Rapid risk assessment

SUMMARY OF RISK ASSESSMENT

<table>
<tr><th colspan="2">A qualitative risk assessment to estimate the likelihood of SARS-CoV-2 infection of rodents from contact with the environment and onward exposure to humans</th></tr>
<tr><td rowspan="2">Risk being assessed:
1. viable virus in sewage
2. contact with rodents and level of infectious dose for variants of concern and “wild type” virus
3. transmission rate in wild rodents
4. exposure to humans – general population and occupational exposure</td><td>Outcome of risk assessment:
P1: What is the likelihood of SARS-CoV-2 to remain viable in the environment and waste water (pre-treatment) such that a rodent could receive an infectious dose? VERY LOW but HIGH uncertainty (unsatisfactory confidence).

P2: What is the likelihood that a variant of concern (VOC) of SARS-CoV-2 which has arisen in the human population could infect a rodent and produce sustained population level transmission? HIGH but MEDIUM uncertainty (satisfactory confidence).

P3: What is the likelihood that a human is exposed to an infectious dose of virus (VOC or otherwise) – either the general public or someone who has regular contact with rodents through pest control, waste management or waste water management? VERY LOW for general public; MEDIUM for occupational exposure; HIGH uncertainty (unsatisfactory confidence).</td></tr>
<tr><td>Key uncertainties:
• Whether mucus or faeces would have a protective effect on the virus. Whether pathogen overdispersal is protective in certain heterogenic environments and rates of decay of virus in different media (faeces, mucus).

• What viral dose is required to infect a wild rodent. Infectious dose to a rodent from different media. With over 8 million rats in the UK, the aggregated risk for one rat to become infected (based on $1-(1-p)^n$) increases when more rats are exposed.

• Transmission rates for the common viral transmission pathways between rats are unknown – faecal oral route, respiratory, mutual grooming. This will also include uncertainty around the magnitude of viral shedding by an infected rodent.</td></tr>
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	• Movement of pest rodents from overseas does occur and would most likely occur at the ports and border control posts. • Endogenous coronaviruses in rodents and risk of recombination with SARS-CoV-2 or selection pressure for SARS-CoV-2 evolution to infect and transmit among rodents.
Type of risk assessment: Rapid	**Confidence in outcome given quality of evidence:** Unsatisfactory overall although for some steps there is satisfactory evidence.

Quality control	
Date of risk assessment	**07/04/2021**
Version number	**1.0**
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Disease Expert		

A qualitative risk assessment to estimate the likelihood of SARS-CoV-2 infection of rodents from contact with the environment and onward exposure to humans

1. Executive Summary

This paper is to inform SAGE on the latest developments in the animal-human interface in SARS-CoV-2 infection. Specifically, Defra was asked to consider the high levels of virus (viable or otherwise) present in wastewater systems or the environment that might be transmitted through rodents, which can act as viral reservoirs. Of particular interest is the possible impact on control strategies addressing the human pandemic, especially considering new variants of concern (VOC) in people, particularly with the N501Y mutation.

The group considered different steps in the pathway of human-environment-animal-environment-human transmission. Quantitative data are used where possible but the final risk estimation is qualitative.

Given the very low likelihood of survival / persistence of the SARS-CoV-2 virus (from human waste) in sewage / rubbish and food waste but the high number of infected people, the large population size of susceptible rodents and their high level of contact with sewage or rubbish we consider there is a high likelihood of a single rodent becoming infected but that there is a high uncertainty to this likelihood and unsatisfactory confidence. This likelihood is reduced as the number of infected humans in the population reduces. The level of close contact between rodents combined with their high population densities means the potential to transmit infection to other rodents is also high and therefore the likelihood that this would lead to sustained population level transmission and persistence would also be high. The level of contact between humans and rats which could potentially lead to new cases is very low for the general population and restricted mainly to occupational exposure. The potential for this to lead to an outbreak (where human to human transmission occurs) will depend on the immune status of the population, the vaccine efficacy and level of circulating variants (i.e. the population attributable fraction). The confidence level will be improved by addressing the knowledge gaps highlighted.

Specifically considering the emergence of VOCs, the likelihood of human to rodent transmission and among-rodent transmission of VOCs is increased because human-derived VOCs' mutations that facilitate rodent infection have arisen during human adaptation as a response to immunity and are only coincidentally adapted for increased replication in rodents. If the "wild type" virus became established in the rodent population, it would be expected to mutate to adapt to the rodent host and most mutations in animals are considered unlikely to lead to increased replication fitness in people.

