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## **Human Animal Infections and Risk Surveillance (HAIRS) group**

Qualitative assessment of the risk that  
SARS-CoV-2 infection in UK captive  
*Mustelinae* populations presents to the  
UK human population

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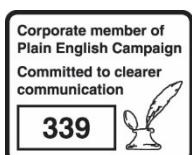


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# About the Human Animal Infections and Risk Surveillance group

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 assessment of the risk that SARS-CoV-2 infection in UK captive *Mustelinae* populations presents to the UK human population

<b>Date of this assessment</b>	10 November 2020
<b>Version</b>	1.0
<b>Reason for assessment</b>	Reports of an emergence of a mink variant of SARS-CoV-2 with reduced sensitivity to neutralising antibodies
<b>Completed by</b>	HAIRS Members
<b>External experts consulted</b>	Christianne Glossop, CVO Wales Richard Griffiths, Welsh Government Anthony J Wilson, FSA Katie Russell, PHE Ian Brown, APHA Matt Heydon, Natural England
<b>Date of previous risk assessment</b>	N/A
<b>Date of initial risk assessment</b>	November 2020

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

<b>Summary of risk assessment for SARS-COV-2 infection in UK captive <i>mustelinae</i> populations and the risk it presents to the UK human population</b>					
<b>Overview</b>	<p>On 4 November 2020, Danish authorities reported the emergence of a SARS-CoV-2 variant in mink and a small number of associated human cases which, on preliminary investigations, demonstrated reduced sensitivity to neutralising antibodies when tested against antibodies collected from people with previous SARS-CoV-2 infection. Although investigations are ongoing, these preliminary findings have raised concerns over the risk of this or other variants arising in <i>Mustelinae</i> species which may potentially hamper COVID-19 intervention efforts (vaccine and therapeutics).</p> <p>In the UK, the only <i>Mustelinae</i> species kept in high-density settings are ferrets in large-scale breeders, working animal collections or in animal research sites. Ferrets kept in low-density domestic premises are not believed to present a significant risk, given large numbers of naïve animals are presumed to be required to allow sufficient virus passage and selection for adapted variants.</p> <p>Thus, individuals in contact with ferrets in high density settings are regarded as the highest risk group for exposure to a <i>Mustelinae</i> adapted variant of SARS-CoV-2 in the UK</p> <p>This risk assessment does not assess the impact in the event of human-to-human SARS-CoV-2 (human or animal variant strain) transmission.</p>				
<b>Assessment of the risk of infection in the UK</b>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 15%; vertical-align: top;"><b>Probability</b></td> <td>General population – very low; High risk group (handlers of ferrets at high density) - high</td> </tr> <tr> <td style="vertical-align: top;"><b>Impact</b></td> <td>Low for animal-to-human transmission, due to the low numbers of likely contacts and available preventive measures</td> </tr> </table>	<b>Probability</b>	General population – very low; High risk group (handlers of ferrets at high density) - high	<b>Impact</b>	Low for animal-to-human transmission, due to the low numbers of likely contacts and available preventive measures
<b>Probability</b>	General population – very low; High risk group (handlers of ferrets at high density) - high				
<b>Impact</b>	Low for animal-to-human transmission, due to the low numbers of likely contacts and available preventive measures				
<b>Level of confidence in assessment of risk</b>	For most of the questions there was a good or satisfactory level of confidence in the assessment. Only for the areas of understanding the disease manifestation and current level of infection in ferrets or wild <i>Mustelinae</i> was the level of confidence either unsatisfactory or poor.				
<b>Action(s) and recommendation(s):</b>	<ul style="list-style-type: none"> <li>• to consider the risk from commercial imports of <i>Mustelinae</i> from countries which have reported mink farm outbreaks (1) or have a large mink or raccoon dog fur farming population</li> <li>• to adapt current content and increase communications and biosecurity messaging to appropriate keepers and veterinarians regarding the potential risks and mitigation strategies,</li> </ul>				

	<p>taking into account recently published OIE draft guidance on working with farmed animals of species susceptible to infection with SARS-CoV-2</p> <ul style="list-style-type: none"><li>• to provide information for the public and animal keepers seeking advice on how to minimise risk of infection</li><li>• to increase surveillance in <i>Mustelinae</i> populations</li><li>• any isolates from <i>Mustelinae</i> species or known human handlers of <i>Mustelinae</i> species should be reported promptly to the relevant incident control team, sequenced and information shared with relevant animal health <b>and</b> human health counterparts</li><li>• review current UK guidance on preventing spread of SARS-CoV-2 infection from humans-to-animals, and animals-to-humans</li><li>• review this risk assessment as new evidence emerges</li></ul>
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**Please note**

This risk assessment addresses:

- i. the risk of SARS-CoV-2 infection in captive *Mustelinae* species (for example, ferrets, weasels, mink and polecats) in the UK and not other potential zoonotic sources (including *Mustelidae* species, for example, badgers and otters) of SARS-CoV-2 infection
- ii. the risk of UK's captive *Mustelinae* population producing *Mustelinae* specific variants
- iii. the risk of direct *Mustelinae*-to-human contact transmission of SARS-CoV-2. While the Group recognises that if or once a *Mustelinae* adapted strain infects direct human contacts, there is a risk of onward, and possibly, sustained transmission within the human population, an assessment of the impact of this possibility sits outside the scope of this risk assessment

As this is an emerging disease, there are knowledge gaps and a degree of uncertainty in the assessment outcomes. According to the established HAIRS risk assessment procedures, uncertainty is clearly documented throughout the risk assessment.

