

Using the MERS-CoV Investigation Protocols


Unity Studies

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Presented by: Anna Funk, PhD

A large, stylized green globe with a grid pattern is positioned on the left side of the slide. The word "Contents" is written in white text on a semi-transparent green rectangular background that is placed over the globe.

Contents

- Choosing an investigation type
 - Introduction to protocol structure
 - Adapting the study protocol for local settings and varying contexts
 - Other considerations
- 
- A decorative graphic consisting of several blue dashed line segments arranged in a curved, upward-sloping path is located in the bottom right corner of the slide.

Case Study

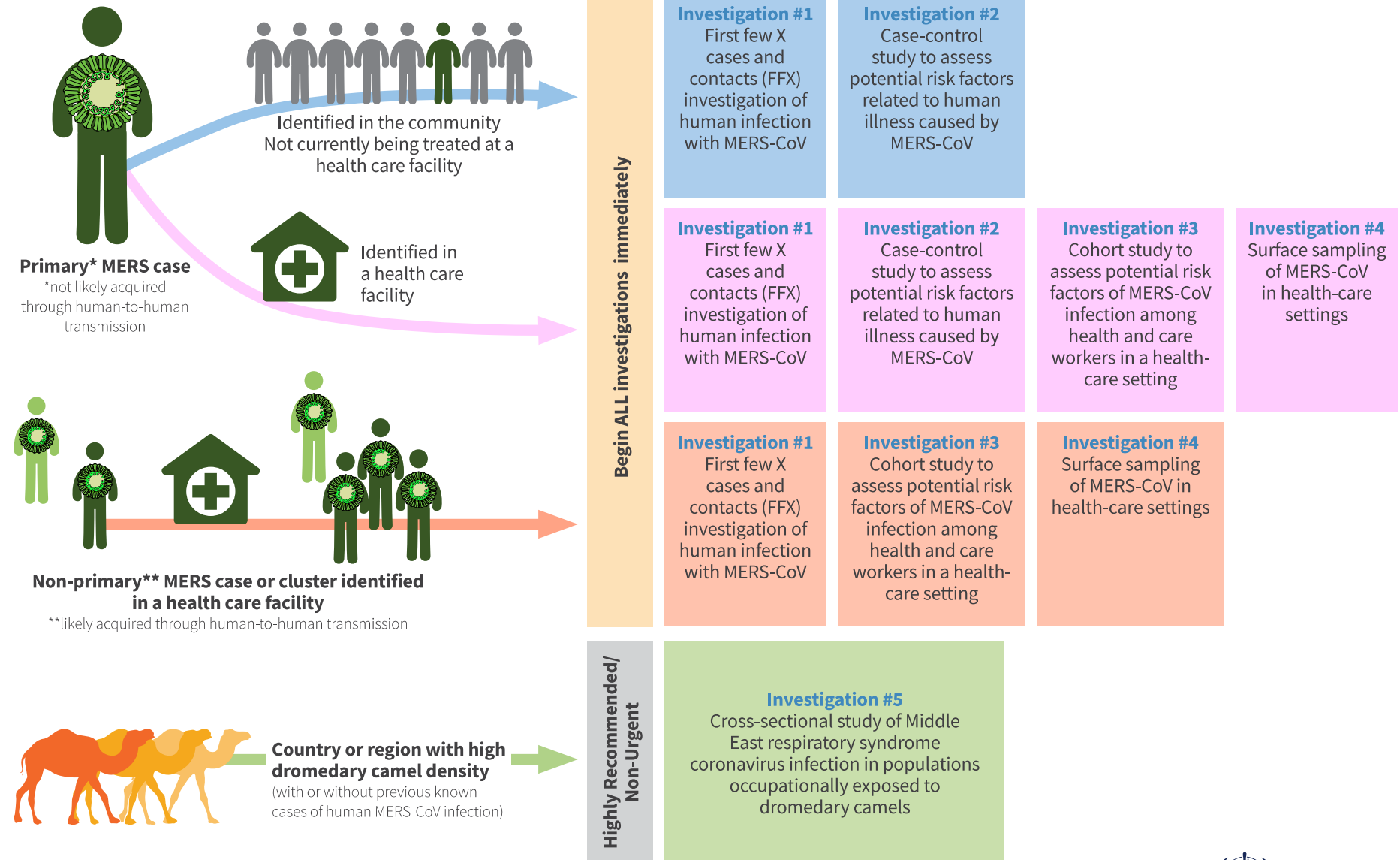
Yesterday, a 50-year-old woman with severe respiratory illness was admitted to the hospital we work at. Testing has just (November 5th) come back positive for MERS-CoV.

