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Applications of mathematical modeling in managing the spread of chronic wasting disease (CWD) in wild deer under alternative harvesting scenarios

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ABSTRACT

The application of a recently developed mathematical model for predicting the spread of chronic wasting disease (CWD) in wild deer was assessed under different scenarios where harvesting is employed in disease management. A process-based mathematical model for CWD transmission in wild deer populations was recently developed and parameterized by Al-arydah et al. (2011) to provide a scientific basis for understanding the factors that affect spread of CWD and evaluate concomitant disease-control strategies. The impact of gender on CWD transmission was shown to have a significant influence on the spread of the disease in the wild. Our model demonstrates a range of harvesting rates in which CWD is controlled and deer populations survive. However, if harvesting rates are too low, the disease remains endemic for decades. Conversely, the Canadian deer population is eradicated if harvesting rates are excessive. Future investigation includes building the model to assess the spread of CWD under different disease-management scenarios.

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) or prion disease that is rapidly spreading across North America (CWD Alliance, 2011). This neurodegenerative disease is known to affect deer, including mule deer (*Odocoileus hemionus hemionus*), white-tailed deer (*Odocoileus virginianus*), black-tailed deer (*Odocoileus hemionus columbianus*), Rocky Mountain elk (*Cervus elaphus nelsoni*), and moose (*Alces shiras*). CWD is currently the only prion disease found in a free-ranging species (Wang, 2008). Clinical symptoms of CWD include gradual weight loss, ataxia, and behavioral changes, eventually leading to death of the infected animal (Williams and Young, 1980; Spraker et al., 1997).

Risk assessment and management of CWD are challenging, due to its long incubation period (Hamir et al., 2008) and environmental persistence (Schramm et al., 2006). Diagnostic challenges, such as difficulty in implementing an antemortem test to diagnose asymptomatic free-ranging deer, make it difficult to implement preemptive risk-management measures on an individual animal basis. Although animals infected with CWD may remain symptom free for 1–3 yr, they are capable of transmitting the disease to other animals during part of this incubation period (Canadian Food Inspection Agency 2014). CWD prions are transmitted from animal to animal (horizontal transmission) or from mother to offspring (vertical transmission) (Heikenwalder et al., 2005; Mathiason et al., 2006; Aguzzi et al., 2007; Sigurdson et al., 2008; Safar et al., 2008; CWD Alliance, 2011). CWD can be also transmitted through deposited CWD agents in soil and water (environmental transmission) (Miller et al., 2006; Sigurdson et al., 2008; Centers for Disease Control and Prevention, 2014). Data suggest that spatial distribution and resultant density of deer are positively associated with prevalence of CWD, indicating that proximity and perhaps direct contact between deer are involved in the spread of the disease (Joly et al., 2006).

The first case of CWD was identified in a captive mule deer in Colorado in 1967. In 1981, the Colorado Division of Wildlife identified CWD in a

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wild elk. The first Canadian case of CWD was detected on a Saskatchewan elk farm in 1996; since then, the disease has spread to wild deer in Saskatchewan and the neighboring province of Alberta (CWD Alliance, 2011). To date, CWD was detected in a total of 18 U.S. states and two Canadian provinces in free-ranging and/or farmed herds. The detection of the first cases of CWD in Missouri, North Dakota, and Virginia as recently as 2010 indicates that CWD is continuing to spread within North America (CWD Alliance, 2011).

An effective risk-management strategy is needed to prevent continued spread of CWD in North America. CWD control measures such as surveillance and regulations on baiting and carcass transportation were implemented in the United States and Canada (CWD Alliance, 2011) but not consistently respected or enforced between provinces and states. Surveillance of Canadian wild deer populations since September 2005 yielded a total of 205 positive cases in Alberta (September 2005 to February 26, 2014; Government of Alberta Sustainable Resource Development, 2014) and 358 positive cases in Saskatchewan (1997 to fall 2014; Canadian Cooperative Wildlife Health Center and Canadian Food Inspection Agency). At present, the primary CWD control strategy involves culling or harvesting herds from infected deer farms or areas in the wild where CWD-positive animals are found. To date, 60 Canadian deer farms were identified as CWD-positive by the Canadian Food Inspection Agency (CFIA) (CFIA, 2011a, 2011b). Despite current management efforts, CWD disease prevalence continues to increase throughout North America. There is also apprehension that CWD might spread to the caribou population in northern Canada or even to humans, as occurred with bovine spongiform encephalopathy (BSE), commonly known as "mad cow disease" (Bovine Spongiform Encephalopathy (BSE) Factsheet, 2008).

