Table 3 **Specific public health questions needing answered for the novel coronaviruses – the what, why and how**

	What do we need to know?	Why do we need to know it?	How will we find out?	Types of studies and notes
1.	Where geographically are the human infections occurring worldwide?	Determining the level of threat: is this an infection only occurring in 1 locality in 1 sub-region or is it more widespread? Alternatively is this an older infection that has been around some time and simply unrecognised? To inform decisions on which patients to test among those who come to Europe with respiratory infections or who subsequently develop respiratory infections within a certain time	Case-finding virologic testing of people fitting the case definition for severe cases and others; Prospectively, among the people fitting the Persons Under Investigation (PUI) definitions in any clusters and outbreaks of severe respiratory disease	Applied epidemiological and laboratory research studies in a number of countries testing patients with unexplained severe lower respiratory tract infection, either using retrospective contemporaneous archives of suitable stored specimen or as prospective planned studies. The ECDC/WHO laboratory survey of European Union countries gives a mechanism by testing people fitting the PUI-with symptoms definition but need to distinguish the different groups therein: • People with severe disease + geographical risk • People with severe disease without geographical risk • Exposed health-care workers Question: Do we need to know the animal reservoir? Question: Have Koch's postulates been demonstrated? Need to think beyond the Middle East and consider the trade/people movements from the Middle East especially migrant workers from South Asia who work in the Middle East
			Serological surveys to agreed protocols with local adaptations [21,22,24].	It should be possible to develop the tools but the importance will be validation and quality assurance from the CONSISE and earlier experience. It will be especially important to include validation with 'sticky' sera from middle East countries remembering the initial HIV serological experience where tests developed and validated in one region lost specificity in another setting[a]
	What is the reservoir of the virus infection?	As for point 1	Environmental and animal surveillance and testing around sporadic unexplained cases	Environmental and animal studies
2.	The estimated incubation period (from exposure to symptoms) and serial interval?	Informing on who to test: "all people developing severe acute respiratory infections within a certain number days of coming from countries X, Y, Z" Determining potential for explosive spread. Comparing infections like influenza (short incubation period and serial interval: impossible to control) and SARS and smallpox (long incubation period and serial interval: possible to control)	Observing and investigating clusters to agreed protocols with local adaptations [21,22].	
3.	How infectious are these cases and what are the sources of infectious virus?	Informing on infection control measures and their stringency	Reviewing the outcome of the case finding around the recognised cases especially in health care staff and household/family contacts	In SARS most cases did not transmit to secondary cases, but 10%–20% transmitted to many secondary (and higher order) cases: super-spreading events [7,19,20].
4.	When are these cases infectious to others	Informing on the duration of infection control measures and the stringency of control measures, as well as possible advice on quarantine of exposed persons	Studies of when and at what levels are the viruses detectable compared to the symptoms and to default cases of influenza and SARS	There are some data from this from Germany (Robert Koch Institute). Note: a positive feature of SARS was that the cases were really not infectious before developing symptoms (c.f. influenza) making quarantine and early isolation of cases especially effective [5].
5.	Are there any super-spreading events?	Informing on infection control measures and the stringency of control measures	Reviewing the outcome of the case finding around the recognised cases especially in health care staff and household/family contacts	Watch for these especially in health-care settings. What actually happened in the clusters in Jordan and Saudi Arabia?
6.	What do cases look like? Who are the high risk groups?	Informing on who to test and understanding the scope of illness manifestations; Understanding the frequencies and severity of organ involvement and secondary bacterial infections to assist in clinical management	Review of the confirmed cases; Serological testing of contacts, especially those with milder symptoms, and virologic testing of contacts exposed in future events [21].	Note: a problem with SARS was that infectious cases were not always recognised in a timely manner. Some were inapparent for example in those hospitalised for other reasons (e.g. post major surgery, people with multiple pathology). In a sense this has happened in the cases that were imported into Germany and the United Kingdom without thinking they might represent serious imported infections.
7.	How best to manage and treat the patients	To optimise care and to avoid doing harm from certain medical interventions	Preparing and agreeing protocols, and those caring for patients applying these and sharing experience and results in real time	Suitable protocols have now been agreed between ISARIC members and approved by WHO [25].
8.	How extensive is patient movement from the Middle East to Europe?	Looking for cases and determining which clinicians to inform; Considering the risk to those caring for patients in transit	WHO Member States asking the referral centre; Work with people who look at transport trends and patient export importations	Note for the cases that came to other countries the long time between the arrival and considering testing for novel infections.

[a]When HIV serological tests validated in Europe and North America were applied in Africa in the 1980s without local validation and the consequent publication of analyses suggesting substantial levels of population prevalence in East Africa which were due to cross-reaction with other antibodies (to malaria) [26].

ECDC – European Centre for Disease Prevention and Control.

WHO – World Health Organization.

CONSISE – consortium for the standardization of influenza seroepidemiology.

HIV – human immunodeficiency virus.

SARS – severe acute respiratory syndrome.

ISARIC – International Severe Acute Respiratory and Emerging Infection Consortium.