However, given the fast pace of availability of new evidence and its potential impact on the outcome of this risk assessment, this caveat is reiterated here and readers should refer to the date stamp on [page 4](#), or contact the HAIRS Group Secretariat ([HAIRS@phe.gov.uk](mailto:HAIRS@phe.gov.uk)) to ensure the latest possible version is reviewed.

Due to the very specific nature of the risk questions addressed in this risk assessment, a number of our standard risk assessment questions have been expanded to clarify the question being addressed.

The impact of a pathogen mutating is not usually considered in the HAIRS risk assessment algorithm, but it was agreed by the group that it is important in this instance to note that it has occurred.

It is noted that the likelihood of mutation of the current dominant human SARS-CoV-2 variant within an animal population will depend on several factors: the mutation (and recombination) rate, the length of time virus is circulating in a population, the number of naïve animals and effective population size. Evidence from Danish mink outbreaks shows the virus enters the mink population and spreads very quickly (within a few days) before an antibody response is raised in mink. But generally, after 2 to 3 weeks the mink have all seroconverted and no virus is detected in samples from these animals. Each farm in Denmark, where mink variants have been detected, had around 1,000 to 3,000 animals per epidemiological group.

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

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

This section of the assessment examines 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 [Annex A](#).

Question	Outcome	Quality of evidence
<p><b>1. Is this a recognised human disease?</b></p> <p>Note: this question also focuses on current knowledge of SARS-CoV-2 infection in <i>Mustelinae</i> species</p>	<p><b>Yes</b></p>	<p><b>Good – humans and mink</b>  <b>Satisfactory – ferrets</b>  <b>Poor – other species</b></p>
<p><b>SARS-CoV- 2</b></p> <p>In December 2019, the World Health Organization was notified of a pneumonia outbreak in the city of Wuhan in Hubei Province of China, by the Health Commission of the city. The cause for the infection was identified as a novel betacoronavirus (1 of 4 genera: Alpha-, Beta-, Gamma-, and Delta-). Subsequently, the virus rapidly spread in China as well as in over 100 other countries causing a global pandemic to be declared in mid-March 2020 (2). As of 9 November 2020, over 50.2 million SARS-COV-2 human infection cases have been confirmed in 235 countries, states and territories. Over 1.25 million associated deaths have been reported (3). In the UK as of 9 November, there have been over 1.2 million confirmed cases, with over 49,000 deaths (within 28 days of a positive test) (4).</p> <p>The origin or source species of SARS-CoV-2 is still unknown, and studies are ongoing (5). However, its genetic sequence shares 96.2% similarity with coronavirus RaTG13 (betacoronavirus, subgenus sarbecovirus) which was detected in horseshoe bats (genus <i>Rhinolophus</i>) in 2016 in Yunnan province, China (6). Similar bat coronaviruses have caused 2 other major outbreaks of severe respiratory disease in the last 2 decades: Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV). Other than these, 4 other coronaviruses belonging to Alpha and Beta subtypes</p>		



have caused zoonotic infections in humans (and infections in other mammals) in the past whereas Gamma and Delta subtypes have mainly infected non-mammals (7).

SARS-CoV-2 is spread by infected respiratory droplets and possibly via faeces, although transmission by contact with contaminated objects or materials is also suggested, as well as spread by aerosols (8, 9). SARS-CoV-2 infection in humans has a wide clinical spectrum, ranging from asymptomatic, or mild symptoms (such as fever, cough, loss of taste and/or smell), to severe pneumonia resulting in respiratory failure (9-11). The current primary diagnosis method used to detect the virus in the UK is RT-PCR using samples from both the upper and lower respiratory tract (9-11). No specific anti-viral treatment or vaccine is currently available.

Genetic sequencing studies suggest that SARS-CoV-2 virus's spike protein (S) binds to the same human cell receptor (Angiotensin I Converting Enzyme 2 -ACE2) which SARS-CoV uses (12, 13). There is considerable interest in host-virus spike protein-ACE2 receptor interactions not only to determine host susceptibility, but also as a target for therapeutics and vaccine development.

There have been several reports of isolation of SARS-CoV-2 by PCR and subsequent serology in companion animals (mostly cats and dogs) in several countries in the world, in a limited number of zoo animals and on mink farms [APHA collated data, (1)]. Domestic cats, big cats, non-human primates, ferrets, mink and raccoon dogs seem to also show signs of infection (virus has been isolated), disease (namely, a combination of fever, inappetence, respiratory and gastroenteric clinical signs), and in the case of mink, increased mortality rate on some farms. The majority of these reports suggest infected humans as the source of infection, or at least the source of the index case for the sustained transmission between animals observed in some animal production facilities (for example, mink farms). Other animals that are known to have low susceptibility to SARS-CoV-2 infection, either naturally derived or experimentally, include dogs, rabbits, cattle and golden hamsters. Poultry, pigs and aquatic finfish or shellfish are unlikely to be susceptible (14).

### **SARS-CoV-2 in *Mustelinae***

*Mustelinae*, a subfamily of the family *Mustelidae*, are a collection of small carnivores, including mink, polecats, weasels and ferrets. This risk assessment is limited to this subfamily and excludes the wild animals of the wider order, *Mustelidae*, present in the UK, such as otters, pine martens and badgers from other families. Reasons for restricting this assessment to only *Mustelinae* species include (i) current available evidence (natural and experimental) suggesting the susceptibility of both mink and ferrets to SARS-CoV-2, (ii) the ability of these species to spread infection within their own species, and in mink, to humans, and (iii) the presence in the UK of ferrets in low- to high-densities in settings with the possibility of close-contact human interactions.

