REVIEW

A review of chronic wasting disease in North America with implications for Europe

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Abstract Cervids are keystone species in ecosystems and are associated with enormous cultural and economic value. Chronic wasting disease (CWD) is a fatal prion disease spreading in North American cervid populations. The 2016 emergence of CWD in Europe makes it urgent to understand the basics of CWD and to assess the extent to which current CWD knowledge is transferable to Europe. CWD is difficult to detect in the early stages due to very low prevalence and slow growth rates. The negative population effect of CWD is mainly due to increased female adult mortality, as infected individuals continue to reproduce. It may take decades before CWD leads to population declines. The population dynamics of mule deer are affected more by CWD than those of white-tailed deer, which in turn are more affected than those of elk, and depending on other factors limiting the populations. Species- and population-specific differences in dynamical consequences are linked to the balance among the rates of transmission, incubation period (linked to the prion protein gene, *PRNP*), and reproductive rates. This make it difficult to predict effects of CWD in Europe with other cervids, but the dynamic impact may be marked to cervid populations over the long term. The process of spillover across the species barrier is not well understood. Occasional spillover to moose without an apparent epizootic suggests specific conditions can limit CWD. Frequency-dependent transmission or weak density-dependent transmission makes it difficult to control CWD using density reductions through harvest and/or culling. CWD is difficult to eradicate once it becomes endemic, and it calls for immediate management actions. These actions involve extensive culling, fencing and ceasing of wildlife feeding and are likely to cause significant controversy.

Key words Frequency-dependent versus density-dependent transmission • direct and environmental transmission routes • spatially targeted harvesting • extermination and fallowing • salt licks and supplemental feeding • genetics and pathology • epizootiology and population dynamics

Introduction

The first case of chronic wasting disease (CWD) in Europe was diagnosed in March 2016 in a female reindeer (*Rangifer tarandus*) in the Nordfjella mountains, Norway (Benestad et al. 2016). Since then, several more CWD-infected reindeer from the same population were detected by testing during the 2016 and 2017 hunting seasons (Viljugrein et al. 2018). Hence, we have the first reported outbreak of CWD in Europe. CWD was first documented in a captive mule deer (*Odocoileus hemionus*) in 1967 in Colorado, USA (Williams & Young 1980), and it appeared in wild mule deer in 1981 (Williams & Young 1992; Spraker et al. 1997; Miller et al. 2000). CWD in the wild has since spread to 25 states and, through sales of farmed elk, has been introduced to two Canadian provinces and to South Korea (Uehlinger et al. 2016); however, the origin of CWD in Norway remains unknown (Benestad et al. 2016).

It is important to realize that although CWD was first identified among wild deer in 1981, it is still spreading to new areas and continuing to increase in prevalence in most, if not all, endemic areas. Evidence of declining populations in endemic areas are recently reported for white-tailed deer (*Odocoileus virginianus*) (Edmunds et al. 2016) and mule deer (DeVivo et al. 2017). There are also increasing impacts on elk (*Cervus canadensis*) populations (Monello et al. 2014; Monello et al. 2017), which is a closely related species to the European red deer (*Cervus elaphus*). Due to the timing and slow rise in prevalence of CWD, it seems likely that more such reports of population declines will appear in the coming years.

Due to the immediate risk of CWD becoming endemic in Norway and spreading geographically in Europe, it is important to know what to expect in affected populations. To what extent are CWD dynamics sufficiently understood in North America? Will CWD prevalence always increase in a population or does it require specific conditions to do so? What are the expected population impacts and how fast will they appear? Will CWD spill over across cervid species, and if so, will the population impacts be species-specific? To what

extent is the current CWD knowledge transferable to Europe? How will CWD change surveillance and cervid management in Europe? We try to give an initial answer to these difficult questions and to highlight the gaps in knowledge to guide research and management efforts.

What are we up against?

The disease agents of CWD are proteinaceous infectious particles called prions (PrP^{CWD}), and hence CWD groups with other prion diseases such as bovine spongiform encephalopathy (BSE), scrapie in sheep, and Creutzfeldt–Jakob disease (CJD) in humans (Prusiner 1998). Prion diseases are invariably fatal, and there are no vaccines or treatments currently available. Susceptibility to CWD is linked to similarity in the structure of the prion protein (PrP), which is present in all mammals. A prion causes misfolding of the normal cellular prion protein (PrP^{C}) into a form (PrP^{res}) not degraded in the organism, which in turn causes a chain-reaction of further misfoldings (Robinson et al. 2012b). Aggregates of PrP^{res} constitutes the prion. The structure of PrP is determined by the prion protein gene (*PRNP*), which is highly conserved and with few polymorphisms within cervids. In general, most cervids are therefore considered susceptible to various degrees, while susceptibility of some species are not determined (Robinson et al. 2012b). The importance of genetics is well covered elsewhere (Robinson et al. 2012b), and we here only cover *PRNP* variation as it relates to population dynamic impacts. Prion diseases are usually not very contagious, the exception being CWD in cervids and 'classical' scrapie in sheep. A type of 'non-classical' scrapie in sheep occur as a sporadic disease mainly in old animals (Benestad et al. 2003). In addition to the 'classical' type of CWD, a new type of CWD was found in two moose in 2016 in Norway, one more in 2017, and also in a moose in 2018 in Finland (Pirisinu et al. 2018). A 'non-classical' type of CWD was also confirmed in one red deer in 2017 in Norway (Våge et al. 2018). The moose cases

appear unrelated to the reindeer cases (Pirisinu et al. 2018). We will focus our review on what can be termed 'classical' CWD, which is highly contagious to be a prion disease.

