Department
for Environment
Food & Rural Affairs

What is the risk of a cervid TSE being introduced from Norway into Great Britain?

Qualitative Risk Assessment

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Summary

This document is the third update of a risk assessment dating from 2012 which originally investigated the risk of incursion of CWD from the USA and Canada. The assessment was updated in March 2016 to include a new import pathway, deer urine lures. In September 2016, a new update followed the report of CWD-like disease reported in Europe for the first time, when Norway reported cases in wild reindeer. Further cases have occurred in reindeer in Norway and it is currently unclear whether these cases are the result of two separate incursions of two different pathogens into two different species, or the same pathogen expressed differently in two species, or an incursion of a transmissible pathogen in the reindeer and cases of atypical CWD in moose (i.e. a spontaneous occurrence with genotypic risk criteria). Experiments have been initiated to answer these scientific uncertainties but during the interim this risk assessment has been updated to review any potential amendments required to the CWD import risk pathways into GB. Any updates which differ from the assessment of September 2016 will appear in blue throughout the main text.

The Norwegian Veterinary Institute reported a wild reindeer (*Rangifer tarandus tarandus)* found moribund and which later died in March 2016, had tested positive for the presence of prions. This was the first case of TSE found in a cervid in Europe and the first ever TSE case in a reindeer or caribou. In regions where chronic wasting disease is commonly found in native deer, there have been no reported cases in caribou (related to reindeer), but this is due to the isolation of the populations, rather than the refractivity of the species. The following month, two further cases were reported in wild moose (*Alces alces*), in a different region and again testing positive for TSE prion protein. In September 2016, a fourth case was detected, again in a reindeer in Nordfjell region, this time in a healthy bull, shot for disease surveillance. In June 2017, one of the animals was caught alive, anaesthetised and a sample of intestinal lymph tissue taken which subsequently tested positive. The animal was released with a radio-label and will be caught and killed. The Norwegian authorities have reported further cases, again in reindeer in the same region throughout June 2017 – June 2018 bringing the total number of cases to 19 in reindeer. The animals were within the region where a mass cull is in progress (due to be completed by May 2018). Surveillance in Norway consists of testing reindeer from the cull region and other cervids from across the country and to date (June 2018) nearly 42,000 animals have been tested. During this period, two other TSE-like cases were detected – and additional one in moose and one in a red dear (*Cervus elaphus*) although all appeared to have limited tissue distribution of the prion protein, restricted to the nervous tissue, and therefore presumed to be a spontaneous or atypical CWD-like disease. Finland has similarly detected a single case of atypical CWD in a moose in March 2018.

The previous assessment focused on the potential routes of entry for a cervid TSE (whether confirmed as chronic wasting disease or another related prion) from Norway. The main conclusions from this assessment were:

- The likelihood of further cases being found in wild reindeer in Norway is high, if confirmed as CWD as opposed to a spontaneous mutation event.

- The likelihood of further cases being found in moose is dependent on whether these are confirmed as a familial (atypical) case or if related to the TSE in the reindeer. Moose are generally solitary animals so the risk of spread will depend on the level of wider environmental contamination, rather than direct contact with other infected cervids.

- The likelihood of spread of a CWD type disease into the farmed reindeer herd or into other farmed cervids in Norway is difficult to assess, and depends on the level of contact between migratory wild reindeer and the semi herded populations in the north or with other farmed cervid species. In the USA, new foci are often detected first in farmed herds, before detection in local wild cervids, so the contact between these two discrete populations is clearly sufficiently high to facilitate transmission in North America. This should be assessed for Norwegian / Scandinavian populations.

- The likelihood of spread into other (wild) deer populations in Norway is medium.

- The possible routes of spread of TSE from Norway to the UK include movements of live animals, imports of deer-related products (urine lures, meat used as pet food), contaminated equipment, including clothing and hunting or skiing equipment and soil surrounding plant imports.

- The likelihood of a reindeer imported from Norway to the UK being infected with TSE is very low as they are imported from farmed herds, but there is uncertainty around this level of risk as it is not known if there is disease in the farmed herds.

- Other cervid species are not generally imported from Norway to the UK and therefore this is a lower risk pathway. If the pattern of trade changes, or if disease is detected over a wider area, the risk will also change.

- For other animals, the movement of pet dogs used for hunting or sledging competitions should be assessed for whether meat of cervid origin is fed to the animals. Where this occurs, this is considered a low risk of disease introduction.

- For other pathways, these are a non-negligible risk which is difficult to evaluate without understanding more on the extent of disease in Norway, but is likely to be between very low or low, depending on the pathway. For lures made from natural deer urine, where the provenance of the animal is unknown, the risk is medium for North American origin urine and Norwegian.

- As a result of the cases in Norway not all the risk levels have increased in comparison to the same risk pathways with an origin in North America.

- Reindeer in the UK are not commonly kept – there are small herds present including in the Cairngorms and Staffordshire and some seasonal imports. However

the poor outcome of reindeer kept in captivity in the UK means it is difficult to ascertain whether any may have been infected with prion disease – a fallen stock programme does not exist for such animals at present.

- Our previous assessment suggested that of the cervid British species, red deer (*Cervus elaphus elaphus*) are susceptible to CWD, fallow deer (*Dama dama*) may be less susceptible and the roe deer (*Capreolus capreolus*) prion gene codes for susceptibility (and are the most closely related to white-tailed deer). More recent experimental data suggest Sika deer, Chinese Water deer and Muntjac deer may also be susceptible. Therefore, it is likely that given exposure to an infectious dose of CWD or a related prion, deer in GB could become infected.

Overall, the probability of importing a TSE into the GB deer herds from Norway and causing infection in British deer is uncertain but likely to be **no greater than very low** via movement of deer hunters, other tourists and British service personnel; **at most, low** via live animal imports or imported (non-ruminant) animal feed; **very low** for the use of lures specifically sourced in Norway and **negligible** for plant imports. However, if it was imported and deer did become infected with CWD, the consequences would be severe as eradication of the disease is unfeasible, it is clinically indistinguishable from BSE infection in deer and populations of wild and farmed deer would be under threat.

Additional information provided now focuses on the risk levels for Norway rather than the USA and Canada and reviews the potential for cross species transmission. The public health aspects of the reindeer and moose atypical CWD / TSE are considered separately by the Food Standards Agency and Public Health England, but three assessments have been written as a joint project (to be published). The conclusions from the joint analysis are as follows:

1. What is the likelihood of any TSE being present in the UK cervid population? [Entry assessment] – **overall very low likelihood**
2. What is the likelihood of a cervid TSE causing infection in other livestock or wildlife species? [Exposure assessment] – **overall high risk for cervids, very low for other livestock.**
3. Does the moose / red deer TSE variant pose a different or greater risk than the reindeer strain present in Norway? [Consequence assessment] – **high uncertainty but considered unlikely**

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Background

Chronic wasting disease (CWD) is a highly infectious transmissible spongiform encephalopathy (TSE) that is circulating in the wild and farmed cervid populations of North America. It is the only TSE maintained in free-ranging wild animal populations. A feature of CWD is that it is able to transmit both directly (animal-to-animal) and indirectly via the contaminated environment. In particular, CWD prions are able to bind to and survive in the soil in a bio-available form for many years without any decrease in infectivity. This makes eradication of the disease from a wild population very unlikely.