Mink appear to be particularly susceptible to SARS-CoV-2 infection and widescale outbreaks have been reported in mink farms, where they are raised for fur production, in the Netherlands, Spain, the United States, Sweden, Italy and Denmark (1). As of 8 November 2020, over 300 mink farms globally have reported SARS-CoV-2 infection with 229 in Denmark (all in North Jutland), 69 in the Netherlands and 20 in Sweden (1, 15) [APHA collated data]. To date, the other large producers of mink fur, Poland and China (16), have not reported infections in their mink farms.

Dutch authorities were first to report outbreaks in mink farms in April 2020. Since then and as of early November, 69 of the 120 mink fur farms in the Netherlands have been affected (1). Sequencing analysis of isolates from mink and in-contact humans from a small selection of these farms (first 16 farms affected) has shown that while workers were likely to have been the source of the mink outbreak in these farms, widescale circulation amongst mink in these high-density settings allowed for the virus to mutate in the animals and to become regarded as distinct mink variants (17). Epidemiological and sequence analysis of mink and human strains showed that although mink-to-human transmission did occur in farm workers, there was limited spread of the observed mink variants in the local or national human population. The Dutch Outbreak Management Team for Zoonoses has advised that people in contact with infected mink on mink farms are at a higher risk of infection with SARS-CoV-2 than transmission within a family/household setting (18, 19). All mink on SARS-CoV-2 positive Dutch mink farms to date have been culled and producers will not be allowed to restart mink farming. The government is discontinuing mink farming from spring 2021 (18, 20, 21).

As of early November 2020, Denmark, one of the world's largest mink fur farming sectors alongside China (16, 22), has reported SARS-CoV-2 infection in animals in 229 mink farms. The first affected farms were detected in June 2020, which were controlled through culling, with a 'second wave' starting in August, which spread very rapidly between mink on each farm premise. Within these farms 7 different groups/clusters of mink-specific variants of SARS-CoV-2 have been identified based on whole genome sequencing. Five of these clusters have been detected in humans (23). In these mink variants, 7 different mutations have been seen in the spike protein on the surface of the virus with between 1 and 4 different changes in the spike protein observed in each cluster. These mink variants have been detected in 214 people among 5,102 samples (4.2%) taken from Danish human cases detected between mid-June to mid-October (23). These individuals infected with SARS-CoV-2 mink variants primarily resided in North Jutland Region (200/214, 94%) and comprised individuals who worked in mink farms, and individuals in local surrounding populations, including a nursing home, many of whom had no known contact with mink. It is possible that not all historical cases of mink variants have been detected in this region due to the low proportion (<15%) of total samples sequenced so far. To date, human-to-mink, mink-to-human and subsequent human-to-human transmission of mink variants of SARS-CoV-2 have been recorded in Denmark (24).

The virus variant with 4 changes in the spike protein, referred to as cluster 5, was found on 5 mink farms and in 12 human cases all residing in North Jutland (ages ranging from 7 to 79 years). Eight of these individuals infected with cluster 5 virus had links to the mink farming industry and the remaining 4 cases are reported from the local community with no known link to mink at this stage (24). All cluster 5 human cases were diagnosed in August and September 2020. Further spread of this cluster 5 variant within and outside Denmark cannot be excluded, but comprehensive actions taken by Danish authorities (including animal culling and enhanced non-pharmaceutical interventions for the population in North Jutland) should reduce this ongoing risk. Based on initial investigations, this cluster 5 virus demonstrates reduced sensitivity to neutralising antibodies when tested *in vitro* against antibodies collected from people with previous SARS-CoV-2 infection (23). Further scientific and laboratory-based studies are ongoing to verify these preliminary findings and to understand any potential implications in terms of diagnostics, therapeutics and vaccines in development (24).

Swedish authorities have reported that none of the mutations described in the Danish Cluster 5 mink variant have been observed in Swedish mink SARS-CoV-2 variants, but work continues to sequence viruses from the latest confirmed positive cases in mink and human cases from the same municipalities as affected mink farms (25) (Personal communications, Swedish authorities).

To date, SARS-CoV-2 natural infection has been reported in a small number of captive ferrets (in Spain) (Personal Communications, Spanish authorities), although 3 studies have shown that infected ferrets are able to transmit the virus to other ferrets under experimental conditions and that transmission was observed under both direct and indirect contact (permeable partition separating infected from uninfected animals) (26-28). For completeness, another small-scale US study that has yet to be peer-reviewed suggests ferrets may not be susceptible under natural exposure conditions after testing several ferrets in 1 household with PCR-positive human cases (29). This study is a pre-print publication and was carried out in 1 domestic setting with only limited virological investigation of the humans in the household. This investigation need to be repeated and results replicated to be considered appropriately.

To date, there are no reports in the scientific literature of SARS-CoV-2 infection in other members of the family of *Mustelinae* (for example, weasels, stoats and polecats), but given their close genetic relationship with mink and ferrets, they are presumed to be susceptible as they will share common receptor binding domains for the virus. The lack of reports of natural infection are likely to be related to their wild/feral status, the limited human contact (identifying humans as the most likely source of SARS-CoV-2 infection) and the absence of mass production facilities of these species.

