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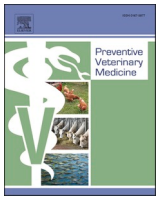

Risk-based surveillance of chronic wasting disease in semi-domestic reindeer

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ABSTRACT

Reindeer pastoralism is a widespread practise across Fennoscandia and Russia. An outbreak of chronic wasting disease (CWD) among wild reindeer (*Rangifer tarandus*) poses a severe threat to the semi-domestic reindeer herding culture. Establishing surveillance is therefore key, but current models for surveillance of CWD are designed for wild cervids and rely on samples obtained from recreational hunters. Targeting animal groups with a higher infection probability is often used for more efficient disease surveillance. CWD has a long incubation period of 2–3 years, and the animals show clinical signs in the later stages of the infection i.e. 1−4 months prior to death. The semi-domestic reindeer are free-ranging most of the year, but during slaughtering in late fall, herders stress the animals in penned areas. This allows removal of animals with deviant behaviour or physical appearance, and such removals are likely to include animals in the clinical stages of CWD if the population is infected. In Norway, the semi-domestic reindeer in Filefjell is adjacent to a previously CWD infected wild population. We developed a risk-based surveillance method for this semi-domestic setting to establish the probability of freedom from infection over time, or enable early disease detection and mitigation. The surveillance scheme with a scenario tree using three risk categories (sample category, demographic group, and deviations in behaviour or physical appearance) was more effective and less invasive as compared to the surveillance method developed for wild reindeer. We also simulated how variation in susceptibility, incubation period and time for onset of clinical signs (linked to variation in the prion protein gene, *PRNP*) would potentially affect surveillance. Surveillance for CWD was mandatory within EU-member states with reindeer (2018–2020). The diversity of management systems and epidemiological settings will require the development of a set of surveillance systems suitable for each different context. Our surveillance model is designed for a population with a high risk of CWD introduction requiring massive sampling, while at the same time aiming to limit adverse effects to the populations in areas of surveillance.

1. Introduction

Chronic Wasting Disease (CWD) is a fatal infection belonging to the transmissible spongiform encephalopathies or prion diseases affecting cervids (Spraker et al., 1997; Benestad and Telling, 2018). Infected animals shed CWD prions in excreta such as saliva, urine and faeces (Haley et al., 2009; Davenport et al., 2018). Susceptible individuals can be infected either by direct contact with infected animals (Miller and Williams, 2003), or due to exposure to environmental prion sources (Miller et al., 2004). Yet, the relative roles of the two transmission routes have not been quantified under field conditions. Even pre-symptomatic individuals can excrete prions (Tamguney et al., 2009), and the minimum infectious dose of prions can be incredibly small in the order of 100–300 ng of CWD-positive brain (Denkers et al., 2020). In white-tailed deer (*Odocoileus virginianus*), inoculation with low-doses of prions prolonged the time to first detection of infection, but not the remaining pathogenesis (Denkers et al., 2020). The incubation time also depends on prion protein gene (*PRNP*) polymorphisms, and is 1.5–2.5 years in mule deer (*Odocoileus hemionus*) (Fox et al., 2006) and 2–5 years in elk (*Cervus canadensis*) (Moore et al., 2018). The geographic distribution of CWD is expanding in North America among both wild and farmed mule deer, white-tailed deer and elk (Bunk, 2004; Haley and Hoover, 2015).

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At the population level, CWD can have low prevalence (<1 %) for up to a decade (Heisey et al., 2010) before rising up to 80 % in some captive deer herds (Keane et al., 2008). Consequently, detecting CWD in early epidemic stages is challenging and a limitation of many current surveillance systems (Belsare et al., 2020, 2021).

Surveillance is key to combatting emerging infectious diseases (Holmes et al., 2018), but it is typically constrained by economic, cultural and logistical factors (Hadorn and Stärk, 2008; Anderson et al., 2017; Gormley et al., 2018). Surveillance of herds adjacent to infected populations is important to avoid geographic spread of infectious diseases, as early detection is often crucial for effective mitigation (Uehlinger et al., 2016). Surveillance that targets groups with higher infection probability, such as fallen stock or animals showing clinical signs of disease, is a common practice to improve early disease detection (Adkin et al., 2016). However, sample sizes of high-risk groups are often limited. On the other hand, massive host sampling for diseases requiring post-mortem clinical diagnosis are invasive (Doherr and Audigé, 2001; Mysterud et al., 2020a). Planning for how to use available samples more efficiently and to target new samples is important to mitigate the economic costs and other adverse effects of disease surveillance (Peeler et al., 2015). More efficient surveillance, termed weighted surveillance, can be achieved by combining ordinary harvest data with fallen stock of different categories, such as traffic kills or animals with clinical suspicion (Heisey et al., 2014). In turn, scenario trees including different risk and detection categories are frequently used to evaluate the efficacy of a given surveillance program when aiming to substantiate probability of freedom from disease (Martin et al., 2007; Rüegg et al., 2018; de la Cruz et al., 2019; Jamin and Rivière, 2020).

The recent emergence of CWD among reindeer (*Rangifer tarandus*) in Norway in 2016 was discovered due to a CWD-surveillance program relying largely on fallen stock (Benestad et al., 2016; Våge et al., 2020). The whole wild reindeer population in the first affected area was rapidly (2017/18) eliminated by culling (Mysterud and Rolandsen, 2018), but CWD was later detected in the neighbouring wild reindeer management area of Hardangervidda in 2020 (VKM et al., 2021). The reindeer inhabit discrete populations due to barriers caused by topography and infrastructure development (Panzacchi et al., 2015; Mysterud et al., 2020b). To detect the disease at early stages and to establish the probability of freedom from disease in each population is a major goal in Europe (Mysterud et al., 2020a). Natural movements of a few animals have been recorded each year between the previously CWD-infected population and an adjacent population of ~3000 semi-domestic reindeer in Filefjell (Fig. 1). This area was identified in an assessment of the Norwegian Scientific Committee for Food Safety, as one of the top three reindeer populations at risk for acquiring an CWD infection (VKM et al., 2018).

There are ~250,000 semi-domestic reindeer in Norway, ~250,000 in Sweden, and ~200,000 in Finland (Pape and Löffler, 2012). In 2018, the European Commission implemented a three-year mandatory surveillance for CWD in member countries with reindeer and/or moose (The European Commission, 2017). The majority of semi-domestic reindeer are owned by Sami people in a management system referred to as reindeer pastoralism (Brännlund and Axelsson, 2011). A potential spillover of CWD to semi-domestic reindeer could ruin this unique cultural legacy (Maraud and Roturier, 2021). Mitigating possible infection is hence an urgent matter to halt the geographic spread of CWD. However, rapidly establishing freedom from infection at a high level of certainty would require excess slaughtering with severe economic consequences.