Appropriate infection prevention and control (IPC) measures are immediately implemented as per standard procedure.

Myself (a clinician) and you (another clinician), as well as an IPC specialist and an epidemiologist, want to use this opportunity to better understand risk factors for transmission of MERS-CoV in healthcare settings.

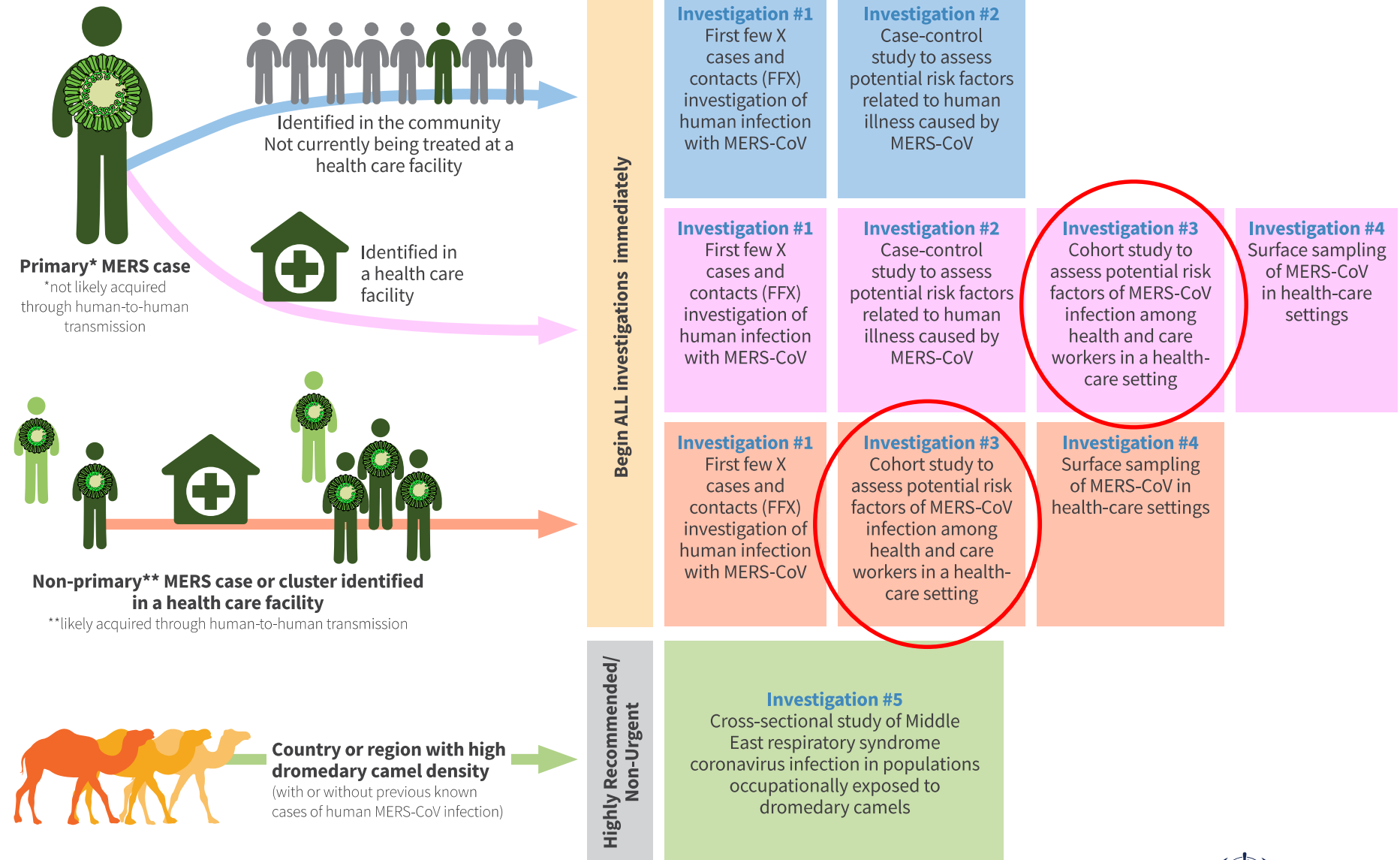
Choosing an investigation

Figure 1. MERS Case Investigation and Surveillance Protocols



Choosing an investigation

Figure 1. MERS Case Investigation and Surveillance Protocols



Protocol Summary → found on page ix of this protocol

Choosing an investigation

Cohort study to assess potential risk factors of MERS-CoV infection among health and care workers (HCW) in a health-care setting	
Study population	Health and care workers (HCW) in a health-care setting in which a patient with a laboratory-confirmed MERS-CoV infection is receiving care, who have any possible contact to the MERS-CoV positive case, regardless of symptoms
Potential output and analysis	Understand transmissibility in health-care settings through estimating: <ul style="list-style-type: none">• secondary infection rate (SIR) among HCW;• range of clinical presentation and risk factors for infection;• serological response following MERS-CoV infection• identification of possible routes of transmission
Study design	Cohort study (protocol is written as a prospective cohort, but this study is likely to be conducted as both a prospective and/or retrospective cohort)
Study duration	From the day that the investigation (data collection) begins, data and specimen collection is complete 21-28 days after the last MERS-CoV-positive contact (this could be the original HCW case, or a secondary HCW case).
Information and specimens to be obtained from participants	<p>Data: Multiple questionnaires at baseline collect information such as: clinical symptoms; exposures in the health-care facility, including contact with confirmed case(s); use of personal protective equipment, other epidemiological data. HCW also complete daily symptom diaries throughout follow-up.</p> <p>Specimens:</p> <ul style="list-style-type: none">• Multiple serum samples per participant• Respiratory specimen(s) to diagnose current MERS-CoV infection if a participant is symptomatic