Transmission routes

CWD can be transmitted both directly from animal to animal (Miller & Williams 2003) and indirectly through the environment (Miller et al. 2004). Though vertical transmission from mother to offspring may occur (Nalls et al. 2013), it is regarded as of minor importance for the epizootic characteristics (Miller & Williams 2003). A major knowledge gap preventing understanding, managing and modelling the development of CWD, is that the quantitative importance of various transmission routes is uncertain. It is likely that direct animal-to-animal contact is the main route of infection in early stages of CWD, while environmental transmission becomes more important in later stages as prions build up in the environment (Almberg et al. 2011). Direct contact is typically higher within than between social groups (Schauber et al. 2015), suggesting that the level of female sociality can be important for transmission. Direct contact of genetically related females, which typically have overlapping home ranges, is a risk factor leading to a higher prevalence of CWD (Grear et al. 2010; Cullingham et al. 2011a). Direct contact rates among females were higher during the rut (autumn) and lowest during summer (Kjær et al. 2008). Female-male contact is highest during rut, while male-male contact is typically higher during summer and pre-rut when social rank is determined. Any action that limits artificial aggregation of cervids is likely to reduce transmission.

Density-dependent or frequency-dependent transmission?

Disease dynamics are affected by the mode of transmission, which can be either density- or frequency-dependent at the population level. Density-dependent infectious diseases are easier to control in wildlife populations because culling efforts can limit transmission. With frequency-dependent transmission, CWD could only be eliminated by removal of the infected

population (Wasserberg et al. 2009), since the lack of clinical signs in the early stages impede selective harvest of infected individuals. Several lines of evidence have been used to evaluate whether CWD is likely to have density-dependent or frequency-dependent transmission. Most evidence suggests CWD has close to frequency-dependent transmission (Table 1). Frequency-dependent transmission is typical of transmission in socially regulated contact networks. The proximity of animals, based on evidence from GPS-marked animals and grouping patterns of deer, is related to population density. However, proximity of animals may not measure the actual direct contact rates necessary for transmission, and hence it is uncertain whether such kind of data can be used to infer density-dependent transmission of CWD. In any case, such a weak impact of population density on transmission does not support culling to reduce density as a tool to control CWD in Europe. Rather, host eradication is required for diseases with frequency-dependent transmission (Wasserberg et al. 2009). The transmission mode for CWD in reindeer is unknown. However, the expectation that transmission would be close to frequency-dependent was an important part of the basis for the aim to remove the whole herd of over 2000 reindeer infected with CWD in Norway (Hansen et al. 2016), which is now completed (Mysterud & Rolandsen 2018).

Table 1 A brief overview of four lines of evidence for whether chronic wasting disease has a density-dependent (DD) or frequency-dependent (FD) mode of transmission at the population level.

Type and approach of study	Parameter or type of data	Mode of transmission	Reference
Mathematical modelling of transmission modes based on empirically estimated functions	Output from transmission models compared to demographic pattern of CWD infection	FD fit data better	(Wasserberg et al. 2009; Jennelle et al. 2014)
Empirical observations of contact rates	Contact rates among GPS-marked animals; group sizes across a population density range	DD or intermediate, season-specific	(Habib et al. 2011; Cross et al. 2013)

Empirical observations of CWD prevalence	Analysing spatial variation in CWD prevalence and the relationship to population density	DD at low density, FD at high density	(Storm et al. 2013)
Culling efforts by state/provincial wildlife agencies	Analysing variation in CWD prevalence before and after management efforts to reduce population density	FD	Reviews in (Conner et al. 2007; Uehlinger et al. 2016)

Epizootic characteristics of CWD

The time from infection to death in the case of CWD is typically 1.5-2.5 years in white-tailed deer and mule deer (Fox et al. 2006; Robinson et al. 2012a), but can be as long as 4 years in elk (Moore et al. 2018); depending on *PRNP*-genotypes. In mice models, also the PrP^{CWD} strain play a role for duration of infection and transmission (Raymond et al. 2007; Angers et al. 2010; Perrott et al. 2012). A long time from infection to death is typical of prion diseases. The basic reproductive number (R_0) measures how fast diseases transmit and grow in a population; it is the expected number of new individuals infected by an infected individual. In captive mule deer, the R_0 values for CWD were determined to be 1.3 and 1.5 in two different epizootics (Miller et al. 2006), and a substantial increase in prevalence may take decades (Wasserberg et al. 2009). CWD in white-tailed deer in endemic areas of Wyoming has now reached a prevalence of 30-40% an estimated 35 years after introduction (Edmunds et al. 2016). However, the R_0 was much higher (in the range of 2.2 to 4.5) even in the early stages of CWD outbreak among mule deer in Alberta, Canada (Potapov et al. 2015). In modelling studies, the estimated R_0 values rarely reach above 2-3 when direct transmission is assumed, but the R_0 can reach considerably higher values with environmental transmission (Almberg et al. 2011; Sharp & Pastor 2011). Other modelling of CWD dynamics suggested that it was not given that R_0 will be >1 under all conditions (Miller et al. 2006), which is required to establish an epizootic. However, the empirical basis for many model parameters are still often weak or absent, and results should be interpreted with caution.

