Chronic wasting disease: possible transmission mechanisms in deer

Alex Potapov[a,b,c,*], Evelyn Merrill[a], Margo Pybus[a,d], David Coltman[a], and Mark A. Lewis[a,b,c]

[a]Department of Biological Sciences,

[b]Centre for Mathematical Biology,

[c]Department of Mathematical and Statistical Sciences,

University of Alberta, Edmonton, AB, T6G 2G1 Canada

[d]Alberta Sustainable Resource Development
6909-116 St., Edmonton, AB, T6H 4P2 Canada
[*]corresponding author

Abstract

We develop a model for the spread of chronic wasting disease (CWD) in a mule deer (*Odocoileus hemionus*) population to assess possible mechanisms of disease transmission and parameterize it for the mule deer population in Alberta, Canada. We consider seven mechanisms of disease transmission corresponding to direct and indirect contacts that change with seasonal distribution and groupings of deer. We determine the minimum set of mechanisms from all possible combinations of mechanisms with different weights for duration of seasonal segregation of sexes that are able to reproduce the observed ratio of CWD prevalence in adult males and females of ~2 and greater. Multiple mechanisms are likely to produce the ratio of male:female prevalence levels and include: (1) environmentally mediated transmission associated with higher food intake by males, (2) female to male transmission during mating of this polygamous species, (3) increased male susceptibility to CWD and (4) increased intensity of direct contacts within male social groups. All of these mechanisms belong to the class of frequency-dependent transmission. Also important is seasonality in deer social structure with an increasing ratio of prevalence in males:females under all mechanisms as the duration of sexual segregation increases throughout a year.

Key words: Chronic Wasting Disease, disease transmission, deer population model, frequency-dependent transmission

1. Introduction

Chronic wasting disease (CWD) is a fatal disease of cervids, including white-tailed (*Odocoileus virginianus*) and mule deer (*O. hemionus*), elk (*Cervus elaphus*) and moose (*Alces alces*) (Williams 2005), which belongs to a class of prion diseases called transmissible spongiform encephalopathies (TSEs). Along with the other well-known TSEs, such as BSE or "mad-cow disease" and Creutzfeldt–Jakob disease in humans, CWD is characterized by the accumulation of an abnormal misfolding of normal forms of proteins, called prions, in lymphatic and neural tissues. The disease was first recognized as a clinical "wasting" syndrome in 1967 in mule deer at a wildlife research facility in northern Colorado, USA, but was later identified as a TSE (Williams and Young 1980). The disease has since spread or been translocated to over fifteen US states and two Canadian provinces.

The exact routes of CWD transmission remain unclear. There is evidence that infection is transmitted horizontally directly from individual to individual during close contact via saliva, urine and feces (Mathiason et al. 2006, 2009), or indirectly through the environment (Miller et al. 2004, Johnson et al. 2007). Environmental transmission may occur via ingestion of soils or plants previously contaminated by an infected animal and the prions may accumulate in the environment and remain infectious for a long time (Schramm et al. 2006, Genovesi et al. 2007,). Once contracted, the incubation period for the disease is about 18 months (Tamgueney et al. 2009), and only in the later, clinical stages is CWD typified by the chronic weight loss and behavioral changes that eventually lead to death. Because infected deer cannot be distinguished from healthy ones during initial stages of the disease, even though they may already be spreading the disease, the primary information about disease infection comes from post-mortem examination of tissues. To develop CWD a deer must contact a sufficient number of prions, although the minimum dosage needed to contract the disease is unknown. Vertical transmission from mother to fawn before or at birth appears to play only a minor role (Miller and Williams 2003).

Because the transmission of infectious diseases in wildlife populations typically is complex (Keeling and Rohani 2008), the problem of deriving adequate models to help guide management of wild populations remains a challenge. The first models describing