Thus far, there have been no reported cases of CWD or other TSE in deer in Great Britain (GB). This is based on surveys of wild and farmed red deer (*Cervus elaphus elaphus*) carried out several years ago (EFSA, 2011). Given the consequences of CWD observed in North America, it is of high importance that GB remains free of the disease. Further, as the clinical signs of CWD in deer are similar to those of deer experimentally infected with bovine spongiform encephalopathy (BSE), all infected deer would need to be tested to differentiate if they were infected with CWD or BSE to minimise the risk of BSE entering the human food chain via affected venison. The public health risk of CWD is not known but current assessments suggest the risk is very low.

In 2015, the British Deer Society (BDS) carried out an online survey of BDS and BASC members to gather evidence about the use of deer urine as a lure. Fifteen percent of respondents (~1,800) answered yes about knowing that deer urine was used as a lure. Of the respondents, less than 2% responded yes to using such a product themselves. Of those that use the product, 50% had sourced the product from the USA, while 20% use more than a litre in volume a year and ~70% is natural (as opposed to synthetic).

UPDATE in September 2016: The report of TSE (CWD like) infection in Norwegian free ranging reindeer and then in European moose has increased the risk to the UK because of the trade in live animals and the different levels of activity for certain pathways, therefore we are reviewing those risk pathways. In addition, a further pathway was identified by a veterinary colleague overseas, which is that of plant and soil imports as well as for movement of hunting dogs so we have included these in the review.

UPDATE in June 2017: Norway is undertaking a mass cull in the Nordfjella region of all reindeer and will then leave the land fallow for a period of at least two years before re-introducing animals. The cull of 12,000 animals will include testing. The risk pathways for GB have not altered and the risk levels for introduction are the same as previously assessed and the ban on movement of cervids from Norway and parts of Sweden and Finland continues. Nevertheless, this assessment will consider any new evidence available to assess any cross-species transmission and the implication of the second, CWD-like atypical TSE infection in moose.

Update in May 2018: The cull in Nordfjella, Norway has finished. Over 41,00 cervids from across Norway have been tested. As part of ongoing enhanced surveillance in Finland during 2018, a 15 year old moose was found dead in Kuhmo region near the Russian

border and has also tested positive for TSE proteins. Tests suggest it is a similar tissue distribution as the other non-reindeer cases found in Norway.

Hazard identification

The hazard is identified as **CWD prions in wild European Reindeer, and atypical CWD prions in Moose and Red Deer**

The current geographic range of the cervid TSE, Chronic Wasting Disease (CWD) is the USA and Canada (and occasional outbreaks in South Korea following imports of infected animals). New foci of infection in the USA continue to be reported in both captive and free ranging cervidae. A new TSE type infection was identified in Norway, in a wild reindeer in March 2016 (NVI, 2016), which is now commonly referred to as CWD (EFSA, 2017), but further detections in moose and red deer will continue to be referred to as atypical CWD (although there is still some uncertainty about the relationship between the two prions in Norway). Recent evidence suggests there are several strains of CWD in the USA and Canada, but it has not been confirmed yet whether the Norwegian TSE prions are similar to any of the North American strains (EFSA, 2017).

In March 2018, a 15 year old wild moose, found dead in Kuhmo region, Finland near the border with Russia. The moose tested positive for prion protein and results were confirmed by the EU reference laboratory. Finland has tested ~2,500 cervids since 2003 and this is the first case to be detected. The Finish Authorities have confirmed the tissue distribution was similar to the cases detected in moose and red deer in Norway (EVIRA, 2018).

The very first case in Norway was a (found dead) adult reindeer cow showing signs of below-average body condition and detected in connection with capture for GPS-collaring, when it died. It was tested as a routine sample for the national surveillance programme for CWD at the Norwegian Veterinary Institute. Prion disease was confirmed in mid-March by both biochemical and immunohistochemical tests. According to the EURL, most of the samples from different organs were strongly positive for TSE prion protein. Samples were sent to the OIE reference laboratory (Canada) for confirmation as Chronic Wasting Disease. However, based on the widespread distribution of PrPCWD in the brain and the case history, the conclusion has been made that the animal had a spongiform encephalopathy compatible with CWD in the an early clinical stage (Benestad *et al.,* 2016). The animal was found in the Nordfjell region (see map below). In a second event, an adult (pregnant) female moose, (*Alces alces*) in the Sør-Trøndelag region was found with signs of poor body condition and lack of response to stimuli. It was culled and samples tested by both ELISA and Western blot tests. A third case was detected in another moose, found dead in a river near by a few days later. It also tested positive. There is approximately 300 km distance between the reindeer and the two elk (moose) cases. In a fourth case, in August 2016, a reindeer bull was shot and tested positive as part of a surveillance programme, also in the Nordfjell region (Sogn og Fjordane) and a fifth case, again in a reindeer (cow) shot by hunters in the same region was detected in September 2016. The North American moose (also *Alces alces*) is susceptible to CWD and cases have been

found across the moose populations in both the USA and Canada. *Alces alces* is different to the North American elk (*Cervus canadensis*) which is also susceptible to CWD.

One case (June 2017) was a healthy reindeer which was caught and anaesthetised in the Nordfjella region. Samples of intestinal lymph node tested positive for CWD. The animal was released with a radio-label tag and will be re-caught and culled.

http://wwweng.vetinst.no/eng/Highlights/Detection-of-Chronic-Wasting-Disease-in-two-Norwegian-moose.html

http://www.mattilsynet.no/dyr_og_dyrehold/dyrehelse/dyresykdommer/skrantesjuke__cwd_/ny_paavisning_av_skrantesjuke.23759

https://www.mattilsynet.no/dyr_og_dyrehold/dyrehelse/dyresykdommer/skrantesjuke__cwd_/ny_paavisning_av_skrantesjuke.26714?utm_campaign=Nyhetsbrev&utm_medium=Epost&utm_source=Mattilsynet&utm_term=Ny_paavisning_av_skrantesjuke&utm_content=Dyrehelse