Spatial pattern of CWD in North America

Management actions, environmental conditions, and the properties of the affected cervid populations may all influence the magnitude to which CWD will affect a given population. Several management actions aimed at limiting CWD have been implemented in Colorado, Wisconsin, and Illinois and the Canadian provinces of Alberta (Uehlinger et al. 2016) and Saskatchewan (Cullingham et al. 2011b), whereas Wyoming has mainly implemented CWD surveillance with no direct action. CWD appear successfully eradicated from New York after detection in two captive and two wild white-tailed deer (Evans et al. 2014). However, spatial variation in infection rates and whether management has been successful in limiting CWD elsewhere in North America remains unclear. It is difficult to estimate prevalence of CWD empirically in the initial stages due to very low prevalence and imperfect detectability (Viljugrein et al. 2018), and hence large sample sizes are required for detecting temporal changes and spatial variation in CWD prevalences. Therefore, if CWD prevalence has remained low for a long period (Geremia et al. 2015), it is difficult to determine whether prevalence is stable, or whether sample sizes are insufficient to detect changes. Changes in the size of monitoring areas are also a problem affecting estimation of prevalence. A formal analysis could not detect spatial variation in the growth of CWD prevalence in Wisconsin (Heisey et al. 2010). The changes in CWD prevalence were determined primarily by the time point of disease introduction (Heisey et al. 2010).

Demographic patterns of CWD prevalence

The observed demographic pattern of CWD infection in a given area results from a combination of time available for exposure and low detectability in early infectious stages, while age- and sex differences in behaviour may lead to different exposure. Prevalence is very low in fawns or calves, and yearlings have about half the infection levels as adults (Miller & Conner 2005; Samuel & Storm 2016). The low infection levels in juveniles may reflect a

shorter time of exposure and less exposure to environmental contamination (when they suckle), in combination with the delay between exposure to PrP^{CWD} and detection using standard CWD tests (Viljugrein et al. 2018). New detection methods are now under rapid development and becoming more sensitive to the early stages of infection (Haley & Richt 2017). Nevertheless, yearlings had lower infection prevalence than adults even after accounting for time of exposure (Samuel & Storm 2016). In both mule deer (Miller & Conner 2005) and white-tailed deer (Heisey et al. 2010), the prevalence of CWD peaked at ages 5-6 years in males, but this result may have been due to biases in age estimation based on tooth wear (Samuel & Storm 2016). CWD prevalence in deer is generally approximately twice as high in males as in females (Miller & Conner 2005; Grear et al. 2006). The higher prevalences in males is likely linked to behavioural differences affecting exposure, but how is not understood. The pattern was slightly reversed between the sexes for white-tailed deer in Wyoming, where the prevalence was as high as 28.8% in males and 42% in females (Edmunds et al. 2016). The extent to which the demographic pattern of infection changes in late epizootic stages remains uncertain.

CWD, mortality and reproduction

Empirical evidence does not indicate markedly reduced reproductive rates in CWD-infected individuals that are pre-clinical for either mule deer (Dulberger et al. 2010a) or white-tailed deer (Blanchong et al. 2012; Edmunds et al. 2016). All CWD infected animals die of clinical disease if they live long enough, and increased adult female mortality is the main effect of CWD on population dynamics (Dulberger et al. 2010b; Edmunds et al. 2016). The effect on populations will further depend on whether mortality from CWD is additive or compensatory to other causes of mortality. Mortality from CWD is in part compensatory to other mortality sources in areas with selective predation (Krumm et al. 2010), hunting (Conner et al. 2000) or accidents (Krumm et al. 2005) of CWD-infected individuals, but a sufficiently large part of

mortality caused by CWD is additive leading to population limitation. Any limiting factor affecting adult female mortality will have the greatest impact on large herbivore populations (Gaillard et al. 1998), and CWD hence has the potential to modulate population dynamics at high prevalence (Edmunds et al. 2016; DeVivo et al. 2017).

Population dynamic effects of CWD

The effect of CWD on populations is driven mainly by the balance between the time since infection, the rate of transmission, the incubation period (linked to the *PRNP* gene), how quickly new offspring (without infection) are produced (Potapov et al. 2016), and it will depend on other limiting factors in a given area. Once CWD is established, prevalence among adult females will rise slowly, to an increasing degree limit population growth, and over decades cause a gradual population decline that may become substantial (DeVivo et al. 2017). The impacts vary between species and geographic location. Individuals or species with host genotypes that are associated with lower susceptibility and longer incubation periods (O'Rourke et al. 1999; O'Rourke et al. 2004; Jewell et al. 2005; Moore et al. 2018) can produce more offspring before death, slowing the rise in CWD prevalence (Table 2). Similarly, the population dynamical consequences will be lower for species and populations with higher reproductive rates, diluting the prevalence by rapidly adding new non-infected individuals to the population (Potapov et al. 2016).