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Protocol structure and adaptation

Implementation tips are provided in boxes throughout the document.

This is a *protocol template* – the user should read through the template and guidance and then modify (and make choices about) the methods according to the local context in which this study will be carried out. If being adapted for use as the investigation protocol, the user should remove any non-relevant sections and modify the language appropriately (e.g. Change the phrase “Investigators should create a detailed map(s) of the facility; within this map(s) and its legend(s), the following details should be included:...” to “We have created a detailed map of facility X, where the MERS-CoV positive patient was identified on [date], this map includes the following details:...”). Background information referenced in this document should be checked for updates by investigators at the time of protocol implementation.

- Modify language – reflect an operational protocol rather than a guidance
- Adjust for your context
- Remove irrelevant sections & add required sections or further methods of interest

Protocol structure and adaptation

1. Scientific background and rationale

- Is it up-to-date?
- Add current situation, regional details
- Objectives to add or remove?

2. Methods

- Specify actual setting, timing, population, estimated number of persons, laboratory tests being used, etcetera
- Adapt 'ideal' methods to situation (e.g. retrospective aspects)

3. Statistical analysis

- This section contains guidance. Use finalized study methods to create a detailed statistical analysis plan with a trained statistician and/or epidemiologist – prior to the study start!

4. Dissemination of results

→ Use prompts and ideas in this section to create a dissemination plan

5. Composition of study team

→ Based on finalized study plan, who else is needed on the team?