Mathematical modeling is increasingly recognized as a valuable tool in disease control and in development and evaluation of risk management interventions. A Bayesian hierarchical survival model based on data collected by hunters from 2002 to 2006 was used to study spatial and temporal aspects of effects on the prevalence of CWD in southwestern Wisconsin (Song and Lawson, 2009; Lawson and Song, 2010). This model included demographic data (gender and age), as well as spatiotemporal random effects. Another Bayesian hierarchical nominal model was applied to hunter and government culling data collected between 2002 and 2007 in southwestern Wisconsin (Osnas et al., 2009). The primary focus of this study was on spatiotemporal change in the probability of infection using linear and nonlinear models to examine interactions between age and gender. Gender and age were significant determinants of CWD risk in all three models considered (Osnas et al., 2009; Song and Lawson, 2009; Lawson and Song, 2010). However, none of these models were able to determine the dynamics or management of CWD due to the nature of their construction. A recent structured-matrix population model by Wasserberg et al. (2009) measured the effects of harvesting and culling in eradicating CWD in a closed population in Wisconsin. A multistate simulation model was used with density-dependent and frequency-dependent transmission schemes that incorporate multiple levels of heterogeneity as well as gender, age, and seasonality but not a spatial component. It was concluded that CWD was present in this region for quite a long time and that it might take decades to eradicate the disease, even in the presence of recreational hunting.

The objective of this investigation is to describe the application of a new mathematical model developed by Al-arydah et al. (2011) in predicting the spread of CWD in the wild under three assumed but plausible disease management strategies: (1) low harvesting, (2) moderate harvesting, and (3) excessive harvesting. This modeling exercise may aid in assessing whether current harvesting rates can eventually control the spread of CWD or whether adjusting harvesting rates might be effective in eradicating CWD in wild Canadian deer populations.

CWD Risk-Projection Model

The model developed by Al-arydah et al. (2011) describes the dynamics of CWD in a density-dependent (logistically) growing but closed population of a single species. Thus, when the deer population increases in size, the natural death rate rises as a result of competition for resources. The model takes into account mortality due to both harvesting of the population and disease death rates. In the present form of the model, the

birth rate depends on both the male and female population through a harmonic mean function (Miller et al., 2007). In addition, one assumes the male-to-female offspring ratio is one-to-one in this population. The reason underlying consideration of the dynamics of the population in our model is that the incubation period is sufficient to have birth and death actions. The present version of the model does not consider immigration to and emigration from the population under study. In the present version of the model, CWD infection is restricted to transmission via direct contact or vertical transmission, where asymptomatic animals with no clinical signs of CWD may become infectious during the latter part of the incubation period for this disease (Miller et al., 2006).

In mathematical terms, our CWD risk-projection model is a compartmental, susceptible–exposed–asymptomatic–infected (SEAI) model. A schematic diagram of the SEAI model compartments with rates of transition is illustrated in Figure 1. Table 1 describes the model compartments and parameters, whereas sample values and ranges of the parameters, used in the sensitivity analysis, are given in Table 2.

In this model, we further divided the population into eight subclasses: (1) susceptible females (S_f), (2) susceptible males (S_m), (3) exposed females (E_f): no clinical signs and noninfectious, (4) exposed males (E_m), (5) asymptomatic females (A_f): infectious without clinical signs, (6) asymptomatic males (A_m), (7) infectious females with clinical signs (I_f), and (8) infectious males with

Table 1. Description of the compartments and parameters of the SEAI (susceptible-exposed-asymptomatic-infected) model.

