



UK Health
Security
Agency

Human Animal Infections and Risk Surveillance (HAIRS) group

Qualitative assessment of the risk that
SARS-CoV-2 infection in UK captive or
wild *Mustelidae* population presents to
the UK human population

Updated December 2021

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About the Human Animal Infections and Risk Surveillance group

This document was prepared by the UK Health Security Agency (UKHSA) 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 the UKHSA, 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.

Information on the risk assessment processes used by the HAIRS group can be found at [HAIRS risk assessment process](#).



Risk that SARS-CoV-2 infection in UK captive or wild *Mustelidae* populations presents to the UK human population

Version control

Date of this assessment: December 2021

Version: 2.0

Reason for the assessment: Reports of findings of SARS-CoV-2 in captive otters and predicted sensitivity in badgers. Update on mink findings.

Completed by: HAIRS members

Non-HAIRS members consulted: Dr Fabian Lean, APHA

Date of initial risk assessment: November 2020

Summary

Overview

This assessment has been conducted using information relating to the dominant variants in the UK at the time of writing. The new Omicron variant has not been assessed as no data is available for susceptibility in animals.

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 *Mustelinae* species which may potentially hamper coronavirus (COVID-19) intervention efforts (vaccine and therapeutics). Since these findings, there has been a single report of a captive Asian small-clawed otter (*Aonyx cinereus*) testing positive in the USA and histological studies which highlight the potential susceptibility of another wild mustelid, the European badger (*Meles meles*). Both these species expand the definition of animals for the purposes of this assessment, to the wider family of *Mustelidae*.

In the UK, the only *Mustelidae* 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.

Thus, individuals in contact with ferrets in high density settings are regarded as the highest risk group for exposure to a *Mustelinae* adapted variant of SARS-CoV-2 in the UK.

In terms of wild species of *Mustelidae*, the badger is the most numerous. They live in sets with often at least 6 adults. Delayed implantation and female gestational dominance mean the population is highest in the Spring when litters of up to 5 young are born. Certain groups of people may be exposed to badgers as part of their occupation or through rescuing animals injured in road traffic accidents and these people should be made aware of the potential risk of infecting the animals during contact.

This risk assessment does not assess the impact in the event of human-to-human SARS-CoV-2 (human or animal variant strain) transmission.

Assessment of the risk of infection in the UK

Probability: General population – very low; high risk group (handlers of ferrets, people working with badgers and at wildlife rescue centres where animal populations are at high density) – high.

Risk that SARS-CoV-2 infection in UK captive or wild *Mustelidae* populations presents to the UK human population

Impact: Low for animal-to-human transmission, due to the low numbers of likely contacts and available preventive measures.

Level of confidence in assessment of risk

For most of the questions there was a good or satisfactory level of confidence in the assessment. Only for the components of understanding the disease manifestation or current level of infection in captive ferrets and wild *Mustelidae* was the level of confidence either unsatisfactory or poor.

Actions and recommendations

To consider the risk from commercial imports of *Mustelidae* from countries which have reported mink farm outbreaks (1) or have a large mink fur farming population.

To adapt current content and increase communications and biosecurity messaging to appropriate keepers and veterinarians regarding the potential risks and mitigation strategies, taking into account recently published OIE draft guidance on working with farmed animals of species susceptible to infection with SARS-CoV-2.

Provide information for the public and animal keepers seeking advice on how to minimise risk of infection.

Increase monitoring and surveillance in *Mustelidae* populations where appropriate,

Any isolates from *Mustelidae* species or known human handlers of *Mustelidae* species should be reported promptly to the relevant incident control team, sequenced and information shared with relevant animal health and human health counterparts.

Review current UK guidance on preventing spread of SARS-CoV-2 infection from humans-to-animals, and animals-to-humans.

Review this risk assessment as new evidence emerges.

Please note

This risk assessment addresses:

- the risk of SARS-CoV-2 infection in captive *Mustelinae* species (for example ferrets, weasels, mink and polecats) in the UK and other potential zoonotic sources (including wild *Mustelidae* species for example badgers and otters) of SARS-CoV-2 infection
- the risk of UK's captive *Mustelinae* population producing *Mustelinae* specific variants
- 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) 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 and Netherlands 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.

Step 1: Assessment of the probability of infection in the UK human 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 found at Annex A.

Is this a recognised human disease?

