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Human Animal Infections and Risk Surveillance (HAIRS) group

Qualitative assessment of the risk that Crimean-Congo haemorrhagic fever (CCHF) presents to the UK population

Version	2.0
Date	14 December 2018

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About the Human Animal Infections and Risk Surveillance group

This document was prepared by Public Health England (PHE) on behalf of the joint Human Animal Infections and Risk Surveillance (HAIRS) group.

This cross-government group is chaired by the PHE Emerging and Zoonotic Infections section. The HAIRS group acts as a forum to identify and discuss infections with potential for interspecies transfer (particularly zoonotic infections).

Members include representatives from PHE, Department for the Environment, Food and Rural Affairs (Defra), Department of Health and Social Care (DHSC), Animal and Plant Health Agency, Food Standards Agency, Public Health Wales, Welsh Government, Health Protection Scotland, Scottish Government, Public Health Agency of Northern Ireland and the Department of Agriculture, Environment and Rural Affairs for Northern Ireland.

Qualitative risk assessment for Crimean-Congo haemorrhagic fever (CCHF) in the UK population

Date of this assessment	14 December 2018
Version	2
Reason for update	A further locally acquired CCHF case described in Spain and detection of an adult *Hyalomma rufipes* tick on a horse with no history of travel in the UK in 2018
Completed by	HAIRS Secretariat and members
Date of previous risk assessment	28 April 2017
Date of initial risk assessment	28 April 2017
External experts consulted	Kayleigh Hansford, PHE

Information on the risk assessment processes used by the HAIRS group can be found at https://www.gov.uk/government/publications/hairs-risk-assessment-process

SUMMARY OF RISK ASSESSMENT FOR CCHF IN THE UK POPULATION		
Note: This risk assessment was completed to assess the current risk that CCHF presents to the UK population		
Overview	Crimean-Congo haemorrhagic fever (CCHF) is not present in the UK nor are there any established populations of *Hyalomma* ticks, the vector of CCHF virus (CCHFV). On 31 August 2016 the Autonomous Community of Madrid, Spain, reported 2 cases of infection with CCHFV. The primary case was a 62 year old man whose exposure to CCHF was in the countryside of the province of Ávila. A secondary case occurred in a healthcare worker who attended the primary case during their ICU admission. In 2018, a third autochthonous case was reported following a tick-bite in the autonomous community of Extremadura, on the Spanish-Portuguese border. These were the first autochthonous clinical cases of CCHF in Spain and in South-Western Europe. Ticks in Spain had first been found to carry CCHF virus in 2010, therefore the occurrence of CCHF cases there was not an unexpected event. A *Hyalomma rufipes* male was detected in the UK during September 2018 on a horse with no history of travel. This suggests possible moulting for the first time of an imported nymph (via a migratory bird) to an adult, despite UK climate constraints previously considered to be a limiting factors for tick development.	
Assessment of the risk of infection in the UK	**Probability**	Very Low
	Impact	Low/Very Low
Level of confidence in assessment of risk	High	
Action(s)/ Recommendation(s):	Monitoring for new evidence as to the presence of *Hyalomma* species in the UK should be continued. Enhanced surveillance should be conducted in 2019 to monitor for any evidence of continued activity of adult ticks that may now be present in the UK following importation as nymphs via migratory birds during the unusually warm weather during the summer of 2018.	

Assessing the risk to the UK population from new and emerging infections

Step 1: Assessment of the probability of infection in UK population

The likelihood of an infectious threat causing infection in the UK human population. Where a new agent is identified there may be insufficient information to carry out a risk assessment and this should be clearly documented.

QUESTION	OUTCOME	QUALITY OF EVIDENCE
i) Is this a recognised human disease?	**Yes**	**Good**

Yes. CCHF was first described in the Crimea in 1944, where an outbreak of an acute febrile illness with a high incidence of shock and bleeding occurred among soldiers and agricultural workers. In 1969, it was recognised that the virus causing this disease was identical to a virus that had been isolated from a child in the Congo in 1956 (1). Humans are the only animal species to manifest clinical CCHF disease (2).

CCHF virus (CCHFV) is a member of the family Bunyaviridae, in the genus Nairovirus (1). CCHFV exhibits great sequence diversity. From analysis of its S, L and M segments, phylogenetic trees have been constructed containing lineages (or genotypes, Gt) I-VI. CCHFV is thought to have originated in Africa 1000-5000 year ago, although strain Ap92 found in Greece is also considered an ancient lineage. The virus was introduced to Central and South Asia in the Middle Ages, but spread into Europe is considered a more recent event, likely via a single introduction into central Russia. Westward spread has since taken place, with further spread considered likely (3, 4).