CWD (Miller et al. 2000; Gross and Miller 2001) included only a basic disease transmission function common to all individuals, and assumed that the number of contacts encountered by an infectious individual was density independent. Two more recent papers illustrate contrasting approaches to CWD modeling. In Wasserberg et al. (2009), a population projection model of white-tailed deer consisting of 160 compartments (20 age classes, two sexes, and 4 disease stages) was developed. The authors considered outcomes of two types of disease transmission, frequency dependent (FD) and density dependent (DD) transmission (McCallum et al. 2001, Begon et al. 2002), but did not include environmental transmission. When they fitted the transmission coefficient from CWD prevalence data in Wisconsin, FD and DD terms fit the observed disease pattern almost equally well. In contrast, Miller et al. (2006) used a simple Kermack-McKendrick type model with minimum population details parameterized by cumulative mortality data from two small captive herds. These authors compared 6 models including different number of disease stages and direct (deer to deer) and indirect (through the environment) transmission and showed that the best two models corresponded to both indirect and direct transmission without explicitly accounting for disease stages. Their study likely reflects realistic DD disease transmission because small numbers of deer were in pens with close contact.

In the case of CWD, sources of complexity in determining transmission include variable contact rates due to seasonal movement, social aggregations, habitat selection and landscape structure (Carnes 2009; Habib et al. 2011). Limited information about potential deer contacts can be obtained using GPS collars (Kjaer et al. 2008; Schauber et al. 2007) or proximity detectors (Prange et al. 2006). However, these studies do not provide population-level transmission, and have not yet been used to infer contact with environmental contamination in wildland situations, despite the potential for environmental persistence to shape deer-CWD dynamics (Almberg et al. 2011, Sharp and Pastor 2011). Inherent differences in susceptibility among individuals of different age, sex, and genetic strains further complicate our understanding.

In this paper we address seven hypothesized mechanisms for CWD transmission. Our approach takes advantage of the consistent evidence that CWD prevalence is about two times higher in adult male deer than in adult females across regions (e.g. , Miller and

Conner 2005, Heisey et al. 2010, Rees et al. 2012). Our goal, therefore, is to select a number of transmission mechanisms capable of producing high enough male to female prevalence ratio as a set of competing hypotheses reflecting the most important transmission paths, and evaluate whether they can produce the observed discrepancy in male and female prevalence. We use a continuous-time population SI model with three categories of both susceptible and infected animals: male adults, female adults, and juveniles (fawns) with density-dependent fawn mortality, density-independent adult mortality, and hunting with different hunting preferences for males, females and juveniles. We incorporate seasonality in grouping patterns among the sexes and explore the effect of duration of sexual segregation across the year. The general scheme of the model is shown in Fig. 1. After addressing mechanisms of transmission, we study the sensitivity of the results to model parameters including hunter harvest and the relative susceptibility of males and females given contact with an infected individual.

2. Model of deer population

In this section we develop the basic model of deer population dynamics with a very general description of disease transmission, which is considered in more detail in Section 3. Notation for model variables and parameters is defined in Table 1. Details of components of the model are found in Appendices A to D.

2.1 Population structure, vital rates and density dependence

The model has two disease-related stages: susceptible (S) and infected (I) deer. Each of the stages includes the simplest sex/age structure commonly used in deer management: adult males (m), adult females (f) and juveniles (j); the latter are assumed to have a 50:50 sex ratio at birth. This gives six compartments for population outputs: three densities of susceptible deer, S_j, S_f, S_m, and three densities of infected ones, I_j, I_f, I_m. The model includes juvenile birth and maturation, natural mortality, harvest and disease transmission:

Rate of change of deer class	Juvenile birth (B, B_{IS}, B_{II}) or maturation at rate τ^{-1}	Natural mortality	Harvest	Disease transmission

$$\frac{dS_j}{dt} = BS_f + B_{IS} I_f - \tau^{-1} S_j - \left(m_{0S,j} + Vm_{1S,j}\right) S_j - h_j S_j - \lambda_j S_j \quad (1)$$

$$\frac{dS_f}{dt} = 0.5\tau^{-1} S_j - m_{0S,f} S_f - h_f S_f - \lambda_f S_f \quad (2)$$

$$\frac{dS_m}{dt} = 0.5\tau^{-1} S_j - m_{0S,m} S_m - h_m S_m - \lambda_m S_m \quad (3)$$

$$\frac{dI_j}{dt} = B_{II} I_f - \tau^{-1} I_j - \left(m_{0I,j} + Vm_{1I,j}\right) I_j - h_j I_j + \lambda_j S_j \quad (4)$$

$$\frac{dI_f}{dt} = 0.5\tau^{-1} I_j - m_{0I,f} I_f - h_f I_f + \lambda_f S_f \quad (5)$$

$$\frac{dI_m}{dt} = 0.5\tau^{-1} I_j - m_{0I,m} I_m - h_m I_m + \lambda_m S_m \quad (6)$$

The model is general enough, but we parameterize it for mule deer, the species in which the most CWD cases occur in free-ranging deer in Alberta. In this paper we do not consider the effects related to deer harvest (see Potapov et al. 2012). However, we parameterized the model from the data for a harvested population, and hence harvest component is present in the model as well.

