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Human Animal Infections and Risk Surveillance (HAIRS) group

Qualitative assessment of the risk that
Usutu virus presents to the UK human
population

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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.

HAIRS is a multi-agency cross-government horizon scanning and risk assessment group, which 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, Public Health 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 Usutu virus in the UK population

Date of this assessment	September 2020
Version	3.0
Reason for assessment	Update to account for latest evidence from Europe and detection of Usutu virus in a small number of birds in the UK in August 2020
Completed by	HAIRS Secretariat and members
Date of previous risk assessment	15 December 2016
Date of initial risk assessment	31 October 2012

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

SUMMARY OF RISK ASSESSMENT FOR USUTU VIRUS IN THE UK POPULATION		
Note: This risk assessment was completed to assess the current risk that Usutu virus presents to the UK population		
Overview	Usutu virus (USUV) was first recognised in Europe, in Austria, in wild birds in 2001 and subsequently expanded its range across Europe. In August 2020, the first Usutu virus infected wild birds in the UK were identified.	
Assessment of the risk of infection in the UK	Probability	Low
	Impact	Low/Moderate
Level of confidence in assessment of risk	Satisfactory	
Action(s)/ Recommendation(s):	<ul style="list-style-type: none"> • Continue to monitor the UK situation with ongoing bird and mosquito surveillance • Continue to monitor situation in European countries for increasing reports of human cases or changes in pathogenicity of human infections • Advise Standing Advisory Committee on Transfusion Transmitted Infections (SACTII) of change to risk assessment for UK population • Advise the Advisory Committee on Dangerous Pathogens and the UK Zoonoses Network of change to risk assessment for UK population 	

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

Step one: 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. Please read in conjunction with the Probability Algorithm following the boxes shaded green. Where the evidence may be insufficient to give a definitive answer to a question the alternative is also considered with the most likely outcome shown in solid colour and the alternative outcome in hatched colour. The text alternative to the probability algorithm can be found in [Appendix A](#).

QUESTION	OUTCOME	QUALITY OF EVIDENCE
i) Is this a recognised human disease?	Yes	Satisfactory
<p>Usutu virus (USUV) is a mosquito borne flavivirus first detected in South Africa in 1959. It is maintained through an enzootic cycle involving birds (predominantly passerine (such as blackbirds) and Strigiformes (such as owls)) as amplifying reservoir hosts and ornithophilic mosquito species as vectors (mainly <i>Culex</i> spp.) (1). Mammals, including humans, are incidental dead-end hosts. USUV is regarded as an emerging infection in humans but the number of confirmed clinical infections to date is low. The first recorded cases were in the Central African Republic in 1981 and in Burkina Faso in 2004. Since then, the vast majority of cases have been reported in Europe, increasing in reporting frequency in recent years. This is either due to raised awareness of the disease or due to increased human exposure as USUV becomes established and is discovered in susceptible bird, mosquito and human populations across a wider geographical expanse in Europe.</p> <p>Although the full spectrum of clinical presentation of USUV infections in humans has yet to be well described, it ranges from the most common asymptomatic, or mild symptoms, to a rare severe neuroinvasive presentation often observed in immunocompromised individuals.</p> <p>Clé and colleagues summarise published reports describing a total of 49 human infections with USUV as of 2018 (2). Of these cases, which were diagnosed using molecular, serological or virus isolation techniques, 25 (51%) were identified in healthy blood donors as part of surveillance, at relatively low rates (<1%) (for example (3-5)). There is evidence in some countries to suggest that seropositivity rates have increased slowly over time (6). Higher rates of seropositivity have also been observed in blood donors in Serbia (7.5%) and in forestry works in northern Italy (18%) (7, 8).</p>		