Variable	Definition
$S_f(t)$	Number of susceptible female deer at time t
$S_m(t)$	Number of susceptible male deer at time t
$E_f(t)$	Number of exposed female deer at time t
$E_m(t)$	Number of exposed male deer at time t
$I_f(t)$	Number of infected female deer at time t
$I_m(t)$	Number of infected male deer at time t
B	Fecundity
β	Transmission rate
h_f	Harvesting rate of females
h_f	Harvesting rate of males
β_A^f	Transmissibility to females from an asymptomatic deer
β_I^f	Transmissibility to females from infected deer
β_A^m	Transmissibility to males from asymptomatic deer
β_I^m	Transmissibility to males from infected deer
β_A	Rate of transmission from asymptomatic deer
β_I	Rate of transmission from infected deer
γ_{mf}	Rate of contact between infected males and susceptible females
γ_{fm}	Rate of contact between infected females and susceptible males
γ_m	Rate of contact between infected males and susceptible males
γ_f	Rate of contact between infected females and susceptible females
L	Incubation period
L_E	Lifespan for exposed deer
L_A	Lifespan for asymptomatic deer
σ	Rate of progression from exposed class to infected class
σ_E	Rate of progression from exposed class to asymptomatic class
σ_A	Rate of progression from asymptomatic class to infected class
μ_f	Natural death rate for females
μ_m	Natural death rate for males
μ_d	Death rate due to disease
α_f^{-1}	Density-dependent reduction rate for females
α_m^{-1}	Density-dependent reduction rate for males
k^{-1}	Average harem size
η	The probability that the newborn of an asymptomatic mother is susceptible

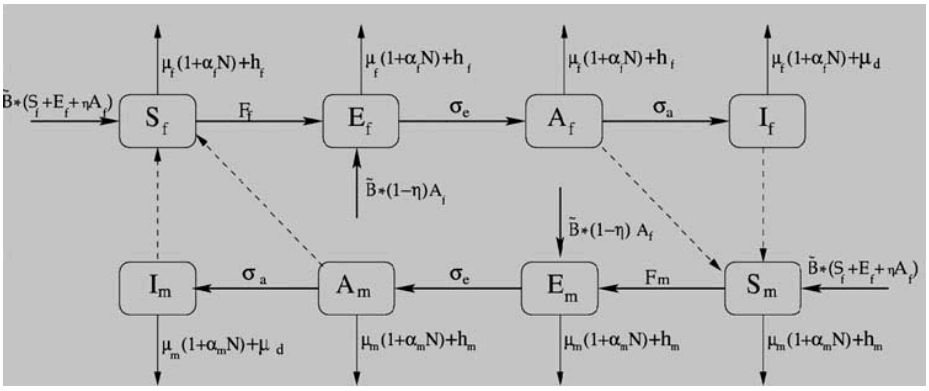

Figure 1. A schematic diagram of the model compartments (in rectangular shapes) with rates of transition indicated beside the arrows; see Table 1 for a description of the model compartments and parameters.

$$\tilde{B} = \frac{bN_m}{kN_f + N_m},\ F_f = \beta_A^f(\gamma_f A_f + \gamma_{mf} A_m) + \beta_I^f(\gamma_f I_f + \gamma_{mf} I_m),$$

$$F_m = \beta_A^m(\gamma_{fm} A_f + \gamma_m A_m) + \beta_I^f(\gamma_{fm} I_f + \gamma_m I_m)$$

Table 2. Sample values and sensitivity ranges of the SEAI (susceptible–exposed–asymptomatic–infected) model parameters.

Parameters	Range s	Sample values	References
b	0.5–0.9	0.57	(Gross, and Miller, 2001)
β	0–0.05	0.226389	(Miller et al., 2006)
h	0–1	1.05	(Binfet and Lutz, 2003)
h_r		0.640278	(Binfet and Lutz, 2003)
h_m		0.195833	(Binfet and Lutz, 2003)
L	1–2	1.05	(Hamir et al., 2008)
L_E		1.5 years	(Hamir et al., 2008)
L_A		0.5 years	(Gross, and Miller, 2001)
μ	0.045–0.15	0.73125	(Gross, and Miller, 2001)
μ_f		0.01	(Gross, and Miller, 2001)
μ_m		0.771528	(Gross, and Miller, 2001)
A	0.002–0.008	0.004	assumed
a, solve for $a\mu_d$	1–4	2	(Miller et al., 2006)
m	0.045–.15	0.05	(Gross, and Miller, 2001)
k		0.02	(Clark and Tait, 1982)
γ_f		0.002	assumed
γ_m		$5\gamma_f$	assumed
γ_{fm}		γ_f	Assumed
γ_{mf}		γ_f	Assumed

clinical signs (I_m). Note that there is a later stage of the incubation period where the animal may become infectious.

Since newborn offspring of infected females have a small chance of surviving because their mothers die quickly, their impact on the dynamics of the disease is minimal. While it is assumed that the offspring of susceptible and exposed individuals enter the susceptible class, one also presumes offspring of asymptomatic individuals are either susceptible or exposed with some probabilities. The offspring of asymptomatic individuals are assumed to be uninfected.