<p><b>2. Is this disease endemic in the UK?</b>                      Note: in this assessment, this question specifically refers to whether SARS-CoV-2 is endemic in the UK <i>Mustelinae</i> population</p>	<p><b>No</b></p>	<p><b>Unsatisfactory</b></p>
<p>Although SARS-CoV-2 is currently endemic in the UK human population, there is currently no evidence to suggest that it is present in either the wild, or captive populations of <i>Mustelinae</i>. Infection of animals with SARS-CoV-2 meets the World Organisation for Animal Health's (OIE's) criteria of an emerging infection, and as a consequence, veterinarians should report any positive test results for SARS-CoV-2 from animals they receive to the chief veterinary officer in the administration where the virus was detected.</p> <p>See:</p> <ul style="list-style-type: none"> <li>• <a href="#">guidance on the case definition, testing and reporting requirements for SARS-CoV-2 for vets</a></li> <li>• <a href="#">advice for veterinarians and clients for pets at the veterinary surgery</a></li> </ul> <p>No reports of SARS-CoV-2 infection in <i>Mustelinae</i> species in the UK have been recorded to date. Due to the wide variation in habitat, human interactions and husbandry of <i>Mustelinae</i> in the UK [APHA collated data], they are considered in 3 separate categories:</p> <p><b>Wild mink, wild ferret and other wild <i>Mustelinae</i></b></p> <p>There are an estimated 120,000 wild mink in Great Britain (GB) of the species <i>Neovison vison</i> (American vison). A non-native species, it became established in the wild following escapes or releases from fur farms in the early twentieth century and is known to be present across the vast majority of GB (30). The European vison mink species (<i>Mustela nutreola</i>) is not known to be present in GB.</p> <p>Ferrets, another non-native species, established in the wild from those recently released from captivity, as well as those from more established feral populations (31). As ferrets are widely kept throughout Britain, feral ferrets are likely to have a broad geographical range. No specific density estimates are available but are likely to be lower than other wild <i>Mustelinae</i> species (30).</p> <p>Wild populations of polecats, including hybrid polecat-ferrets, are widely established throughout Wales and in western and southern England, with the population expanding eastwards. Only small numbers have been reported in Scotland, most of which will be hybrids or feral ferrets. The GB population is estimated at 83,000 (30).</p> <p>Wild populations of weasels and stoats are also present in GB in high numbers (450,000 and 438,000) respectively (30).</p>		

To date, there is no evidence to suggest infection in wild *Mustelinae* populations in the UK. It is our understanding that no SARS-CoV-2 testing has been undertaken in these species to date, but no increased reports of clinically unwell animals or increased mortality events have been recorded by or reported to the APHA wildlife team.

**Domestic ferrets kept at low to medium density**

The UK domestic pet ferret population is estimated at between 800,000 to 1,000,000 (32). Within households, they are often kept in low density (the minimum recommendation is pairs). Small-scale breeders (for domestic pet purposes) and small collections of working ferrets may have low to medium density collections of ferrets (where low would be single numbers, and medium several tens) [APHA collated data].

To date, information collated by the small animal veterinary surveillance network (SAVSNET) show no records of suspected SARS-CoV-2 infection in ferrets, or ferrets being tested for SARS-CoV-2 (Personal communications, SAVSNET).

**Ferrets kept at higher density**

In the UK there are a small number of holdings with high densities of ferrets (more than 100). These animals are produced mostly for, and used in, medical research or used as working animals for vermin control or flushing rabbits. As of 9 November, no SARS-CoV-2 infection in these higher-density premises have been officially reported in the UK, but this may reflect a lack of testing to date. Enhanced surveillance in these populations is required.

Further evidence gained from enhanced surveillance is required to provide an accurate answer to this question.

**3. Are there routes of introduction into the UK?**

**Yes**

**Satisfactory**

Note: in this assessment, this question specifically refers to possible routes of SARS-CoV-2 (human and *Mustelinae* adapted variants) introduction into the UK *Mustelinae* population

Since March 2020, SARS-CoV-2 has been endemic in the UK human population at varying prevalences over time, and infected individuals would be regarded as the most likely source of SARS-CoV-2 infections for UK *Mustelinae*. As of 6 November, only 1 confirmed case and 1 suspect case (which was positive on unofficial tests only) of SARS-CoV-2 infection in animals have been reported in the UK, both in cats for which the most likely source was determined to be an infected owner. There have been no reports of any *Mustelinae* adapted strains in *Mustelinae* in the UK.

Testing and sequencing are ongoing in the UK to determine if any of the mink-adapted strains reported from Denmark or other countries are present in the UK human population. This risk assessment will be reviewed based on the outcome of these investigations.

The following sections look at the risk of human contacts introducing SARS-CoV-2 into specific *Mustelinae* populations

### **Wild mink, wild ferret and other wild *Mustelinae***

Due to the limited human contact with wild *Mustelinae* species, direct human to wild *Mustelinae* transmission is thought unlikely. People involved in working with wild animals are advised to wear protective equipment but not full PPE. Natural England is providing guidance to these settings (Personal communications, Natural England). There is a theoretical possibility of indirect transmission via contact with contaminated human waste.

### **Domestic ferrets kept at low density**

Given the endemic nature of SARS-CoV-2 in the human population, and the close contact between most owners and their ferrets in domestic or other low-density settings (for example, petshops), ferret exposure to SARS-CoV-2 from infected in contact humans is possible. Prior to November 2020, there was no specific guidance for owners on how to prevent SARS-CoV-2 spread to ferrets, but general advice included good hygiene practice to prevent transmission of SARS-CoV-2 to pets. Due to COVID-19 restriction on gatherings, there have been very limited opportunities for interactions between ferrets from different households since early in 2020 at shows, fairs, racing events, therefore ferret-to-ferret transmission of infection is likely to be restricted to within these low-density settings.