Note: this question also focuses on current knowledge of SARS-CoV-2 infection in species included in *Mustelidae* family.

Outcome: Yes

Quality of evidence: Good for humans and mink, satisfactory for ferrets and poor for other species

SARS-CoV- 2

Yes. 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 (one 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 23 November 2021, over 257.4 million SARS-COV-2 human infection cases have been confirmed in 235 countries, states and territories. Over 5.1 million associated deaths have been reported (3). In the UK as of 23 November 2021, there has been nearly 9.9 million confirmed cases with over 143,000 deaths (within 28 days of a positive test) (4). This pandemic continues to be predominantly a human to human infection.

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 *Rhinolophus*) 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 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 or smell), to severe pneumonia resulting in respiratory failure (9 to 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 to 11). Multiple vaccines are currently available which induce immunity against SARS-CoV-2 in humans. There have also been some limited vaccines produced for use in animals, mostly targeted at mink populations in Russia and USA, and non-human primates in the USA.

Genetic sequencing studies suggest that SARS-CoV-2 virus's spike protein (S) binds to the same 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.

SARS-CoV-2 in animals

There have been several reports of SARS-CoV-2 detections by PCR and subsequent serology in companion animals (mostly cats and dogs but also ferrets) in several countries in the world, in a limited number of zoo animals and on mink farms [APHA collated data, (1)]. In captive collections, big cats, non-human primates, ferrets, mink, raccoon dogs, Asian small-clawed otters, beavers, hyaenas, white tailed deer, coatimundi and binturongs may show usually mild signs of infection (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 rabbits, cattle, fruit bats, ferrets, mice and golden hamsters. Poultry, pigs, sheep and aquatic finfish or shellfish are less (or otherwise not) 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.

Mink appear to be particularly susceptible to SARS-CoV-2 infection and widescale outbreaks have been reported in captive mink farms, where they are raised for fur production, in Canada, Denmark, France, Greece, Italy, Latvia, Lithuania, Netherlands, Poland, Spain, Sweden and the United States (where wild mink have also tested positive) (1). As of November 2021, over 445 mink farms globally have reported SARS-CoV-2 infection including 290 in Denmark, 69 in the Netherlands, 23 in Greece, 17 in USA, 16 in Spain and 13 in Sweden (1, 15) [APHA collated

data]. To date, the other large producer of mink fur, China (16), has 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, 49). 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 (49). 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 or 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 has discontinued mink farming since spring 2021 (18, 20, 21).

In May 2021, Denmark, one of the world's largest mink fur farming sectors alongside China (16, 22), had 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 2020, which spread very rapidly between mink on each farm premise. Within these farms 7 different groups or 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 one 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 (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). Similarly, no other countries which had SARS-CoV-2 outbreaks in farm minks have reported the Cluster 5 mink variant, but work continues to sequence viruses from the latest confirmed positive cases in mink and human cases (1) ((Personal communications). Like in the Netherlands, respiratory symptoms as well as occasional increase in mortality were reported in the animals in the farms by these countries as well (1).

There have been reports of positive detections of SARS-CoV-2 in free-ranging, wild mink in the USA and Spain (1,44). But these animals are almost always caught near or within a roaming distance of mink farms where the virus had also circulated. Therefore, such infections may occur due to escaped animals establishing in the local wildlife or when wild animals come into close proximity to captive animals.

So far these mink-related variants including Cluster 5 have not been shown to be more transmissible or to cause more severe impact in human populations, compared with other circulating SARS-CoV-2; the circulation of mink-related variants in the human population has decreased since the end of 2020 and mink farming in Denmark has been paused for 2021. 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 to 28). The first natural infection of a ferret that was kept as a pet in a SARS-CoV-2 positive household was reported to the OIE by Slovenia at the end of November, further proving the susceptibility of ferrets to SARS-CoV-2 infection (1). However, further studies suggest that even though natural SARS-CoV-2 infection could occasionally occur in kept ferrets, high viral circulation in the human population may be required for this to occur regularly (46). Additionally, studies support the conclusion that ferrets kept at low density are probably unable to maintain prolonged virus circulation (46). 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 one household with PCR-positive human cases (29). This study is a pre-print publication and was carried out in one domestic setting with only limited virological investigation of the humans in the household. This investigation needs to be repeated and results replicated to be considered appropriately. The USA has however reported the finding of SARS-COV-2 in a wild mink, found near a mink farm. This was the first report of free ranging animal being infected with the virus.