The passive surveillance system in Norway has been running since 2003 and involves testing samples from wild native cervid species of which there are four, red deer (*Cervus elaphus*), roe deer (*Capreolus capreolus*), moose (*Alces alces*) and reindeer (*Rangifer tarandus*) and from captive deer (Sviland et al, 2015). Red deer predominate along the west coast, wild reindeer live in high mountain areas in southern Norway (see map above). In 2013, the numbers of hunted cervids were nearly 35,000 moose, over 36,000 red deer, over 25,000 roe deer and nearly 8,000 reindeer. There is also a semi-domestic (herded) reindeer population of 250,000 which are located in north Norway and managed by the Sami people, and some of these animals will also be tested. There are 90 deer farms which mainly keep red deer and some keep fallow deer (*Dama dama*). Scrapie is present in sheep in areas where there are free ranging red deer populations. The number tested each year is very small; in 2014, only 10 deer were tested (all negative), and none of them reindeer. In 2013, again, just ten animals were tested (all negative) (Sviland et al, 2014) and in 2012, 21 animals were tested (all negative) and none were reindeer (Vikoren et al., 2013). This level of surveillance means that when a single positive sample is recorded, it suggests a high prevalence level is likely but the statistical confidence in such sampling is very low. It is not known how many animals have been tested in 2015/2016 for CWD under the Norwegian programme. The Norwegian Authorities are proposing a large surveillance programme to start in the autumn of 2016, to test around 15,000 animals (moose, roe deer, red deer and reindeer) for fallen stock, hunted animals and at game slaughter houses and approved locations. By the end of May 2018, 41,685 animals had been tested (including 10,627 moose, 4,658 free ranging reindeer, 14,914 semi-domesticated reindeer and 6,711 red deer). In Nordfjella the Norwegian authorities have analysed 2,469 free ranging reindeer and with 19 positive, this suggests a cluster prevalence of around 1% (http://apps.vetinst.no/skrantesykestatistikk/NO/). Recently the Norwegian authorities have announced a mass cull of reindeer in the Nordfjella region has been completed in an effort to eliminate the disease. The land will be left fallow for a period of 5 years following the end of the cull.

The pattern of prion infectivity in the brain of the Norwegian TSE cases in reindeer and moose or red deer show differences when compared by immunohistochemistry and western blot profiles. The reindeer CWD type seems to be similar to what is found in North America. The moose / red deer TSE type seems to be unidentified previously. Bioassay work is ongoing in collaboration with several international laboratories to address the strain properties of the Norwegian CWD cases. This was presented (oral presentation) at the Prion2017 meeting In Edinburgh (Sylvie Benestad, November 2016, Amie Adkin pers comm.).

In Europe and North America, moose or elk (*A.alces*) are solitary animals, coming together primarily in the mating season, although young stay with their mothers for several months until the next offspring is born. There is a wide level of variation in their movement behaviour with some undertaking very long range migrations, and others being more sedentary. These movements can be categorised as migration, dispersal, nomadism or residence. In Scandinavia, seasonal migration is more likely in northerly populations (regions north of 66^{o}N) than those in the southern regions (regions between 56^{o}N and 66^{o}N) and mean distances decline from ~100 km to 5 km. Seasonal migration can also change with time, depending on the environmental changes, climate or urbanisation. A recent study into the population genetics of *Alces alces* in Europe suggests there are genetically distinct populations, with the Scandinavian cluster showing low genetic diversity and separate to the other European populations (Niedziałkowska et al. 2016). Nevertheless, the low genetic mixing does not preclude mixing of animals at common grazing areas and therefore having access to contaminated land.

The genetic sub-structuring of the *A.alces* population in Scandinavia could be partly due to geographic barriers, such as the Scandes mountain range which separates Sweden and Norway. This supports the understanding that there is a lower risk of direct disease transmission to other populations of cervids, even of the same species, which are separated by semi-permeable geographic boundaries. However, if there has been widespread environmental contamination over time from a common source of prion, then the risk to other populations will be more difficult to assess.

Chronic Wasting Disease was first identified as a clinical disease of captive mule deer in Colorado in 1967 and later classified as a TSE in 1978 (Williams & Miller, 2003). The origin of the disease is unknown and may have been a spontaneous TSE that arose in deer. Currently, natural infections of CWD have been reported in the USA and Canada in mule deer (*Odocoileus hemionus hemionus*), black-tailed deer (*Odocoileus hemionus columbianus*), white-tailed deer (*Odocoileus virginianus*), Rocky Mountain elk (*Cervus elphus nelsoni*), Shira's moose (*Alces alces shirasi*) and mule deer and white-tailed deer hybrids (Hamir *et al*., 2008). CWD has a significant impact on the population of white tailed deer in the USA where it is currently causing a 10% population decline (Edmunds et al. 2016).

Caribou (*Rangifer tarandus caribou*, *R.t. granti* and *R.t. goenlandicus*) are a subspecies of the Eurasian reindeer, *Rangifer tarandus* and several populations overlap with the current CWD distribution in Canada. The disease has not been reported in the scientific literature

in caribou as natural infections. However, experimental infection of six reindeer resulted in TSE in two of the six animals via oral inoculation (Mitchell et al, 2012). In this study on experimental infection in reindeer, Mitchell and colleagues showed that the two out of three reindeer infected with CWD prion protein (PrP) from brain homogenates of infected white-tailed deer started to show clinical signs between 17 and 18 months after oral inoculation. The same infection route using PrP from infected elk brains did not result in clinical infection in three further reindeer. Results from histopathology showed PrP present in peripheral lymphoid tissue, in the kidney, the pituitary and adrenal glands, in nerves associated with the gastro-intestinal tract and of course the brain and central nervous system.

A recent publication of an experimental infection in reindeer (Moore et al., 2016) showed that the species is susceptible to CWD PrP derived from a range of hosts (elk, mule deer and white tailed deer) when infected intracranially, that clinical signs are seen on average 20 months post infection and that both direct and indirect horizontal transmission to naïve reindeer can occur (i.e. through contact with contaminated environment or secretions from infected animals).

The widespread distribution in the USA and two Canadian provinces may be detected because of enhanced surveillance but may have increased because of natural movements of cervids and translocation of infected animals by humans (EFSA, 2011). Within affected areas, the prevalence varies. In the endemic area of Wyoming, for example, the prevalence of CWD in mule deer has increased from approximately 11% in 1997 to 36% in 2007 (Almberg *et al*., 2011). In such areas, population declines of deer of up to 30 to 50% have been observed (Almberg *et al*., 2011; Edmunds, *et al,* 2016) and diseased deer are more represented in the hunting bag, which is important when considering the public health risk. In areas of Colorado, the prevalence can be as high as 30% (EFSA, 2011). However the separation between caribou populations in Canada and affected cervids is probably the main reason for disease not being detected.

The clinical signs of CWD in affected adults are weight loss and behavioural changes that can span weeks or months (Williams, 2005). In addition, signs might include excessive salivation, behavioural alterations including a fixed stare and changes in interaction with other animals in the herd, and an altered stance (Williams, 2005). These signs are indistinguishable from cervids experimentally infected with bovine spongiform encephalopathy (BSE). Given this, if CWD was to be introduced into countries with BSE such as GB, for example, infected deer populations would need to be tested to differentiate if they were infected with CWD or BSE to minimise the risk of BSE entering the human food-chain via affected venison.