Pet ferrets, accompanied by their owners, may travel to the UK provided animals are compliant with the pet travel rules: ferrets must (i) be identifiable by microchip, (ii) have a valid passport and (iii) have a current rabies vaccination. These animals are likely to have significant human contact and could be exposed to SARS-CoV-2 if their owner, handler or a household member is infected. In these circumstances, ferret-to-human transmission of infection presents no greater risk than human-to-human transmission. Guidance is being updated to ensure any pet ferrets arriving into the UK with people who are required to self-isolate should also remain in isolation and not leave the house or property for 3 weeks following return to the UK. Note, this is a longer period specified for self-isolation compared to current human guidance, but it is based on experimental infections of ferrets where virus is cleared after 2 to 3 weeks.

### **Ferrets kept at higher density**

The risk of exposure of ferrets kept in high density settings will be dependent on biosecurity measures applied. But extrapolating from outbreaks in other *Mustelinae* high-density settings (mink farms), infected workers have been identified as the source of infection for substantial outbreaks in these settings. In the UK, no specific guidance for keepers was available before November 2020. The OIE released draft guidance for these circumstances in early November 2020 (33). It should be noted that for ferrets used in medical research they are likely raised and managed in strict biosecurity so as to minimise the effect of external factors on outcomes of the research.

### **Other sources**

**Non-human sources (for example, infected companion animals)** – cats and dogs have tested positive for SARS-CoV-2 in households with infected humans. It would not be possible to differentiate between the likely exposure of a companion ferret in such a household to the other infected companion animals or to an infected human (or contaminated environment). Nevertheless, evidence suggests dogs are unlikely to become infectious, while cats have only limited transmission potential under experimental conditions. In COVID-19 positive households with multiple companion animals, not all become infected (1).

**Legal importations of infected *Mustelinae*** – commercial imports of *Mustelinae* must be in accordance with European Directive 92/65 (EEC) and accompanied by a veterinary health certificate. They should be consigned to approved or registered premises, and for entry into the UK must enter with a licence under the Rabies Import Order. There are no requirements for pre-import testing for SARS-CoV-2; all health conditions relate to rabies. All people keeping mink, which are invasive non-native species, must apply for a license from their relevant authority.

**Illegal importations or stowaways of infected *Mustelinae*** – it is not possible to provide data to support an estimate of this risk, but this pathway of introduction is thought to be unlikely. In Denmark, there are few wild-living mink (estimated between 4,000 and 10,000) (Personal communications, Danish authorities) and mink farms are very secure due to the value of the pelts, thus wild-farmed mink interactions are unlikely to occur. Wild mink are wary of humans, therefore it is not believed they would readily enter a vehicle or cargo.

<p>At this time, if <i>Mustelinae</i> exposure to SARS-CoV-2 were to occur, it will most likely to be one of the UK human circulating variants. In low density settings, it is presumed that there would be an insufficient naïve population to permit enough virus passage to allow functional mutations to occur and be maintained within that population.</p> <p>The highest risk of functional <i>Mustelinae</i>-adapted mutations occurring to human variant strains in the UK are likely to be in high ferret density settings.</p>		
<b>4. Are there effective control measures in place to mitigate against these?</b>	<b>No</b>	<b>Satisfactory</b>
<p>At this current stage of the COVID-19 pandemic, humans in the UK present a persistent source of onward transmission of SARS-CoV-2 virus until eradication or significant management is achieved by non-pharmaceutical or pharmaceutical interventions. Guidance does exist on ways to prevent onward transmission of SARS-CoV-2 from infected individuals to in-contact animals and on having animals tested, but it is unclear how widely this guidance is followed (33-38).</p> <p>The Group recognises that given the latest developments in our knowledge on infection in <i>Mustelinae</i>, there needs to be more awareness raised on these guidance documents and recommendations.</p>		
<b>5. Do environmental conditions in the UK support the natural reservoirs?</b>	<b>Yes</b>	<b>Good</b>
<p>In this circumstance, and at this point in the epidemic, humans will be regarded as the natural reservoir of SARS-CoV-2.</p>		
<b>6. Will there be human exposure?</b>	<b>No - general population</b>	<b>Good</b>
<p>Note: in this assessment, this question specifically refers to will or could there be human exposure to SARS-CoV-2 infected <i>Mustelinae</i> in the UK?</p>		
<p>For the majority of the UK human population there will be no contact with <i>Mustelinae</i> species, wild or domesticated, thus no risk of exposure to infected <i>Mustelinae</i>.</p> <p><b>Wild mink, wild ferret and other wild <i>Mustelinae</i></b></p> <p>Given the propensity for wild <i>Mustelinae</i> to avoid human contact, there will be very limited risk of exposure to infected wild <i>Mustelinae</i> for the general public. The risk of exposure to these infected animals will be those involved in care of wild <i>Mustelinae</i>. We estimate there are over 50 wildlife rescue centres in GB and 20 ferret rescue centres. For this small group of individuals, given the risk of SARS-CoV-2 infection in these <i>Mustelinae</i> species is believed to be very low, there will be only a limited risk of exposure.</p>		



**Domestic ferrets kept at low density**

In low-density settings, there is a possibility of human exposure to infected ferrets if SARS-CoV-2 has been introduced by infected handlers. As discussed above, in these domestic or low-density settings the strain of exposure will most likely be those circulating in the human population, and not ferret-adapted strains. Nevertheless, there would also be a risk of transmission from human-to-human in the same household setting, not involving the ferrets.

**Ferrets kept at higher density**

In high-density ferret settings, there is also a possibility of human exposure to infected ferrets if SARS-CoV-2 has been introduced by infected human handlers. In these circumstances, depending on housing and management arrangement (for example, contact of different age groups) and biosecurity (APHA collated data), there may be sufficient transmission and naïve populations to allow for the possibility of strains circulating in the ferrets to adapt functional mutations. Thus, it is this group who would be regarded as the highest-risk group for contact with ferret- adapted strains of SARS-CoV-2.