CCHF is both the most widespread tickborne viral infection of humans, and the most widespread of the haemorrhagic fevers. It is endemic in many countries in Africa, the Middle East, Eastern Europe and Asia, with the distribution of cases corresponding to those areas where the tick vector(s) is found (2). The nearest country within eastern Europe which regularly reports cases is Kosovo. There have been case reports, virological or serological evidence of human infection in at least 62 countries (2, 5).

Spain reported its first autochthonous cases in August 2016, the first in Western Europe. One was a fatal case which followed a tick-bite acquired in the Castilla-Leon region (northwest Spain) and the second a nosocomial transmission which occurred during care of the first case (6, 7). A subsequent fatal case was reported in August 2018 (8). While this case was also diagnosed in the Castilla-Leon region, the patient reported a recent tick bite acquired during a hunting trip to the autonomous community of Extremadura, on the Portuguese border. Spain first reported CCHFV infected ticks in 2010 (7, 9, 10), in areas including the Extremadura region (11).

CCHF disease has varying manifestations from asymptomatic infection through to fulminant haemorrhage. The incubation period

varies by mode of transmission but is always less than 14 days. The onset of symptoms is sudden with fever, severe headache, dizziness, photophobia, malaise, myalgia and back pain. Sore throat, nausea, vomiting and diarrhoea may also feature. Hepatomegaly and lassitude develop after 2-4 days (1, 12, 13). The haemorrhagic forms of the disease are more diverse that any of the other viral haemorrhagic fevers, starting with a petechial rash and progressing through extensive bruising and cutaneous ecchymoses (bleeding under the skin), to excessive bleeding (13). Cerebral haemorrhage has been described (14). In fatal cases, death occurs from haemorrhage, multi-organ failure and shock, usually between days 5 and 14 of illness (1). Reported overall case fatality rates have varied from 5% to more than 40%, though this disparity is likely skewed by small sample sizes and failure to detect and report less severe cases (1).

ii) Is there zoonotic or vector borne spread?	**Yes**	**Good**

Yes. CCHF is maintained in several ixodid (hard) tick genera and these are responsible for spreading the virus to a wide range of wild and domestic animals. In these mammals, illness does not occur but there is a transient viraemia, for up to 15 days (15). Some mammals and probably some avian species act as amplifying hosts that can subsequently infect ticks feeding on them (1, 16).

Human disease from an animal source follows exposure to blood and body fluids of infected animals (particularly livestock), via tick bites, or following contamination due to crushing a tick (1, 12).

While CCHFV has been detected in many tick species, only some ticks have been confirmed as vectors (17). The virus is mainly transmitted by tick species of the genus *Hyalomma*. Within this genus, the main vector is *Hyalomma marginatum*, but other species also implicated as vectors include *H. rufipes.* Some species of the genus *Dermacentor* and *Rhipicephalus* have also been shown to be capable of transmitting CCHFV (16). In Spain, the CCHFV detected in the 2 human cases in 2016 was determined to correspond to the virus found previously in indigenous *H. lusitanicum.* Infected *H. lusitanicum* are more widely geographically dispersed in Spain than previously recognised (11).

Infection within generations of ticks is maintained by transstadial (between stages) and transovarial transmissions ie by both horizontal and vertical transmission. Via these routes, the virus can be maintained in ticks for extended periods even in the absence of susceptible vertebrate hosts (16).

iii) Is this disease endemic in the UK?	**No**	**Good**

No. The virus is not found in UK mammals, nor are relevant tick species found except as occasional importations via migratory birds or imported animals. A distribution map for *H. marginatum* in Europe is shown in the Appendix.

Historical tick records have demonstrated that importations of *H. marginatum* have occurred via migratory birds, although a study in 2004 (18) collected 38 ticks from more than 10,000 birds examined, and none were *Hyalomma*. A subsequent UK study carried out

in the spring of 2010 and 2011 examined 971 migratory birds of 29 species. From 53 infested birds of 9 species, 68 ticks were recovered. These were mostly (54/68, 79%) *Ixodes* species, but 14/68 (21%) were *H. marginatum.* The *H. marginatum* were found on 4 species of bird and all ticks were negative for CCHF virus by PCR (17).

As of November 2018, 6 *Hyalomma* ticks have been received by PHEs passive Tick Surveillance Scheme (TSS) (see table below).