Birth and mortality rates are the key components of deer population dynamics models because they describe population self-regulation. We incorporated density-dependent fawn survival but not fecundity rate because density-fecundity relationships for mule deer are not as well developed in the literature as density-dependent juvenile mortality (Bartmann et al. 1992, Gaillard *et al*. 1998; Unsworth et al. 1999, Heffelfinger et al. 2003). Although birth rates could decline if there were not enough males to fertilize all the females, we assume there are always sufficient males because a threshold in buck:doe ratios below which recruitment declines rapidly has not been reported for mule deer (White et al. 2001, Erickson et al. 2003, Bishop et al. 2005). For example, the data in White et al. (2001) show only a minor decline in fawn:doe ratio with a major decline of buck:doe ratio, whereas the effect of other factors was much more prominent. Furthermore, very low buck to doe ratio never occurred in our results.

For modeling density-dependent mortality we used an approach similar to Powers et al. (1995) that relates mortality to the available food, where the amount of required food in a critical season (assumed to be winter in Alberta) is proportional to densities in the deer sex and age groups. For the sake of simplicity we do not include

stochasticity in summer food (Hurley et al. 2011) and in snow accumulation in winter that influences energy expenditures for locomotion (Parker et al. 1984) and reduces forage availability (Visscher et al. 2006). Hence, we scale mortality as a simple starvation index V, which depends on the ratio of available winter food F_A and required food F_R:

$$V = \max\left\{0, 1 - \frac{F_A}{F_R}\right\}. \quad (7)$$

If there is excess food, i.e., the population is below winter carrying capacity, then $F_A > F_R$ and $V=0$. If F_A is much less than F_R and starvation rates are high, V approaches 1. When the population is at a food-based equilibrium (at carrying capacity), V takes some value V_0 between 0 and 1, corresponding to partial food limitation. Derived estimates of F_R, F_A, and V from deer population data are given in the Appendix A. Thus in model (1)-(6) we assume that density dependent juvenile mortality is determined by food limitation as:

$$m_{S,j} = m_{0S,j} + V m_{1S,j}, \quad (8)$$

where $m_{0S,j}$ corresponds to density-independent mortality and $m_{1S,j}$ to its density-dependent part. For healthy adult males and females there is little evidence of strong density-dependent mortality (Gaillard et al. 1998; Bonenfant et al. 2009); therefore we assumed $m_{1S,f} = m_{1S,m} = 0$.

For mortality of infected deer, it is known that the disease remains in the latent stage for about eighteen months, then switches to the clinical stage, and the mean time from oral infection to death is 20-25 months (Williams and Miller 2002). The mortality rate of infected deer should increase above that of uninfected deer by the value close to inverse mean duration of the disease. The difference between the two rates has been estimated by Miller et al. (2006) for the model of SI-type as $\mu=0.57$ year^{-1}. There are no data on density dependence or on sex-related difference in disease duration; therefore we take

$$m_{0I,f} = m_{0S,f} + 0.57\,\text{year}^{-1}, \quad m_{0I,m} = m_{0S,m} + 0.57\,\text{year}^{-1}, \quad m_{1I,f} = m_{1I,m} = 0. \quad (9)$$