Population dynamic effects are larger in mule deer than in white-tailed deer, while elk populations are less affected. In endemic areas of Wyoming, CWD led to a 10.4% annual population decline in white-tailed deer (Edmunds et al. 2016) and a 21% annual decline in mule deer (DeVivo et al. 2017). The lower reproductive potential of mule deer may explain the larger population effects of CWD compared to in white-tailed deer populations. Elk populations have consistently lower CWD prevalence (Miller et al. 2000). In elk, a CWD incidence above 15% is not reported. The annual incidence of CWD was estimated at 0.08

[0.05-0.12] in a high-density elk herd in the Rocky Mountains, USA, after 25 years (Monello et al. 2014). The elk population in Wind Cave National Park, South Dakota had a prevalence reaching 14% (12-15%) in adults during the winter of 2016-2017 (Glen Sargeant, pers. comm.). CWD develops slower, with longer incubation periods (Moore et al. 2018), in elk than in deer (Race et al. 2007); this was assumed due to the substitution in the *PRNP* gene at residue 226 (Angers et al. 2010). However, even in elk, the CWD prevalence may rise sufficiently to become population limiting. In Colorado, population declines were predicted at 13% [0-35%] adult female prevalence for elk (Monello et al. 2014) and at 26% for white-tailed deer in Wyoming (Edmunds et al. 2016).

Over longer time scales, less-susceptible host genotypes may become more common and dampen the population effects of CWD (Williams et al. 2014; DeVivo 2015; Monello et al. 2017). The very long-term effects (century scale) are currently not known, and it is therefore unclear if CWD will cause local extinctions.

Predicting the population dynamic impact of CWD on European cervids without any empirical evidence is uncertain even to a very coarse level (Table 2). The variation in the *PRNP* gene is low in moose and roe deer, while it is somewhat higher in red deer and reindeer leading to a potential for larger individual variability in susceptibility. Moose and roe deer are generally more solitary than other cervids. Moose have quite high and roe deer have very high reproductive rates (Table 2). Both these factors may limit the growth of CWD in a population. Anecdotal evidence from North America suggests occasional spillover to moose (Baeten et al. 2007; Haley & Hoover 2015), but it is uncertain whether the absence of subsequent epizootics is due to the solitary behaviour of moose alone. Group sizes typically increase with the openness of the habitat (Pays et al. 2007), with increasing population density (Vincent et al. 1995), and aggregation in agricultural fields or at supplementary feeding sites can increase

Table 2. An overview of susceptible species' risk factors related to the effects of chronic wasting disease (CWD) on population dynamics. Variation in social organization and population growth rates are considerable within species. The normal incubation period is considered 1.5-2.5 years, but can be longer. There are varying levels of susceptibility based on host prion protein gene (*PRNP*) allele variation (Robinson et al. 2012b; EFSA Panel on Biological Hazards (BIOHAZ) et al. 2016). For annual population growth rates, we based this on the maximum expected growth from Gaillard et al. (2000), and pers. comm.), mainly varying depending on the number of offspring produced; such population growth rates will depend on the ecological conditions in a given area. Amino acid abbreviations: A = alanine; E = glutamic acid; F = phenylalanine; G = glycine; H = histidine; I = isoleucine; L = leucine; M = methionine; P = proline; Q = glutamine; S = serine; T = threonine; V = valine.

Continent Species	*PRNP* allele variation	Pathology, incubation	Social organization	Maximum population growth rates (λ_{max})	Population impact
North America					
Mule deer *Odocoileus hemionus*	3 *PRNP* genotypes (Jewell et al. 2005; Robinson et al. 2012b): 225SS, SF, FF; susceptibility varies by genotype	Normal (Race et al. 2007); *PRNP* genotype differences vary by incubation period[3]	Large groups	Intermediate (1.40-1.45)	Moderate (Geremia et al. 2015) to large impact (Dulberger et al. 2010a)
White-tailed deer *Odocoileus virginianus*	9 *PRNP* genotypes (O'Rourke et al. 2004; Velásquez et al. 2015): 95QQ, QH, HH ; 96GG, GS, SS ; 116AA, AG, GG (O'Rourke et al. 2004); susceptibility varies by genotype	Normal (Race et al. 2007), 1.8-2.6 years; incubation period vary by *PRNP* genotype (Johnson et al. 2011)	Small familial groups; larger groups in winter in northern latitudes	Very high (> 1.6)	Intermediate impact; normal incubation but rapid population growth; may cause population declines (Edmunds et al. 2016; Foley et al. 2016).
Elk *Cervus canadensis*	3 *PRNP* genotypes (O'Rourke et al. 1999; Robinson et al. 2012b): 132MM, ML, LL	Slow (Race et al. 2007); incubation period vary by *PRNP* genotype (Moore et al. 2018)	Large groups	Slow (1.30-1.35)	Low-to-moderate impact; long incubation but slow population growth and close to population decline levels (Monello et al. 2014)