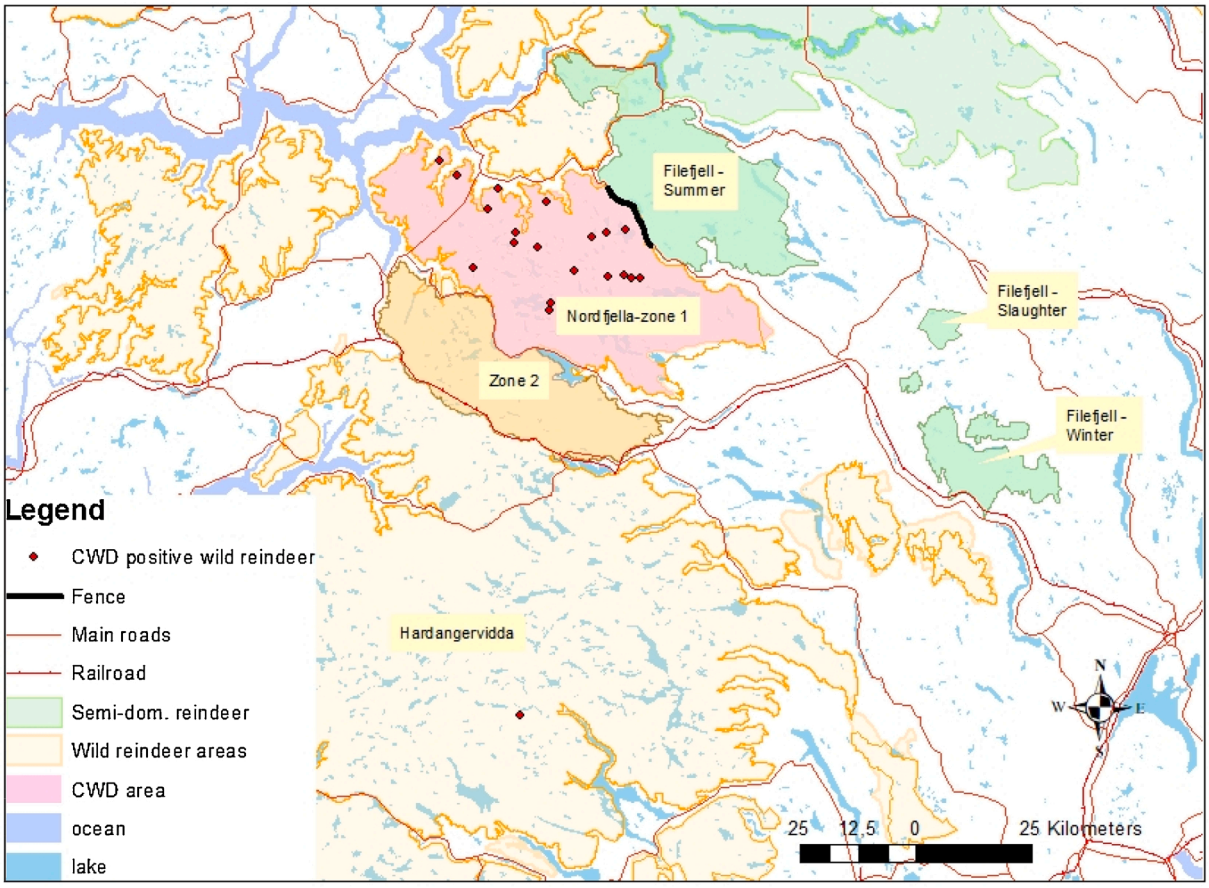

Fig. 1. An overview of wild and semi-domestic reindeer populations and CWD detections in Norway in 2016-2020. Our study population was the semi-domestic reindeer population of the Filefjell area, the neighbouring area north-east to the now eradiated CWD-infected population in the Nordfjella management zone 1. The fence between Nordfjella zone 1 and Filefjell was first erected in 2017 and extended in 2018 targeting alpine habitat only.

Previously, the concept of weighted surveillance of mixed samples was applied to estimate the prevalence of CWD in wild white-tailed deer in the USA (Jennelle et al., 2018). Adult males have higher infection rates (Miller and Conner, 2005), which can be used to target harvesting in wild deer populations (Rees et al., 2012; Mysterud et al., 2020a). However, some populations of semi-domestic reindeer have only a few adult males in the standing stock (Lenvik, 1989). Hence, the high relative risk of adult males is of limited value to increase the efficiency of the surveillance, as few high risk males would be available for testing. Therefore, managing CWD in semi-domestic reindeer has different challenges for surveillance as compared to wild populations in North America (Nusser et al., 2008; Rees et al., 2012; Jennelle et al., 2018; Belsare et al., 2020).

We aim to establish the probability of freedom from infection for a population of semi-domestic reindeer, using risk-based sampling (i.e., in this context deliberately obtaining more samples from groups where individuals have a higher probability of being infected) and weighted surveillance (i.e., how samples with different likelihood of infection are incorporated in calculations). We develop an alternative surveillance strategy based on the long infection period of CWD, and the late appearance of clinical signs (Wild et al., 2002; Tamguney et al., 2009; Johnson et al., 2011). Stress is known to trigger the appearance of some clinical signs (Williams, 2005), and semi-domestic reindeer management involves gathering herds in fall for slaughter. In this period, the animals are captured and handled. The increased stress can elicit clinical signs of CWD and make it possible for herders to observe and remove those individuals with suspected infection. Using our knowledge of the infection duration and the time for onset of clinical signs of CWD, we can estimate the probability that a CWD-infected animal shows clinical signs. Here we present a novel method for risk-based surveillance of semi-domestic reindeer, which involves an explicit probability distribution of the proportion of infected individuals showing clinical signs. The scenario tree includes a hierarchy of three risk categories (sample category [ordinary harvest, fallen stock and animals showing clinical signs], demographic group [age group and sex] and deviations in behaviour or physical appearance), giving rise to seven groups with different probabilities of CWD infection, hereafter referred to as 'risk groups'. We also simulate the effect of anticipated low and high genetic susceptibility to CWD, linked to variation in the prion protein gene (*PRNP*), which in other deer species is known to impact both incubation time and symptom onset.

2. Material and methods

2.1. Study population

Filefjell is one of four areas with semi-domestic reindeer in southern Norway that is not within the Sami culture. The Filefjell reindeer company was founded in 1945, but the tradition of herding reindeer dates back at least to the 19th century (Opdal and Maristuen, 2019). The population comprises approximately 3000 semi-domestic reindeer before slaughter. After slaughtering in late fall, they aim for a demographic composition of about 2400 adult (≥1 yrs) females, 10 adult (≥1 yrs) males, 300 female calves and 300 male calves. The herd is largely free-ranging with limited herding during summer (Fig. 1). In contrast, when reindeer are moved between the seasonal areas and during winter, there is active herding on a daily basis. The herding is either on foot or during winter with snowmobiles. In November, the herd is gathered for slaughter, before entering the winter range. The specific winter ranges vary across years in order to avoid overgrazing of lichen heaths. After winter, the herd is moved to a calving area, a smaller section of the summer range, where they remain from late April to 20th of May. After calving, they remain in the wider summer range until the fall period (Opdal and Maristuen, 2019).

2.2. Collection of samples

We divided between samples originating from (1) ordinary harvest of apparently healthy animals (mainly slaughtering; 2016−2020: n = 2876), (2) fallen stock (n = 29), and (3) animals showing clinical signs removed during herding (n = 8). Samples were collected from all slaughtered animals above two years old in 2016 and one year old in 2017–2020 (Supplementary Table S1). Information on age (yearling or adult) and sex were collected. We obtained population size data with age and sex categories from the resource accounts from Filefjell reindeer company (Supplementary Table S2).

Fallen stock are animals wounded or killed by accidents (e.g. stuck in fences), roadkill, predators, or with an unknown cause of death. Animals showing clinical signs included all animals reported as 'killed due to disease/clinical signs', regardless of showing signs typical for CWD. It was mandatory to test all animals that showed clinical signs and were found dead (except calves), but only approximately 3–28 % (range for 2016−2020) of these were tested according to the self-reported data from the Filefjell reindeer company. The semi-domestic reindeer are ear-tagged allowing for individual identification. Semi-domestic reindeer from Filefjell that were shot during the depopulation of reindeer from Nordfjella zone 1 (Mysterud and Rolandsen, 2018), and other individuals later found outside their main range (crossing towards the border or into the adjacent Nordfjella zone 1) were also tested for CWD (Supplementary Table S1). These animals were apparently healthy and most of them were tested and added to the category of ordinary harvest animals (if found in the register).