The likelihood of a VOC (to humans) emerging as a result of adaptation in a rodent is low, and certainly lower than in the human population.

Nevertheless, the overall risk (likelihood x impact) would increase if the virus was controlled in the human population through vaccination (where the levels of vaccination remain stable but do not achieve eradication) yet remained aa an animal

reservoir. The combination of an appropriate mutation arising in rats resulting in exposure to humans is lower than mutation arising in humans plus exposure in human to human. Therefore the relative risk might change because the risk for human driven variation should go down as the number of infected humans reduces but not the absolute risk.

Given the number of people involved in environmental work with rodents (controlling pests and rubbish, working in wastewater systems) and using the proxy of people being infected each year with Weill's disease (a rodent zoonotic bacteria found in rat urine) and Hanta virus (transmitted by aspiration of rat urine, faeces, blood), the likelihood of a person to become exposed to an infected rodent is very low to medium (depending on the population group) (high uncertainty). This is using a proxy of other human infections with rat-origin Hanta virus (HAIRS risk assessment, 2013), where the risk to the general public is far lower than to those who may have direct exposure to rats through working with them for pest control for example. It is less likely that owners of pet rats would be at the same level of risk, given the limited contact a pet rat would have with a wild rat. Nevertheless, the impact of each human infection and the capability of giving rise to a new outbreak should not be underestimated and will depend on the attributable population distribution, the reduction in the force of infection due to natural and vaccine induced immunity and the Ro of the variant of concern.

There is a very high level of uncertainty (unsatisfactory level of confidence) concerning (i) the persistence of virus in sewage or other waste and (ii) the transmissibility, duration of an infection and level of virus in rodents. New variants may be less sensitive to degradation in certain environmental conditions. Additional research in this area will reduce the uncertainty.

Increased knowledge of experimental infections in rodents, particularly rats (non-inbred laboratory strains), viral surveys of wild rodents and testing of people who are in contact regularly with any rodents through environmental work would reduce the level of uncertainty. Information on the level of surveillance in other countries, where SARS-CoV-2 is circulating more widely, where public health protection / sanitation and human / animal interactions are more likely would be very informative. Further understanding of the rodent viral excretion routes (urine/faecal/respiratory) and relative risk is desirable.

2. Introduction

There is considerable scrutiny around the possible origin of SARS-CoV-2 from animals, involving monitoring and surveillance of domestic livestock and wildlife, experimental infections of livestock and captive laboratory animals and culminating in the WHO Origins Mission to China, the results of which have not definitively identified any animal reservoirs. The most likely animal origin is a bat, with Rhinolophid bats such as horseshoe bats having coronaviruses most closely related. However the sequence data suggest there is an as yet unidentified intermediate host.

We have previously provided updates to SAGE on the likely risk of SARS-CoV-2 infection of cats and dogs, and of Mustelinae (including mink and ferrets). As a

result, the detection of SARS-COV-2 in any animal sample is now legally reportable under the Zoonoses Order (relevant in all four Devolved Administrations). The requirement to register large breeding groups of ferrets is going through consultation and stakeholders have reacted positively.

The latest information on animal infections with SARS-CoV-2 of interest to SAGE are:
Pet cats and dogs testing positive for SARS-CoV-2 continue to be reported, although the most recent article suggesting myocarditis in cats and dogs associated with infection with the UK B.1.1.7 variant has not been confirmed by the APHA laboratory (using viral and antibody detection methods and histopathology). Pet and working ferrets have tested positive in Europe as well. For a full list, see https://www.oie.int/en/scientific-expertise/specific-information-and-recommendations/questions-and-answers-on-2019novel-coronavirus/events-in-animals/

In the USA, gorillas tested positive for SARS-CoV-2, prompting the veterinary services to vaccinate all the primates with a vaccine developed for mink in Russia.

Mink continue to be farmed in many countries and the JBC with Defra has a subgroup looking at mink risk, which assigns a risk level to countries according to their mink populations and reporting capability.

There have been reports of positive detections in wild mink in Spain and USA but these are almost always animals caught near or within a roaming distance of mink farms where the virus had also circulated. A recent report of Asian short clawed otters testing positive in a zoo in the USA is also not unsurprising given the close relationship within the Mustelid family.

Defra have been involved in the recent scientific opinion from EFSA / ECDC on surveillance for mink farming countries, and the OIE guidance on trade in live mink and raw mink pelts.