<p>Mild clinically apparent human cases of USUV present with fever, myalgia, headache, asthenia and rash (9). Severe human cases are rare but cases of USUV related meningoencephalitis (for examples see (10-13) and facial paralysis (14) have been reported. Immunosuppression is believed to have been a contributory factor to many of the severe cases described so far. No USUV associated fatalities have been reported to date.</p>		
ii) Is this disease endemic in the UK?	No	Good
<p><u>Birds</u> Two studies carried out in the early 2000's looking for evidence of arbovirus infection in birds in the UK reported detection of USUV antibodies in wild and farmed birds (15, 16). As neither RNA or USUV virus was isolated from these animals and the data not repeatable, these studies were not thought to provide convincing evidence of USUV presence in the UK. APHA surveillance for USUV in wild birds in Great Britain from 2005-2019 did not result in any detections of USUV.</p> <p>In late August 2020, USUV RNA was detected in samples from a small number of wild birds (blackbirds and house sparrow) submitted to APHAs wildlife disease surveillance programme from a site in Greater London. This is regarded as the first detection of USUV in wild birds in the UK. Repeated detections over a wider geographical expanse as well as in multiple years would be required to confirm endemicity of USUV in the UK.</p> <p><u>Mosquitoes</u> A joint PHE/APHA study in 2013 in North Kent tested over 1000 <i>Cx. modestus</i> mosquitoes for USUV and all were negative (17).</p> <p><u>Humans</u> As of August 2020, no human cases of USUV infection have been reported in the UK.</p> <p>Thus, current evidence suggests USUV is not endemic in the UK.</p>		
iii) Are there routes of introduction into the UK?	Yes	Good
<p>Four routes of introduction into the UK are possible:</p> <ul style="list-style-type: none"> (i) short distant migration of infected birds from eg Europe (ii) long distance infected migrant birds from eg Africa (iii) active/passive infected mosquito dispersal (iv) importation of infected captive birds. 		

Although phylogenetic analyses of USUV strains suggest that the initial appearance of USUV in Europe (into Austria) was introduced by migratory birds from Africa (18), short distance movement of infected wild birds is considered the most important factor for the extension of geographical range of USUV in Europe. Short distance migration of infected birds is also thought the most probable route of introduction to the UK. See also v) below.

To date, infected birds have been reported in many Western European countries including Austria, Belgium, Croatia, France, Germany, Greece, Italy, Poland, Spain, Switzerland, the Netherlands (19), and now the UK. The source of the infection in the birds detected in Greater London in August 2020, or whether the birds had migrated from an infected country, are still under investigation. There is a possibility that this information will not be elucidated, however information from the site is that captive bird imports this year are ruled out (due to COVID-19 restrictions).

iv) Are there effective control measures in place to mitigate against these?	No	Satisfactory
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The implementation of mitigation strategies to prevent the introduction of USUV by bird migration or mosquitoes is impractical. No USUV specific plans are in place to deal with an incursion. However, on such an occurrence the implicated mosquito species would be identified and control measures suggested if practicable. There are options for management of mosquitoes if particular species caused nuisance biting and pose a vector risk to humans. [Advice on management of aquatic habitats for *Cx pipiens* s.l. and *Culiseta annulata* around the home and in urban areas can be found here.](#)

v) Do environmental conditions in the UK support the natural reservoirs?	Yes	Good
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The primary vector of Usutu virus in Europe is *Cx pipiens* s.l. and most of the USUV positive pools are associated with this species of mosquito (1, 20, 21). Other *Culex* species have been implicated (*Cx. neavei*, *Cx. perexiguus*) but neither of these occur in the UK.

Although a small number of positive pools of other mosquito species trapped in continental Europe have been found positive, this does not always confirm that they play a role in transmission, as many mosquito species acquire bloodmeals from birds and may be positive, but are then not involved in onward transmission of the virus. Of those species that also occur in the UK, these include *Ae. caspius*, *An. maculipennis* s.l., *Cs. annulata*, *Ae. vexans*, *Cx. modestus*, *Ae. detritus* (22-28).

Positive pools of the invasive mosquitoes *Ae. albopictus* and *Ae. japonicus* have also been found (1, 20, 21, 27, 29, 30).