The duration of clinical disease is highly variable and death can occur within 4 weeks but some infected animals may survive as long as a year (Williams, 2005). The incubation period is a minimum of approximately 16 months and is more likely to be between 2 and 4 years (Williams, 2005). In affected American elk, the incubation period is between 1.5 and 3 years after which they become clinically affected and may succumb less than 12 months

after initial clinical signs appear (Miller *et al.*, 1998). During the pre-clinical period, the animal is infectious (Almberg *et al*., 2011).

The CWD agent or Prion Protein (P_rP^{CWD}) in affected animals is distributed firstly in the gut associated lymphoid tissues, digestive tract (e.g. tonsils, Peyer's patches, mesenteric lymph nodes) and then in the brain and spinal cord as the disease progresses (Sigurdson, 2008). Prions of CWD have also been found in muscle tissue (Angers *et al.*, 2006) (see Figure 1). The distribution and levels of PrP^{CWD} in tissues differ between species (e.g. American elk versus white tailed or mule deer).

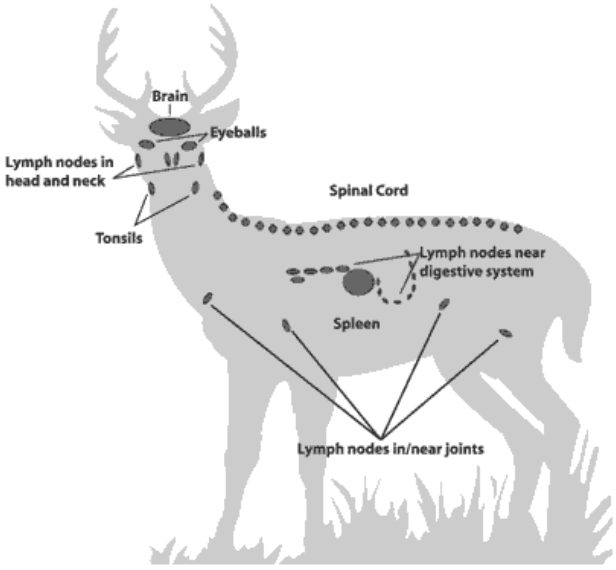


Figure 1: Diagram displaying the main organs affected by CWD in infected cervids (http://www.dnr.state.mn.us/mammals/deer/cwd/index.html)

Given its propensity to colonise the digestive tract, evidence suggests the prion is excreted in faeces (Safar *et al*., 2008), urine and saliva potentially leading to direct and indirect transmission between cervid species. Indeed, the disease is transmitted horizontally with high efficiency and circumstantial evidence suggests that environmental contamination with CWD prions contributes to the maintenance of CWD in affected areas (Safar *et al*., 2008; Nalls *et al.*, 2013). The rate of transmission of CWD has been reported to be as high as 30% and can approach 100% among captive animals in endemic areas (Safar *et al*., 2008). The efficiency of CWD transmission is unparalleled among TSE diseases (EFSA, 2011). Trifilo *et al*., (2007), using a murine tg mouse model, established that CWD can be transmitted via the oral route. Indeed, the distribution of PrPres in the orally infected mice (e.g. in the spleen and lymph nodes) mimicked what has been reported in deer developing CWD via natural infection (Trifilo *et al.,* 2007). Modelling studies also support the theory that transmission of CWD in deer herds is maintained by contact with a prion contaminated environment (Almberg *et al*., 2011). Scavenging of CWD-infected carcasses provides another route of releasing the prion into the environment and exposure of non-cervid species (Sigurdson, 2008). This indirect transmission route is problematic as it not only increases the basic reproductive number but also because there are very few effective mitigation strategies for reducing the risk from indirect transmission. This is due to the fact that the agent is extremely resistant in the environment and able to bind to soil particles

making eradication and control of CWD a major obstacle in both farmed and free-ranging cervid populations.

The hypothesis that disease can be transmitted between cervid species has been supported by recent experimental studies that have demonstrated that European red deer become infected with CWD after oral inoculation with brain tissue from infected Rocky Mountain elk (Balachandran *et al*., 2010). Specifically, two of the four 2-month old red deer challenged, showed clinical signs by 585 days p.i. and all deer had CWD prion in the brain, spinal cord and other organs at necropsy (Balachandran *et al*., 2010). Further, Martin *et al*., (2009) demonstrated in a similar study of four European red deer, that red deer can become infected upon inoculation with 5g of infected brain homogenate from four CWD elk and hence the species is susceptible to CWD.

Hamir *et al*., (2008) undertook a study to ascertain if fallow deer (*Dama dama*), another British deer species, could be experimentally infected with CWD brain suspension from infected elk or white-tailed deer. The authors concluded that it is possible to transmit CWD to fallow deer via the intracerebral route but the pathological features of CWD in the deer differs from those observed in white-tailed deer or elk (Hamir *et al*., 2008). It was further concluded that it might not be possible to transmit CWD via a more natural route or, alternatively, a higher dose of inoculum is required leading to a longer incubation period (Hamir *et al*., 2008). However it should be noted that these animals were all sourced from a single breeder therefore genetic diversity would be low and it cannot be ruled out that other fallow deer sourced from other breeders with greater heterogeneity would behave differently.

Initial studies into the PRioN Protein (PRNP) gene variability in European red deer and roe deer suggest that these species have a PRNP genetic background that is compatible with TSE susceptibility, including CWD (EFSA, 2011). It is important to note, however, that no experimental studies on roe deer have been conducted verifying this hypothesis.

Recent data on the susceptibility of the other free-ranging deer species present in Britain (muntjac (*Muntiacus reevesi*), sika (*Cervus nippon*), Chinese Water deer (*Hydropotes inermis*)) to CWD also suggests variability in susceptibility for these species (Robinson et al., 2012; Nalls et al., 2013). Further experimental studies would be required to investigate the susceptibility of these species to CWD. Therefore, on the basis of current scientific understanding, it is likely that given exposure to an infectious dose to CWD, most deer species in GB could become infected with CWD.

Recent research on reindeer also suggests that direct transmission is possible between reindeer and therefore these populations, albeit not native to the UK, would also be susceptible (Moore et al, 2017).

A study funded by the Defra and the British Deer Society is investigating the sequences of the genes coding for the PrP protein in those deer present in the British cervid population for mutations which would suggest susceptibility (Fiona Houston, Roslin Institute, Pers Comm). Initial conclusions suggest that the PrP protein sequence shared by British red, roe and sika deer is identical to that found in CWD-susceptible North American cervids;

British red deer express at least three additional PrP sequence variants but whether this changes susceptibility is not known.