→ Include collaborators (e.g. statisticians) from earliest stages

Protocol structure and adaptation

Annex 2: Questionnaires

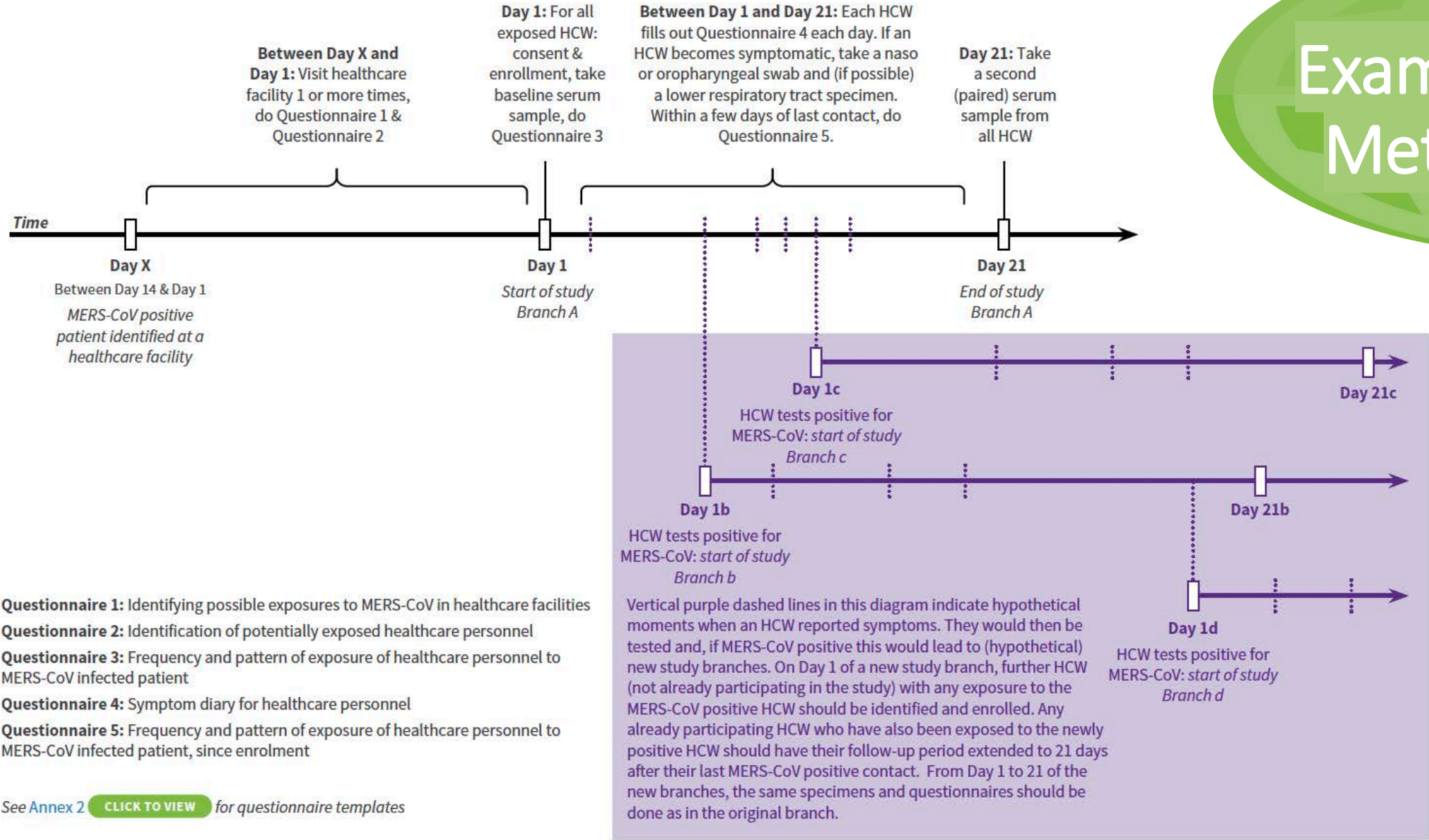


Questionnaire 1: Identification of possible exposures to MERS-CoV in a health-care facility

→ Add and/or remove questions as per final study objectives (and feasibility, appropriateness)