Table 1 ***Hyalomma ticks received by the PHE passive Tick Surveillance Scheme (TSS)***

Tick species	Year	Host species	Reference
H. marginatum	2009	Horse	(19)
H. lusitanicum	2016	Dog	(20)
H. lusitanicum	2017	Human	TSS data
H. truncatum	2017	Human	TSS data
H. lusitanicum	2018	Dog	TSS data
H. rufipes	2018	Horse	TSS data

All but the *H. rufipes* were linked to overseas travel to *Hyalomma*-endemic regions. The detection of a *H. rufipes* male tick on a horse in Dorset with no history of travel was possibly the result of importation of a nymph on a migratory bird, and subsequent moulting to an adult during the unusually warm summer of 2018 (Hansford *et al*., in prep). CCHFV was not detected in this tick. To date there is no evidence that any imported *Hyalomma* ticks have led to established populations in the UK, but continued monitoring at the site where *H. rufipes* was detected in Dorset will be required to confirm this.

Travel associated human CCHF cases have very rarely been confirmed in the UK. Only 2 laboratory-confirmed clinical cases have been diagnosed; 1 imported from Afghanistan in 2012 (21) and the other from Bulgaria in 2014 (22). No onward transmission resulted from either case.

iv) Are there routes of introduction into the UK?	**Yes**	**Satisfactory**

Yes, via tick infested bird migration and animal movements. The latter route does not appear to have been commonly documented (15), although in the UK *Hyalomma* species have been detected on an imported horse (19), 2 travelling dogs (20) and a human (TSS data) (Table 1).

The risk of CCHF introduction into Western Europe, including via animal movement, has been assessed and considered a very low

risk (23).

Livestock and horses are currently freely traded between EU member states on an Intra Trade Animal Health Certificate, which has no specific requirements for CCHF freedom, no testing or tick treatment requirements. Importation from outside EU is strictly controlled, with few countries approved for trade in live ruminant livestock (206/2010/EU) and few approved bodies for trade in exotic ruminants. None of the approved third countries have endemic CCHF. Horses can however enter from many third countries, including the Middle East and North Africa and there are no tick treatment requirements.

Jameson *et al* (17) estimated that there could be tens of thousands of *H. marginatum* being imported annually via birds migrating from Africa. However, no established populations are known to have resulted from importation of this nature, and it has previously been considered that there is a climatic limitation with UK being too wet or too cold during the summer may be a limiting factor for *Hyalomma* development from nymph to adult. However, during periods with increased summer temperatures like those experienced during 2018 (24), nymphal moulting may take place in the UK, as suggested by the 2018 detection of a male *H. rufipes* on an horse in Dorset with no history of travel (TSS data). CCHFV was not detected in this tick (Hansford *et al*., in prep).

Gale *et al* modelled the absolute risk of CCHFV infections of livestock through immature ticks via migratory birds as being very low (25). An assessment of the risk ticks on northward migrating birds present to Great Britain was conducted in Spain and examined 564 birds. 65 *Hyalomma* species ticks were found on 26 birds (2.2%), none of which were positive for CCHFV (26). Tick infestation rates on birds entering UK is estimated at <1%, and such migratory birds are considered more likely to have originated in north Africa or southern Europe. The conclusion was that migratory birds present an extremely low but not negligible risk of CCHFV being introduced into Great Britain.

Hyalomma lusitanicum has been imported into the UK on 2 occasions (in 2016 and 2018) on dogs which had a recent history of travel to Portugal (20) and Spain (TSS data). Nonetheless, these importations are considered likely to be extremely rare events. The role of this tick species in transmission of CCHF is unclear, though it was found to harbour CCHFV in Spain (9).

Spur-thighed tortoises (*Testudo graeca*) imported into the UK have been found to be infested with *Hyalomma aegyptium (27)*, a species known to be infected with CCHFV in Turkey and Syria, however, this tick species is not known to be associated with virus transmission.

v)	**Are there effective control measures in place to mitigate against these?**	**No**	**Satisfactory**

This is not possible for migratory birds. There are no statutory controls for ticks on imported livestock. There are no tick controls in the PETS passport scheme. Tick treatment is voluntary but recommended to all pet owners, whether their cat or dog is travelling or

not.

The presence of a viraemia due to CCHFV in a livestock species would most likely be silent, thus importation of infected animals could pass unrecognised. However, there are controls on trading of livestock animals within/between EU members and on importation from outside the EU. Importation from many CCHFV endemic countries is illegal, due to EU legislative requirements, based on disease status of the country and the competency of the veterinary authorities.