Miller et al. (2008) present data for yearly survival of free-ranging female mule deer, and show that for infected individuals it is reduced by factor 0.53/0.82=0.64, which corresponds to $\mu=\ln(0.64)\approx 0.43$ year^{-1}. Since the values of μ, 0.57 year^{-1} and 0.43 year^{-1}, are close, in our calculations we use $\mu = 0.57\,\text{year}^{-1}$. To account for uncertainty in μ we

studied sensitivity of the results towards it. Fawns, even if they are infected, remain in the latent stage as fawns; therefore we assume that mortality for infected fawns is the same as for susceptible, uninfected fawns, that is

$$m_{1I,j} = m_{1S,j}, \quad m_{0I,j} = m_{1S,j}. \tag{10}$$

To estimate natural mortality rate of adult deer, we used data obtained at Canadian Forces Base Wainwright (CFBW; courtesy CFBW Environmental Services), Alberta, Canada, where population numbers and harvest have been monitored for the period 1966 to 2010 (Appendix A). We assumed that average population sex-age proportions approximately reflect the equilibrium state and with this knowledge we could estimate annual survival and hence the combination of natural and harvest mortality (Appendix A). Hunter harvest rates alone were estimated from the number of harvested animals per year at CFBW, which is recorded at mandatory check stations. Because under general seasons hunters typically prefer to shoot males when encountered (Erickson et al. 2003), we used different per capita harvest rates for each deer sex and age group (Table 1). The harvest rate for each deer category was represented as a product of overall harvest intensity *h* and hunter preference coefficient h_{Pj}, h_{Pf}, h_{Pm} for each deer category. Values for the latter were obtained from CFBW harvest data and are shown in Table 2 and Appendix A. Because hunters prefer to shoot males, we set h_{Pm}=1, $h_{Pj}, h_{Pf} < 1$. We assumed that the increase of the number of hunters changes overall harvest intensity *h*, but not the hunter preferences.

3. Transmission rates

We consider two types of disease transmission in the model: direct (animal-to-animal) and environmental (animal-to-environment) contact. Direct contact includes both vertical and horizontal transmission. Vertical transmission is considered constant and occurs only during the birth. Horizontal transmission is characterized by several force of infection terms λ that do not reflect a latent stage but represent seasonal changes depending on the dynamics in deer grouping behaviour. The absence of a latent stage follows from Miller et al. (2006) who found the best model did not have the latent compartment. We discuss the implications of this decision below and provide more

detailed comparison of the SI model (1)-(6) and the extension of the model to include the latent class (SLI) in Appendix D. We incorporated seasonal contact rates implicitly by assuming simplified dynamics in groupings of deer as: 1) *Summer* (May to October): males and females stay in separate groups and there are practically no direct contacts between them, fewer interactions among both female and male groups in this season due to spatial dispersion after migration, but high intra-group contacts. 2) *Rut*: (November to December): male and female groups remain separated but new types of contacts appear: mating contacts between males and females and fights between some males. 3) *Winter* (January to April): deer form larger, mixed-sex groups. Migration to winter locations where food is more accessible under winter snows results in groups staying near each other, and between-group contacts are more frequent but within group contact rates remain similar to other seasons.

Seasonal changes in direct and environmental contacts by deer require different expressions for the force of infection terms during different seasons when groups are separate (summer and rut) and mixed (winter) together on winter ranges. To avoid introduction of too many parameters, we accounted for seasonality implicitly: we combine terms corresponding to different seasons into a weighted sum, and use it for the whole year; see Appendix B for mathematical derivations. If we have several seasons with the relative durations of w_S, w_R, w_W, and different expressions for force of the infection during each season, then the effective term in our model is

$$\lambda(I) \approx w_S \lambda_S(I) + w_R \lambda_R(I) + w_W \lambda_W(I), \qquad w_S + w_R + w_W = 1. \tag{11}$$

If the expressions for the force of infection for two seasons coincide, as for within group contacts during summer and rut, then effectively there are only two seasons, summer+rut and winter. If contacts take place only during rut, then the corresponding weight can be incorporated into the value of transmission coefficient (see details below). Therefore, terms for the rut contacts, for example, appear without explicit seasonal weight. Similarly, seasonal weights are integrated into the values of between-group transmission coefficients. This approach allows us to use a minimum set of parameters — an explicit description of each season would require a different set of transmission coefficients for every season.

We consider seven transmission mechanisms, four of which act throughout the year, and three act only during the rut. The expressions for the corresponding force of infection terms are shown in Table 3. Here we explain only the meaning of the terms and parameters in Table 3, but give the detailed derivations and all assumptions necessary for the force of infection terms in Appendix B.