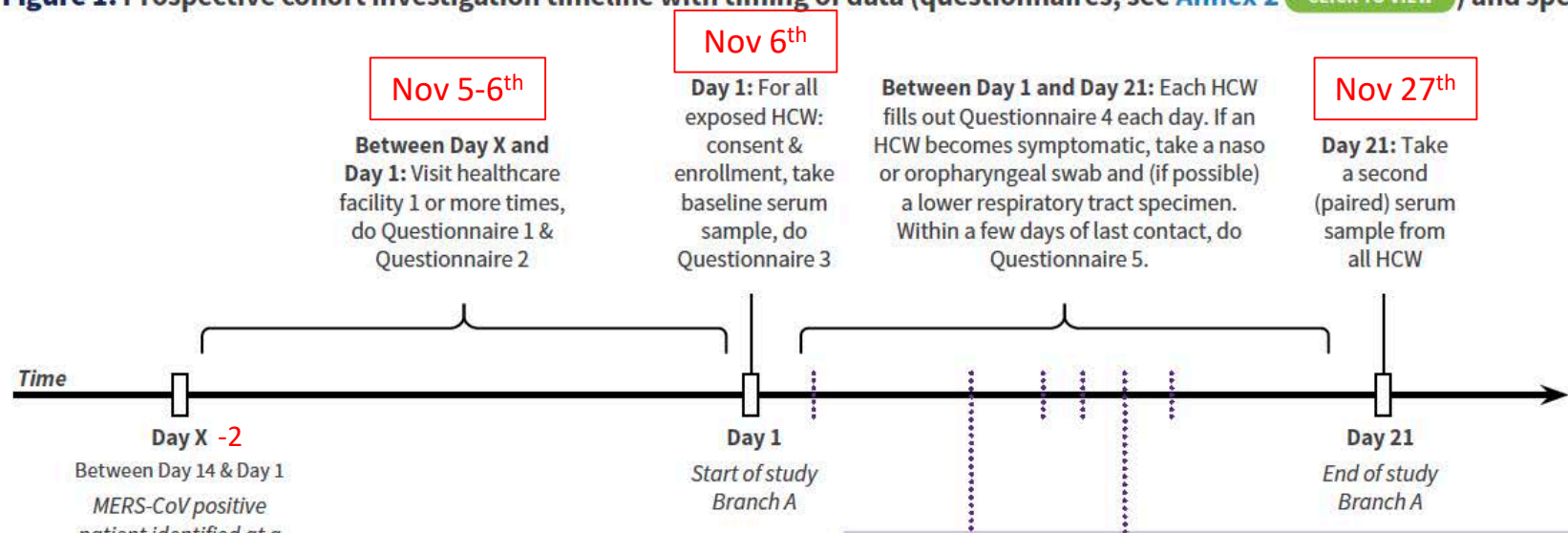
→ Adapt response options to local context

Figure 1: Prospective cohort investigation timeline with timing of data (questionnaires, see [Annex 2](#) [CLICK TO VIEW](#)) and specimen collection



Example 1: Methods

Figure 1: Prospective cohort investigation timeline with timing of data (questionnaires, see [Annex 2](#) [CLICK TO VIEW](#)) and specimen collection



Example 1: Methods

- Questionnaire 1:** Identifying possible exposures to MERS-CoV in healthcare facilities
- Questionnaire 2:** Identification of potentially exposed healthcare personnel
- Questionnaire 3:** Frequency and pattern of exposure of healthcare personnel to MERS-CoV infected patient
- Questionnaire 4:** Symptom diary for healthcare personnel
- Questionnaire 5:** Frequency and pattern of exposure of healthcare personnel to MERS-CoV infected patient, since enrolment