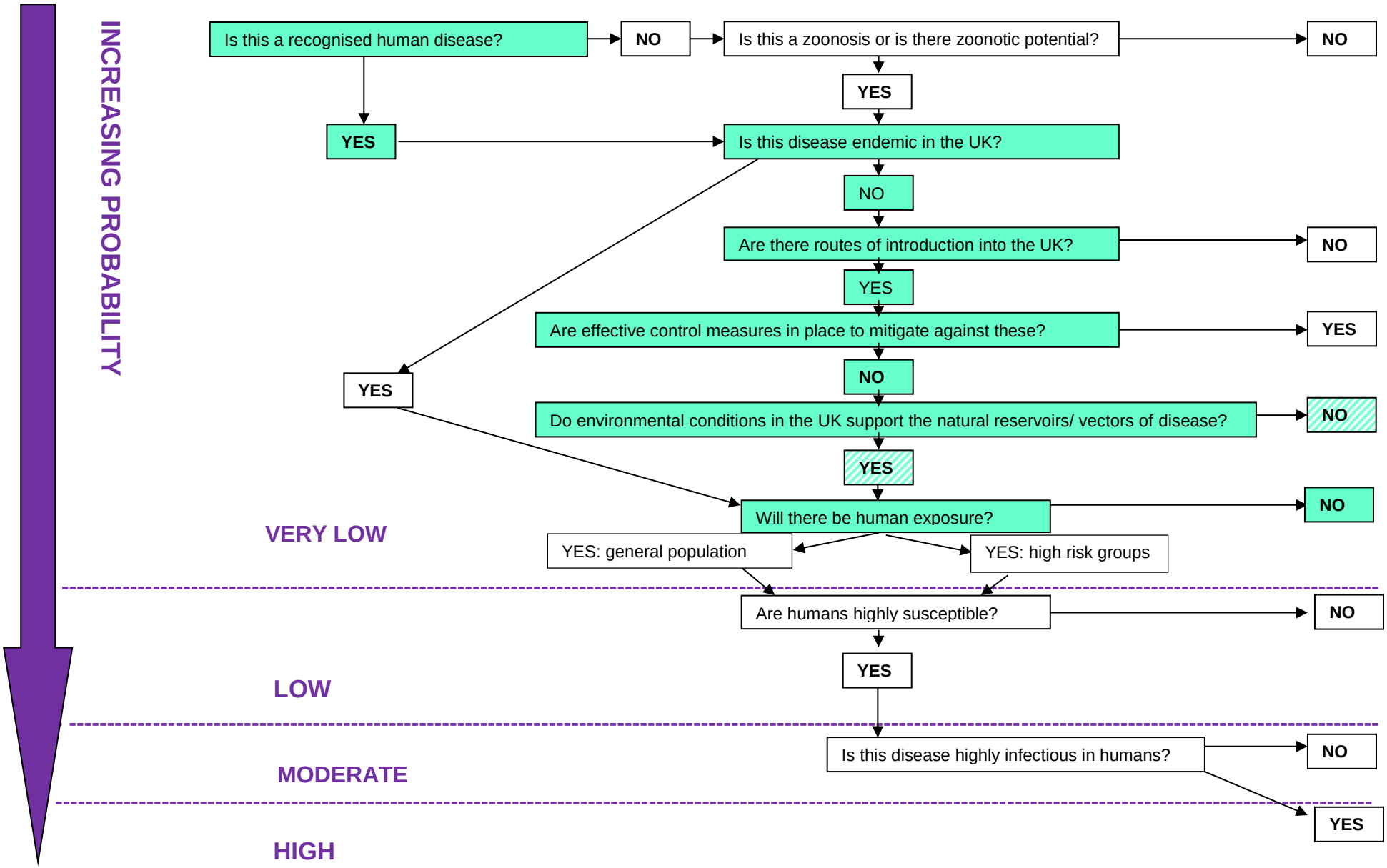
vi)	**Do environmental conditions in the UK support the natural reservoirs?**	**No/Yes**	**Poor/satisfactory**

There have been no established *Hyalomma* tick populations in the UK despite presumed frequent incursions via migratory birds. This is considered likely due to a climatic limitation with UK being too wet or too cold during the summer for *Hyalomma* development (16).The recent detection of a single *H. rufipes* male on a horse from Dorset with no history of travel suggests that increased summer temperatures (24) may support nymphal moulting in the UK following introduction via migratory birds. However the lack of occurrence of this tick in other parts of Europe with similar climatic conditions (eg see ECDC *H. marginatum* map) suggests that survival in the UK may be restricted.

vii)	**Will there be human exposure?**	**Not currently**	**Good**

Not at the current time. There is no evidence to suggest CCHFV is present in the UK and to date, only a limited number of imported *Hyalomma* species have been detected without any indication of establishment.