We aimed to collect samples from both brainstem tissue (if possible at the level of the *obex* area) and, following the recommendation of EFSA Panel on Biological Hazards (BIOHAZ) et al. (2016), the retropharyngeal lymph node (RLN). Tissues were sent by express over-night transport to the Norwegian Veterinary Institute (NVI), the national reference laboratory of animal TSE and OIE reference laboratory for CWD, where they were analysed the day they arrived in the laboratory. The collection of RLN was less common from fallen stock and animals showing clinical signs (mean 2018−2020: 49 % for fallen stock compared to 92 % for normal slaughtered when sampling was planned ahead and performed by veterinarians). However, fallen stock represented a small amount of samples (~1 % of total animals tested), and the low proportion of RLN did not represent a major problem for the surveillance system.

2.3. Diagnostic tests

Until July 2019, the initial screening for CWD in Norway was done with a pooled sample of both brain tissue (the usual required amount of tissue) with some additional RLN tissues (Viljugrein et al., 2019), using an ELISA test, the TeSeE® ELISA SAP, Bio-Rad, Hercules, CA, USA. Thereafter, NVI used IDEXX HerdChek BSE-Scrapie AG Test, IDEXX Laboratories, Westbrook, USA. A positive or inconclusive test result was retested on separate tissues by western blot (TeSeE® Western Blot, Bio-Rad, Hercules, CA, USA). These analytical tests have near perfect specificity according to EFSA (European Food Safety Authority EFSA, 2005). Due to the use of mixed samples of brain and RLN tissue, we assumed that the analytical test sensitivity was 95 %, which was a compromise based on the test performance using brain and RLN separately (Table 1).

2.4. A model of infection development

Previously, we have built a stochastic model for how the likelihood of discovering an infection develops during the course of infection given the test regime implemented (Viljugrein et al., 2019). The disease detection model relies on an understanding of the ability of the ELISA method to detect abnormal prion protein (PrP^{Sc}) during the course of CWD infection from samples of brain and RLN tissue. By taking this into account, the test sensitivity is increasing as a non-linear function of time

Table 1
Input parameters and outcomes in a stochastic simulation model for the evaluation of CWD surveillance of semi-domestic reindeer from Filefjell from 2016 to 2020. Stochastic input parameters are specified by a beta-pert (Pert) distribution of the expected, minimum and maximum values.

	Notation	Expected	Distribution	Comment	Reference
Parameters defining relative risks (RRs, sensitivity analysis performed)					
RRs of sample categories (ordinary harvest, fallen stock, clinical) (RR)	RRsample_cat	1, 1, 9	Fixed		Walsh and Miller (2010), Jennelle et al. (2018)
RRs of demography (yearlings, adult females, adult males) (RR)	RRdemo	1, 2, 6	Fixed		Mysterud et al. (2019a, 2020a)
Probability of a CWD-infected individual for showing clinical sign of disease (probability)	PrCWDclinic	0.125	Pert(0.125, 0.04, 0.17)	3 (1−4) months clinical period relative to 2 year duration of infection	Wild et al. (2002), Tamguney et al. (2009), Johnson et al. (2011)
Number of adult females (<10 years) in the population (individuals)	Nadf9	2218 [a]	Fixed	Annual data	This paper, Table S2
Number of harvested adult females (<10 years) showing a deviating sign (individuals)	nAdf_Deviating	24 [a]	Fixed	Annual data	This paper, Table S1
Probability that an adult female with a deviating sign is infected, given one infected (probability)	PrCWDadfDeviating	0.006 [a]	PrCWDclinic / nAdf_Deviating + (1–PrCWDclinic) / Nadf9	Stochastic output	
Probability that a random adult female without deviating signs is infected, given one infected (probability)	PrCWDadfNonDev	0.0004 [a]	(1–PrCWDclinic) / (Nadf9 –nAdf_Deviating)	Stochastic output	
RR of adult females showing a deviating sign (RR)	RRdeviating	14.4 [a] Fig. S2	PrCWDadfDeviating / PrCWDadfNonDev	Stochastic output	Eq. (5)
Parameters related to diagnostic test sensitivity					
Analytical test sensitivity - pooled sample (%)	aSe	95	Fixed		Viljugrein et al. (2019)
Diagnostic test sensitivity (%)	dSe	See ref.	Stochastic	Dependent on random time since infection, sample type and quality	Viljugrein et al. (2019)
Diagnostic test sensitivity at (or close to) the terminal stage of disease (%)	dSeHigh	95	Fixed (dSeHigh = aSE)		Viljugrein et al. (2019)
Probability of low sample quality (brain) from fallen stock or hunted animals (probability)	PrLQ	0.22	Pert(0.22, 0.02, 0.60)		Viljugrein et al. (2019)
Probability of low sample quality from slaughtered animals (probability)	PrLQS	0	Fixed	High quality when scheduled sampling are performed by a veterinarian	Expert assessment by S.L. Benestad, 2021 [b]
Time from infection to expected death from disease (years)	Infection length	2	Fixed	2 an 3 years tested in Viljugrein et al. (2019)	Wild et al. (2002), Tamguney et al. (2009), Johnson et al. (2011)
Probability of animals with clinical signs being in the last part of the infection phase, if CWD-infected (probability)	pClinic	0.80	Fixed		Expert assessment by S.L. Benestad, 2021 [b]
Annual input data (empirically known 2016−2020)					
Population size of risk group g	$GroupSize_g$		Fixed	Annual data; The RRs separate the population in 7 risk groups (Fig. 2)	This paper; Table S1 & Table S2
Number of individuals sampled from risk group g	n_g		Fixed	Annual data	This paper; Table S1
Proportion of ordinary harvest samples that included RLN (%)	pRLN of ordinary harvest	84 [a]	Fixed	Annual data	This paper
Proportion of fallen stock samples that included RLN (%)	pRLN of fallen stock	50 [a]	Fixed	Annual data	This paper
Proportion of adult females showing a deviating sign (%)	pAdf_Deviating	1.1 [a]	$\begin{cases} \frac{nAdf\_Deviating}{Nadf9} for < 2021 \\ \text{Pert}(1.1,\ 0.8,\ 1.6)\ for > 2020 \end{cases}$	Annual data	This paper; Table S1 & Table S2
Parameters set by management authorities					
Design prevalence (individuals)	P*	4 [a]	Fixed from 2020	2 in 2016−2017, 3 in 2018−2019	Mysterud et al. (2020a)
Annual probability of introduction	pIntro	0.001 [a]	Fixed from 2018	0.05 for 2016−2017	Mysterud et al. (2020a)
Prior probability of infection	$PFree_1$	0.5			Uninformed prior

RR: Relative risk.
[a] Input (expected) value in 2020.
[b] S.L. Benestad is head of the National Ref Lab for TSE and expert for the OIE Ref lab (Oslo) for CWD.

since infection. We assumed a typical infection time of two (or three) years from infection to death from disease. In the simulations, infected individuals are given a random infection time within the assumed duration of infection, and depending on their expected age at slaughter in early December (being ~19 and ~7 months for yearlings and calves, respectively).