Because the rate and types of contact between deer differ markedly between males and females, gender plays an important role in the rate of infection of susceptible animals, referred to as the force of infection. Since male deer fight at least seasonally among themselves, the probability of contact between males is assumed higher than female–female and male–female contact. This might help explain the observation that prevalence of CWD is twice as high in males as in females (Conner et al., 2007).

In the CWD risk-projection model employed here, transmission of the disease was assumed to be density dependent, since population density exerts a positive influence on the probability of transmission (Williams et al., 2002; Potapov et al., 2012, 2013). It is also assumed that the length of time in each of the exposed, asymptomatic, and infectious states is exponentially distributed with different means. Other important parameters are also embodied in the model, including harvesting rates of males and females, average harem size, fecundity, and gender-specific transmission rates for the asymptomatic and infected animals. Although the model is gender based, two special cases were also investigated: one-sex non-asymptomatic and one-sex asymptomatic. These two simpler models allow for detailed analysis and derivation of explicit disease thresholds, which were then used to compare and contrast with the full gender-structured model.

In our analysis of the two one-sex special cases and the gender-structure model, three important indicators of the CWD epidemic were derived: (1) the disease eradication threshold (Lloyd-Smith et al. 2005; Heffernan et al., 2005), reflected by the basic reproductive number R_0, which is defined as the average number of new infections due to one infectious deer in a completely susceptible population; (2) the critical carrying capacity, which is the epidemic threshold such that if the carrying capacity is below it, the disease starts to vanish; and (3) the critical rate of transmission above which CWD persists in the population and becomes endemic.

These three indicators are used to determine the existence of the endemic equilibrium (when the disease persists within the population over the long term) and to describe the stability of both the disease-free equilibrium (when only the uninfected population survives) and the endemic equilibrium (when infection stabilizes). An equilibrium state is stable if disease states that start from somewhere close to the point of equilibrium return to equilibrium. If the disease-free equilibrium is unstable, then the disease can invade an uninfected population or persist in an already-infected population.

Numerical simulations are used to support the theoretical results and to show how sensitive the basic reproductive number is to harvesting. In fact, a range of harvesting rates was found in which the disease is controlled and the population survives. For low harvesting rates, however, the disease persists, whereas too much harvesting results in eradication of the population in Canada.

Application of the Model to Canadian CWD Epidemic

The gender-structured non-asymptomatic risk-projection model is applied to data for mule deer in

wildlife management unit 150-Alberta (WMU 150), which has an area equal to 1841 km^2 (Pybus, 2006). (For simplicity, one considers only one class for both asymptomatic deer and infected deer.) This area is not closed and includes different species of deer. In 2006, intensive herd reduction was conducted in three local areas, all within approximately 10 km of previous cases of CWD in wild deer in Alberta or Saskatchewan (Government of Alberta Sustainable Resource Development, 2014; Pybus, 2006). As a result of this culling, one may consider this area almost isolated for the next few years, which makes this a reasonable baseline for parameterizing our model.

The population of interest is composed of the 650 deer remaining in this region after the 2006 culling program. It is estimated that 24 of these are exposed, according to the prevalence in culled animals, while the rest are considered susceptible (413 females and 213 males). One assumes that CWD prevalence in males is initially twofold higher than in females, resulting in 16 exposed males and 8 exposed females.

Our risk-projection model for CWD may be used to evaluate culling strategies with moderate harvesting rates as a method of controlling the disease. The harvesting rate was estimated to be 0.0922 for females and 0.282 for males using data for Alberta in 2000 (Binfet and Lutz, 2003), which is considered to be a low harvesting rate.

Under the above assumptions, the optimal harvesting rate was investigated in a gender-structured, non-asymptomatic model (Figure 2). The optimal harvesting strategy to theoretically eradicate the disease without driving the population to extinction lies between the disease-eradication threshold and the population-extinction threshold curves, which are functions of the gender-specific harvesting rates h_f and h_m for females and males, respectively. In other words, any point (h_f, h_m) that lies between the two thresholds implies that the disease is controlled and the population survives. For instance, (h_f, h_m) = (0.0922, 0.282), (0.4, 0), and (0.6, 0) are three points lying in the three regions shown from left to right (Figure 2): (1) disease persists, (2) disease is eradicated but population survives, and (3) population is eradicated. These sets of points and percentages correspond to low harvesting, moderate harvesting, and excessive harvesting, respectively. Note that these harvesting numbers are rates and not percentages; thus, a rate of 0.4 corresponds to an average female life span of 2.5 years, while a rate of 0.6 corresponds to an average female life span of 1.67 years. Practical strategies that might increase the harvesting include rising number of hunting licenses (e.g., by reducing the price of hunting licenses), elevating the number of hunted animals per license, and increasing the hunting season period.