There are over 800 sequences of mink-origin SARS-CoV-2 viruses logged in the GISAID database. Whole genome sequencing of virus from 40 farms revealed 170 different mutations

(50). It appears that SARS-CoV-2 mutates more rapidly in mink than in humans, with mutations occurring every 2 weeks, however, the close contact between several thousand animals as seen in the mink farms may be driving rapid host adaptation (50). The finding of some of these strains in humans following contact with mink farms indicates the public health significance of such findings.

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 or 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.

SARS-CoV-2 in *Lutrinae*

Lutrinae is a subfamily of the family *Mustelidae*, and refers to otters. There has been a recent report of Asian short clawed otters testing positive in a zoo in the USA with SARS-CoV-2 (1,45). These are the first otters known to be infected with SARS-CoV-2 worldwide. Samples from these otters were collected for testing after they showed clinical signs including sneezing, runny noses, mild lethargy, and coughing. Early epidemiological analysis shows that the otters may have acquired the infection from an asymptomatic animal caretaker (45). Additionally, research conducted at APHA has identified ACE2 in the bronchiolar epithelium of the Asian short-clawed otter by microscopy analysis (publication under preparation).

SARS-CoV-2 in Badgers (*Melinae*, *Helictidinae*, *Mellivorinae* and *Taxidiinae*) and Pine Marten (*Guloninae*)

To date, there are no reports in the scientific literature of SARS-CoV-2 infection in wild animals belonging to these subfamilies. Given their close relationship with the other animals in family *Mustelidae* they are also 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 or 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. Findings from a published ACE2 receptor mapping study in tissues reveals presence of receptor in the bronchiolar epithelium in the European badgers but not the alveoli of the lungs (51). Further work has also been conducted in the upper respiratory tract, in which preliminary data shows ACE2 is also present in the nasal mucosa of the European badger (unpublished findings from APHA). Infection of the alveoli may be very important in pathogenesis of SARS-CoV-2 infection, whereas ACE2 distribution in the nasal mucosa (as observed in ferrets and mink) may influence transmission. Ubiquitous distribution in the small intestine may support the finding in many human cases of digestive symptoms, but may also play a role in oral-faecal transmission (51).

Is the disease endemic in the UK?

Note: in this assessment, this question specifically refers to whether SARS-CoV-2 is endemic in the UK *Mustelidae* population.

Outcome: No

Quality of evidence: Unsatisfactory

No. 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 *Mustelidae*. 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.

There is [guidance on the case definition, testing and reporting requirements for SARS-CoV-2 for vets](#), and [advice for veterinarians and clients for pets at the veterinary surgery](#).

No reports of SARS-CoV-2 infection in *Mustelidae* population in the UK have been recorded to date. Due to the wide variation in habitat, human interactions and husbandry of *Mustelidae* in the UK [APHA collated data], they are considered in 4 separate categories:

Wild mink, wild ferret and other wild *Mustelinae*

There are an estimated 120,000 wild mink in Great Britain (GB) of the species *Neovison vison* (American vison). A non-native species, it became established in the wild following escapes or releases from fur farms in the early 20th century and is known to be present across the vast majority of GB (30). The European vison mink species (*Mustela lutreola*) is not known to be present in GB, as is an IUCN listed species as critically endangered.

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 *Mustelinae* species (30).

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 of wild so called polecats have been reported in Scotland, most of which will be hybrids or feral ferrets. The GB population is estimated at 83,000 (30).

Wild populations of weasels and stoats are also present in GB in high numbers (450,000 and 438,000) respectively (30).

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,

Risk that SARS-CoV-2 infection in UK captive or wild *Mustelidae* populations presents to the UK human population

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 to be approximately 800,000 to 1,000,000 (Pers.Comm, Dr M. Livingstone). Within households, they are often kept in low density (the minimum recommendation from a welfare perspective is to keep animals in pairs). Small-scale breeders (for domestic pet purposes) and small collections of working ferrets may be considered low to medium density collections of ferrets (where low would be single numbers, and medium several tens but fewer than 100) [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.