The **PROBABILITY** of human infection with CCHF in the UK population: **VERY LOW**


INCREASING PROBABILITY
Is this a recognised human disease?
NO
Is this a zoonosis or is there zoonotic potential?
NO
YES
YES
Is this disease endemic in the UK?
NO
Are there routes of introduction into the UK?
NO
YES
Are effective control measures in place to mitigate against these?
YES
NO
YES
Do environmental conditions in the UK support the natural reservoirs/ vectors of disease?
NO
YES
Will there be human exposure?
NO
VERY LOW
YES: general population
YES: high risk groups
Are humans highly susceptible?
NO
YES
LOW
Is this disease highly infectious in humans?
NO
MODERATE
YES
HIGH

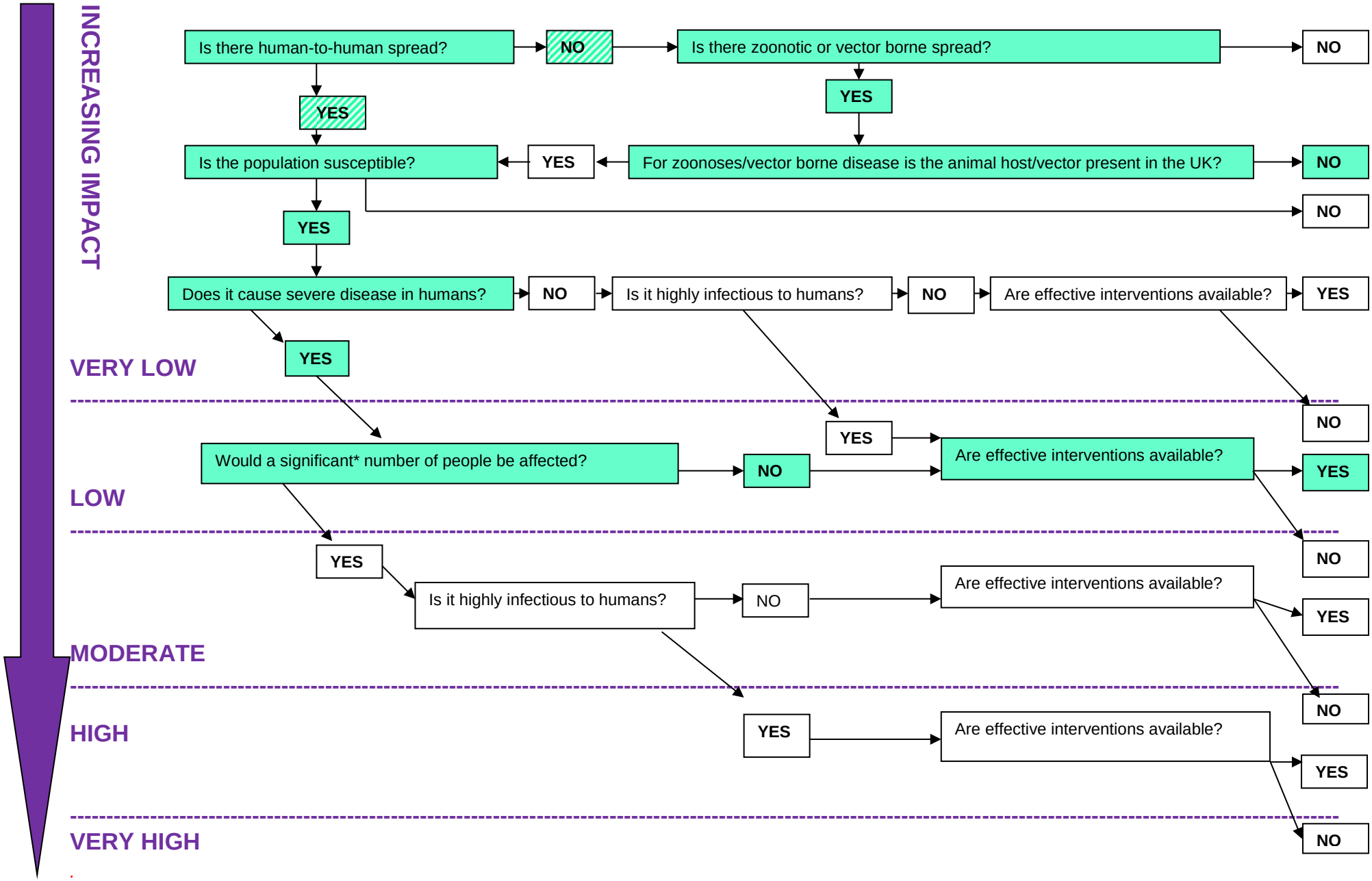
Step 2: Assessment of the impact on human health