Sheep and cattle may be exposed to CWD via common grazing areas with affected deer but so far, appear to be poorly susceptible to mule deer CWD (Sigurdson, 2008). In contrast, cattle are highly susceptible to white-tailed deer CWD and mule deer CWD in experimental conditions but no natural CWD infections in cattle have been reported (Sigurdson, 2008; Hamir *et al*., 2006). It is not known how susceptible humans are to CWD but given that the prion can be present in muscle, it is likely that humans have been exposed to the agent via consumption of venison (Sigurdson, 2008). Initial experimental research suggests that human susceptibility to CWD is low and there may be a robust species barrier for CWD transmission to humans (Sigurdson, 2008), however the risk appetite for a public health threat may still find this level unacceptable. Recent experimental data suggests cynomolgus macaques can be experimentally infected with CWD when intracranially injected with homogenised brain samples from infected cervids. However, intracranial injection is a more productive transmission route than oral transfection. Nevertheless, when fed meat from infected animals, the macaques also developed clinical signs (HPFB, 2017). This suggests some cross-species infection may be possible, and has prompted some health messages from the Canadian government associated with the consumption of infected deer meat. However, a second study by Race et al. (2018) reported that experimental infection of Cynomolgus macaques over 13 years however showed no evidence of clinical signs or infection with highly specific prion screening tests. There were some anomalies in PrP deposits in some of the animals (including the non-inoculated controls) but these deposits were not associated with PrP^{Sc}, the disease-associated form.

Surveys of wild and farmed cervid populations in the European Union between 2006 and 2010 did not identify any TSEs (EFSA, 2011). As part of this survey, 601 farmed and 598 wild red deer (*Cervus elaphus elaphus*) were tested (EFSA, 2010). These included clinical/sick animals, fallen stock, healthy shot/slaughtered animals and road killed animals. Based on the survey results, it was concluded that the prevalence of CWD in the EU is less than 0.5%. The results in Norway, where only five reindeer have tested positive out of several thousand tested, agrees that this is a disease with very low prevalence.

Risk Question

This risk assessment considers the risk posed to the Great Britain (GB) deer population if chronic wasting disease (CWD) is confirmed in Norway. The specific risk question addressed has been updated to cover the request from the Chief Scientist's Office in 2017 and is:

What is the risk of any TSE being introduced into Great Britain (GB) from Norway and causing infection in deer or other livestock or wildlife populations?

To answer the above question, the risk assessment follows the OIE framework of release (or entry), exposure and consequence assessment. Specifically, it is divided into the three key areas:

4. What is the likelihood of any TSE being present in the UK cervid population? [Entry assessment]
5. What is the likelihood of a cervid TSE causing infection in other livestock or wildlife species? [Exposure assessment]
6. Does the moose TSE variant pose a different or greater risk than the deer strain present in Norway? [Consequence assessment]

Risk Assessment

Terminology related to the assessed level of risk

For the purpose of the risk assessment, the following terminology will apply (OIE, 2004):

Negligible	So rare that it does not merit to be considered
Very low	Very rare but cannot be excluded
Low	Rare but does occur
Medium	Occurs regularly
High	Occurs often
Very high	Event occurs almost certainly

Entry assessment

The routes by which any TSE may be introduced into GB from Norway include:

- Importation of live deer (including reindeer, other cervids, other animals)
- Importation of deer urine lures
- Importation of meat and other products derived from cervid species (e.g. trophy items including antlers, semen)
- Importation of animal feed
- Hunters and other tourists (skiers and walkers) and British servicemen travelling from affected areas to GB with contaminated equipment (e.g. boots, clothing, knives)
- Importation of plants, shrubs and trees with root balls where the soil could be contaminated with prion protein

UPDATE IN JUNE 2017: The estimated risk of each of these risk pathways into GB remains as follows:

- Very low for the entry pathway involving meat or other products of animal origin (skins, antlers, semen)

- Very low for animal feed due to the low level of pet food produced in Norway for the European market derived from wild reindeer and exported.

- Very low for deer urine lures - the risk was considered medium for exports from the USA, but is considered to be very low for Norway given the lower number of hunters and lack of evidence of these products, produced from Norwegian stock, being sold over the internet.

- Non-negligible risk from movement of equipment or people from Norway, however the risk would depend on the frequency of movement and there is considerable uncertainty as to the exact areas within Norway where environmental contamination may be considered to be of risk. .

- Very low risk (high uncertainty) for live animal trade from Norway, as the electronic trade notification system indicates that in the last five years there have been no consignments of reindeer or moose to the UK. Other cervids have been consigned, but these populations are not considered to be infected. Going forward, live cervid trade is not permitted from Norway, parts of Sweden and Finland for the foreseeable future into GB.

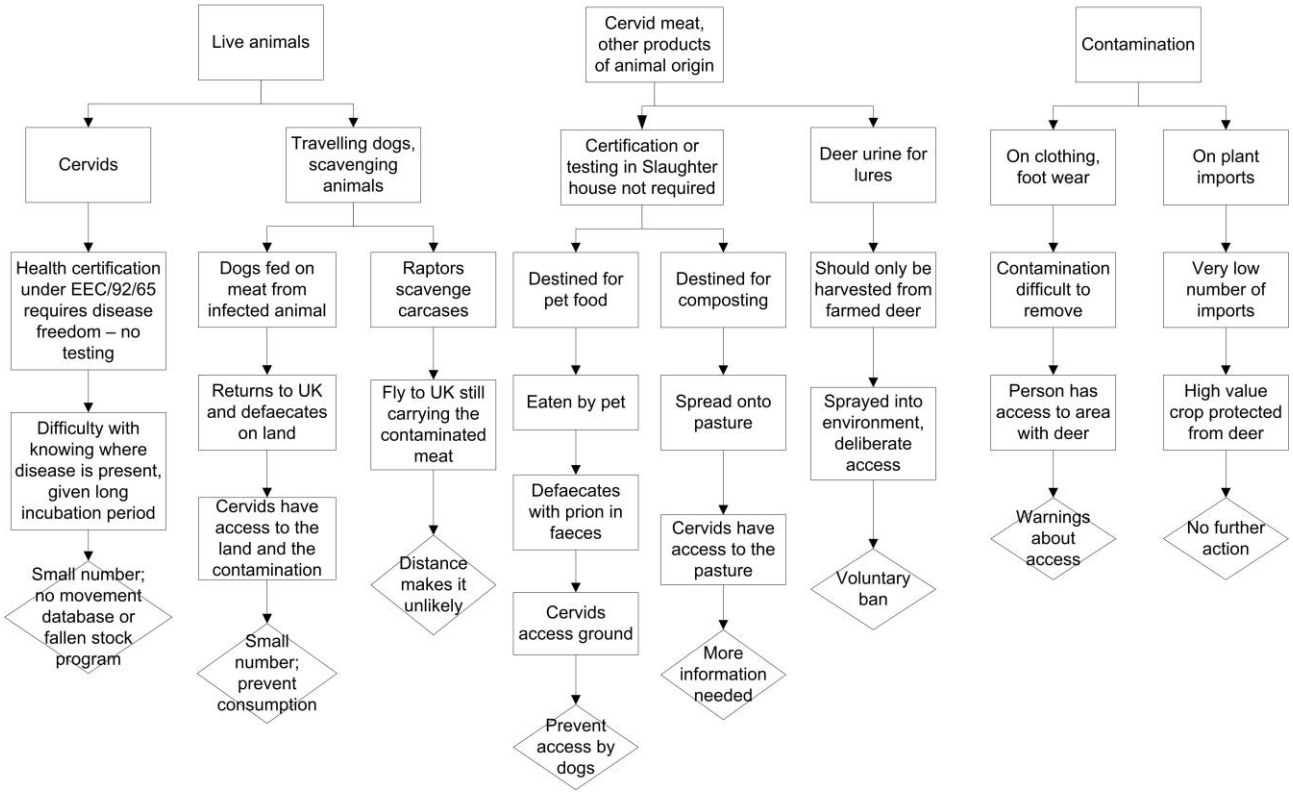
- Low risk (high uncertainty) for the live animal trade of other animals, such as working dogs which may have been fed CWD-infected pet food or meat in Norway.