It is important to note that exposure will not always lead to infection from infected *Mustelinae* to human contacts.

7. Are humans highly susceptible?	Yes	Good
<p>Naïve humans are highly susceptible to SARS-CoV-2 infection, with clinical presentations ranging from asymptomatic or mild to severe and fatal infections, depending on age, sex and underlying health conditions. Latest estimates according to SAGE, is a population level hospital case fatality rate of 15% (where only 5% of all those testing positive enter hospital) (39). Research is ongoing to determine the susceptibility of individuals to repeat infections with SARS-CoV-2. To date, a relatively small number of re-infections have been reported in the scientific literature (40).</p> <p>Evidence from Denmark suggests that humans are susceptible to mink variants of SARS-CoV-2. In total, 214 human infections with mink variants have been reported out of 5,102 isolates sequenced since mink farm infections have been reported in Denmark. These infections have been reported in individuals with direct and indirect contact with mink, as well as in individuals with no contact with mink (24).</p> <p>For the cluster 5 mink variant to date only 12 people are known to have been infected with this variant. In this group, 8 had a link to the mink farming industry and 4 cases are from the local community with no known contact with mink at this stage (24).</p>		

Based on investigations to date there is no evidence to suggest increased transmissibility or pathogenicity in humans from these Danish mink variants (Personal Communications, Statens Serum Institut, Denmark). Testing is still ongoing on antibody neutralisation studies. However, according to the most recent information, rabbit antisera will neutralise the mink variant (Personal Communications, Statens Serum Institut, Denmark). Although further research is required, these initial studies suggest that naïve humans infected with this mink variant will mount an antibody response to this variant but limited immunological protection may be provided by previous infections with other SARS-CoV-2 variants.

**8. Is this disease highly infectious in humans?**

**Yes**

**Good**

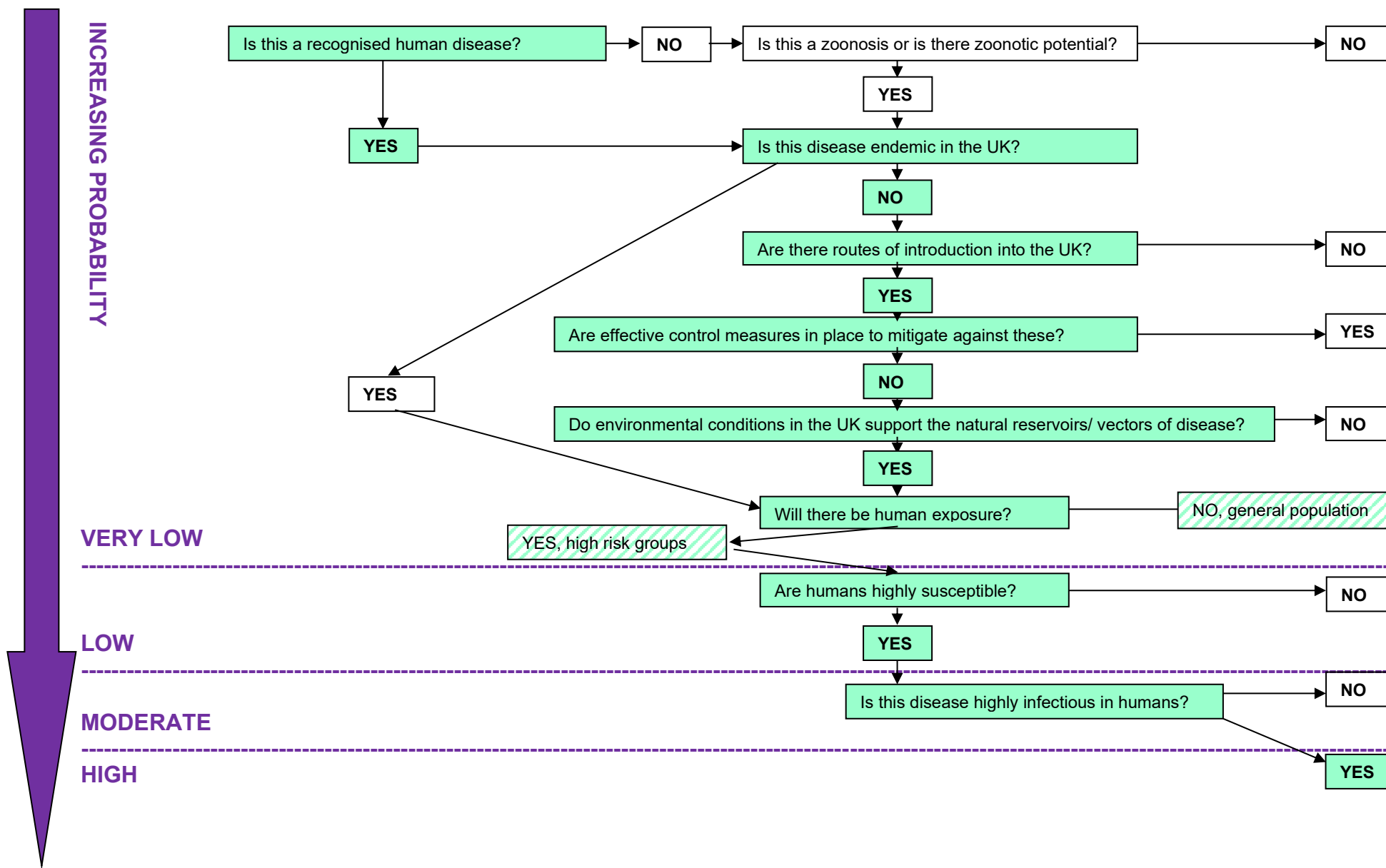
The basic reproduction number ( $R_0$ ) for SARS-CoV-2 has been estimated to be between 2 and 6 depending on the setting under investigation (41). Based on currently available information it is not thought that there is any significant variation in  $R_0$  or  $R_t$  between different SARS-CoV-2 strains circulating in the human population. Information from Danish authorities indicates that mink variants are understood to have the same transmissibility and pathogenicity as other strains circulating in the human population. Although further investigations are ongoing, initial research has indicated the possibility that limited immunological protection may be provided by previous SARS-CoV-2 infections against the Danish cluster 5 mink variant. The potential implications of this finding in terms of transmission dynamics, including the  $R_0/R_t$  in human populations are still being evaluated.