3.1 Direct vertical transmission.

Vertical or maternal transmission is implemented through two different birth rates for infected females: they produce healthy juveniles at the rate B_{IS} and infected juveniles at the rate B_{II}. Although some fawns born at late stages in the disease may not be viable (Mathiason et al. 2010), reducing fertility (Dulberger et al. 2010), we assume that fertility for infected and healthy females coincide, $B_{IS} + B_{II} = B$ (see Discussion below). If we denote the probability of vertical transmission by p_V, then $B_{IS} = (1 - p_V)B$, $B_{II} = p_V B$. According to studies on penned mule deer (Miller et al. 2000), for CWD p_V does not exceed 0.05; when vertical transmission occurs in our models, we use this value.

3.2 Direct horizontal transmission

Direct horizontal transmission assumes that with direct contact, such as grooming and mating, the host infects a healthy individual with some probability. At present there are no measures of the frequency of direct transmission, although several studies provide metrics of pair-wise proximity based on GPS-telemetry as surrogates for contact rates (Schauber et al. 2007, Kjaer et al. 2008, Habib et al. 2011). To keep our approach general, we assumed three types of deer social groups (matrilinear family group of females + juveniles, males only groups, and mixed groups) whose proportion in the population varied by season, and the efficiency of transmission for pairs of deer within these groups varied as described below.

3.2.1 Direct contacts within a group. Deer group structure changes seasonally: in summer and autumn there are separate male and female groups and in winter males and females typically combine in larger mixed groups. Therefore, the expressions for the force of infection terms include parts corresponding to the segregated sexes and mixed-

sex groups. For the mixed-sex groups, force of infection depends on the ratio of densities of infected deer and total population density. The ratio arises because we assume the groups are representative, when the proportions of infected and susceptible individuals within a group on average coincide with those for the whole population. Sexually segregated groups we consider as two independent subpopulations, one of which consists of males and the other consists of females and juveniles, and the corresponding force of infection terms contain proportions of infected individuals in each of the subpopulations.

The general expression for force of infection in males is

$$\lambda_{m1} = \beta_1 \left[w_{S1} \frac{\psi_{mm} I_m}{S_m + I_m} + w_{M1} \frac{\psi_{mm} I_m + \psi_{mf} I_f + \psi_{mj} I_j}{D} \right], \quad (12)$$

and for family groups

$$\lambda_{x1} = \beta_1 \left[w_{S1} \frac{\psi_{xf} I_f + \psi_{xj} I_j}{S_f + I_f + S_j + I_j} + w_{M1} \frac{\psi_{xm} I_m + \psi_{xf} I_f + \psi_{xj} I_j}{D} \right], \quad x = f, j. \quad (13)$$

Here the first term in the brackets corresponds to transmission during the period when males are segregated from groups of females and fawns, the second one to transmission when males are in mixed-sex groups; coefficients w_{S1} (Segregated) and w_{M1} (Mixed), where $w_{S1} + w_{M1} = 2$, show proportional contribution of each term into overall disease transmission due to the duration of time the sexes are segregated and changes in group size; and β_1 is the transmission coefficient for direct within group contacts. The matrix of coefficients ψ_{xu}, $u, v = j, f, m$, represents relative intensity of transmission between each category of deer. We assume the values of relative intensity of contacts do not change with seasons. Coefficients ψ_{xu} may be important for accurate description of disease transmission through direct contact, and thus we present the general form above (12)-(13). However, because there are no data on direct disease transmission among age/sex groups, for our initial simulations we assume relative transmission coefficients are equal among age and sex classes, or all ψ_{xu}=1, and only β_1 and the ratio w_{S1}/w_{M1} reflecting the duration of seasonal segregation of sexes are varied in our initial simulations. This results in the simplified expression for the force of infection for males of

$$\lambda_{m1} = \beta_1 \left[w_{S1} \frac{I_m}{S_m + I_m} + w_{M1} \frac{I_m + I_f + I_j}{D} \right], \quad w_{M1} + w_{S1} = 2, \tag{14}$$

and for family groups of

$$\lambda_{x1} = \beta_1 \left[w_{S1} \frac{I_f + I_j}{S_f + I_f + S_j + I_j} + w_{M1} \frac{I_m + I_f + I_j}{D} \right], \quad x = f, j. \tag{15}$$

After initial simulations, we provide an alternative choice for ψ_{xu} based upon sex-related susceptibility (see below).