The scale of harm caused by the infectious threat in terms of morbidity and mortality: this depends on spread, severity, availability of interventions and context. Please read in conjunction with the Impact Algorithm following the boxes shaded green.

Question		Outcome	Quality of Evidence
i)	**Is there human-to-human spread?**	**No/Yes**	**Good**
The most common route of acquisition of CCHF is tickborne or via animal contact. However, person-to-person spread can occur via contact with the blood and body fluids of infected persons (1, 12). Nosocomial transmission is known to occur and has been well-documented in many countries (28), including in Spain in 2017 (6, 8). Nosocomial transmission has not occurred in the UK. Possible sexual transmission has also been described (29).			
ii)	**Is there zoonotic or vector borne spread?**	**Yes**	**Good**
Yes, both. It is a tickborne infection, but disease may also be acquired via contact with blood/body fluids of infected animals (1).			
iii)	**For zoonosis/ vector-borne disease, is the animal host/ vector present in the UK?**	**No**	**Satisfactory**
No. The virus is not found in UK animals and there are no established *Hyalomma* tick populations in the UK. Detection of a single adult *H. rufipes* on a horse with no history of travel during 2018 suggests moulting of nymphs has taken place in this instance in the UK. Winter temperatures in the UK would not be a limiting factor for continued survival of adults which may therefore result in questing of adult *Hyalomma* next spring. It is possible that future human exposure to *Hyalomma* ticks in the UK could occur following warm summers permissive for nymphal moulting following importation of ticks.			
iv)	**Is the population susceptible?**	**Yes**	**Satisfactory**
Yes. There is no reason to suspect that the UK population is any different in susceptibility to CCHFV than populations in endemic countries. Two UK travellers to date have acquired confirmed clinical CCHF overseas, as have a number of other tourists; more than twenty travel-related cases have been documented to date in the literature (30, 31).			
v)	**Does it cause severe disease in humans?**	**Yes**	**Good**
Yes. Although asymptomatic infection occurs, it is not clear what proportion of infections lead to overt clinical disease. However, when it occurs, CCHF can be a severe illness with a high mortality. In endemic countries, the case fatality rate is very variable,			

ranging from 5% to more than 40% (1). In a series of travel-related infections, 12/21 (57%) had a fatal outcome (30).			
vi)	**Would a significant number of people be affected?**	**No**	**Satisfactory**
The burden of disease due to CCHFV even in endemic countries appears to be comparatively low, although there is great variation in surveillance, detection and reporting. In the UK, it is unlikely that a significant number of cases would occur from environmental exposures. There are robust and tested procedures for managing and caring for patients with viral haemorrhagic fevers (32). There has been no transmission to healthcare workers involved in the care of patients with any viral haemorrhagic fever in the UK (33).			
vii)	**Are effective interventions available?**	**Yes**	**Satisfactory**
Preventive measures in endemic countries focus on tick avoidance (34), minimising contact with blood/body fluids of livestock animals (35), and infection prevention and control measures in healthcare settings (28). There is no internationally available vaccine. The use of the antiviral ribavirin for treatment may be beneficial provided it is commenced early in the course of illness, but the quality of studies reporting its use has been inconsistent (1). Ribavirin has also been suggested as post-exposure prophylaxis following percutaneous exposure (36). Intensive public messaging about preventive measures would take place in response to the first detection of a locally acquired human case in the UK.			

The **IMPACT** of CCHF on human health in the UK: **VERY LOW/LOW**



**This question has been added to differentiate between those infections causing severe disease in a handful of people and those causing severe disease in larger numbers of people. 'Significant' is not quantified in the algorithm but has been left open for discussion and definition within the context of the risk being assessed.*

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Appendix

ECDC *Hyalomma marginatum* distribution in Europe map – May 2018