There is still no evidence to implicate livestock in the transmission cycle; while experimentally pigs have become infected with large infectious doses administered intranasally, no onward transmission was observed. No other livestock have been infected successfully. White tailed deer have been experimentally infected, and there was evidence for limited onward transmission, but the significance of this in the wider pandemic context is not understood yet.

3. Risk question

To answer the overall assessment, there are three risk questions:

- What is the likelihood of SARS-CoV-2 remaining viable in the environment and waste material (pre-treatment) such that a rodent could receive an infectious dose?

- What is the likelihood that a variant of concern (VOC) of SARS-CoV-2 that has arisen in the human population could infect a rodent and produce

sustained population level transmission in rats or that SARS-CoV-2 may mutate / recombine in a rodent?

- What is the likelihood that a human is exposed to an infectious dose of rat origin SARS-CoV-2 virus (VOC or otherwise) – either the general public or someone who has regular contact with rodents through pest control, waste management or wastewater management – leading to a new human infection and outbreak?

4. Hazard identification

The SARS-CoV-2 virus, specifically the spike variants that have different ACE2 fidelity and the host range.

Variant of Concern: B.1.1.7; B.1.351; P2 (descendant of B.1..1.28); P1 (descendant of B.1.1.28). Case definition for VOC (confirmed) where all lineage defining positions are called as alternative (variant) bases in the S gene (particularly N501Y which is base change of 23063A->T.

While this document does not consider the potential for new variants to be carried by rodents from other countries where there are high levels of infection, there is now a methodology which looks at countries where mink are farmed and the level of risk to the humans. This methodology could be applied to other such situations if considered necessary. Particularly when the number of human cases in the UK has dropped and this could be a source for new introductions.

5. Risk assessment

5.1 Risk assessment terminology

The terminology used to define the level of risk and the level of confidence (degree of certainty) in the risk estimate based on the supporting evidence is in Tables 1 and 2.

Table 1: Definitions for the qualitative risk terms based on EFSA (2006) and OIE (2004) with expanded descriptions adapted from NHS (2008), IPCC (2005), and Kahn *et al.*, (1999)

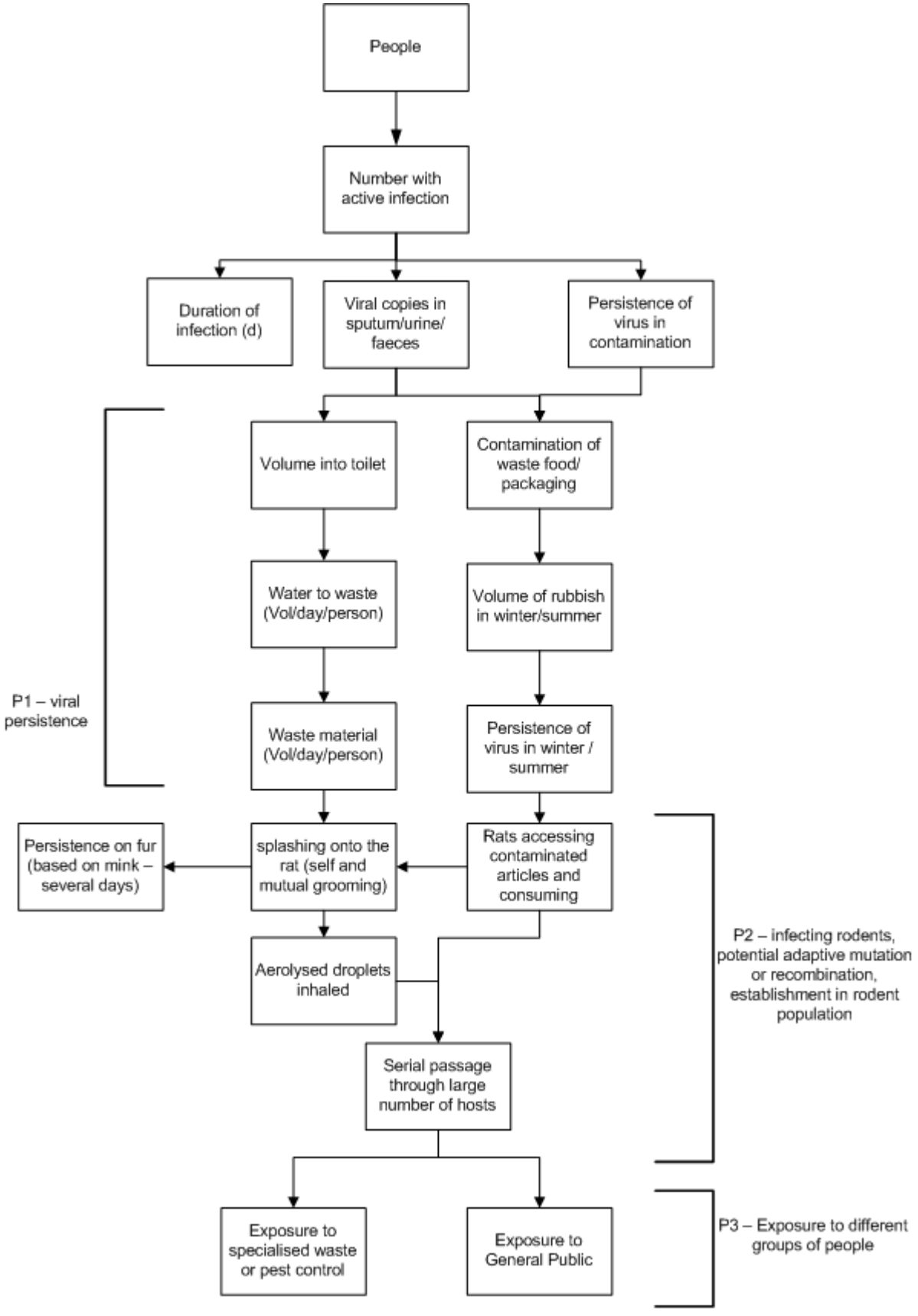
Risk level	Definition	Expanded description
Negligible	Event is so rare, does not merit consideration	The chance of the event occurring is so small it does not merit consideration in practical terms (i.e. < 0.1% probability); it is not expected to happen for years;
Very low	Event is very rare, but cannot be excluded	The event is not expected to occur (very rare) but it is possible (i.e. >0.1-1% probability); it is expected to occur at least annually