- Very low, if not negligible risk, for plant imports where root balls may be associated with soil contaminated with prion protein.

Below is a schematic of the different pathways which could potentially lead to entry of CWD to the UK. Note, the human exposure pathway is not included here.

For each pathway, the end point is the possible action which could be put in place.

Schematic pathway for introduction of Chronic Wasting Disease through movement of live animals, products or contamination



Exposure assessment

Imports of live animals

Should an infected animal be imported into the resident herds in GB, there is a **high probability** disease would spread to other in-contact conspecifics, but the level of contact with wild deer may not be as high as for other species (as these are valuable animals kept for a limited time until slaughter weight). It is nevertheless, difficult to prevent contact between wild and farmed deer and in the USA, disease is often detected first in farmed deer where there are more regular inspections. Since our last assessment, awareness campaigns has been initiated for all keepers of cervids, including reindeer and report cases should be expected on an occasional basis.

Moose (*Alces alces*) are not a widespread species in the UK naturalised or in captivity. There are some individuals in collections (zoos for example) and two herds in Scotland, one at the Alladale Estate and one at the Scottish Deer Centre in Fife. These premises have not had any animals recently imported into the herds from Scandinavia.

Importation of animal feed or products of animal origin

Assuming the TSE Feed Ban and ABP regulations are adhered to correctly, the risk of farmed deer which are enclosed, being exposed to animal feed containing deer protein from Norway is considered **negligible** but with associated low uncertainty.

There are a number of pathways by which wild deer could gain access to different categories of imported animal by-products.

Wild deer may gain access to non-ruminant feed (e.g. pig, fish and chicken feed) on farms near their habitat. Alternatively, wild deer may be exposed to TSE prion in the faeces of pets that have consumed and digested imported, contaminated pet feed. Food may be diverted to composting and the resulting effluent spread on pasture to which wild deer have access. The frequency in which these routes may occur is unknown and is considered to be a **greater than negligible** risk with associated medium uncertainty.

Exposure to environmental contamination

Whether through imported urine lures, faecal or urine-contaminated feed and salt licks or soil contamination on boots, equipment and clothing, these are all pathways for exposure which are possible, but highly difficult to quantify at the current time and therefore are assigned a **very low** risk score, based on the likelihood of entry and the contact with cervids in the UK.

Exposure to other livestock species

Bovine Spongiform Encephalopathies (BSE) in cattle

According to the most recent EFSA report on slaughter house, fallen stock and clinical report case surveillance carried out in the European Union since 2001 (EFSA, 2016), approximately 114 million bovine animals have been tested for BSE. Since 2002 8.4 million small ruminants were tested for scrapie. In addition, in 2015 alone 580 samples from other species such as domestic cats, foxes and mink were also tested and all were negative. In terms of scrapie infection in sheep, the classical type represents around 95% of cases. Any flock with atypical scrapie cases will undergo intensified surveillance for two years. In terms of BSE, three types can currently be differentiated: H-BSE, L-BSE or C-BSE, with only the latter giving significant cause for concern in terms of public health risk as for any herd with C-BSE, all animals over 18 mo old will be culled out. There is a very low occurrence of H-type and L-type over time, with very few not defined as one of the three types. Therefore it is reasonable to suggest that given the level of awareness and testing at the EU level, if CWD had been present in Europe for many years and if spill over had occurred into livestock it would have been detected.

The recent EFSA opinion (2017) intracerebral transmission to cattle results in ~40% of cattle testing positive for PrP^{Sc}. In sheep, low rate of disease was observed, depending on host genotype. Experimental data with transgenic mice (expressing deer PrP) have shown that the species barrier is not complete where it comes to transmission in experimental circumstances, although transmission to some species such as ferrets and other mice is less efficient. However the widespread environmental contamination in certain regions of the USA where CWD is present in free ranging and captive deer has not resulted in detected of infection in other species through natural transmission.

Consequence assessment

We were asked specifically to consider whether a possible difference between the two cervid TSEs present in Norway would pose a difference in the level of risk and if there was a greater risk from the moose variant than the reindeer variant. According to the Norwegian authorities, there are differences in the pattern of distribution of the prion protein in the affected reindeer and moose, which may suggest two separate TSEs circulating in Norway.

We consider that the likelihood of the reindeer variant spreading from one cervid to another, both conspecifics and different species is high. Evidence from the USA and Canada confirms that spread from wild to domestic or farmed deer is possible and that eradication is difficult and costly; in fact eradication has only been successful where an early incursion is detected. This is a slow moving disease, and eventually it could have a substantial impact on the national herd, if left uncontrolled, and could also impact on trade, biodiversity, tourism (access to the countryside) and agriculture.

There are uncertainties about the moose variant, which from initial reports, appears to be a genetic mutation in a familial group. It is too early to say however, whether environmental contamination would be seen with these atypical CWD infections, and therefore whether the likely entry pathways for disease incursion associated with this prior are the same as for CWD. However we would consider there be a no greater risk than that from the pathways associated with typical CWD infections. In BSE infected cattle, where PrP^{Sc} is restricted similarly to the nervous tissue, there is little environmental contamination as prions are not found in the saliva, faeces or other tissues, unlike CWD and scrapie (Davenport et al., 2018).

In terms of either TSE variant being capable of infecting other livestock species, field evidence from the USA and Canada suggests this is unlikely for the reindeer CWD, but the species barrier in experimental circumstances does not provide confidence that other species may become infected. However, we suggest it is too early to say for the atypical moose CWD and even comparing the American situation with Europe may be precipitous, but the restricted tissue distribution suggests transmissibility in the field is less likely.