The **PROBABILITY** of human infection with SARS-CoV-2 from *Mustelinae* in the UK:

**General population: very low**

**High-risk population: high**

Flowchart showing the 'probability of infection in the UK population' algorithm (for an accessible text version see page 27)



## Step 2: Assessment of the impact on human health of high-risk groups

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
<b>1. Is there human-to-human spread?</b>	<b>Yes</b>	<b>Good</b>
<p>The basic reproduction number (<math>R_0</math>) for SARS-CoV-2 widely circulating in human populations has been estimated to be between 2 and 6 depending on the setting under investigation (41).</p> <p>To date, there has only been limited community transmission of the mink variants (214 of 5102, 4.2% of sequenced strains since significant mink outbreaks started to occur in Denmark) (23). Based on currently available evidence, there is no reason to think this would not be capable of transmitting easily between humans, similar to the human variants. Other variants with mutations in the S protein (for example, D614G) have spread very quickly and regionally between humans (42).</p>		
<b>2. Is the population susceptible?</b>	<b>Yes</b>	<b>Good or satisfactory</b>
<p>Naïve humans are highly susceptible to SARS-CoV-2 infection. Investigations are ongoing to determine the susceptibility of individuals to repeat infections with SARS-CoV-2. To date, a relatively small number of re-infections have been reported in the scientific literature (40), thus re-infections are possible, but the degree to which they occur, and the impact of different variants, is yet to be determined.</p> <p>Information from Denmark suggests that humans are susceptible to mink variants of SARS-CoV-2 and are understood to have the same transmissibility and pathogenicity as other strains circulating in the human population.</p> <p>The Danish cluster 5 mink variant virus was tested <i>in vitro</i> against antibodies from people who had been infected with SARS-CoV-2 viruses commonly circulating in humans and there was a variable but reduced neutralising affect (23, 24). However, recent Danish experiments with rabbit antisera show good neutralising activity (Personal Communications, Statens Serum Institut, Denmark), suggesting naïve humans could possibly have a normal immune response to this particular variant if these <i>in vitro</i> outputs can be replicated with natural infection. The impact of this on the efficacy of candidate vaccines has yet to be determine but Danish authorities are believed to be working with the World Health Organization and vaccine producers to investigate.</p>		