Continent Species	*PRNP* allele variation	Pathology, incubation	Social organization	Maximum population growth rates (λ_{max})	Population impact
Moose *Alces alces*	2 *PRNP* alleles (Robinson et al. 2012b); 209M, 209I	Uncertain, likely normal	Solitary summer, small groups in open habitat	Intermediate (1.40-1.45)	Repeated spillover, no known epizootic (Baeten et al. 2007; Haley & Hoover 2015)
Caribou *Rangifer tarandus*	8 *PRNP* alleles (Robinson et al. 2012b), one Alberta population with alleles with some resistance (Cheng et al. 2017); 2V, M (Robinson et al. 2012b); 129GG, GS; 138SS, SN, NN (Cheng et al. 2017); 169V, M (Robinson et al. 2012b)	Normal (Moore et al. 2016)	Very large groups all year	Slow (1.30-1.35)	Uncertain, likely very high
Europe	In general, uncertain due to previously low interest				
Reindeer *Rangifer tarandus*	See above for North America	Normal (Viljugrein et al. 2018), terminal CWD 18.5-20 months post inoculation (Mitchell et al. 2012)	Very large groups all year	Slow (1.30-1.35)	Uncertain, likely very high; outbreak in Nordfjella, Norway
Red deer *Cervus elaphus*	8 *PRNP* alleles; 59G, S; 98T, A, 168P, S, 226E, Q (Robinson et al. 2012b)	As in elk (Schwabenlander et al. 2013)	Small groups in summer; larger in open habitat; larger in winter/spring	Slow (1.30-1.35)	Uncertain, likely moderate impact
Moose *Alces alces*	2 *PRNP* alleles	Uncertain, likely normal	Solitary summer, small groups occur in winter	Intermediate (1.40-1.45)	Uncertain, likely low (depending on population density & supplemental feeding?)

Continent Species	*PRNP* allele variation	Pathology, incubation	Social organization	Maximum population growth rates (λ_{max})	Population impact
			(Bonenfant et al. 2004)		
Roe deer *Capreolus capreolus*	1 *PRNP* allele (Robinson et al. 2012b)	Uncertain	Solitary, small groups occur winter in agricultural landscapes	Very high (> 1.5)	Uncertain, likely low (depending on population density & supplemental feeding?)
Introduced species					
White-tailed deer	See above for North America				
Axis deer *Axis axis*	Uncertain	Uncertain	Solitary and small groups, larger groups in winter	Slow (1.30-1.35)	Uncertain
Fallow deer *Dama dama*	No *PRNP* allele variation (Robinson et al. 2012b)	Delayed; 4-5 yrs of incubation post inoculation (Hamir et al. 2011)	Large groups year-round	Slow (1.30-1.35)	Long incubation, lower impact despite being highly social; seem not to be infected via the natural route (Rhyan et al. 2011)
Sika deer *Cervus nippon*	4 *PRNP* alleles; 100S, G; 226E, Q (Robinson et al. 2012b)	Uncertain	Small groups	Slow (1.30-1.35)	Uncertain, likely intermediate
Muntjac *Muntiacus reevesi*	Uncertain	Normal (Nalls et al. 2013)	Solitary	Very high (>1.5)	Uncertain, likely low

transmission of parasites in general (Milner et al. 2013). Social group size of red deer in Europe differ depending on the habitat; group sizes as small as only 2-3 females occur during summer, but can be much larger during winter, especially when they are aggregating on feeding sites or agricultural pastures. Additionally, in an open habitat, such as in Scotland, they occur in large herds. Farmed red deer is known to contract CWD (Schwabenlander et al. 2013), but impact of CWD on red deer populations may differ from elk due different *PRNP* genotypes (Table 2). Due to the gregarious nature of reindeer, we would expect higher contact rates among individuals of this species than for any other deer species and, hence, more rapid development towards endemic CWD. Hence, many aspects of cervid biology likely to affect transmission of CWD differ markedly within Europe even for the same species.

Effects of predation

Any factor causing increased mortality of CWD-infected deer relative to non-infected deer may aid in limiting CWD, as it would decrease the period infected individuals can transmit and spread disease. Predators vary widely in the degree to which they target weak animals, and the effect of predators on infectious disease depends on epizootic detail. Predators can keep herds healthy when the disease agent is highly virulent and aggregated in prey, prey are long-lived, and predators are selective for infected individuals (Packer et al. 2003). CWD meets the conditions of having a strong impact on infected prey and with a clear distinction between infected and non-infected individuals that are long-lived, so the key question is the level of selectivity. This is not a trivial issue due to the long incubation period. In the early stages, the animals appear healthy but can spread disease (Tamguney et al. 2009) before they slowly change behaviour and become more vulnerable to predation. Modelling wolf predation on CWD-infected mule and/or white-tailed deer suggests that if predation is sufficiently selective for CWD-infected individuals, it could cause a marked decline in CWD prevalence (Wild et al. 2011). Empirical evidence for selective predation on CWD-infected individuals

is, however, not consistent. CWD-infected mule deer were more likely to be depredated by mountain lions (*Puma concolor*) than non-infected mule deer (Krumm et al. 2010). Predation can thus, to some extent, remove a higher proportion of CWD-infected individuals than is present in the population. However, empirical evidence found that remarkably high CWD infection rates of mule deer were sustained even in the face of intense selective mountain lion predation (Miller et al. 2008).