Other wild *Mustelidae*

Wild populations of otters (*Lutrinae*), in the UK are estimated to be around 11,000 (47). These are of the species *Lutra lutra* (Eurasian otter). These otters are the only otter species found in the wild in the UK. Their habitats include wetlands, rivers, and coastlines. Though still considered rare, the species is widespread in the UK and is more common in Scotland, the west coast of Wales, East Anglia, and South-West England. The only recorded SARS-CoV-2 positive so far belongs to otter species native to South and Southeast Asia (Asian small-clawed otter). This species (*Aonyx cinereus*) is not known to be present in the wild in UK, only in captive populations. Research conducted at APHA has identified ACE2 in the bronchiolar epithelium of the Asian short-clawed otter by microscopy analysis (publication under preparation).

The European badger (*Meles meles*) is widespread in the UK reaching highest densities in the west of the country. This species may be found in a variety of habitats including woodlands and open meadows but also on some farmland and can be found in towns, parks, and large gardens. There are an estimated 562,000 wild badgers in the UK (47). European badgers belong to subfamily *Melinae* and the other subfamilies *Helictidinae* (ferret-badgers), *Mellivorinae* (honey badger) and *Taxidiinae* (American badger) are present only in America, Asia or Africa.

The other wild *Mustelidae* found in the UK are pine martens (*Martes martes*), belonging to the subfamily *Guloninae*. There are an estimated 3,700 of these animals in the UK (47). Further

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

Are there routes of introduction into the UK?

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

Outcome: Yes

Quality of information: Satisfactory

Since March 2020, SARS-CoV-2 has circulated widely 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 November 2021, only a handful of confirmed cases of SARS-CoV-2 infection in domestic (pet) animals have been reported in the UK, in cats and dogs, for which the most likely source was determined to be an infected owner. There have been no reports of any *Mustelidae* adapted strains in *Mustelidae* in the UK.

Testing and sequencing of human viruses are ongoing in the UK to determine if any variants of concern arise which could be associated with strains found in animals. This risk assessment will therefore 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 *Mustelidae* 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 pet shops), 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

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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.

Since this risk assessment was first written in November 2020, the presence of SARS-CoV-2 has been made reportable in any animal species in the UK. This requires all laboratories to report positive test results to the UK Competent Authority. In addition, the registration of all premises where ferrets are kept in large numbers (>10 adults) is also now required (on a voluntary basis while the legislation is made). A central database will enable the authorities to conduct additional surveillance should it be necessary.

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

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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.

Other wild *Mustelidae*

Some of these wild mustelid species, such as European badger and Eurasian otter can approach and live in or close to urban areas. Although they would have limited human contact as they are elusive animals. Additionally, animals such as Eurasian otters and pine martens maintain a low population density in the UK. Therefore, direct SARS-CoV-2 transmission from human or other SARS-CoV-2 susceptible domestic animals to these wild *Mustelidae* is thought unlikely, but where humans feed pine martens to attract them, this cannot be ruled out as indirect contact. Due to their low population density the opportunity for any onward transmission is also limited.

European badgers may be an exception to these features of wildlife (low population density and limited human contact) due to their nature of living in social groups, the number of badger injuries in road traffic accidents and the UK's badger management interventions such as vaccination, trapping and relocation. These activities could facilitate virus transmission from humans to badgers, and transmission between badgers in close contact and allo-grooming cannot be ruled out. There are guidelines and COVID-19 advice for Badger Groups that are involved in handling these animals (48). Additionally, people involved in working with wild animals are advised to wear protective equipment but not full PPE and not to work with wildlife if they are self-isolating following a positive lateral flow test. Natural England is providing guidance for these settings (Personal communications, Natural England).

At this time, if *Mustelidae* exposure to SARS-CoV-2 were to occur, it will most likely 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.

The highest risk of functional *Mustelidae* adapted mutations occurring to human variant strains in the UK are likely to be in high ferret density settings.

Are effective control measures in place to mitigate against these routes of introduction?

Outcome: No

Quality of evidence: Satisfactory

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 to 38).

The Group recognises that given the latest developments in our knowledge on infection in *Mustelidae*, there needs to be more awareness raised on these guidance documents and recommendations.

Do environmental conditions in the UK support the natural reservoirs or vectors of disease?

Outcome: Yes

Quality of evidence: Good

In this circumstance, and at this point in the epidemic, humans will be regarded as the natural reservoir of SARS-CoV-2.

Will there be human exposure?

Note: in this assessment, this question specifically refers to will or could there be human exposure to SARS-CoV-2 infected *Mustelidae* in the UK.

Outcome: No for the general population. Yes for high risk group.