Low	Event is rare, but does occur	The event may occur occasionally (rare) (i.e. >1-10% probability); expected to occur at least monthly
Medium	Event occurs regularly	The event occurs regularly (i.e. >10-66% probability); expected to occur at least fortnightly
High	Event occurs very often	The event will happen more often than not (i.e. ≥66-90% probability); expected to occur at least weekly
Very high	Event occurs almost certainly	The event will undoubtedly happen (i.e. >90% probability); expected to occur at least daily

Table 2: Definitions for the level of confidence in the risk estimate given the available evidence used; based on definitions within (EFSA, 2006; ECDC, 2011, Spiegelhalter & Riesch, 2011)

Level of confidence	**Definition**
Unsatisfactory	Further research very likely to have impact on confidence of information and likely to change assessment
Satisfactory	Further research likely to have impact on confidence of information and may change assessment
Good	Further research unlikely to change confidence in the information

5.2 Risk pathway



5.3 Estimation of each probability on the risk pathway

An assessment for each probability on the risk pathway highlighted in Figure 1 is given in the tables below.

P1. Persistence of viable virus in environment

Pathway	Data/evidence available	Assumptions, uncertainties, known variability and conclusions
Waste water (sewage)	SARS-CoV-2 is shed in the faeces of people with asymptomatic and symptomatic infection (Guo et al. 2021; Wang et al., 2020; Xiao et al. 202; Zhang et al. 2020). Other enterotropic coronaviruses (eg MHV, PED) are shed in faeces and transmitted via the faecal oral route. PED virus persists in pig waste and sewage for up to 9mo at 4^{o}C and is capable of infecting Vero cells (Tun et al, 2016). Viral RNA fragments detected in waste water but no evidence yet on recovering culturable virus from real-world samples known to contain high levels of SARS-COV-2 RNA (artificially spiked samples can harbour infectious virus when added at very high titres) (Alex Corbishley, Edinburgh Uni, pers. comm., Davey Jones, Bangor Uni pers. comm). Current estimates are that this type of wastewaters surveillance testing can detect 1 infected person in 1000, although this is influenced by local plumbing and on the significant variability in faecal shedding rates of SARS-CoV-2 from individuals (SAGE, 2020; Jones et al., 2021). Assumption is 60 million people in the UK, each using 200 l waste water a day. 16 million infected people a year (based on estimated case reporting rates; Colman et al. 2021) with 10d infectious period (although viral shedding has been detected up to 33 days beyond initial clinical signs, this will vary (Aguilar-Oliveira et al. 2020)); volume per day of infected material (faeces, urine, sputum) leads to a	Unknowns: If the virus survived in sputum, stool mucus or nasal secretions on a piece of material, could there be a higher concentration and a protective effect of the mucus. Low concentrations and low levels of light in sewage systems. Rate of decay of any viable virus in sewage.

