

Chemotherapy therapy Radiation

Other, please specify \_\_\_\_\_

3.9.8. Blood disorder such as chronic anemia? 1 yes 0 no 9 unknown  
*if no, go to question 3.10*

3.9.8.1. Describe specific condition: \_\_\_\_\_

3.10. Are you currently taking corticosteroids? 1 yes 0 no 9 unknown

3.11. Do you take medications regularly? 1 yes 0 no 9 unknown *if no, go to question 3.12*

3.11.1. What medications do you regularly take? (list) \_\_\_\_\_

3.12. Have you taken any traditional medications in the study period? 1 yes 0 no 9 unknown

3.12.1. Which traditional medications? \_\_\_\_\_

3.13. If female, are you currently pregnant? 1 yes 0 no 9 unknown

3.13.1. How many weeks? \_\_\_\_\_ weeks