Cx. pipiens s.l. is a widespread species in the UK (PHE unpublished data and [see map here](#)). There are two physiological forms. The more ubiquitous typical form of *Cx. pipiens* is almost exclusively ornithophilic, and it is only thought to rarely bite humans. It breeds in a range of natural and artificial habitats and is common in urban and rural areas. It is a container breeding species and will exploit a range of habitats around the home as well as areas of flooded water and nutrient-rich waters. It overwinters in the adult female stage and this begins from late August, with mosquitoes entering houses and cool outbuildings. The *molestus* form of *Cx. pipiens* does bite humans but appears to be limited in distribution and is associated with underground aquatic habitats and specific sewage treatment systems in London

A recent report from Belgium (31) demonstrated endemicity of USUV in local birds and *Pipistrellus* sp. of bats (which are also present in the UK) with over-wintering of USUV in *Cx. pipiens* pools; extension of the host range in wild bird species, including waterbirds; ongoing virus introduction by wild birds from outside the country and ongoing USUV viral evolution. The authors speculate on whether bats could be an amplification host. This hypothesis requires further investigation.

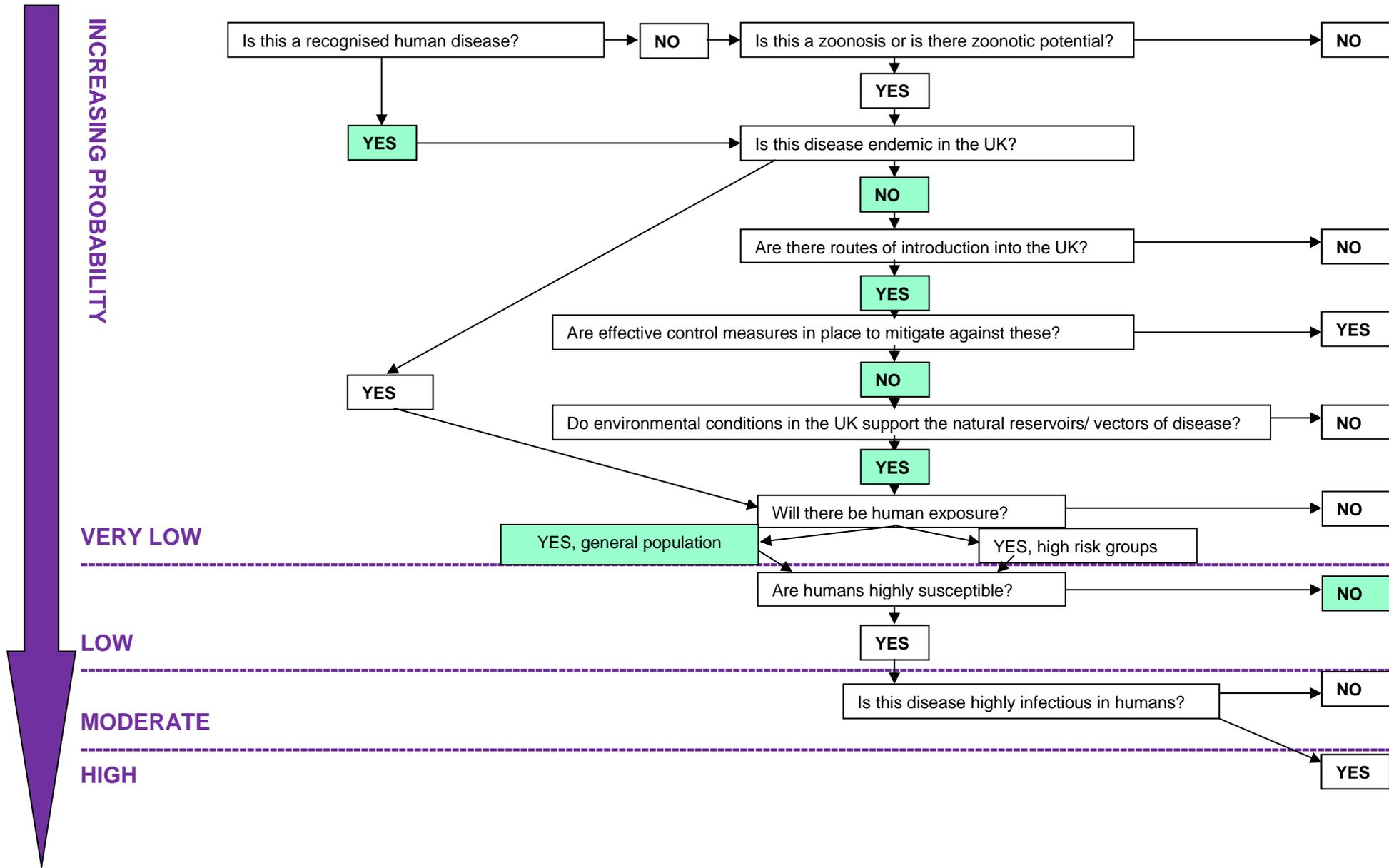
The combination of endemicity of USUV in near-continental countries to the UK, combined with short distance infected migrant birds and possibly mosquito movements, increases the likelihood of repeated incursions of USUV into the UK by these species, which could occur potentially in the spring, summer and autumn months, when native *Culex* mosquitoes will be active. Together these factors may lead to autochthonous transmission of USUV in the UK via native *Culex* mosquitoes. as opposed to the previous most probable incursion route via USUV infected long-distance migrant species from Africa with a different seasonality, arriving on UK shores when local *Culex* mosquitoes would not be active.