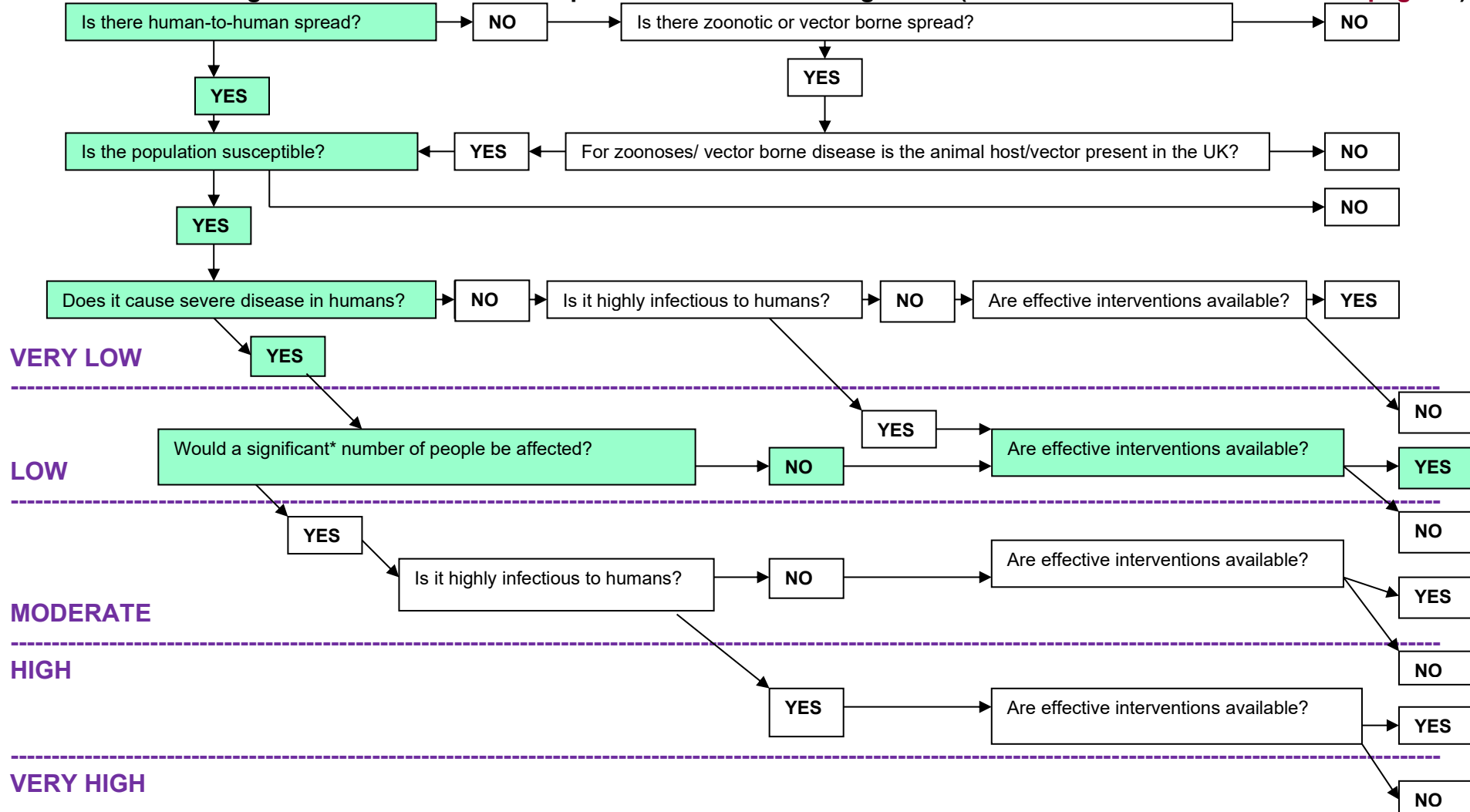
3. Does it cause severe disease in humans?	Yes	Satisfactory
<p>Clinical presentations of human infections with SARS-CoV-2 range from asymptomatic or mild to severe and fatal infections, depending on age, sex and underlying health conditions. Latest estimates according to SAGE is a population level hospital case fatality rate of 15% (where only 5% of all those testing positive enter hospital) (39). The long-term impacts of COVID-19 on human health are not yet fully appreciated, but as many as 1 in 20 people can suffer symptoms for more than 8 weeks post infection (43). Current information provided by Danish authorities suggests that mink variants observed in human populations display no discernible differences in terms of ability to cause severe disease compared to SARS-CoV-2 viruses that commonly infect humans.</p>		
4. Would a significant number of people be affected?	No	Good
<p>It is anticipated that direct <i>Mustelinae</i>-to-human transmission would occur in very low numbers. In domestic and low/medium density ferret settings, care of animals is generally restricted to a small number of individuals or occurs within a household. Due to COVID-19 non-pharmaceutical interventions across the UK, situations where more individuals could interact with infected ferrets (for example, petting farms) are under restrictions limiting visitor, and thus, exposure numbers.</p> <p>In higher density ferret settings, that is, populations where specific variants are deemed most likely to occur, care of animals is undertaken by a restricted number of people. Although there will be some seasonal variability in ferret numbers coinciding with breeding seasons, the animal densities in these facilities in the UK are much lower than what is described in mink farming in Denmark and other countries with commercial farming of mink for fur. Thus in the UK, seasonal workers are unlikely to be widely employed, and the workforce would be a more static, low number.</p> <p>Outside the scope of this risk assessment is the risk of indirect transmission of mink SARS-CoV-2 variants if human-to-human transmission were to occur. Uncontrolled spread in this circumstance could result in a significant number of people being affected, as seen with other SARS-CoV-2 viruses. Surveillance should be enhanced to ensure early detection of such an event. Any isolates from <i>Mustelinae</i> species or known handlers of <i>Mustelinae</i> species should be reported promptly to the relevant incident control team, whole genome sequenced, and information shared with relevant animal health and human health counterparts across the UK.</p>		

5. Are effective interventions (preventative or therapeutic) available?	Yes	Satisfactory
<p>The employment and correct use of appropriate PPE when handling ferrets and other <i>Mustelinae</i>, as well as preventing SARS-CoV-2 infected individuals contacting these species, could prevent infection occurring in these populations.</p> <p>The OIE recognises the importance of human-to-animal transmission and has produced guidelines on working with free-ranging wildlife (38). The guidance is to avoid handling mammals as much as possible and collect environmental samples instead (reduce, replace and refine), so that if an individual has been exposed or is infected with SARS-CoV-2 she/he should postpone handling animals and, finally, that individuals should adopt practices to reduce exposure – face coverings, gloves and disinfection procedures.</p> <p>It is recognised that, in the household setting, the application of PPE for handling ferrets where they are likely to share living space with owners is not always feasible, but good hand hygiene and the use of face coverings should be encouraged. In these circumstances, if owners become unwell with COVID-19 symptoms, they are advised to not be involved in the care of their ferrets if possible. They should self-isolate from their pets, avoid kissing and cuddling them, and avoid sharing food or other items with them. If a ferret does develop clinical signs suggestive of SARS-CoV-2 infection, owners are advised to contact their vet who will provide guidance on testing and care of the animal.</p> <p>In higher density ferret facilities and holdings, appropriate PPE should be worn by all handlers, and any staff members with symptoms suggestive of COVID-19 should not be permitted to handle ferrets as recommended by the OIE guidance on working with farmed animals of species susceptible to infection with SARS-CoV-2 and WHO (24, 33).</p>		

**The *IMPACT* of SARS-CoV-2 infection in UK *Mustelinae* on human health in the UK: **Low****

Flowchart showing the 'assessment of the impact on human health' algorithm (for an accessible text version see [page 28](#))

INCREASING IMPACT



## References

Effort was made to include mainly peer-reviewed articles related to SARS-CoV-2. However, due to the rapidly changing situation when important novel or unique information has been made available online through rapid pre-print releases, government reports or official press releases, these have been included, despite not being peer-reviewed.

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## Annex 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 – high-risk groups: Go to question 8 ✓
- No – general population 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