Conclusions

There is significant uncertainty associated with estimating the risk of TSE entering the UK from Norway via imports of live animals, movement of people (tourists, hunters and British servicemen) and importation of animal feed or urine lures. This stems from the lack of data on the current distribution of disease, not only in wild reindeer and moose in Norway, but also in herded animals and more widely in other wild cervids across the region and neighbouring counties. Notwithstanding this uncertainty, the probability of importing TSE

into GB from Norway and causing infection in British deer is likely to be **greater than negligible** via movement of deer hunters, other tourists and British servicemen and **low** via live animals, **very low** via products of animal origin or imported (non-ruminant) animal feed. However the risk of natural deer urine lures from Norway is lower than for those products sourced from the USA and the probability of such a commodity, if used in significant volumes, leading to CWD infection in GB populations is considered to be **very low** (potentially reduced susceptibility in certain species and limited use by hunters and stalkers in GB) but with a high level of uncertainty, around the volumes which may be imported and used.

The consequences of CWD, however, are severe with the minimal possibility of eradicating the disease from a wild cervid population and populations of both wild and farmed deer in the UK would be under threat.

Current research indicates that of the six free-ranging deer species in the UK, red deer, and muntjac are susceptible to CWD, while roe deer, which is the closest related to white-tailed deer, Japanese sika and Chinese water deer are likely to also be susceptible. Farmed fallow deer are numerous in the UK and while those studied to date have lacked the PRNP polymorphisms associated with higher susceptibility to CWD, our populations are genetically heterogenous so the risk of infection cannot be ruled out. Wild roe deer are even more numerous, so again, understanding the susceptibility of this species will be important.

While we test for BSE in cattle and scrapie in sheep and goats, we do not know what CWD infection in livestock would manifest as, in terms of tissue distribution and if it would be identified in conventional tests during passive surveillance. It remains important, therefore, that the risk of any species being exposed to TSE is minimised by taking appropriate precautionary measures.

This assessment will be kept under review and updated as more information becomes available.

References

Almberg, E.S., Cross, P.C., Johnson, C.J., Heisey, D.M. & Richards, B.J. (2011) Modeling routes of chronic wasting disease transmission: environmental prion persistence promotes deer population decline and extinction. *PLos ONE*, 6(5), e19896.

Angers, R.C, Browning, S.R, Seward, T.S., Sigurdson, C.J., Miller, M.W., Hoover, E.A., & Telling, G.C. (2006) Prions in skeletal muscles of deer with chronic wasting disease. *Science*, 311, 1117.

Anon (2015a) http://www.fieldandstream.com/blogs/field-notes/virginia-bans-deer-urine-lures

Anon (2015b) http://www.bloomberg.com/bw/articles/2012-08-31/odd-jobs-deer-urine-farmer

Anon (2015d) Tink's natural attraction http://www.trophybucklure.com/

APHIS (2015) Voluntary National Herd CWD Certification Programme. See APHIS website at Link Accessed August 2015.

Balachandran, A., Harrington, N.P., Algire, J., Soutyrine, A., Spraker, T.R., Jeffrey, M., Gonzalez, L., & O'Rourke, K.I. (2010). Experimental oral transmission of chronic wasting disease to red deer (*Cervus elaphus elaphus*): Early detection and late stage distribution of protease-resistant prion protein. *Canadian Veterinary Journal-Revue Veterinaire Canadienne*, 51, 169-178.

Benestad, S.L., Mitchell, G., Simmons, M., Ytrehus, B. & Vikoren, T. (2016) First case of Chronic Wasting Disease in Europe in a Norwegian free-ranging reindeer. Veterinary Research 48:88 DOI: 10.1186/s13567-016-0375-4.

Dalgleish, M.P., Martin, S., Steele, P., Finlayson, J., Siso, S., Hamilton, S., Chianini, F., Reid, H.W., Gonzalez, L., & Jeffrey, M. (2008) Experimental transmission of bovine spongiform encephalopathy to European red deer (Cervus elaphus elaphus). *BMC Veterinary Research, 4,* 17.

Davenport, K.A., Christiansen, J.R., Bian, J., Young, M., Gallegos, J., Kim, S., Balachandran, A., Mathiason, C.K. Hoover, E.A & Telling, G.C. (2018) Comparative analysis of prions in nervous and lymphoide tissues of chronic wasting disease-infected cervids. Journal of General Virology 2018;99:753–758

Defra (2016) Qualitative risk assessment: risk of chronic wasting disease being introduced into Great Britain. https://www.gov.uk/government/publications/qualitative-risk-assessment-risk-of-chronic-wasting-disease-being-introduced-into-great-britain Published 6 April 2016.

Edmunds, D.R., Kauffman, M.J., Schumaker, B.A., Lindzey, F.G., Cook, W.E., Kreeger, T.J., Grogan, R.G., Cornish, T.E. (2016) Chronic Wasting Disease drives population decline of white-tailed deer. PLoS One 11(8):e0161127. doi:10.1371/journal.pone.0161127

EFSA (2004) Annex to the EFSA Journal (2004) 70 On the Opinion on a surveillance programme for Chronic Wasting Disease in the EU.

EFSA Panel on Biological Hazards. (2011) Joint Scientific Opinion on any possible epidemiological or molecular association between TSEs in animals and humans. *EFSA Journal*, 9(1), 1945.

EFSA Panel on Biological Hazards. (2010). Scientific Opinion on the results of the EU survey for Chronic Wasting Disease (CWD) in cervids. *EFSA Journal*, 8(10), 1861.

EFSA (2016) The European Union summary report on data of the surveillance of ruminants for the presence of transmissible spongiform encephalopathies (TSEs) in 2015. doi:10.2903/j.efsa.2016.4643
http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4643/epdf

EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Fern_andez Esc_amez PS, Giron_es R, Herman L, Koutsoumanis K, Lindqvist R, Nørrung B, Robertson L, Sanaa M, Skandamis P, Snary E, Speybroeck N, Kuile BT, Threlfall J, Wahlstr€om H, Benestad S, Gavier-Widen D, Miller MW, Ru G, Telling GC, Tryland M, Ortiz Pelaez A and Simmons M (2017) Scientific opinion on chronic wasting disease (CWD) in cervids. EFSA Journal 2017;15(1):4667, 62 pp. doi:10.2903/j.efsa.2017.4667

EVIRA (2018) Moose found dead in forest with chronic wasting disease. https://www.evira.fi/en/animals/current_issues/2018/moose-found-dead-in-forest-with-chronic-wasting-disease/

Gale, P. (1998) Quantitative BSE risk assessment: relating exposures to risk. Letters in Applied Microbiology, 27, 239-242.

Gale, P., Young, C., Stanfield, G. & Oakes, D. (1998) Development of a risk assessment for BSE in the aquatic environment. Journal of Applied Microbiology, 84, 467-477.

Gale, P. (2006) The infectivity of transmissible spongiform encephalopathy agent at low doses: the importance of phospholipids. Journal of Applied Microbiology, 101, 261-274.

Georgsson, G., Sigurdarson, S., & Brown, P. (2006) Infectious agent of sheep scrapie may persist in the environment for at least 16 years. *Journal of General Virology*, 87, 3737-3740.