Spillover among cervid species

The evidence for population-level effects of CWD is derived from white-tailed deer, mule deer, and elk in North America. How fast CWD will grow, spread and spillover among the cervid species in Europe remain uncertain. From a genetic perspective, there is a low barrier for transfer of CWD among most cervid species (Robinson et al. 2012b). However, fallow deer (*Dama dama*) housed together with infected mule deer did not become infected via the natural route (Rhyan et al. 2011), even though fallow deer can contract CWD via intracerebral inoculation (Hamir et al. 2011). In North America, CWD is known to have been transferred from mule deer to white-tailed deer, mule deer to elk, and elk to mule deer and white-tailed deer (Williams 2005); it is likely CWD was transferred from one or all of those three species to moose as well. A main uncertainty is whether CWD in reindeer in Norway will transmit across species as has happened in North America. From experiments with mice, it is known that the first transmission of a new prion strain to a new host may be difficult, but that subsequent transmission (serial passage) becomes easier within the new species (Raymond et al. 2007; Angers et al. 2010; Velásquez et al. 2015).

Hence, the process of spillover from one cervid species to another in the wild is not well described or understood. It is likely that such transmission among species is indirect (i.e., through environmental contamination), as direct contact between individuals of different species is rare. Even though the transmission of CWD within a species is not strongly density-

dependent, it is likely that a spillover event would be linked to: 1) the population density of the receiver species, 2) the spatial overlap of the two species, and 3) the density of infected individuals in the donor population (Hansen et al. 2016). Contact points attracting multiple species, such as common mineral licks (Plummer et al. 2018), supplemental feeding and watering sites, or riparian habitats (Edmunds et al. 2018), are likely to be risk factors. Similar feeding niches linked to feeding on low vegetation may be risk factors, as it is more likely to transfer prions through ingestion of soil (Johnson et al. 2006; Johnson et al. 2007) and vegetation (Pritzkow et al. 2015). It is suggested that the lower levels of prions in the lymph nodes of elk compared with white-tailed deer and mule deer reduces the risk of elk transmitting CWD to other species (Race et al. 2007). There is no direct empirical evidence to support these hypotheses, so they are all inferred from general knowledge about CWD transmission.

Geographic spread of disease

The spread of CWD in North America results from the movement of deer, which is often linked to the dispersal of male yearlings (Lang & Blanchong 2012), but spread is also due to the movement of infected deer by farming (Rorres et al. 2018). Male-biased dispersal is the common pattern in cervids. Male yearlings typically have the longest dispersal distances for all the affected North American species: white-tailed deer, mule deer and elk. In Europe, red deer also have male-biased dispersal (Loe et al. 2009), but this is not the case for roe deer (Wahlström & Liberg 1995; Gaillard et al. 2008) and likely not for moose. Juvenile dispersal of roe deer is longer and a higher proportion takes place in low-quality than in high-quality habitats (Wahlström & Liberg 1995), so expansion of CWD will likely be faster in low-quality habitats with low population density and slower in areas with good habitats (Andersen et al. 2004). There is also extensive long-distance migration of moose across the borders of Norway and Sweden (Bunnefeld et al. 2011; Singh et al. 2012). In the case of deer movement,

major roads and rivers appear as semipermeable barriers (Blanchong et al. 2008; Long et al. 2010; Robinson et al. 2013). For both white-tailed deer (Cullingham et al. 2011a) and mule deer (Cullingham et al. 2011b) in western Canada, limited evidence of natural barriers for dispersal based on genetic structure were found, and even the Mississippi River in the USA had little impact on genetic differentiation (Lang & Blanchong 2012). In Scandinavia, highways are increasingly barriers to cervid movement and the barrier effect is often strengthened by wildlife fencing to avoid traffic accidents. Often these fences have wildlife passages, which could be closed to limit the spread of disease by deer movement. The spread of CWD at a broader scale is not easy to predict, as humans have played a major role in long-distance spread of CWD in North America, partly linked to transport of farmed deer (Rorres et al. 2018). Spread of CWD to Canada (Bollinger et al. 2004) and South Korea (Kim et al. 2005) was through sales of farmed elk. If CWD becomes endemic in Scandinavia, human transport of infectious material to continental Europe will be a risk factor to consider. In a European setting, restrictions on the movement of farmed cervids are likely to hinder such spread; there is already a regulation on the export of live cervids from Norway.