2.5. Model overview

We have previously presented a disease detection model as a stochastic scenario tree model of wild reindeer, including the framework to estimate the probability of freedom given the specific samples tested (Viljugrein et al., 2019; Mysterud et al., 2020a). Here, we extended the

previous model to also separate between three categories with assumed different relative risk of CWD infection (RRsample_cat): 1) harvest data of apparently healthy animals, 2) fallen stock and 3) animals showing clinical signs removed during herding (clinical suspects). Additionally, we separated the ordinary harvest data in two risk categories (RRdeviating) depending on whether adult females were slaughtered due to deviations in behaviour or physical appearance (as defined below) versus old age (Fig. 2). The structure of the scenario tree model acknowledges that the experienced herders are inspecting every animal when the reindeer are gathered and herded through the enclosures at the slaughter location. In addition, due to the active herding of reindeer during winter and the moving of animals between seasonal areas, there is also an increased probability of discovering animals showing clinical signs and fallen stock in semi-domesticated reindeer as compared to wild reindeer. Briefly, the scenario tree model estimates the likelihood of detecting CWD infection in a given individual, depending on the sample category, sex and age class of the animal, presence of deviations in behaviour and physical appearance, knowledge about the infection development, and the sensitivity of the given testing regime. For the Filefjell population, all adult females less than 10 years old showing deviations in behaviour or physical appearance are slaughtered, while the females with no deviations are not. All older females (≥10 years old) are slaughtered irrespective of deviations in behaviour and physical appearance. For risk categories in the model, the relative risks of infection were adjusted according to the population proportion of risk groups within each risk category (Supplementary Table S2). Thereby, we ensured that the average adjusted risk (AR) for a representative sample of the reference population was 1, while the relative ratios were maintained as specified by Martin et al. (2007). For the sample category, however, we kept ordinary harvest as the reference population.

The sensitivity of the diagnostic test is dependent on the time after infection and the type of tissue tested. In the simulations (10,000 iterations), we randomly drew the hypothetical time after infection for each of the tested individuals (see 2.4 above), and the resulting diagnostic sensitivity for individual i in group g in the simulation j (dSe_{gij}) was determined by the pathway of individual i through the scenario tree. The pathway of an individual through the tree was randomly drawn according to probabilities and proportions specified by the testing regime.

2.6. Estimation of probability of freedom from disease

Estimation of probability of freedom from infection usually implies to document that the prevalence of infection, if present, is below a predefined level, the so-called design prevalence (Cannon, 2002). A probability formula assuming that infected reindeer are distributed according to the hypergeometric distribution, is used to calculate the annual surveillance sensitivity (SSe), which is the probability of detecting the infection (at least one sample testing positive) from the specific sampling regime and at the specified design prevalence. For each iteration (j) of the model, the effective probability of infection (EPI_{gj}) in a risk group (g) is the design prevalence (P^*) weighted by the relevant adjusted relative risks (AR_g). For ordinary harvest animals (reference population), $AR_{sample\_category}$ is set to 1.

- For fallen stock and animals showing clinical signs, $EPI_{gj} = AR_{sample\_category} \times P^*$.

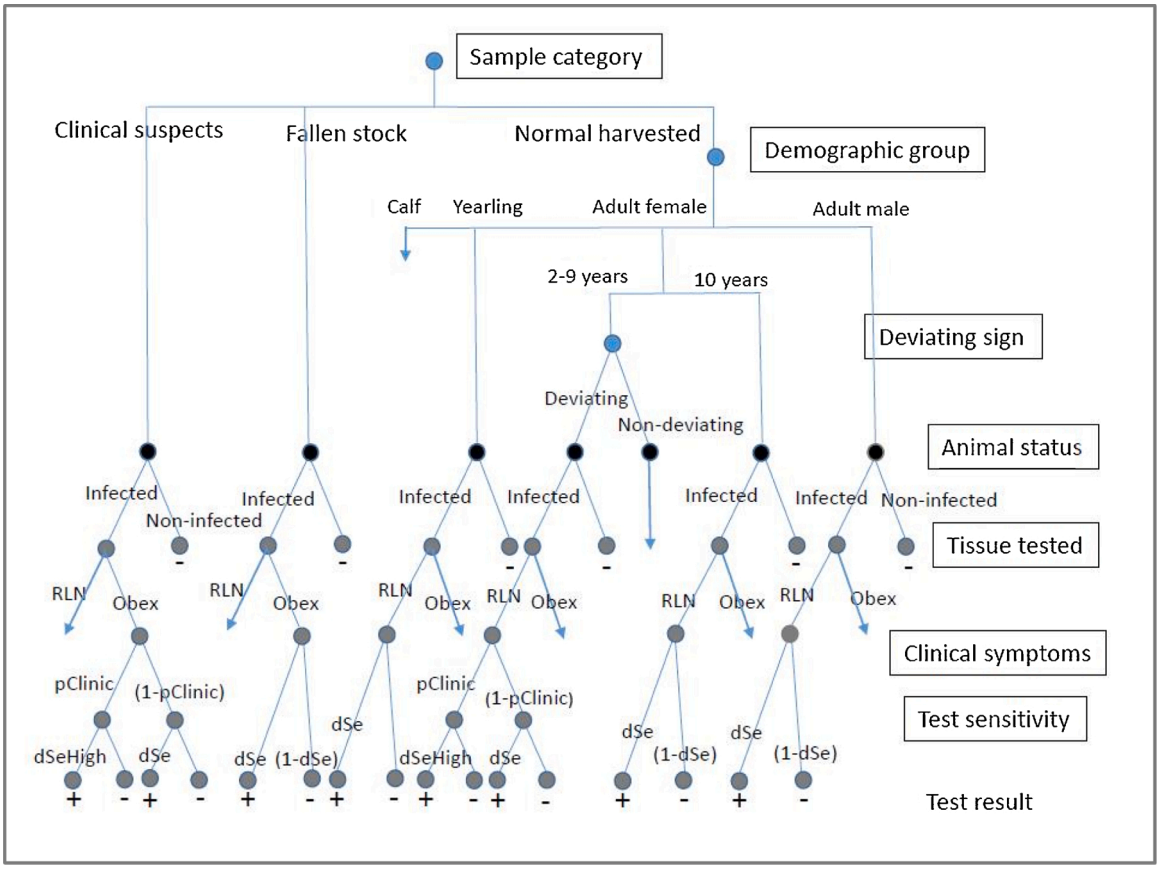

Fig. 2. An overview of the scenario tree with the different risk and detection categories. The pathway of an individual through the tree was randomly drawn according to probabilities and proportions specified by the population proportions, relative risks and testing regime. The probability of an animal testing positive, if infected, depends on the risk group and the diagnostic test sensitivity (dSe). dSe is dependent on sample tissue type and random time since infected, and animals in the risk group of clinical signs or adult females with a deviation in behaviour or physical appearance had a higher probability (pClinical) of being closer to the terminal phase of the infection period (high test sensitivity). Arrows denote branches that for simplicity are not shown, but are similar to a nearby completed branch.

- For yearlings, adult males and old females of ordinary harvest, $EPI_{gj} = AR_{demo} \times P^*$.
- For adult females slaughtered less than 10 years old, with or without a deviation in behaviour and physical appearance, $EPI_{gj} = AR_{demo} \times AR_{deviating,j} \times P^*$.