Hamir, A.N., Kunkle, R.A., Miller, J.M., Greenlee, J.J., & Richt, J.A. (2006) Experimental second passage of chronic wasting disease ($CWD^{mule\ deer}$) agent to cattle. *J. Comp. Path*, 134, 67-73.

Henderson, D.M., Davenport, K.A., Haley, N.J., Denkers, N.D., Mathiason, C.K. & Hoover, E.A. (2015) Quantitative assessment of prion infectivity in tissues and body fluids by real time quaking-induced conversion. Journal of General Virology 96: 210-219.

HPFB (2017) Health Products and Food Branch Risk Advisory Panel: Potential health risks from Chronic Wasting Disease. https://www.thetyee.ca/Documents/2017/06/24/Risk-Advisory-Opinion-CWD-2017.pdf

ITC (2016) Trade Map: Trade statistics for international business development: Monthly, quarterly and yearly trade data. Import & export values, volumes, growth rates, market shares, etc. http://www.trademap.org/Country_SelProductCountry.aspx

Johnson, C.J., Philips, K.E., Schramm, P.T., McKenzie, D., Aiken, J.M., & Pedersen, J.A. (2006) Prions adhere to soil minerals and remain infectious. *PLoS Pathogens*, 2 (4), e32.

Johnson, C.J., Pedersen, J.A., Chappell, R.J., McKenzie, D., & Aiken, J.M. (2007) Oral transmissibility of prion disease is enhanced by binding to soil particles. *PLoS Pathogens*, 3 (7), e93.

Martin, S., Jeffrey, M., Gonzalez, L., Siso, S., Reid, H.W., Steele, P., Dagleish, M.P., Stack, M.J., Chaplin, M.J., & Balachandran, A. (2009) Immunohistochemical and biochemical characteristics of BSE and CWD in experimentally infected European red deer (*Cervus elaphus elaphus*). *BMC Veterinary Research*, 5:26.

Miller, M.W., Wild, M.A., & Williams, E.S. (1998) Epidemiology of chronic wasting disease in captive rocky mountain elk. *Journal of Wildlife Diseases*, 34 (3), 532-538.

Mitchell GB, Sigurdson CJ, O'Rourke KI, Algire J, Harrington NP, et al. (2012) Experimental Oral Transmission of Chronic Wasting Disease to Reindeer (Rangifer tarandus tarandus). PLoS ONE 7(6): e39055. doi:10.1371/journal.pone.0039055.

Moore S, Kunkle R, Greenlee M, Nicholson E, Richt J, Hamir A, et al. Horizontal Transmission of Chronic Wasting Disease in Reindeer. Emerg Infect Dis. 2016;22(12):2142-2145. https://dx.doi.org/10.3201/eid2212.160635

Nalls, A.V., McNulty, E., Powers, J., Seelig, D.M., Hoover, C., Haley, N.J., Hayes-Klug, J., Anderson, K., Stweart, P., Goldmann, W., Hoover, E.A. & Mathiason, C.K.(2013) Mother to offspring transmission of Chronic Wasting Disease in Reeve's Muntjac deer. PLoS One http://dx.doi.org/10.1371/journal.pone.0071844

NVI (2016) The first detection of Chronic Wasting Disease (CWD) in Europe. Norwegian Veterinary Institute. http://www.vetinst.no/sykdom-og-agens/chronic-wasting-disease/the-first-detection-of-chronic-wasting-disease-cwd-in-europe

OIE, (2004). Handbook on import risk analysis for animals and animal products. World Organisation for Animal Health, 12, rue de Prony, 75017 Paris, France, p.59.

Race, B., Williams, K., Orru, C.D., Hughson, A.G., Lubkei, L. & Cheesebro, B. (2018) Lack of transmission of chronic wasting disease to Cynomolgus macaques. J. Virol. doi:10.1128/JVI.00550-18

Robinson, S.J., Samuel, M.D., O'Rourke, K.I. & Johnson, C.J.. (2012) The role of genetics in chronic wasting disease of North American cervids. Prion 6 (2): 153-162.

Russo, F., Johnson, C.J., Johnson, C.J., McKenzie, D., Aiken, J.M., & Pedersen, J.A. (2009) Pathogenic prion protein is degraded by manganese oxide material found in soils. *Journal of General Virology*, 90, 275-280.

Saunders, S.E., Bartz, J.C., Vercauteren, K.C., & Bartelt-Hunt, S.L. (2010) Enzymatic digestion of chronic wasting disease prions bound to soil. *Environ. Sci. Technol.*, 44, 4129-4135.

Seidel, B., Thomzig, A., Buschmann, A., Groschup, M.H., Peters, R., Beekes, M., & Terytze, K., (2007) Scrapie agent (strain 263K) can transmit disease via the oral route after persistence in soil over years. *PLoS Pathogens*, 5, e435.

Sigurdson, C.J. (2008) A prion disease of cervids: Chronic wasting disease. *Veterinary Research*, 39, 41.

Strauser, K. (2014) Detection of Urine-Based Deer Lures to Mitigate CWD Transmission in Pennsylvania Keystone Journal of Undergraduate Research 2(1): 1-7. 2014

Sviland S, Vikøren T, Hopp P, Benestad SL. The surveillance programme for Chronic Wasting Disease (CWD) in wild and captive cervids in Norway 2014. Surveillance programmes for terrestrial and aquatic animals in Norway. Annual report 2014. Oslo: Norwegian Veterinary Institute 2015.

Sviland S, Vikøren T, Hopp P, Benestad SL. The surveillance programme for Chronic Wasting Disease (CWD) in wild and captive cervids in Norway 2013. Surveillance programmes for terrestrial and aquatic animals in Norway. Annual report 2013. Oslo: Norwegian Veterinary Institute 2014.

Trifilo, M.J., Ying, G., Teng, C. & Oldstone, M.B.A. (2007) Chronic wasting disease of deer and elk in transgenic mice: oral transmission and pathobiology. *Vaccine*, 365, 136-143.

Vikøren T, Sviland S, Hopp P, Benestad SL. The surveillance programme for Chronic Wasting Disease (CWD) in wild and captive cervids in Norway 2012. Surveillance programmes for terrestrial and aquatic animals in Norway. Annual report 2013. Oslo: Norwegian Veterinary Institute 2013.

VKM. (2017) CWD in Norway – a state of emergency for the future of cervids (Phase II). Opinion of the panel on Biological Hazards, ISBN: 978-82-8259-266-6, Oslo, Norway.

Williams, E.S. (2005) Chronic wasting disease. *Vet Pathol.*, 42, 530-549.

Williams, E.S., & Miller, M.W. (2003) Transmissible spongiform encephalopathies in non-domestic animals: origin, transmission and risk factors. *Rev. Sci. Tech. Off. Int Epiz.*, 22, 145-156.

Wilkinson, D.M. (2010) Have we underestimated the importance of humans in the biogeography of free-living terrestrial microorganisms? *Journal of Biogeography*, 37, 393-397.