See [Annex 2](#) [CLICK TO VIEW](#) for questionnaire templates

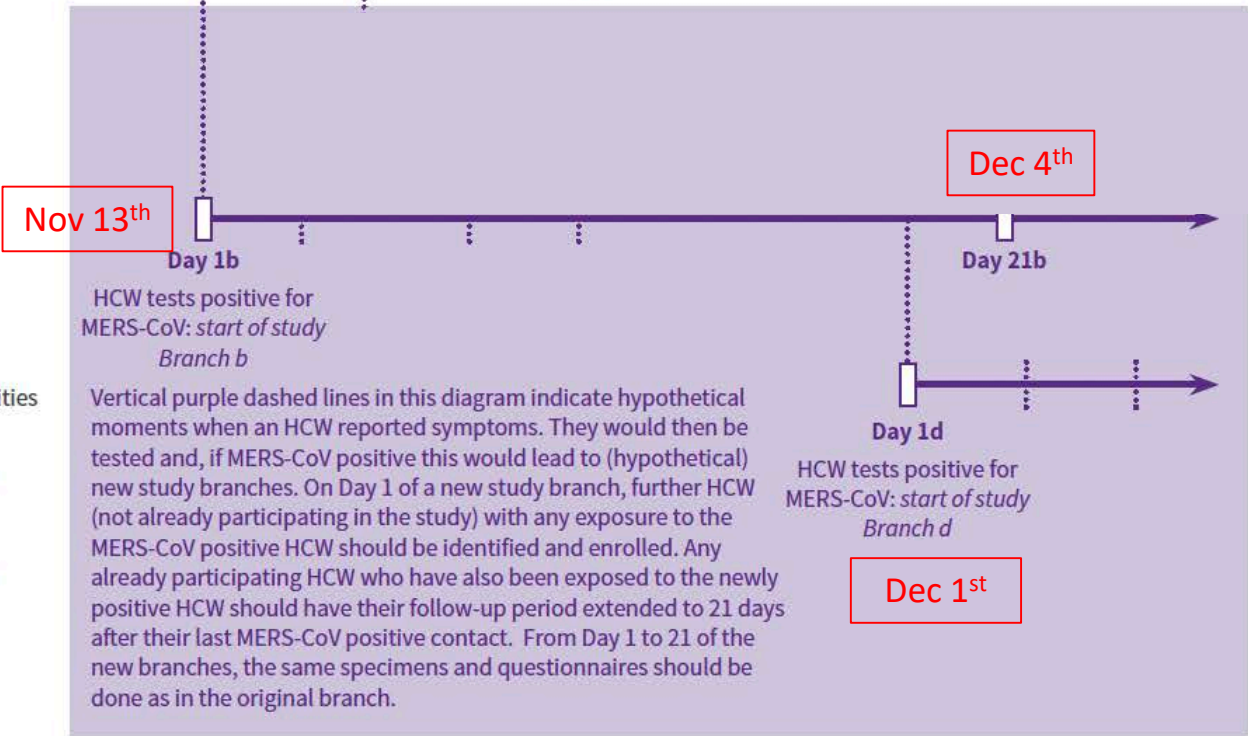
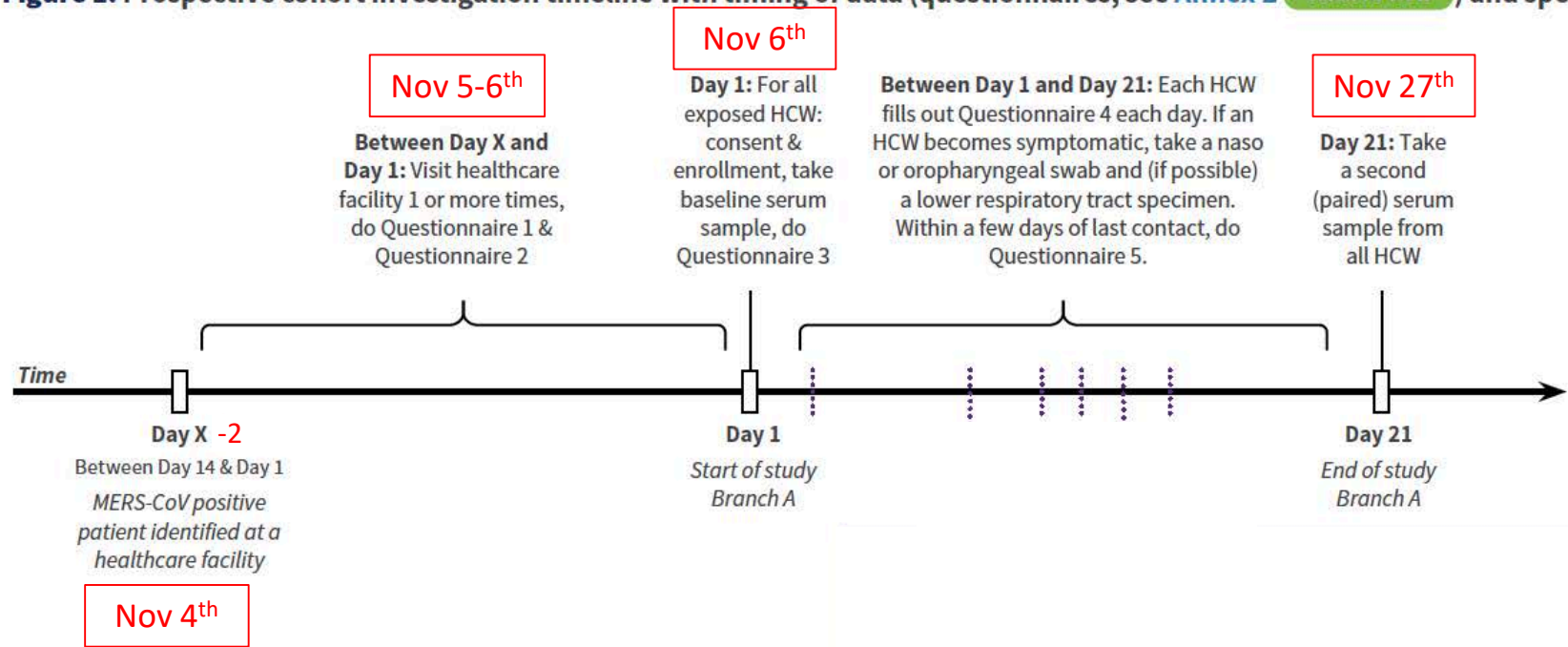