Let $ProbAllSampleNeg_{gj}$ denote the probability that there were no test-positive animals found in iteration j of n_g samples from risk group g for the EPI_{gj}. According to MacDiarmid (1987), a hypergeometric distribution can be approximated by:

$$ProbAllSampleNeg_{gj} = (1 - \sum_{i=1}^{n_g} dSe_{gij} / GroupSize_g) \text{ ^ } (EPI_{gj} \times GroupSize_g) \quad (1)$$

where dSe_{gij} is the diagnostic sensitivity of individual i in group g in iteration j (see above) and $GroupSize_g$ denotes the population size (ignoring calves) of the risk group g. In the scenario tree, there are three risk categories (sample category, demographic group and deviating sign) giving rise to seven risk groups in total (Fig. 2). For each of 10,000 iterations, we then calculated the surveillance sensitivity:

$$SSe_j = 1 - \prod_{g=1}^{7} ProbAllSampleNeg_{gj} \quad (2)$$

To estimate the probability of freedom from infection, PFree (i.e., estimate the probability that the prevalence of the infection is not higher than the design prevalence) an updated posterior probability of freedom after each year of testing is calculated using the Bayes theorem, as described by Martin et al. (2007). Assuming perfect specificity, the calculation of probability of freedom for each year t is based on the prior probability of the population being infected, $priorPInf_t$, and the surveillance sensitivity, SSe_t, at the given design prevalence:

$$PFree_t = (1 - priorPInf_t) / (1 - priorPInf_t \times SSe_t) \quad (3)$$

Further, the calculation of $priorPInf_t$ is based on the probability of introduction of infection, $pIntro_t$, and the posterior probability of infection from the previous year (t-1), $postPInf_{t-1}$:

$$priorPInf_t = postPInf_{t-1} + pIntro_t - (postPInf_{t-1} \times pIntro_t) \quad (4)$$

where $postPInf_{t-1} = 1 - PFree_{t-1}$ (= 1 - prior probability of freedom). The prior probability of infection was set to 0.5 for the first year. The simulation model is stochastic and model output for each simulated year ($PFree_t$) will be in the form of frequency distributions (summarized by the median and 95 % credible interval).

2.7. The model input parameters

2.7.1. Relative risk of sample category (RRsample_cat)

Relative risks for CWD infection in fallen stock and animals showing clinical signs compared to ordinary harvest individuals were chosen based on CWD studies from North America (Walsh and Miller, 2010; Walsh, 2012; Jennelle et al., 2018). For example, white-tailed deer reported from hunters as clinical suspects and fallen stock (excluding road kills) were given 9.1 times and 7.3 times higher weight relative to harvested male yearlings (Jennelle et al., 2018). The relative risk of CWD infection has been found both higher (Krumm et al., 2005) and lower (Jennelle et al., 2018) for vehicle-killed deer compared to hunted deer. On this basis, we chose the same infection rate between fallen stock and ordinary harvest, and a 9 times higher infection likelihood for animals showing clinical signs compared to apparently healthy harvested individuals (Table 1). We also assessed the impact of uncertainties in the values for the relative risks of the sample categories as part of a sensitivity analysis (see 2.9).

2.7.2. Relative risk of demography (RRdemo)

There is a well-documented sex and age-specific pattern of CWD infection in deer in North America (Miller and Conner, 2005; Samuel and Storm, 2016), which appeared similar to the smaller sample from wild reindeer in Norway (Mysterud et al., 2019a). In wild reindeer harvested during the hunting season (August-September), we have used relative risk of infection 0:1:2:6 for calves: yearlings: adult females: adult males (Mysterud et al., 2020a). In the semi-domestic setting of Filefjell, the high relative risk of adult males is of limited value to increase the efficiency of the surveillance, since males are slaughtered out at a young age and the majority of slaughtered animals are either calves, yearling males or adult females (Supplementary Table S1).

2.7.3. Relative risk of animals with a deviation in behaviour or appearance (RRdeviating)

We defined an animal with a 'deviating sign', as an animal showing any physical or behavioural deviation, such as being blind, skinny, limp, having poor body condition, or showing abnormal behaviour. There were no available data on the number of individuals showing clinical signs consistent with CWD. However, by utilizing data on the number of deviating adult females at age 2–9 years (nAdf_Deviating) and modelling the probability of an infected animal for showing clinical signs of CWD (PrCWDclinic, see below), we were able to estimate the relative risk of being infected with CWD for adult females (below 10 years) showing a deviation relative to non-deviating adult females (RRdeviating). Let *PrCWDadfDeviating* denote the probability that an adult female with a deviating sign is infected, given one infected adult female (age < 10 years), and *PrCWDadfNonDev* denote the probability that a random adult female without deviating signs is infected, given one infected adult female (age < 10 years). The ratio of these two probabilities is defined as RRdeviating (Table 1):

$$RRdeviating = PrCWDadfDeviating / PrCWDadfNonDev \quad (5)$$

2.7.4. Probability of a CWD-infected individual for showing clinical sign of disease (PrCWDclinic)

We used the length of the clinical phase relative to the incubation period to estimate PrCWDclinic. We defined this variable as a stochastic distribution (beta-pert distribution) defined by expected, minimum and maximum values, in order to take into account individual variability in these parameters (Table 1). For the baseline model, we assumed that the period from infection to death was two years and included a clinical phase of 3 months (expected value) with range 1−4 months (Johnson et al., 2011). The impact of the uncertainty in the variables defining this distribution was assessed by a sensitivity analysis.

2.7.5. Diagnostic test sensitivity (dSe)

The diagnostic sensitivity is modelled as a stochastic distribution to account for individual variation in disease progression (see 2.4–2.5 above), and is dependent on tissue type and quality. We assumed that, if infected, adult females slaughtered because of deviations and animals removed during herding because of clinical signs, had a high probability of being close to the terminal stage of the disease (pClinic), which corresponded to a high test sensitivity (dSeHigh), equal to the analytical test sensitivity (Table 1).

2.7.6. Design prevalence (P*)

We used a design prevalence set as a number of infected individuals increasing from 2 in 2016 to 4 from 2020, based on the assumed epidemic growth of CWD after the first introduction in a population and to be able to detect a relatively recent introduction (Mysterud et al., 2020a). This is similar to the design prevalence used in the population of wild reindeer in Nordfjella zone 2, bordering the CWD-infected population in Nordfjella zone 1, opposite Filefjell (Fig. 1).

2.7.7. Probability of introduction (pIntro)

We also used the same level of probability of introduction of infection, which was 5 % annually, and reduced to 0.1 % annually (i.e. 1 introduction per 1000 year) after depopulation of the source population and setting up fences (Mysterud et al., 2020a).

2.8. Baseline scenario and sampling regimes

We ran the model with baseline values as defined in Table 1. We do not know the exact size and structure of the population and the samples being tested in 2021, but we assumed that they will be similar to those in 2020 (baseline scenario). We also tested a sampling regime of harvesting 400 extra adult females in 2019. We reran the model for a version excluding both the relative risks of sample category and the risk group introduced for adult females showing a deviation (corresponding to wild reindeer model). For each scenario, there were 10,000 iterations, and the model was run using R version 4.0.3 (R Development Core Team, 2019). Convergence of results was assessed by running three independent runs of the model scenarios.

2.9. Sensitivity analysis

Sensitivity analyses were performed by testing alternative values to the baseline (Table 2).

2.9.1. Sensitivity of sample category (RRsample_cat)

For fallen stock, we tested a scenario of increasing the relative risk of infection compared to the ordinary harvest from 1 to 7 (scenario 6), and for animals showing clinical signs we tested two scenarios, one increasing and the other decreasing the relative risk compared to the baseline of 9, using 12 (scenario 7) and 7 (scenario 8) times higher risk of infection compared to ordinary harvest. The parameter variations reflected a range of values reported from North-American CWD studies (see references in Table 1).

2.9.2. Sensitivity of the probability of a CWD-infected individual for showing clinical signs (PrCWDclin)

PrCWDclin is a required parameter for estimating RRdeviating. Uncertainty in PrCWDclin was addressed by four scenarios representing alternatives to the baseline distribution. We first assessed sensitivity in the estimate of PrCWDclin by increasing the period from infection to death from 2 to 3 years (PrCWDclin2, scenario 2), while keeping the assumed duration of the clinical phase unchanged (expected value 3, range 1−4 months). Based on experimental infection studies in white-tailed deer, a longer incubation period is not necessarily associated with a longer clinical period (Johnson et al., 2011). In additional scenarios, we used measurements of incubation- and clinical-period lengths from low and high susceptible *PRNP* from Fig. 2 in Johnson et al. (2011). A scenario of high susceptible *PRNP* (scenario 3) was represented by the infection pattern of individuals surviving three years or shorter, while a scenario of low-susceptible *PRNP* (scenario 4) was represented by the infection pattern of two individuals surviving around four years. We also included a scenario assuming that the population consists of a 50 % mix of hosts with low and high susceptibility genotypes (scenario 5). A limited sample (n = 29) suggests the Filefjell population consists of about 65 % *PRNP* genotypes with assumed high susceptibility to CWD (Güere et al., 2021). The assumed high susceptibility *PRNP*s (variants with A or C allele) was based on the pattern of CWD infection in Norwegian wild reindeer from Nordfjella (Güere et al., 2020).