	large number of viral RNA copies (fragments) per year but this would be diluted to several copies (fragments) per litre of waste water. SARS-CoV-2 RNA is occasionally detected in urine but more frequently reported in faecal samples but still at levels lower than for enteric viruses (Jones et al, 2020). Live virus degradation is lowered in aquatic ecosytems where there are lower light levels.	
Household waste (including food waste left in public bins in parks)	This is about people having picnics in parks or disposing of their weekly rubbish. If they are asymptomatic and excreting virus, not using hand sanitiser and leaving the wrappings in the bin. Anecdotal evidence of rats around parks visiting waste bins; moving out of areas with catering establishments to forage domestic refuse. There is no food safety issue of livestock being infected and a source of virus. Experimental evidence of cattle, pig and poultry infections suggests these animals are unlikely to be involved in the human to human transmission cycle. While other wild animals, captive (farmed for fur) or companion animals may also be susceptible to infection, persistence within the population and ability to transmit to other species has not been reported as playing a significant role (Delahay et al. 2021).	
Risk estimate:	VERY LOW	The persistence of viable virus cannot be ruled out, although at present all experimental evidence points to this being unlikely
Confidence in outcome given quality of evidence:	HIGH UNCERTAINTY (UNSATISFACTORY CONFIDENCE)	Limited evidence in an experimental setting is only a bound on the likelihood that something will occur in nature where the number of “samples” is multiple orders of magnitude greater than any experiment, but the expected dose is much

		lower, so this could still have a greater impact if the next step (P2) is more likely.

P2. Infection of and establishment in large populations of wild rodents

Pathway	Data/evidence available	Assumptions, uncertainties and conclusions
Infecting a rodent	Experimental infection of rodents. Serial passage of virus infecting BALB/c by intranasal inoculation with the (mouse adapted) MASCp6 strain caused replication in the trachea and lung. The main VOC's which include the Spike N501Y mutation, e.g. B.1.1.7, B1.351 all have increased tropism for mouse and rat ACE2. These VOCs do not affect hamster ACE2 usage therefore these VOCs may have a broader tropism rather than an adaptation towards rodents. Mouse (*Mus musculus*) ACE2 protein does not effectively bind the viral spike protein of SARS-CoV-2 virus (wild type) but the new VOCs are better able to bind murine ACE2 and replicate in lungs. Sequential passaging in lab mouse lungs leads to adaptation and increased binding affinity (Gu et al. 2020). North American deer mice (*Peromyscus maniculatus*) were intranasally infected with SARS-CoV-2 human isolate and tested positive for 21 d in oral swabs and 14 d in lungs. Second passage high proportion of virus sequences with insertion of 4 aa in N terminal of spike protein – possible purifying selection. Other permissive hosts include the hamster, based on ACE2 binding. While further experimental evidence also points to ACE-2 protein of cattle, cats and dogs binding the Spike protein of SARS-	Known efficacy for new variants of concern (P1 and B1.351 (Montagutelli et al., 2021)) to bind the murine ACE2 and lead to viral replication in lungs Assume the wild rodents in the UK have same ACE2 characteristics as lab rodents and assume that wild rodents do not have any diversity of ACE2. There are an estimated 8 million rats in the UK. They live in colonies and have close contact with one another.