Surveillance for CWD in Europe

Whether or not classical CWD is present in countries of Europe other than Norway remains to be established. A survey during the period 2006–2010 across Europe detected no CWD in either farmed or wild cervid populations (EFSA Panel on Biological Hazards (BIOHAZ) et al. 2016). However, the sample sizes were quite low. After the discovery of CWD in Norway, the European Food Safety Authority proposed a 3-year surveillance program for Estonia, Finland, Latvia, Lithuania, Norway, Poland and Sweden (EFSA Panel on Biological Hazards (BIOHAZ) et al. 2016). This surveillance program for CWD will include both farmed and wild cervids, and it will consist of random sampling at a population unit level and convenience sampling targeting high-risk animals, typically fallen stock. The surveillance in

EU is aimed to detect CWD, and if present, intentions are to contain (avoid geographic spread) and to limit CWD transmission (actively stabilize or reduce infection rates) in an infected population (EFSA Panel on Biological Hazards (BIOHAZ) et al. 2016). This surveillance started in 2018, and the fallen stock sampling has already revealed the 'non-classical' type of CWD in a moose in Finland. The countries included in the surveillance program were based on the distribution of reindeer and moose, which at the time were the only species with CWD detected in Europe. Later (2017), 'non-classical' CWD was also discovered in red deer in Norway (Våge et al. 2018), and surveillance may become geographically extended to countries with red deer (EFSA Panel on Biological Hazard (BIOHAZ) et al. 2018). If the 'non-classical' CWD is a sporadic type of prion disease, which remains uncertain, it should be found at low prevalence in older animals with no clear geographic clustering of cases (Pirisinu et al. 2018). If correct, the discovery of 'non-classical' CWD will likely not require the same drastic management actions as 'classical CWD', which we describe in the following section.

Hunting management strategies

Controlling CWD with hunting is difficult and has typically had limited success once established in the landscape (Uehlinger et al. 2016). We briefly go through the main principles of the different options (Table 3).

Depopulation or host eradication. Complete eradication of an infected herd, fallowing and subsequent restocking is the option typically used for farmed deer. Herd reduction to eradicate CWD was the aim of management when first detected in Wisconsin, but it was unsuccessful as significant herd reduction was not accomplished (Heberlein 2004). In Norway, the open habitat and use of professional marksmen made it possible to take out the entire reindeer population with detected CWD in the Nordfjella mountain range (Mysterud & Rolandsen 2018), though the success in terms of CWD eradication is still uncertain. In forested areas, the

removal of all animals is difficult to achieve. This strategy is hence intended mainly for smaller populations, but it may be an option in some of Europe's fragmented landscapes. The recommended fallowing period is usually 5 years, but this limit was set without rigorous scientific testing. Due to the prion contamination of soil, it is uncertain whether this tactic works once CWD has become established, and early management action appears important.

Spatially targeted harvesting. In the early stages of an epizootic, CWD is mainly transmitted by direct contact (Almberg et al. 2011). Therefore, non-selective harvest in a spatially confined region can take out infected individuals and limit the spread of CWD. The sharpshooter programme in Illinois is controversial, but it is the best evidence that such an effort may limit growth of CWD. They target deer non-selectively within blocks of 64 km^2 when an infected deer is discovered (Mateus-Pinilla et al. 2013; Manjerovic et al. 2014). For Europe, this appears to be a promising strategy for forest-living cervids. However, the distribution of CWD on the landscape is important, and the actual spatial scale of such targeted efforts should follow evidence about functional connectivity and migration of the given infected population. This is, however, not an alternative for species such as reindeer with no marked home range behaviour.

Male-targeted harvest. CWD infection rates are strongly sex and age-specific (Jennelle et al. 2014; Samuel & Storm 2016). Hunting (and predation) that targets specific sex and age groups may hence change the population prevalence of CWD due to changes in the demographic composition. Targeting males, who usually have higher CWD infection prevalence, are a management alternative (Jennelle et al. 2014; Uehlinger et al. 2016). The efficacy of such an action is not well established, and we regard it likely to slow, rather than stop, the growth rate of CWD.

Targeting clinical suspects. Targeting clinical suspects when hunting may be either intentional or non-intentional. The active targeting of clinical suspects appears to have limited success due to prion shedding soon after infection (Hoover et al. 2017). CWD changes the behaviour of animals (Edmunds et al. 2018), and this can make them more exposed to hunters even with no active targeting. There was a selective harvest of CWD-positive white-tailed deer in Wyoming (Edmunds et al. 2016) and for mule deer in Colorado (Conner et al. 2000). For white-tailed deer in Wisconsin, the male offspring with CWD-infected mothers were harvested more often than would be expected by chance (Blanchong et al. 2012). However, a larger study of white-tailed deer in Wisconsin found no difference in the proportional harvest of CWD-infected and non-infected deer over the hunting season (Grear et al. 2006; Heisey et al. 2010). In heavily infected populations, hunters may also avoid shooting deer with unusual behaviour to avoid getting infected meat (Conner et al. 2000). Relying on such measures is not sufficient to limit CWD.

Capture-test-and-cull. An attempt was made in a mule deer population to capture, test and mark individuals with GPS collars (Wolfe et al. 2018). Individuals later established to be CWD-positive were removed from the population. These actions were only partly successful, and they are highly invasive, economically costly and only likely to be an option in small populations.