Table 2
Model results for stochastic simulations of different model scenarios reported as the probability of freedom from CWD in the Filefjell semi-domesticated reindeer population, after testing samples from 2016 to the end of production in 2018 (PFree_2018) and 2020 (PFree_2020), and including the surveillance sensitivity of 2020 (SSe_2020). Results are given as medians and 95 % credible intervals (the lower and upper 2.5 and 97.5 percentiles). A sensitivity analysis was performed by varying parameters one-by-one (as defined by scenarios) compared to the Baseline (scenario 1, Table 1). Parameter values are specified as fixed or stochastic, and if stochastic, described by a beta-pert (Pert) distribution of the expected, minimum and maximum values. The scenarios 6-14 resulted in minor change of estimates (less than 0.010) compared to the baseline.

No	Scenario	Baseline	Expected	Distribution	SSe_2020	PFree_2018	Pfree_2020
1	Baseline (PrCWDclin1)	0.125	0.125	Pert(0.125, 0.04, 0.17)	0.79 (0.68, 0.85)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)
2	PrCWDclin2 (3 yr infection)[a]	0.125	0.08	Pert(0.08, 0.03, 0.11)	0.70 (0.61, 0.76)	0.88 (0.82 0.91)	0.98 (0.96, 0.99)
3	PrCWDclin3 (high)[b]	0.125	0.35	Pert(0.35, 0.15, 0.50)	0.97 (0.90, 0.99)	1.00 (0.98, 1.00)	1.00 (1.00, 1.00)
4	PrCWDclin4 (low)[c]	0.125	0.07	Pert(0.07, 0.06, 0.08)	0.68 (0.64, 0.71)	0.86 (0.84, 0.88)	0.98 (0.97, 0.99)
5	50−50 high and low susceptibility	0.125	50 %: 0.35, 50 %: 0.07	50 %: Pert(0.35, 0.15, 0.50), 50 %: Pert(0.07, 0.06, 0.08)	0.79 (0.64, 0.99)	0.93 (0.84, 1.00)	0.99 (0.97, 1.00)
6	RRsample_cat = RRfsc2 (harvested, fallen stock, clinical)	(RRfsc1) 1, 1, 9	1, 7, 9	fixed	0.80 (0.69, 0.86)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)
7	RRsample_cat = RRfsc3	1, 1, 9	1, 1, 12	fixed	0.79 (0.68, 0.85)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)
8	RRsample_cat = RRfsc4	1, 1, 9	1, 1, 7	fixed	0.79 (0.68, 0.85)	0.93 (0.86, 0.96)	1.00 (0.98, 1.00)
9	pClinic = pClinicLow	0.8	0.7	fixed	0.79 (0.68, 0.85)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)
10	pClinic = pClinicHigh	0.8	0.9	fixed	0.79 (0.68, 0.85)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)
11	Stochastic RRdemo (yearlings, adf, adm)	1, 2, 6 (fixed)	1, 2, 6	RRadf: Pert(2, 2, 2.3), RRadm: Pert(5, 2.5, 6.5)	0.79 (0.67, 0.85)	0.93 (0.86, 0.96)	1.00 (0.98, 1.00)
12	PrLQS	0	0.10	fixed	0.79 (0.68, 0.85)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)
13	Infection length (years)	2	3	fixed	0.79 (0.68, 0.85)	0.93 (0.86, 0.96)	1.00 (0.98, 1.00)
14	pIntro (from 2018)	0.001	0.01	fixed	0.79 (0.68, 0.85)	0.93 (0.87, 0.96)	1.00 (0.98, 1.00)

[a] Increasing assumed infection length from 2 to 3 years, while keeping the assumed duration of the clinical phase unchanged.
[b] High susceptible PRNP represented by the infection pattern of nine individuals surviving three years or shorter (Wt/G9gS or wt/wt in Johnson et al., 2011).
[c] Low susceptible PRNP represented by the infection pattern of two individuals surviving around four years (Q95 H/G96S and wt/Q95H in Johnson et al., 2011).

2.9.3. Sensitivity of other parameters

We added a scenario for testing the impact of including stochasticity (individual variation) to the relative risk of demography (scenario 11). Scenarios with alternative values for the probability of infected animals with clinical signs or deviations to be in the terminal stage of the disease, were run to test the effect of the uncertainty of the baseline value (scenario 9–10). To account for the possibility that samples from ordinary harvest may have included brain samples of low quality, we also ran a scenario with the probability of low-quality samples increased to 10 % (scenario 12). As a baseline, the diagnostic test sensitivity was modelled according to an assumption of an infection length of two years. We tested the effect of increasing the infection length to three years (scenario 13). Finally, we tested the effect of increasing the probability of new introductions from 0.1 % to 1 % from 2018 (scenario 14).

3. Results

The time required to reach a specified probability of freedom from infection was markedly improved by including surveillance of adult females showing deviations in behaviour or physical appearance, compared to a surveillance system based only on targeting demographic patterns of infection as applied in wild populations of reindeer (Fig. 3). Compared to the wild reindeer scenario, where variability in parameters is related to the diagnostic sensitivity, the inclusion of a relative risk for adult females with deviations, led to a profound increase in the variation of the model estimates of the probability of freedom from CWD. However, the surveillance was clearly improved, despite greater uncertainty in the model estimates.

Increasing the ordinary harvest of adult females by 400, increased the estimated probability of freedom where the prior probability was low, but the effect was small if the prior probability was high, and when compared to the effect of targeting females with deviations in behaviour or physical appearance (Fig. 3). The total effect of harvesting additional adult females is uncertain because the remaining stock of adult females would lead to lower sample sizes in the coming years.

The time to reach a given level of probability of freedom from infection was only marginally shorter if the probability of a CWD-infected individual to show clinical sign of disease was estimated based on an assumption that the duration from infection to death was 2 years compared to 3 years, for the same clinical period (Fig. 4a). When using the incubation period and clinical period in white-tailed deer,

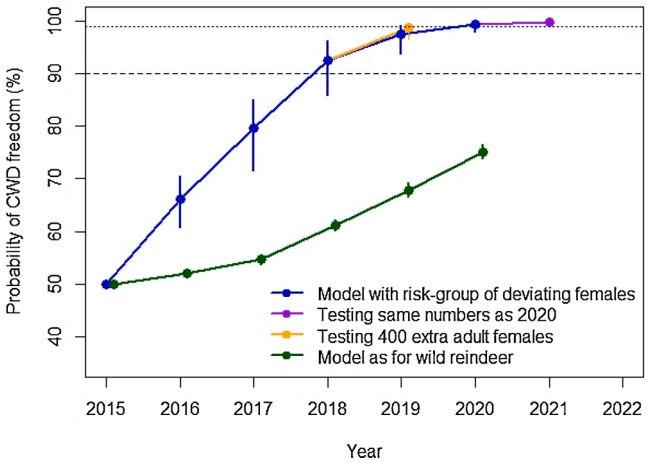

Fig. 3. The annual change in probability of freedom from infection in a population of semi-domestic reindeer in Filefjell, Norway, given different scenarios. Curves describing the effect of the risk-based surveillance including a risk-category of adult females with or without a deviation in behaviour or physical appearance (i.e., adult females that were slaughtered for reasons other than old age) relative to surveillance developed for wild reindeer. The annual error bars represent 95 % credible intervals (in some cases too narrow to be visible).