	COV-2. Nevertheless viral entry will also be a key component to susceptibility to infection and transmissibility in rodents. Humanised (ACE2) mouse models are not relevant to this paper.	
Infecting a rodent in the sewer	Belgian study on small number (35 to 40) of wild sewer rats (*Rattus norvegicus)* in an area where there were high levels of SARS-CoV-2 were circulating in the human population, resulted in no PCR positive samples (oral, swabs, faeces and tissues) and all negative VNT, although some non-specific IgG seropositives (3/35) (Colombo et al. 2021) Of the 8 water samples tested, 4 samples had detectable Ct values for SARS-CoV-2. Two samples were positive below the LLOQ and two samples had Ct values that equalled ± 7 gene copies per ml of wastewater.	Unknown: Infectious dose to a rodent. If 1 litre contained tens of viral RNA copies, that's a lot of water to be exposed to, although virus may not be uniformly distributed.
Infecting a rodent from contact with contaminated rubbish	Temperature and UV light dependent; higher volume of rubbish left in public parks in the summer; dependent on the number of people actively shedding virus and contributing to the contamination. Virus may remain on plastic and stainless steel surfaces for up to three days. Virus remains on mink pelts for up to 10 days (European Food Safety Authority et al., 2021). However, the virus would probably need to be aerosolized which is less likely on a dry surface.	Exact route to infect an animal *in vivo*. Consumption, contact with mucous membranes, inhaling aerosolised virus? Can they be infected from self and mutual grooming? Main transmission pathways between rats are unknown – faecal oral route, respiratory, mutual grooming.
Risk estimate:	HIGH	Given the experimental work carried out on VOCs and rodents, and the likely abrogation of host specificity, it is highly likely that a rodent could become infected and could transmit infection to another rodent.

Confidence in outcome given quality of evidence:	MEDIUM UNCERTAINTY (SATISFACTORY CONFIDENCE)	While it is known airway cells would be infected so the respiratory transmission pathway is highly likely, other transmission pathways (faecal / oral) are not understood. Satisfactory evidence that VOCs infect laboratory rodents. Unsatisfactory evidence for infection scenarios in sanitation systems.

P3. **Infected rat is capable of exposing a human to an infectious dose**

Pathway	**Data/evidence available**	**Assumptions, uncertainties and conclusions**
General public	For other animal models or production systems, only mink have been proven to be capable if infecting humans. In mink farms, once the virus is introduced, it circulates rapidly between animals with virus replication mainly taking place in the respiratory tract and only minor involvement of the digestive tract. Virus excretion lasts a few days. Therefore faecal contamination is less likely to be a route for infecting humans. However in establishments with a high density of infected mink, the most likely transmission pathways to humans are via air droplets, dust particles, aerosols and fomites (European Food Safety Authority et al., 2021). Mink associated variants have not become established in the community to date. No data available on the mutation rate of SARS-CoV-2 in a rodent model and the degree of abrogation such variants would pose to infecting humans and causing new human to human outbreaks, but based on the mink work, this would be very low (satisfactory uncertainty).	Very low risk to the general public where the public health / sanitary protection is good. However even a very low risk if this is of a variant that is easily transmitted between people, then the potential impact is greater. While a large proportion of the adult public is vaccinated, the duration of immunity is unknown. Recent data from Denmark suggest six months after natural infection 20% of adults under 65 yrs and 53% of over 65's can be reinfected (Boynton & Altmann, 2021)

	Based on data from Hanta virus and Leptospirosis cases, there are very few cases in humans each year who do not have close contact with rodents or their habitats. Annual cases of infection with these pathogens in the UK is around 50 – all of whom belong to the at risk groups with occupational exposure to rats. This level of rodent-human transmission of SARS-COV-2 could be enough to seed a new outbreak in the human population with low immunity or if the VOC evades the vaccine induced immunity.	
Someone handling rats or working with rodent control	HAIRS risk assessment for Hanta virus summarised known studies of seropositive people. The highest positive group were those owning pet rats (10 times higher than any other group) while for those working in the waste water, pest control groups had prevalence of <3% seropositive. Jones et al. (2020) concluded the likelihood of human infection due to contact with sewage-contaminated water (from non-occupational exposure) or food such as salads or shellfish is very low if not negligible, based on very low predicted abundances and limited environmental survival or SARS-CoV-2.	Moderate likelihood level for this group being exposed and infected (using the HAIRS algorithm but applying the SARS-CoV-2) and assuming that the rodents are infectious, and including pet owners. The risk is reduced if we do not include pet owners.
Risk estimate:	VERY LOW for the general public. MEDIUM for the people in specialised roles. LOW for pet owners. Pet rats are unlikely to come into contact with wild rats or with sewers / waste water. They are more likely to be infected by their owners and this therefore may result in limited household spread but the occupiers are at a likely greater risk from the infected source individual and it would be challenging to unravel the transmission pathways.	Vaccine considerations: as vaccine is rolled out, failure to protect against certain VOCs will become a greater issue than the proportion of unvaccinated to vaccinated people. Nevertheless, at present there are more people unvaccinated who are likely to be in the specialised roles than not (age related and social group related).