vi) Will there be human exposure?	Yes	Satisfactory
<p>Yes, but not to any great extent.</p> <p>USUV is thought to be maintained in a similar mosquito-bird-mosquito cycle as for West Nile virus (32). The most likely vector (<i>Cx pipiens</i> s.l.) exists in the UK, although the bird-biting biotype rarely, if ever, bites humans. Nuisance biting in the UK is a regional phenomenon (33), due to a variety of species including <i>Cs. annulata</i>, although the role of this mosquito and other human-biting species in USUV transmission is not clear. The invasive species <i>Aedes albopictus</i> and <i>Aedes japonicus</i> are not currently established in the UK.</p>		

vii) Are humans highly susceptible?	No	Satisfactory
<p>No. Human disease has been described, but apparent moderate to severe clinical disease is rare. The recent increasing numbers of reports of asymptomatic human USUV infections as well as cases of mild to severe neuroinvasive USUV infections in humans in Europe may be due to changes in awareness and surveillance but may also be an effect of increased human exposure to this zoonotic risk.</p>		

The **PROBABILITY** of human infection with Usutu virus in the UK population: **LOW**

Qualitative assessment of the risk that Usutu virus presents to the UK human population



Step two: 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. Where the evidence may be insufficient to give a definitive answer to a question the alternative is also considered with the most likely outcome shown in solid colour and the alternative outcome in hatching. The text alternative to the impact algorithm can be found in [Annex A](#).