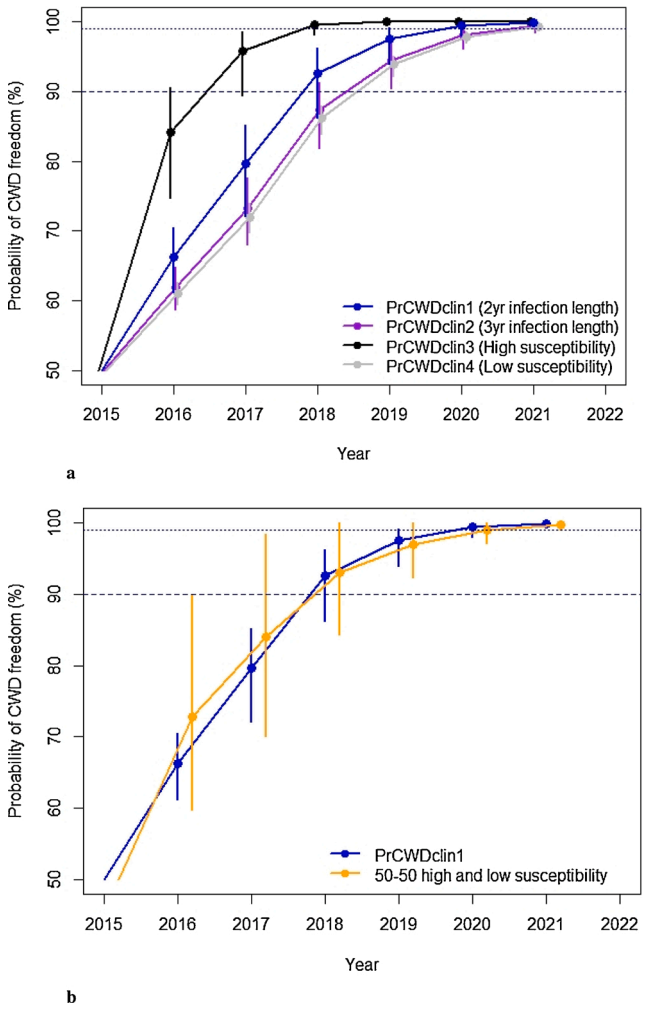

Fig. 4. The effect of how variation in incubation period and duration of visible signs of disease linked to variation in the prion protein gene (*PRNP*) would affect time to establish probability of freedom from infection at a given level. a) The effect of 2 (PrCWDclin1) or 3 (PrCWDclin2) years infection duration (with an assumed 3 months period of clinical signs), compared to the effect of a long incubation period linked to a short period of clinical signs (PrCWDclin4) or a short incubation period linked to a long period of clinical signs (PrCWDclin3), as has been documented in white-tailed deer. b) The effect of having a 50/50 mix of high (PrCWDclin3) and low (PrCWDclin4) susceptibility among individuals, relative to a fixed 2 year infection duration (PrCWDclin1). The annual error bars represent 95 % credible intervals.

reaching a high probability of freedom from infection was more rapid in a population with only 'high' compared to only 'low' susceptibility individuals, as expected (Fig. 4a). This was reflected in a very high relative risk of adult females with a deviation in behaviour or physical appearance for the scenario with 'high'-susceptibility individuals (Supplementary Fig. S2). The time to reach a given level of probability of freedom from infection for a hypothetical population with a 50/50 mix of low and high susceptibility among individuals was similar on average to our baseline model, but with markedly increased variance (Fig. 4b).

Changing the relative risks of fallen stock and animals with clinical signs relative to ordinary harvested animals had a negligible effect on the estimate of probability of freedom from infection (Supplementary Fig. S1, Table 2). This is primarily due to the low number of fallen stock (1 %) and animals with clinical signs (~0.3 %) relative to the total number of animals tested. Secondly, as the design prevalence is specified relative to the sample category of ordinary harvest, the effective probability of infection in this group does not change by changing the relative risks. Changing the relative risks of demographic classes from fixed

parameters to stochastic distributions, or increasing/decreasing the probability of CWD-infected animals with clinical signs or deviations to be in the terminal stage of the disease, also had minor effect on the estimated probability of freedom (Table 2).

4. Discussion

Pastoralism requires extensive areas that are often shared with wildlife (Dyson-Hudson and Dyson-Hudson, 1980; Frachetti, 2012), and this cohabitation may cause pathogen spillover between livestock and wild populations (Roug et al., 2014; Zinsstag et al., 2016). The first CWD-infected wild reindeer population in Norway was successfully depopulated (Mysterud and Rolandsen, 2018; Mysterud et al., 2019b). A key focus of current CWD management in Norway is to detect infections early, if present, or to document freedom from CWD infection particularly in the adjacent populations (Mysterud et al., 2020a). CWD is a notifiable disease in Norway and the European Union (European Parliament and Council, 2001). A 3-year mandatory surveillance program for CWD was implemented (2018–2020) in Norway and EU member states having populations of reindeer and/or moose (The European Commission, 2017). Within these countries, there are more semi-domestic than wild reindeer. No CWD cases have been detected in any semi-domestic reindeer populations, but developing surveillance methods fitting the European context is urgent as the disease has been detected in their wild counterparts. Here we present a surveillance system for CWD applicable to semi-domestic reindeer management when herders remove (and provide samples from) animals showing clinical signs or deviations in behaviour or physical appearance. The method combines the information from sampling high-risk groups with that from ordinary harvest of apparently healthy animals. The method depends on reliable data on the population size and composition and number of samples being tested from the various risk groups. If such data are available, the weighted surveillance will be less invasive and may reduce the time required to establish the probability of freedom from infection or increase the likelihood of early detection. The novelty of our surveillance approach lies in calculating the expected relative risk for CWD of animals harvested due to deviations in behaviour or physical appearance, based on the probability that an infected individual presents clinical symptoms. This probability is estimated based on the assumed length of the clinical phase relative to the incubation period. We further simulate how variations in the incubation time and onset of clinical signs (linked to *PRNP*) would affect the time necessary to establish a probability of freedom from infection. Although there is both a large parameter uncertainty and variability in the relative risk of females with a deviation in behaviour or physical appearance, including this risk factor in the surveillance significantly improved the surveillance system.

4.1. Surveillance of disease fitted to pastoralist reindeer management

The presence of pre-symptomatic individuals severely complicates our ability to combat infectious diseases in general (Fraser et al., 2004), including CWD (Haley et al., 2009). For wild reindeer, adult males had a 2–3 times higher infection rate than adult females (Mysterud et al., 2019a). Previously, this was used to develop harvest strategies targeting adult males to maximize disease detection (Mysterud et al., 2020a). In contrast to wild reindeer, the Filefjell population of semi-domestic reindeer have a very low proportion of adult males, since they follow the so-called Røros-model for herd composition to maximize meat production (Lenvik, 1989). Therefore, targeting mostly adult male reindeer for surveillance, as adopted for hunted wild reindeer, is not effective for this semi-domestic production system. Moreover, increasing the harvest of adult females would negatively impact the profitability of the reindeer herders. It is a fair assumption that most CWD-infected females will show clinical signs of disease at some point, as they are generally not slaughtered before 10 years of age. The clinical features of progressive CWD are weight loss and behavioural changes (Williams, 2005). Visible signs vary and include excess salivation and urination, ataxia, head tremors and abnormal movement behaviour. Stress is known to trigger the appearance of some clinical signs (Williams, 2005). Here we take advantage of the indigenous knowledge of the reindeer herders and based on their experience assume that, when stressing the animals, they can identify and remove females deviations in behaviour or physical appearance, forming a basis for testing of high-risk groups.