3.2.2 Direct contacts between groups. For between group contacts we assume that any two groups may encounter, and hence the whole population can be considered as one big group, and force of infection is proportional to the total number of infected deer or to the density of infected deer. We also assume that relative intensity of contacts between deer belonging to different groups can be described by the same matrix ψ_{xu}. The general expression for between group transmission,

$$\lambda_{x2} = \beta_2 \left(\psi_{xm} I_m + \psi_{xf} I_f + \psi_{xj} I_j \right), \qquad x = j, f, m, \tag{16}$$

β_2 is the transmission coefficient for direct between group contacts.

As above, initially we assume all ψ_{xu}=1 and we obtain the simplified expression

$$\lambda_{m2} = \lambda_{f2} = \lambda_{j2} = \beta_2 \left(I_m + I_f + I_j \right), \tag{17}$$

which is used in numerical results below.

3.2.3 Mating contacts, female to male transfer. For this type of transmission we assume that on average each female can participate only in a finite number of mating contacts, and the number of new infections is proportional to the product of the density of infected females (proportional to their total number in the population) and number of mating contacts with susceptible males. The latter is the product of the mean number of mating contacts and the proportion of susceptible males in the population. Since the force of infection is per susceptible capita number of new infections, the resulting expression is

$$\lambda_{m3} = \beta_3 \frac{I_f}{S_m + I_m}. \tag{18}$$

The denominator arises as a part of expression for the proportion of susceptible males, and all constant factors are aggregated into the transmission coefficient β_3.

3.2.4 Mating contacts, male to female transfer. This expression is derived in a similar way as λ_{m3}, but now we use density of susceptible females and the proportion of infected males. The result is

$$\lambda_{f4} = \beta_4 \frac{I_m}{S_m + I_m}.$$

3.2.5 Male fights. Fights during the rut typically occur between males from different social groups, and they should be distinguished from sparring matches that contribute to contacts within male groups. We model transmission during fights similarly to between-group disease transmission by assuming that the number of contacts where the disease can be transmitted is proportional to the product of the densities of susceptible and infected males, assuming random mixing. This gives disease transmission due to fighting as

$$\lambda_{m5} = \beta_5 I_m. \qquad (20)$$

3. 3. Environmental transmission

For environmental transmission, we model both the accumulation of prions in the environment and transmission from the environment to deer at both the level of the social group and between groups. We do not explicitly model the environmental compartment *E* for disease transmission, but follow an approach described by Haken (1983) where slowly changing variables "enslave" ones with "fast relaxation", and the latter can be approximated by functions of just the slow variables. As a result, the complex model including both slow and fast variables can be replaced by a simpler model containing slow variables only. Accuracy of the approach depends on the difference between characteristic times for slow and fast modes: the greater is the difference, the more accurate is the method.

The equation for the prion content *E* in the environment is a generalization of the Miller et al. (2006) model:

$$\frac{dE}{dt} = \varepsilon_m I_m + \varepsilon_f I_f + \varepsilon_j I_j - \tau E, \tag{21}$$

where ε_x denote rates of environment contamination for the 3 deer age-sex classes, and τ is the rate that prions become inaccessible to deer due to decay or degradation (Rapp et al. 2006) or movement in soils or water (Smith et al. 2011). Miller et al. (2006) reported τ =2.55 year^{-1} for CWD transmission in penned deer. This rapid rate of removal means that a portion of prions left in the environment decreases with time as $\exp(-\tau t)$ and reduces to 0.078 of its original amount in one year and to 0.006 in two years. Note that these calculations account for the amount of prions actively participating in the disease transmission rather than the total amount of prions in the environment.

The deer density and hence deer infection, $I_x(t)$, changes slowly compared to this rate of prion decline. For example, in Alberta the detected prevalence of CWD increased about 6 fold in 5 years after it was first detected (Alberta Fish and Wildlife), which corresponds to a growth exponent about one-tenth τ reported by Miller et al. (2006). In such a situation a "fast" variable (prion content in the environment) is determined by current density of CWD infected deer $I_x(t)$, while the influence of the number of infected deer in the past is waning. The solution to (21), assuming $E(0) = 0$, can be written as