Figure 1: Prospective cohort investigation timeline with timing of data (questionnaires, see [Annex 2](#) [CLICK TO VIEW](#)) and specimen collection



Example 1: Methods

Questionnaire 1: Identifying possible exposures to MERS-CoV in healthcare facilities

Questionnaire 2: Identification of potentially exposed healthcare personnel

Questionnaire 3: Frequency and pattern of exposure of healthcare personnel to MERS-CoV infected patient

Questionnaire 4: Symptom diary for healthcare personnel

Questionnaire 5: Frequency and pattern of exposure of healthcare personnel to MERS-CoV infected patient, since enrolment

See [Annex 2](#) [CLICK TO VIEW](#) for questionnaire templates



Example 2: specimen collection and testing

Table 1: Type of specimen to be collected and timing of collection

Specimen collection	Timing of collection
Serum sample (required)	Baseline (Day 1): at the time of recruitment - as soon as possible after exposure. Day 21 to 28 (once): collection of a second ('paired') serum sample from the same individuals who had baseline samples taken. If one HCW has multiple MERS-CoV positive contacts, this should be conducted repeatedly, once during the 21 to 28 days following each contact.
Combined nasopharyngeal and oropharyngeal swabs (if HCW symptomatic)	Day X (≤21 days since exposure): if HCW contact experiences any symptoms during follow-up (within 21 days of exposure to a MERS-CoV positive case) a respiratory specimen should be collected and tested as soon as possible
Lower respiratory specimen (optional)	Day X (≤21 days since exposure): if HCW contact experiences any symptoms during follow-up (within 21 days of exposure to a MERS-CoV positive case) a lower respiratory sample can also be collected as soon as possible

Implementation tip For serum samples, the specific volume of blood is to be determined by study personnel, bearing in mind that the minimum required volume is 5 mL.

Some serologic assays or full genome sequencing may not be possible to perform in country, therefore specimens should be aliquotted so that specimens remain in country and only aliquots are sent to a reference laboratory.