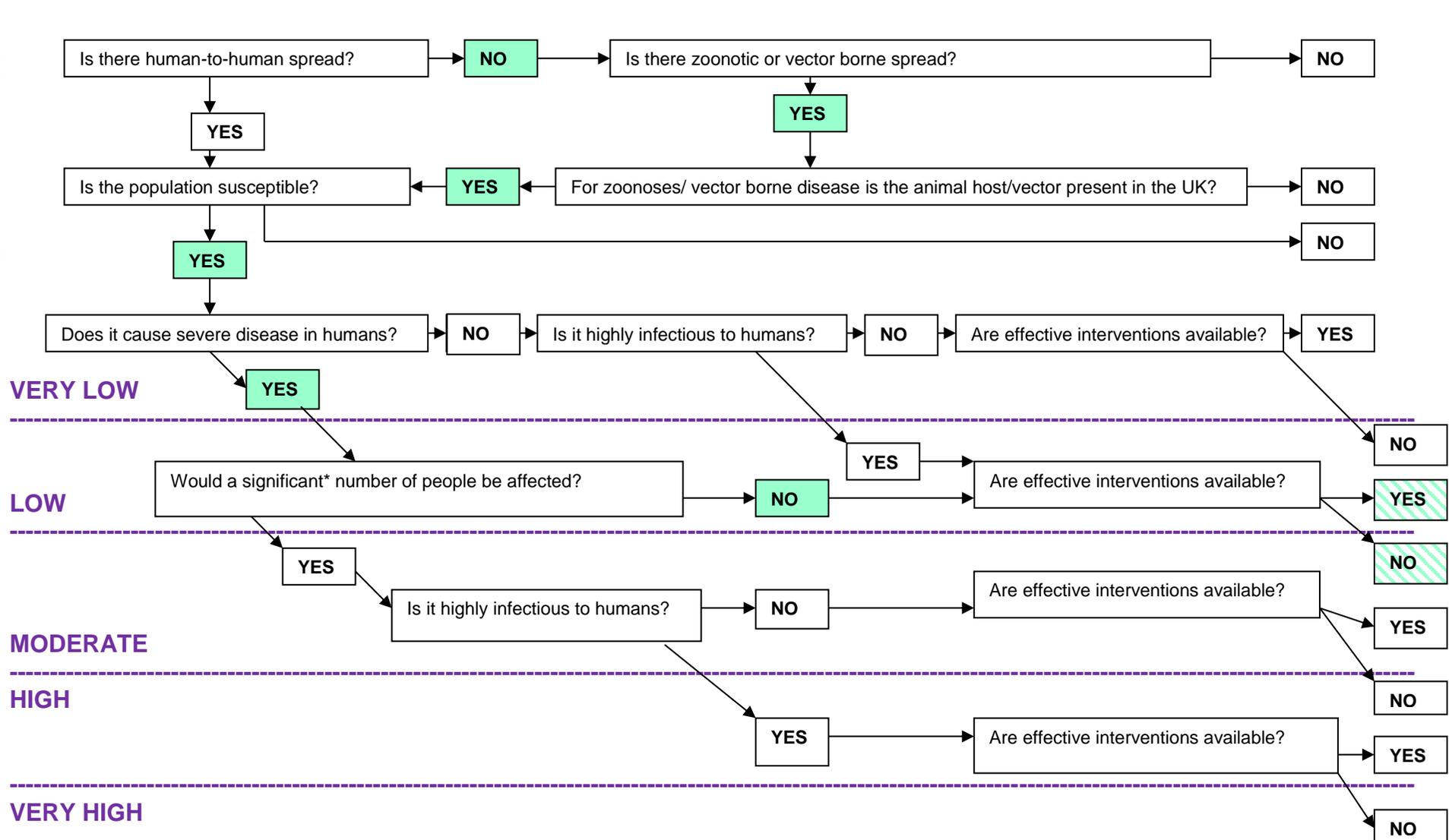
QUESTION	OUTCOME	QUALITY OF EVIDENCE
i) Is there human-to-human spread?	No	Satisfactory
There is no known human-to-human spread. Transmission has been hypothesised through blood products (34) and possibly transplantation, but the main route of human transmission is through the bite of an infected vector.		
ii) Is there zoonotic or vector borne spread?	Yes	Satisfactory
USUV is transmitted to birds by mosquitoes, particularly <i>Culex</i> species. Human cases are rare, and infection is assumed to occur from the bite of an infected mosquito.		
iii) For zoonoses / vector-borne disease is the animal host/ vector present in the UK?	Yes	Good
The hosts of USUV are birds, particularly blackbirds, and the vectors are mosquitoes, principally <i>Culex</i> species. Both hosts and vectors are present in the UK.		
iv) Is the population susceptible?	Yes	Satisfactory
Available data suggest that human disease is rare, even in Europe where epizootics have taken place in wildlife. Asymptomatic or mild infection has been reported in healthy individuals, but the majority of severe infections have occurred in immunosuppressed individuals.		
v) Does it cause severe disease in humans?	Yes	Satisfactory
Yes, but very rarely		