$E(t) = \int_0^t \left(\varepsilon_m I_m(t') + \varepsilon_f I_f(t') + \varepsilon_j I_j(t')\right) \exp\left(-\tau(t-t')\right) dt'$ Due to the exponential factor, the essential contribution to $E(t)$ comes only from the time interval $t - \Delta t < t' < t$ where $\Delta t \sim 1/\tau$ and in our case is close to 1 year. If $I_x(t')$ does not change significantly at this interval, then $I_x(t') \approx I_x(t)$ and the integral easily evaluates. Neglecting the term $\exp(-\tau t) << 1$, one obtains

$$E(t) \approx \frac{\varepsilon_m I_m(t) + \varepsilon_f I_f(t) + \varepsilon_j I_j(t)}{\tau}. \tag{22}$$

We further discuss this approach and compare it to the findings of Miller et al. (2006) and Almberg et al. (2011) as part of our model assessment in Appendix B.

For modeling environmental transmission, we assume that both prion deposition and uptake (transmission) is associated with the consumption of soil or food. We assume that the rate of contamination of the environment by excrement ε_u is proportional to the

rate of food consumption of an infected individual F_{Iu}, $u=\{j,f,m\}$. The rate of intake of contaminated food we assume proportional to the rate of food consumption of a healthy individual F_{Sx}, $x=\{j,f,m\}$. We incorporate spatial heterogeneity in environmental transmission implicitly by modeling environmental exposure both within-groups and between groups, which changes seasonally due to spatial mixing patterns of deer.

3.3.1 Environmental transmission within a group.

Derivation of the force of infection for this case resembles the case of direct within group contacts with one exception. Here instead of the matrix of intensity of transmission ψ we use another matrix ϕ related with food consumption rates of infected individuals $F_{I,u}$ and of susceptible individuals $F_{S,x}$:

$$\phi_{xu} = \frac{F_{I,u}F_{S,x}}{\max_{v,w}\{F_{I,v}F_{S,w}\}}. \qquad (23)$$

We assume that both the rate of the environmental contamination by an infected individual and the rate of infection intake by a susceptible individual are proportional to their food intake rates. The final expression for the force of infection for environmental transmission within groups is

$$\lambda_{m6} = \beta_6\left[w_{S6}\frac{\phi_{mm}I_m}{S_m + I_m} + w_{M6}\frac{\phi_{mm}I_m + \phi_{mf}I_f + \phi_{mj}I_j}{D}\right], \qquad (24)$$

$$\lambda_{x6} = \beta_6\left[w_{S6}\frac{\phi_{xf}I_f + \phi_{xj}I_j}{S_f + I_f + S_j + I_j} + w_{M6}\frac{\phi_{xm}I_m + \phi_{xf}I_f + \phi_{xj}I_j}{D}\right], \quad x = f, j, \qquad (25)$$

where the segregated and mixed state weights satisfy $w_{S6} + w_{M6} = 2$. Because the weights may depend not only the duration of the seasons, but on possible seasonal variation of transmission intensity as well (e.g. due to grouping behaviors or environmental exposure), w_{S6}, w_{M6} may differ from w_{S1}, w_{M1}. As in direct transmission within groups (Section 3.2.1), only the transmission coefficient β_6, and of the ratio w_{S6}/w_{M6} reflecting in particular seasonal duration of segregation by the sexes will be varied when we simulate disease spread to explain the observed disease patterns.

3.3.2 Environmental transmission between groups. Between group transmission arises when home ranges of deer from different groups intersect and deer from one group are exposed to areas infected by the second group. This is less frequent in summer in Alberta

because deer are relatively more dispersed across the landscape than in winter (Habib et al. 2011). However, we do not account for spatial structure in between group transmission based on segregation of the sexes, and all weights and parameters can be aggregated into single a effective transmission coefficient β_7. The expression for the force of infection for environmental between group contacts is

$$\lambda_{x7} = \beta_7 \left(\phi_{xm} I_m + \phi_{xf} I_f + \phi_{xj} I_j \right), \quad x = j, f, m. \tag{26}$$