Targeting adult females with deviations in behaviour or physical appearance significantly improved our ability to substantiate the probability of freedom from infection and early detection, due to the high probability of infected animals to show a deviation or clinical sign in late stages of CWD infection. Our modelled risk-based surveillance requires detailed knowledge about development of infection and visible sign of disease. There is quite limited information even for mule deer and white-tailed deer about the duration of the clinical period and on the proportion of individuals showing clinical signs of CWD infection. The duration of the clinical period was 1–4 months prior to death in mule deer and white-tailed deer, with a few exceptions of up to 9–13 months (Wild et al., 2002). Clinical signs started 18 months post infection in intracerebrally inoculated white-tailed deer, but the study was terminated due to welfare concerns after 26 months (Hamir et al., 2008). A review suggested the clinical course of CWD usually ranges from a few weeks up to 3–4 months (Williams and Miller, 2002). A study in mule deer reported clinical signs for the last four months (16–20 months post-infection) in all infected deer that survived longer than 490 days post-infection (Tamguney et al., 2009). The duration of clinical signs prior to death averaged 7.5 months in elk, but varied from 5 to 12 months (Miller et al., 1998). Therefore, we designed scenarios to capture different possibilities in order to assess the sensitivity to these assumptions. We found, as expected, that the relative risk of females with a deviation to be infected with CWD was lower with a short clinical disease phase relative to the duration of the incubation period. Compared to the relative risk of females with a deviation in behaviour or physical appearance, uncertainties and variabilities tested for the other risk factors included in the surveillance had minor impact on the model results.

4.2. Surveillance, PRNP-variation and data gaps

Including knowledge of genetic variation in pathogens or hosts can improve disease surveillance (Valdazo-González et al., 2015). Susceptibility to prion disease and infection development is linked to variation of the prion protein gene (*PRNP*) encoding the prion protein in some species (Collinge, 2001). Knowledge of *PRNP* variation is included in scrapie surveillance to estimate freedom from infection (Schulman and Lyytikäinen, 2018), but *PRNP* information does not appear to be used in surveillance of CWD in North America. For CWD, *PRNP* has been linked to variation in susceptibility and the incubation period for elk (Moore et al., 2018) and white-tailed deer (Johnson et al., 2011). We also know that there is substantial variation in *PRNP* among reindeer (Robinson et al., 2012) and caribou (Arifin et al., 2020). For Norwegian reindeer, some variants had lower susceptibility to CWD (Güere et al., 2020). The prevalence of less susceptible *PRNP* variants, defined as those with lower CWD infection probability in Nordfjella (Güere et al., 2020), was about 35 % (n = 29) in the Filefjell population (Güere et al., 2021). There is limited experimental transmission data on reindeer (Mitchell et al., 2012; Moore et al., 2016), and the CWD strain detected among Norwegian reindeer is different from those found in North America (Nonno et al., 2020; Bian et al., 2021). The assumption of a link between low susceptibility and long incubation period, and the length of clinical phase relative to incubation period being dependent (or not) on the *PRNP,* is therefore uncertain. Even for white-tailed deer, a longer duration of infection was not always linked to a longer period with visible signs (Johnson et al., 2011). We used data from Fig. 2 in Johnson et al. (2011) as a basis to model how this might affect the sensitivity of

the surveillance system (Table 2). For classical scrapie in sheep, it is a known paradox that to substantiate freedom from disease, more testing is required in genetically less susceptible flocks, even though they are less likely to be infected (Durand et al., 2009). We found similar results for reindeer when comparing a theoretical population composed of only highly susceptible individuals with a population of only less susceptible individuals (Fig. 4a). However, with a mix of *PRNP* genotypes as in Filefjell, the effect was limited to a remarkably increased variance in the estimated probability of freedom (Fig. 4b), rather than a change in mean time to establish a probability of freedom from CWD infection.

Knowledge about individual variation in infection dynamics of CWD is still sparse, and the limited data from reindeer were performed with North-American CWD strains (Mitchell et al., 2012; Moore et al., 2016). Hence, there is considerable uncertainty in setting reliable parameter estimates for both duration of the incubation period and the period with clinical signs of infection. Refinement of the current surveillance scheme would require inoculation studies with the Norwegian CWD strains in reindeer, including testing for any differences in infection dynamics between the relevant *PRNP* variants. Unfortunately, CWD-transmission experiments in reindeer are challenging due to the long time frame needed, the large costs and not the least, animal welfare concerns.

4.3. Model considerations with many risk groups and low design prevalence

The probability of freedom estimated according to a given design prevalence is relative and must be interpreted in combination with all the assumptions built into the model. The results are also sensitive to the detailed choices of model setup. For example, we calculated the probability of detecting at least one positive animal for each risk group by using the hypergeometric approximation and the effective probability of infection for the risk group. In our case, the number of risk groups (seven) is larger than the design prevalence of four infected animals for the category of normal slaughtered animals. If we instead, for each iteration, had used a multinominal distribution to randomly distribute the number of infected animals between risk groups according to the effective probability of infection for an individual within the risk group, the estimated mean probability of freedom from infection would have decreased due to increased variance and a left-skewed frequency distribution (results not shown). The model and the relative probability of freedom being estimated is still a valuable tool for evaluating and comparing different sampling strategies and surveillance systems.

4.4. Management considerations

Uncertainties about disease outbreaks in wildlife are typically high (Webb et al., 2017), and surveillance is key to lower these uncertainties especially in our situation where semi-domesticated reindeer are free-ranging much of the year. The Norwegian Food Safety Authority has chosen a proactive approach to surveillance of reindeer populations adjacent to the CWD-infected area. The aim is to establish probability of freedom from infection rapidly and with high certainty, or to enable early detection as a basis for rapid action. Therefore, the design prevalence was set very low (~0.1 %). Here we report the current status for semi-domestic reindeer in Filefjell (Fig. 1). After 5 years of surveillance, a 99 % likelihood for CWD freedom for the given design prevalence was reached, or was close to being reached, for most model scenarios (Fig. 3, Table 2).

The low design prevalence used for the Filefjell reindeer population required surveillance longer than the 3 years mandatory surveillance period of the EU. The duration of a given surveillance program should reflect the design prevalence, which again may depend on the management situation and objective. The short duration of the EU surveillance program may be sufficient for a higher design prevalence (e.g. 1 %). However, 3 years was too short when aiming for early detection and using a low design prevalence, as in our case chosen with the aim to contain a known and likely recent CWD outbreak in the same main region. The process of establishing probability of freedom from infection was nevertheless relatively rapid due to efficient use of risk groups, compared to the method applied for hunting of wild reindeer. Reaching a similar aim for a wild reindeer population involves excessive harvesting (Mysterud et al., 2020a).

The result relies on the assumptions of random sampling and homogenous mixing within risk groups, likely being valid with apparently full mixing of individuals within the herd. The result was also robust even if assuming a relatively long incubation period relative to expected clinical phase. The model uses a low risk of infection introduction reflecting that the adjacent wild population was eliminated and fenced off. With the recent detection of CWD in the Hardangervidda wild reindeer management area (Fig. 1), the risk of spread will increase if an outbreak develops, and risk of infection introduction into Filefjell may become an issue again in the future. It has been questioned whether the battle to keep Europe free of CWD is already lost (Dagleish, 2016), and consequences for reindeer pastoralism can be substantial (Maraud and Roturier, 2021). The uncertainties regarding disease status are likely to remain for decades in Europe.

Declaration of Competing Interest

None declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.prevetmed.2021.105497.

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