The percent of infected animals was examined in the low and moderate harvesting scenarios (Figure 3, Figure 4) and the mule deer population in the excessive harvesting scenario (Figure 5) in WMU 150 over a 100-yr observation period. In the case of low harvesting, our theoretical results predict that the disease will be endemic in 70 yr, with approximately 20% of does and bucks infected. In the case of moderate harvesting, the disease will be eradicated in about 40 yr. However, it was also predicted that excessive harvesting might lead to extinction of the population in approximately the same period (40 yr). These simulations support the notion that culling is a viable way to eradicate CWD, but harvesting rates should not be excessive.

Discussion

Although harvesting is one of the main CWD management strategies currently used, it remains unclear whether it is efficient in controlling and/or eradicating this disease. Risk-projection models such as the one presented here provide valuable guidance in disease management. Specifically, the results of our model-based analysis indicate whether the three harvesting scenarios (low, moderate, or excessive harvesting) are able to control or eradicate CWD in wild infected mule-deer populations.

Wasserberg et al. (2009) compared a density-dependent transmission model and a frequency-dependent transmission model for CWD. Data showed that the latter model provides a slightly better fit to the values than the former model. The time since the introduction of the disease in the density-dependent transmission model was shown to be approximately 80% less than for the frequency-dependent transmission model. The study also found that it will take a long period of time to

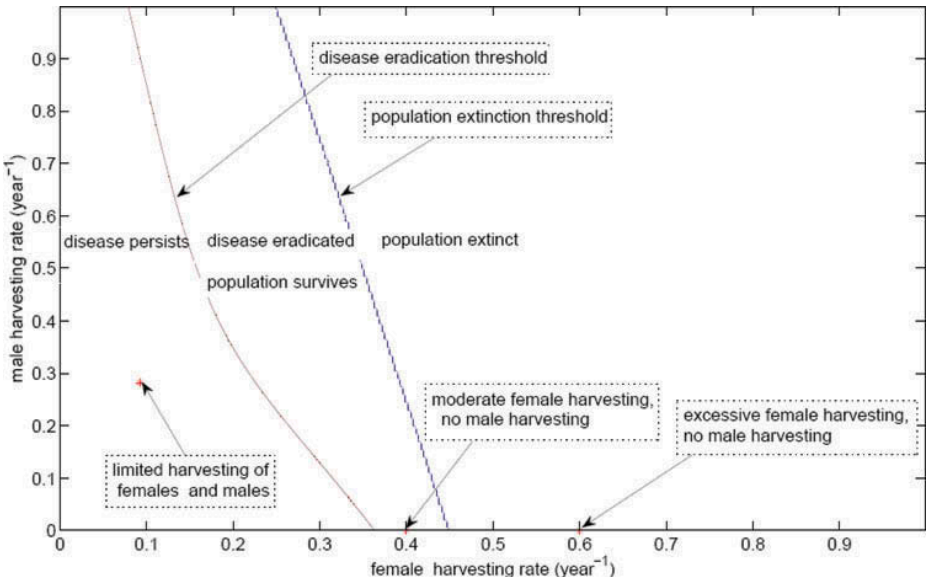

Figure 2. Critical harvesting rates in the gender-structured model. Too little harvesting results in disease persistence. Too much harvesting eradicates the population. Note that the outcome varies with the harvesting of females much more than with the harvesting of males.