Confidence in outcome given quality of evidence:	HIGH UNCERTAINTY (UNSATISFACTORY CONFIDENCE)	There is considerable uncertainty regarding the transmission pathways from rodents back to humans. The P3 step considers the number of direct transmissions from rats, based on other infections where human to human transmission is unlikely, The next step would consider the number of infections that would be expected to arise because of rats (i.e. including all infections in the chain arising from rats) and therefore the number of direct exposures is the key figure). This has not been fully assessed as the Ro in the human population can change according to control measures put in place, including vaccination policy, movement restrictions and non-therapeutic interventions.

5.4 Final Risk Estimation –

P1: What is the likelihood of SARS-CoV-2 to remain viable in the environment and waste water (pre-treatment) such that a rodent could receive an infectious dose? **VERY LOW but HIGH uncertainty (unsatisfactory confidence).**

P2: What is the likelihood that a variant of concern (VOC) of SARS-CoV-2 which has arisen in the human population could infect a rodent and produce sustained population level transmission? **HIGH but MEDIUM uncertainty (satisfactory confidence).**

P3: What is the likelihood that a human is exposed to an infectious dose of virus (VOC or otherwise) – either the general public or someone who has regular contact with rodents through pest control, waste management or waste water management? **VERY LOW for general public; MEDIUM for occupational exposure; HIGH uncertainty (unsatisfactory confidence).**

The risk level would depend on the overall level of virus circulation in the human population; the risk declines with fewer human infections. Where the virus has been brought under control through vaccination and good immunity, and/or continued non-

pharmaceutical measures, fewer people are contributing to the infection and there is a lower likelihood of animals being exposed to any new variants. Where any SARS-CoV-2 virus (VOC or not) is not under control in the human population, there is a greater risk of rodent infection which may act as a reservoir. However there are anecdotal reports that lockdown has changed rat foraging behaviour and wide fluctuations in estimated population sizes as a result.

6. Summary of key uncertainties

Whether mucus or faeces would have a protective effect on the virus. Whether pathogen overdispersal is protective in certain heterogenic environments and rates of decay of virus in different media (faeces, mucus).

What viral dose is required to infect a wild rodent. Infectious dose to a rodent from different media. If 1 litre contained merely tens of viral RNA copies, infection may require exposure to a lot of water, but the same number of copies may be present in a fraction of a gram of faeces which will increase the likelihood of infection following exposure for any rat. With over 8 million rats in the UK, the aggregated risk for one rat to become infected (based on $1-(1-p)^n$) increases when more rats are exposed.

Transmission rates for the common viral transmission pathways between rats are unknown – faecal oral route, respiratory, mutual grooming. Contact experiments may provide some answers for the expected rates which would be seen in wild populations. This will also include uncertainty around the magnitude of viral shedding by an infected rodent.

Movement of pest rodents from overseas does occur and would most likely occur at the ports and border control posts.

Endogenous coronaviruses in rodents and risk of recombination with SARS-CoV-2 or selection pressure for SARS-CoV-2 evolution to infect and transmit among rodents.

7. Summary of key assumptions

Known efficacy for new variants of concern (P1 and B1.351 (Montagutelli et al., 2021)) to bind the murine ACE2 and lead to viral replication in lungs.

Wild rodents in the UK have same ACE2 as lab rodents and there is no diversity between species.

8. Conclusions

There is a plausible pathway for infection of rodents with new variants of concern (VOC) from infected humans following contamination of an environment.

Experimental evidence has shown SARS-CoV-2 with N501Y has increased affinity for lab rodents and there is nothing to suggest the same would not be true for wild rodents.

There is a lot of uncertainty about whether SARS-CoV-2 would persist as viable virus in wastewater and sewage and this likelihood would impact the rest of the steps in the assessment. Current work suggests not, but there may be some overdispersal of the virus in certain media which would have a protective effect.

In the event that the circulation of SARS-CoV-2 in the human population is controlled, there would be a lower level of environmental contamination.

There are key uncertainties around whether the VOC would become established in a rodent population, or would the virus become adapted to the rodent host and would no longer be able to infect a human or establish a new outbreak. Therefore there remain some important questions about whether these populations could act as reservoirs for future outbreaks but targeted surveillance in human populations at a higher risk of exposure would answer some of those questions in time.

For the general public in the UK where public health and sanitation would protect from regular exposure to rat-derived pathogens, the likelihood of infection is reduced considerably.