Quality of evidence: Good

For the majority of the UK human population there will be no contact with *Mustelidae* species, wild or domesticated, thus no risk of exposure to infected *Mustelidae*.

Wild mink, wild ferret and other wild *Mustelinae*

Given the propensity for wild *Mustelinae* to avoid human contact, there will be very limited risk of exposure to infected wild *Mustelinae* for the general public. The risk of exposure to these infected animals will be those involved in care of wild *Mustelinae*. We estimate there are over fifty 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 *Mustelinae* species is believed to be very low, there will be only a limited risk of exposure.

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.

Other wild *Mustelidae*

Due to their elusive behaviour there will be very limited risk of exposure to infected wild *Mustelidae* for the public. The risk of exposure to these infected animals will be those involved in care of wild *Mustelidae* such as badger vaccinators and rescuers. For this small group of individuals, given the risk of SARS-CoV-2 infection in these *Mustelidae* species is believed to be very low, there will be only a limited risk of exposure

It is important to note that exposure will not always lead to infection from infected *Mustelidae* to human contacts. Vaccination may reduce transmission to humans, although the use of physical barriers to aerosol and oral-faecal transmission will be more effective.

Are humans highly susceptible?

Outcome: Yes

Quality of evidence: Good

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).

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).

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).

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.

Is this disease highly infectious in humans?

Outcome: Yes

Quality of evidence: 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

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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.

Outcome of probability assessment

The probability of human infection with SARS-CoV-2 from *Mustelinae* and certain wild *Mustelidae* in the UK:

General population: very low

High risk population: high

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 found at Annex B.

Is there human-to-human spread of this pathogen?

Outcome: Yes

Quality of evidence: Good

The basic reproduction number (R_0) for SARS-CoV-2 widely circulating in human populations has been estimated to be between 2 and 6 depending on the setting under investigation and depending on the circulating variant (41).

To date, there has only been limited community transmission of the mink variants (214 of 5,102, 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).

Is the population susceptible?

Outcome: Yes

Quality of evidence: Good/Satisfactory

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. Vaccination which is now at a high level in the UK human population, is not going to prevent transmission *per se*. The use of physical barriers to transmission will be more effective.

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.

The Danish cluster 5 mink variant virus was tested in vitro 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, Danish experiments with rabbit antisera showed 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 in vitro outputs can be replicated with natural infection. The impact of this on the efficacy of candidate vaccines has yet to be determined.

Does it cause severe disease in humans?

Outcome: Yes

Quality of evidence: Satisfactory

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. Estimates for an unvaccinated (or where vaccination protection has waned) population, 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 one in 20 people can suffer symptoms for more than 8 weeks post infection (43).

Information provided by Danish authorities suggests that mink variants observed in human populations displayed no discernible differences in terms of ability to cause severe disease compared to SARS-CoV-2 viruses that commonly infect unvaccinated humans.

Would a significant number of people be affected?

Outcome: No

Quality of evidence: Good

It is anticipated that direct *Mustelidae*-to-human transmission would occur in very low numbers. In domestic and low or 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 in situations where more individuals could interact with infected ferrets (for example petting farms) are still recommended.

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.

In terms of contact with badgers, wildlife rehabilitators and badger vaccinators or veterinarians will be aware of the potential for animals to be infected with bovine TB, which can be transmitted through aerosol, therefore precautions should already be in place.

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 *Mustelidae* species or known handlers of *Mustelidae* 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.

Are effective interventions (preventative or therapeutic) available?

Outcome: Yes

Quality of evidence: Satisfactory

The employment and correct use of appropriate PPE when handling ferrets, badgers and other *Mustelidae*, as well as preventing SARS-CoV-2 infected individuals contacting these species, could prevent infection occurring in these populations.

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 or he should postpone handling animals and, finally, that individuals should adopt practices to reduce exposure – face coverings, gloves and disinfection procedures.

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

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SARS-CoV-2 infection, owners are advised to contact their vet who will provide guidance on testing and care of the animal.

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).

Outcome of impact assessment

The impact of SARS-CoV-2 infection in UK *Mustelinae* and certain wild *Mustelidae* on human health in the UK: Low.