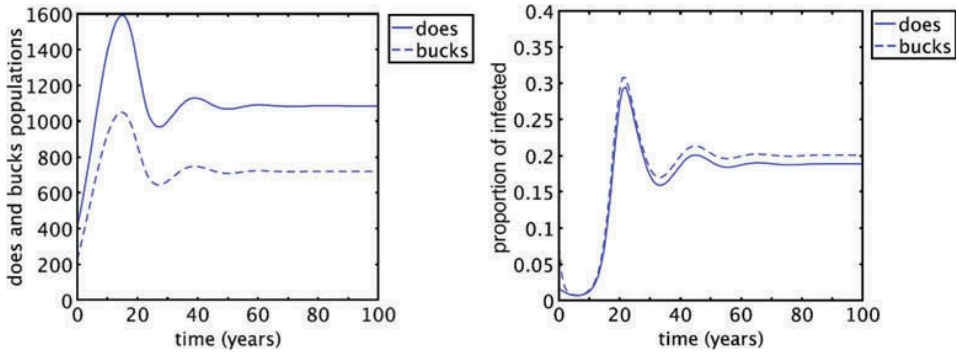

Figure 3. Low harvesting. On the left, deer population in the WMU 150 area for the gender-structured model for (h_f, h_m) = (0.0922, 0.282). The solid curve represents the female population and the dashed curve represents male population. In this case, the disease persists. The percentages of infected deer are given in the right-hand graph. The prevalence is greater in males.

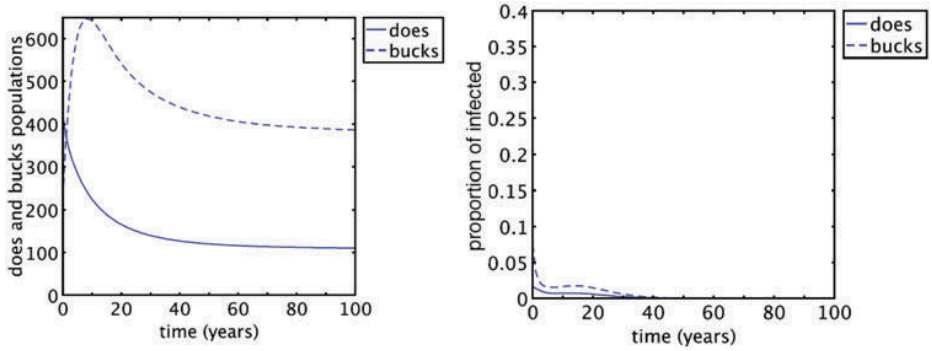

Figure 4. Moderate harvesting. On the left, deer population in the WMU 150 area for the gender-structured model for (h_f, h_m) = (0.4, 0). The solid curve represents the female population and the dashed curve represents male population. In this case, the disease can be controlled and the population survives. The percentage of infected deer is given in the right-hand graph. The prevalence is higher in males.

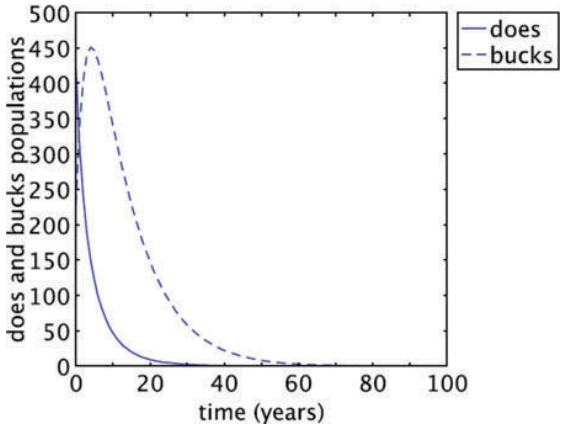

Figure 5. Deer population in the Alberta WMU 150 area for the gender-structured model for (h_f, h_m) = (0.6,0). The solid curve represents the female population and dashed curve represents the male population. In this case, the population is eradicated. Since only females are culled, their numbers decline quicker than those in males.

eradicate CWD, ranging from a few decades to a few centuries, depending on the transmission scheme and the control strategies, and that CWD prevalence decreases in hunted populations. In addition, a high culling rate was indicated as a method of eradicating the disease, although this would diminish the abundance of deer.

In our risk-projection model, culling strategies were examined using different harvesting rates as a method of controlling CWD in the absence of an effective treatment or vaccine for the disease. Based on our model predictions, current low harvesting levels have not been effective in controlling the spread of CWD and will not eradicate the disease in wild deer in the foreseeable future. For low harvesting rates, the disease persists, while excessive harvesting results in extinction of the population. There is a range of harvesting rates in which the disease is controlled and the population survives. An interval for rates of harvesting male and female deer that predict disease control and population survival was found. The results indicated that higher female harvesting rates are expected to induce disease eradication if selected within the moderate harvesting range (Figure 2).