vi) Would a significant number of people be affected?	No	Satisfactory
<p>It appears that infection occurs only in a minority of those who are exposed to and bitten by infected mosquitoes. Although there is limited information on the incidence of mosquito biting in the UK, sustained human biting is currently considered to be a localised event (33).</p>		
vii) Are effective interventions available?	Yes/No	Satisfactory
<p>The risk of contracting the disease could be reduced by preventing exposure to mosquitoes (use of repellent, long sleeves, avoiding being outside at dusk and dawn when mosquito vectors are most active) [by extrapolation from West Nile virus].</p> <p>There are options for management of mosquitoes if particular species caused nuisance biting and pose a vector risk to humans. <i>Advice on management of aquatic habitats for <i>Cx pipiens</i> s.l. and <i>Culiseta annulata</i> around the home and in urban areas can be found here.</i></p> <p>There is no human vaccine available and no specific antiviral therapy.</p>		

The **IMPACT of USUV on human health in the UK: **LOW / MODERATE****

Qualitative assessment of the risk that Usutu virus presents to the UK human population

INCREASING IMPACT



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Appendix A

Accessible text version of the assessment of the probability of infection in the UK population algorithm

Outcomes are specified by a ✓ beside the appropriate answer. Where the evidence may be insufficient to give a definitive answer to a question, the alternative is also considered with the most likely outcome shown with ✓✓ and/or the alternative outcome(s) with a ✓

Question 1: Is this a recognised human disease?

- Yes: go to question 3 ✓
- No: go to question 4

Question 2: Is this a zoonosis or is there zoonotic potential

- Yes: go to question 3
- No: probability of infection in UK population is very low

Question 3: Is this disease endemic in the UK?

- Yes: go to question 7
- No: go to question 4 ✓

Question 4: Are there routes of introduction into the UK?

- Yes: go to question 5 ✓
- No: probability of infection in UK population is very low

Question 5: Are effective control measures in place to mitigate against these?

- Yes: probability of infection in UK population is very low
- No: go to question 6 ✓

Question 6: Do environmental conditions in the UK support the natural reservoirs/vectors of disease?

- Yes: go to question 7 ✓
- No: probability of infection in UK population is very low

Question 7: Will there be human exposure

- Yes – General population or high-risk groups: Go to question 8 ✓
- No: probability of infection in UK population is very low

Question 8: Are humans highly susceptible?

- Yes: go to question 9
- No: probability of infection in UK population is low ✓

Question 9: Is this disease highly infectious in humans?

- Yes: probability of infection in UK population is high
- No: probability of infection in UK population is moderate

Accessible text version of the assessment of the impact on human health algorithm

Outcomes are specified by a ✓ beside the appropriate answer. Where the evidence may be insufficient to give a definitive answer to a question, the alternative is also considered with the most likely outcome shown with ✓✓ and/or the alternative outcome(s) with a ✓

Question 1: Is there human-to-human spread?

- Yes: go to question 4
- No: go to question 2 ✓

Question 2: Is there zoonotic or vector borne spread?

- Yes: go to question 3 ✓
- No: impact on human health in the UK is very low

Question 3: Is the animal host or reservoir present in the UK?

- Yes: go to question 4 ✓
- No: impact on human health in the UK is very low

Question 4: Is the population susceptible?

- Yes: go to question 5 ✓
- No: impact on human health in the UK is very low

Question 5: Does it cause severe human disease?

- Yes: go to question 8 ✓
- No: go to question 6

Question 6: Is it highly infectious to humans?

- Yes: go to question 9
- No: go to question 7

Question 7: Are effective interventions available?

- Yes: impact on human health in the UK is very low
- No: impact on human health in the UK is low

Question 8: Would a significant number of people be affected?

- Yes: go to question 10
- No: go to question 9 ✓

Question 9: Are effective interventions available?

- Yes: impact on human health in the UK is low ✓
- No: impact on human health in the UK is moderate ✓

Question 10: is it highly infectious to humans?

- Yes: go to question 12
- No: go to question 11

Question 11: Are effective interventions available?

- Yes: impact on human health in the UK is moderate
- No: impact on human health in the UK is high

Question 12: Are effective interventions available?

- Yes: impact on human health in the UK is high
- No: impact on human health in the UK is very high