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

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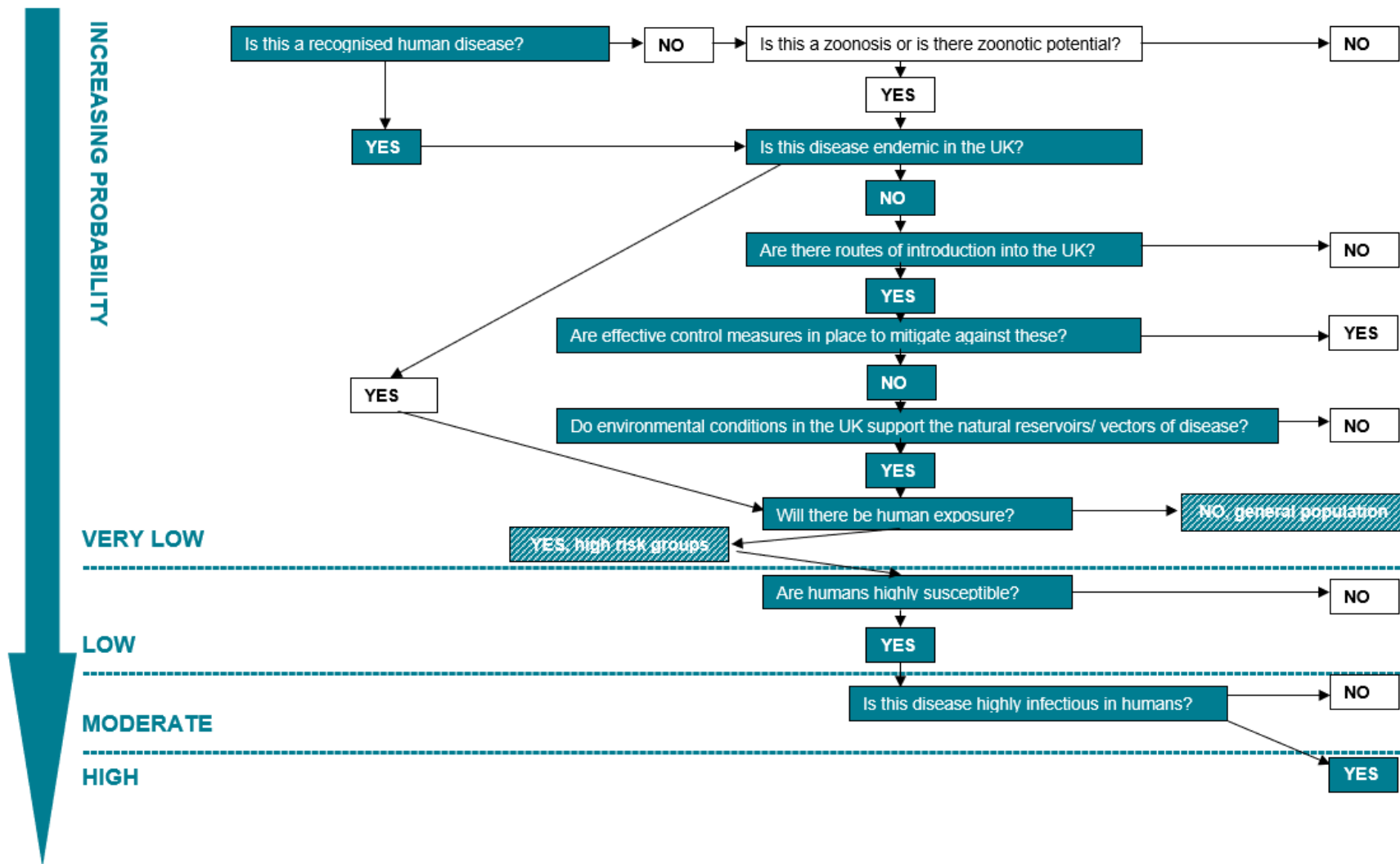
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Annex A: Assessment of the probability of infection in the UK population algorithm



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

Outcomes are specified by a ✓ (tick) 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 ✓✓ (2 ticks) and or the alternative outcome(s) with a ✓ (tick).

Question 1: Is this a recognised human disease?