Sensitivity analysis of the disease eradication threshold to the choice of model parameters demonstrates that the threshold is most sensitive to harvesting rates (Figure 6). Moreover, data show that culling is more effective in females than in males in the asymptomatic, SEAI model.

Due to uncertainty in the parameter values, practical harvesting rates should not be chosen too close to the thresholds because small variations

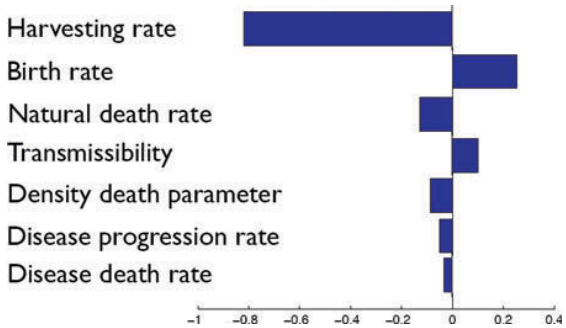

Figure 6. Tornado plot for the sensitivity of the disease threshold to variations in each parameter. Each parameter was varied in turn, with all other parameters held at median values. Parameters that decrease the disease when they are increased have negative rankings, while those that increase the disease when they are increased have positive rankings.

in meteorological parameters or stochastic variation in transmissibility may cause the threshold boundary to be inadvertently crossed. Instead, harvesting rates need to be selected from well within the desired region. Note that adaptive management might be necessary to monitor populations and effectiveness of control strategy to ensure population viability.

Environmental contamination with CWD prion proteins, a factor that might affect our CWD risk predictions, was not considered in our model because of limited data. Some studies indicated that soil and water act as a reservoir for prions and therefore may contribute to the transmission of CWD and scrapie (Almberg et al., 2011; Miller et al., 2004; Schramm et al., 2006). Since herbivores such as deer consume soil both deliberately and incidentally (Weeks and Kirkpatrick, 1976; Beyer et al., 1994), ingestion of prion-contaminated soil may contribute to the natural transmission of CWD (Johnson et al., 2006, 2007). The next step in developing this model will be to include environmental transmission. As new data become available on the etiology and transmission of CWD, our risk-projection model might be easily updated to perform simulations with a new array of factors that may affect the transmission of CWD, helping us better understand the spread of this disease.

Although surveillance programs monitoring the distribution of wild deer populations and CWD testing programs exist, programs that monitor effectiveness of implemented disease-management practices are lacking. Future applications of the risk-projection model might include evaluating the efficiency of a broader range of disease-management options beyond harvesting in controlling and eradicating CWD. CWD management strategies that have been employed in Canada include regulations on feeding deer in areas of game hunting, regulations on baiting of wild deer, use of double fencing on deer farms to prevent contact between farmed and wild deer, and regulations on the transportation of live animals, carcasses, and animal parts (CWD Alliance, 2011). Our results indicate that harvesting at the current rate is not sufficient in controlling or eradicating CWD. However, culling still needs to be considered as a disease-control strategy in the future at rates indicated by our model, using rates falling between the disease-eradication and disease-extinction thresholds shown in Figure 2.

Our model has some limitations, which need to be acknowledged. Many of our parameters have uncertainty, which were partially accounted for. Density dependence may not be the best method of modeling contact, as several recent findings indicate (Habib et al., 2011; Potapov et al., 2013; Schauber et al., 2007; Storm et al., 2013). Indirect transmission was also omitted, leaving transmission due to environmental factors to future investigations. Further, our thresholds are theoretical; there has been little empirical evidence for population thresholds for wildlife disease eradication. Consequently, as with any modeling study, any application of our results needs to begin by testing in an experimental management area.

The underlying risk-projection model is based on the assumption that the disease transmission is density dependent and not frequency dependent, while the latter showed a slight best fit using the Akaike information criterion (AIC) for the structured matrix model in (Wasserberg et al., 2009). This assumption is based on the fact that high prevalence is found in farmed deer and deer aggregation at winter feeding and for salt licking (Wasserberg et al., 2009). An extension to assume both frequency-dependent and density-dependent transmissions interchanging based on seasons, as well as modeling environmental transmission of the disease, is underway. The risk-projection model was built also on another assumption that the death rate is density dependent. Birth rates that are density dependent will be also taken into consideration in the future.

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