Human dimension and consequences for wildlife management

The above harvest management actions towards CWD are all rather drastic measures. In addition, since aggregation of hosts is a risk factor for disease transmission, the governments are likely to implement bans on both wildlife feeding and use of artificial mineral licks. This is common practice in CWD-endemic areas in North America. Such bans have already been implemented for the whole of Norway (Landbruks- og matdepartementet 2016), even though CWD was only discovered in one location. During the severe winter of 2018 in Norway, this

cessation of supplemental feeding resulted in massive die-off of cervids locally; this was not without controversy. Hunters in CWD-infected areas must take care of offal and several more minor restrictions will likely be implemented to avoid spatial spread, such as fencing (Mysterud & Rolandsen 2019). Therefore, the management actions of the government may have a far-reaching impact on wildlife management, even if CWD is discovered at a very low prevalence. These drastic management actions to combat CWD have been controversial and politically contentious in North America (Heberlein 2004; Vaske 2010; Holsman et al. 2010; Vaske et al. 2018). Local resistance towards the depopulation strategy to fight CWD in the reindeer herd in Nordfjella was massive in Norway (Mysterud & Rolandsen 2018), and the public resistance towards a ban on winter feeding of wildlife appear common. In Wisconsin, the number of hunting licenses sold declined initially even though the management tactic was for herd reduction to eradicate CWD; this decrease resulted from uncertainty among hunters regarding the zoonotic potential of eating CWD-infected meat (Heberlein 2004) and from reluctance to reduce deer density. Similarly, in Norway, the effectiveness of recreational hunters was low compared to professional marksmen in the eradication process (Mysterud & Rolandsen 2018), but it is typically unpopular among hunters and landowners to use professionals. We can say with certainty that the emergence of CWD in any country will cause considerable controversy and become a game changer for wildlife management. There is an overabundance of deer in many areas of North America and Europe. Some may argue CWD can be positive since it will contribute towards lowering deer densities. However, since CWD has a mainly frequency-dependent rather than density-dependent transmission (Table 1), CWD is unlikely to regulate deer numbers in a moderate way around a stable lower equilibrium. Also, the uncertainty regarding the zoonotic potential require testing of meat to avoid exposure. Both the surveillance for and combat of CWD are economically costly. The

discovery of CWD may lead to a ban on the export of cervid meat and products from the affected areas, which will affect livelihoods in many rural areas.

Table 3 An overview of harvest management strategies aimed to eradicate or limit increases in the prevalence of CWD.

Management strategy	Biological basis	Rationale	Aim	Comment	Reference
Depopulation/host eradication	CWD has frequency-dependent transmission	Host eradication, fallowing and restocking	Eradication of CWD	Mainly for small and closed populations, or new outbreak with limited distribution	(Williams et al. 2002)
Spatially targeted non-selective harvest	CWD spread among related females with overlapping home ranges	Spatial clustering of positives allows lowering of overall prevalence	Limit growth in prevalence	Main option for CWD management in forested areas and open populations	(Manjerovic et al. 2014)
Male-targeted harvest	Higher infection prevalence in males, male-biased dispersal	Removing males will lower the overall prevalence and may limit spread	Limit growth in prevalence	For large populations where other options are not feasible, efficacy unknown	(Jennelle et al. 2014; Potapov et al. 2016)
Targeting clinical suspects	Late stage CWD associated with visible clinical signs of disease	Selective removal of positives lowers prevalence	Limit growth in prevalence	Most animals are asymptomatic until late stage, low efficacy	(Gross & Miller 2001)
Capture-test-and-cull	Mark animals, test for CWD, remove infected	Selective removal of positives lowers prevalence	Limit growth in prevalence	Costly and intrusive, for small populations, some effect	(Wolfe et al. 2018)

The future of cervids in Europe with CWD

The future of many cervid populations in North America with CWD appears grim from a long-term perspective. The endpoint of the CWD epizootic has not been observed even in North America. Will endemic CWD progression lead to local extinction? We are potentially up against a disease that may have a devastating effect on cervid populations for as long as 50-100 years or more. Indeed, a 50 year time period is regarded as the early stage of a CWD epizootic (Wasserberg et al. 2009; Almberg et al. 2011). The main uncertainty about the biological effect of CWD in Europe is linked to the following question: How transferable is the knowledge from different species in North America? Most populations are likely susceptible. It is entirely clear that the European Union (EU) will not allow free growth of such a serious disease without attempting management actions (EFSA Panel on Biological Hazards (BIOHAZ) et al. 2016), partly because of the experience with the mad cow disease (BSE) and the uncertain zoonotic potential of CWD (Waddell et al. 2018). Therefore, the impact on cervid populations through management countermeasures aiming to limit disease spread may have a large indirect impact on populations, even in early stages with low direct impact of CWD. However, even such drastic management countermeasures are not very effective, at least partly due to high levels of environmental contamination, if CWD becomes endemic (Uehlinger et al. 2016). The coming years will therefore be critical to avoid taking such risks. Early action require early detection and rigorous surveillance is key. We currently can only hope that early management actions will be successful in the quick eradication of CWD from Europe (Hansen et al. 2016; Stokstad 2017); the first stage of eradication of the whole reindeer herd infected with CWD in Norway were successful (Mysterud & Rolandsen 2018). Due to the keystone role of cervids across ecosystems in Europe and their high associated economic and cultural importance (Apollonio et al. 2010), the consequences of failure may be dramatic.

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