9. References

Aguiar-Oliveira, M.d.L.; Campos, A.; R. Matos, A.; Rigotto, C.; Sotero-Martins, A.; Teixeira, P.F.P.; Siqueira, M.M. Wastewater-Based Epidemiology (WBE) and Viral Detection in Polluted Surface Water: A Valuable Tool for COVID-19 Surveillance—A Brief Review. *Int. J. Environ. Res. Public Health* **2020**, *17*, 9251.

Boynton, R. & Altmann, D.M. (2021) Risks of SARS-CoV-2 reinfection after natural infection. The Lancet 397, (10280) 27 March–2 April 2021, Pages 1161-1163.

Colman, E. Enright, J., Puspitarani, G.A. & Kao, R.R. (2021) Estimating the proportion of SARS-CoV-2 infections reported through diagnostic testing. MedRxiv 2021.02.09.21251411

Colombo VC, Sluydts V, Mariën J, et al. (2021) SARS-CoV-2 surveillance in Norway rats (Rattus norvegicus) from Antwerp sewer system, Belgium. bioRxiv; 2021. DOI: 10.1101/2021.03.06.433708.

Delahay, R.; de la Fuente, J.; Smith, G.; Sharun, K.; Snary, E.; Flores Giron, L.; Nziza, J.; Fooks, A.; Brookes, S.; Lean, F.; Breed, A.; Gortazar, C. Assessing the Risks of SARS-CoV-2 in Wildlife. *Preprints* 2020, 2020120283 (doi: 10.20944/preprints202012.0283.v2).

European Food Safety Authority and European Centre for Disease Prevention and Control, Boklund, A., Gortazar, C., Pasquali, P., Roberts, H., Nielsen S.S., Stahl, K., Stegeman, A., Baldinelli F. Broglia, A., Ven der Stede, Y., Adloch, C., Alm, E., Melidou, A. & Mirinaviciute, G. (2021) Scientific opinion on the monitoring of

SARS-CoV-2 infection in mustelids. EFSA Journal 2021; 19(3):6459 68 pp. Guo, M., Tao, W., Flavell, R.A. *et al.* Potential intestinal infection and faecal–oral transmission of SARS-CoV-2. *Nat Rev Gastroenterol Hepatol* **18,** 269–283 (2021).

Gu, H, Chen, Q. Yang, G. et al. (2020) Adaptation of SARS-CoV-2 in BALB/c mice for testing vaccine efficacy. Science 369 (6511), 1603-1607

Jones DL, Baluja MQ, Graham DW, Corbishley A, McDonald JE, Malham SK, Hillary LS, Connor TR, Gaze WH, Moura IB, Wilcox MH, Farkas K. Shedding of SARS-CoV-2 in feces and urine and its potential role in person-to-person transmission and the environment-based spread of COVID-19. Sci Total Environ. 2020 Dec 20;749:141364. doi: 10.1016/j.scitotenv.2020.141364. Epub 2020 Jul 31. PMID: 32836117; PMCID: PMC7836549.

Montagutelli, X., Prot, M., Levillayer, L., Baquero Salazar, E., Jouvion, G., Conquet, L., Donati, F., Albert, M., Gambaro, F., Behillil, S., Enouf, V., Rousset, D., Jaubert, J., Rey, F., van der Werf, S. & Simon-Loriere, E. (2021) The B1.351 and P.1 variants extend SARS-CoV-2 host range to mice. bioRxiv 2021.03.18.436013; doi: https://doi.org/10.1101/2021.03.18.436013

SAGE (2020) Waste water C19 monitoring. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/940919/S0908_Wastewater_C19_monitoring_SAGE.pdf

Tun, H. M., Cai, Z., & Khafipour, E. (2016). Monitoring Survivability and Infectivity of Porcine Epidemic Diarrhea Virus (PEDv) in the Infected On-Farm Earthen Manure Storages (EMS). *Frontiers in microbiology*, *7*, 265. https://doi.org/10.3389/fmicb.2016.00265

Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA. 2020;323(18):1843-1844.

Xiao F, Sun J, Xu Y, Li F, Huang X, Li H, et al. Infectious SARS-CoV-2 in Feces of Patient with Severe COVID-19. Emerg Infect Dis. 2020;26(8).

Zhang Y, Chen C, Zhu S, Shu C, Wang D, Song J, et al. Isolation of 2019-nCoV from a stool specimen of a laboratory-confirmed case of the coronavirus disease 2019 (COVID-19). China CDC Weekly. 2020;2:123-4.