Example 2: specimen collection and testing

Table 1: Type of specimen to be collected and timing of collection

Specimen collection	Timing of collection
Serum sample (required)	Baseline (Day 1): at the time of recruitment - November 6 th and Day 1 of future study branches Day 21 (Nov 27*) : collection of a second ('paired') serum sample from the same individuals who had baseline samples taken. If one HCW has multiple MERS-CoV positive contacts, this will be conducted repeatedly, at 21 days following each contact. * and Day 21 of any further study branches
Combined nasopharyngeal and oropharyngeal swabs (if HCW symptomatic)	Day X (≤21 days since exposure): if HCW contact experiences any symptoms during follow-up (within 21 days of exposure to a MERS-CoV positive case) a respiratory specimen will be collected and tested within 24 hours

In this study, 10ml of blood will be collected for each HCW participant at Day 1 (Nov 6th for those in the initial study branch and the first day of any new study branch) of the study as well as on Day 21 (Nov 27th, and subsequent 'Day 21' dates for further study branches). The serological assay being used is Euroimmun. To add more details later.

Serum samples will be processed immediately; if not possible, they will be stored at a temperature of 2 to 8°C for no more than 48 hours. Positive nasopharyngeal and oropharyngeal swabs will be sent to XXX? for genome sequencing.

*Confirm
highlighted points
with Julie in lab
asap*

Example 3: Questionnaires

Questionnaire 3: Frequency and pattern of exposure of health and care workers (HCW) to a MERS-CoV infected patient (continued)

3. Participant demographic information and role within health-care facility

Sex	<input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Not known <input type="checkbox"/> Prefer not to answer
Age (years, months)	____ years ____ months <input type="checkbox"/> Unknown
Nationality	
Ethnicity [optional, at discretion of study investigators. If using, please input checkbox style options with relevant ethnicities in the right-hand column]	
Country of residence	
Highest level of education <i>finished</i>	<input type="checkbox"/> None or not finished primary school <input type="checkbox"/> Primary school (approximately 6 years) <input type="checkbox"/> Secondary school (total of approximately 12 years) <input type="checkbox"/> College or university undergraduate degree or postsecondary diploma <input type="checkbox"/> Graduate studies (e.g. Masters, PhD)
Does the participant live in a shared living facility (e.g. dormitory) with other HCW?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown If Yes, provide general address information for living facility (e.g. building block number, etc) If Yes, are there camels present in or close to the living facility? <input type="checkbox"/> Yes <input type="checkbox"/> No

Example 3: Questionnaires

Questionnaire 3: Frequency and pattern of exposure of health and care workers (HCW) to a MERS-CoV infected patient (continued)

3. Participant demographic information and role within health-care facility

Sex	<input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Not known <input type="checkbox"/> Prefer not to answer
Age (years, months)	____ years ____ months <input type="checkbox"/> Unknown
Nationality	<input type="checkbox"/> Country 1 <input type="checkbox"/> Country 2 <input type="checkbox"/> Other (specify) _____
Country of residence	_____
Highest level of education <i>finished</i>	<input type="checkbox"/> None or not finished primary school <input type="checkbox"/> Primary school (approximately 6 years) <input type="checkbox"/> Secondary school (total of approximately 12 years) <input type="checkbox"/> College or university undergraduate degree or postsecondary diploma <input type="checkbox"/> Graduate studies (e.g. Masters, PhD)
Does the participant live in a shared living facility (e.g. dormitory) with other HCW?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown If Yes, provide general address information for living facility (e.g. building block number, etc) If Yes, are there camels present in or close to the living facility? <input type="checkbox"/> Yes <input type="checkbox"/> No



Other considerations for protocol use

External support – within country, international

- Data pooling (e.g. case control study)
- Contact WHO (MERSHQ@who.int) to inquire about support with genomic analysis and other laboratory support, data sharing, and statistical support

Linked Investigations

- Check for other MERS Unity Study protocols
- Example: Protocol 2 (Case-control investigation) and Protocol 4 (Environmental sampling) would compliment Protocol 3 (Health and care worker cohort investigation)

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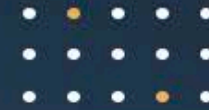
**MERS-CoV
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Thank you!

<https://www.who.int/initiatives/mers-cov-investigations-and-studies>



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& PANDEMIC
PREPAREDNESS
& PREVENTION**