- Yes: go to question 3 ✓ (tick)
- 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 ✓ (tick)

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

- Yes: go to question 5 ✓ (tick)
- 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 ✓ (tick)

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

- Yes: go to question 7 ✓ (tick)
- 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 ✓ (tick)
- No – general population probability of infection in UK population is very low ✓ (tick)

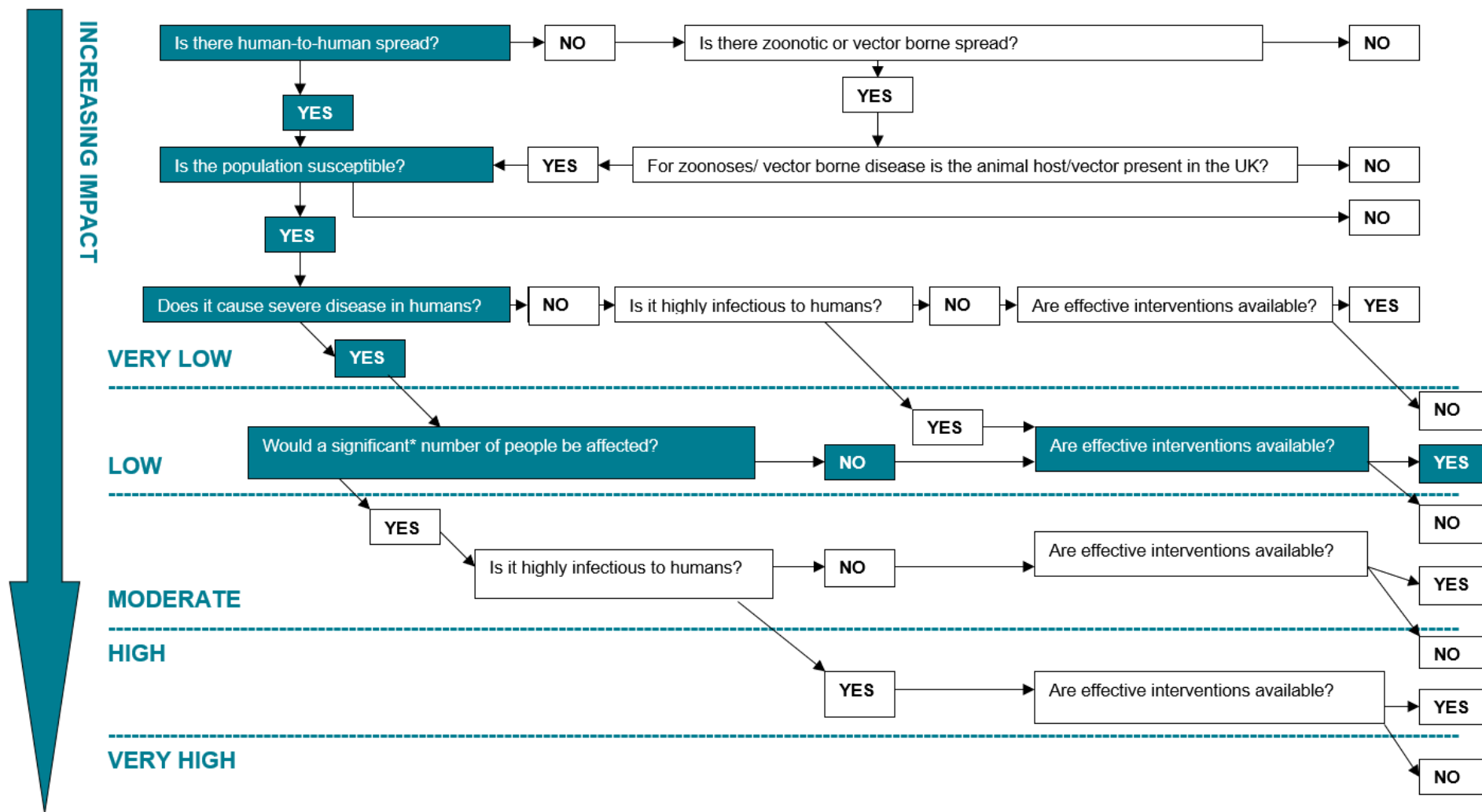
Question 8: Are humans highly susceptible?

- Yes: go to question 9 ✓ (tick)
- 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 ✓ (tick)
- No: probability of infection in UK population is moderate

Annex C: Assessment of the impact on human health algorithm



Annex D: Accessible text version of assessment of the impact on human health algorithm

Outcomes are specified by a ✓ (tick) 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 ✓✓ (2 ticks) and or the alternative outcome(s) with a ✓ (tick).

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

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

Question 5: Does it cause severe human disease?

- Yes: go to question 8 ✓ (tick)
- 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 ✓ (tick)

Question 9: Are effective interventions available?

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

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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

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