3.4 Susceptibility differences between males and females.

The above derivations used the assumption that all deer categories are equally susceptible to the disease given similar exposure to prions (i.e., all $\psi_{xu} = 1$). However, there is evidence that in some species males may be more susceptible to certain infections than females due to immunological or hormonal differences (Folstad and Karter 1992, Nunn et al. 2009); that is males may have higher probability to develop the disease being subjected to the same amount of pathogen. Although it is unknown whether there is differential susceptibility to CWD between the sexes, we evaluated this as a hypothesis for higher prevalence in male deer. To this end, we introduced a relative susceptibility to the disease, Y_m, Y_f, Y_j, such that $Y_f = 1$. In our case we hypothesize greater male susceptibility, $Y_m > 1$. To evaluate this hypothesis we use the null hypothesis about contacts, that is, assume that the rate of contacts between each of the deer categories is equal; for the case of direct transmission this means that $\psi_{xu} = Y_x,\ u, x = \{m, f, j\}$, where we alter Y_m from 1 to 5. Then for force of infection we use expressions (12), (13) for within-group contacts, and (16) for between group contacts. For rut transmission mechanisms each expression is related only to one sex, and hence the relative susceptibilities can be incorporated into the effective transmission coefficient e.g. for males as

$$\lambda_{m3} = Y_m \beta_3 \frac{I_f}{S_m + I_m} = \beta'_3 \frac{I_f}{S_m + I_m}. \tag{27}$$

Additionally, in case of environmental transmission, the expression (23) for the intake of food takes the form

$$\phi_{xu} = Y_x \frac{F_{I,u} F_{S,x}}{\max_{v,w} \{F_{I,v} F_{S,w}\}}. \quad (28)$$

such that ϕ_{xu} is scaled by the relatively higher susceptibility of males than females when exposed to environmental sources of prions.

3.5 Frequency- and density-dependent transmission

The seven mechanisms can be classified as frequency dependent (FD) and density dependent (DD). This classification is often used in disease modeling. It is related to the dependence of force of infection on population density: for FD transmission the force of infection is proportional to disease prevalence and remains constant as density increases, for DD transmission the force of infection is proportional to the number of infected individuals or their density and scales with density (McCallum et al. 2001, Begon et al. 2002). When the population density changes, e.g. due to population control measures, but the proportion of infected individuals remain the same, the force of infection corresponding to FD mechanisms does not change, but that of DD mechanisms increases or decreases proportionally to density. For the expressions λ_1 to λ_7 in Table 3, we see that λ_1, λ_3, λ_4 and λ_6 are invariant to density change because both numerator and denominator are proportional to density, while λ_2, λ_5, and λ_7 scale proportionally to population density. For this reason we refer to the former group as frequency-dependent (FD) transmission mechanisms, and the latter as density-dependent (DD) mechanisms.

4. Numerical simulations and CWD prevalence

Combining all possible mechanisms of transmission described above, the most general relation for the transmission of CWD for an age/sex class rate is:

$$\lambda_x = \lambda_{x1} + \lambda_{x2} + \lambda_{x3} + \lambda_{x4} + \lambda_{x5} + \lambda_{x6} + \lambda_{x7} \quad (29)$$

This expression denotes the cumulative force of infection for each age/sex class (x) and each hypothesized mechanism. Corresponding formulas of hypothesized transmission mechanisms 1-7 described above are listed in Table 3. The mechanisms 1, 2, 6, and 7 are in effect year round and affect all deer categories and below we call them "basic". The rut mechanisms 3, 4, and 5 involve only one or two deer categories, and any one of them

cannot explain the observed pattern. Therefore the minimum combination of transmission mechanisms must include at least one basic mechanism.

With numerical simulations using the above model and parameters values in Table 2, we sequentially combined different transmission mechanisms in (29) by either turning some of them off (i.e., setting the respective β_i=0), or turning them on to their full extent (i.e., setting the respective β_i=β). We also varied the amount of horizontal transmission between females and juveniles at birth for p_V=0 and 0.05 (Miller et al. 2000) and weights of seasonal grouping patterns of deer to determine their effects on male:female prevalence ratio. We altered the weights of seasonal segregation by the sexes by varying the ratios of w_{S1} / w_{M1} and w_{S6} / w_{M6} as: 10:90, 50:50, and 90:10 as the ratio of time spent in separate:mixed groups during the year.

All simulations were started from an initial state close to the healthy, disease-free equilibrium with population density D_0, and a small number of infected deer were introduced, such that the disease prevalence was 0.1% both in males and females. To exclude the influence of the initial state, we allowed the process to converge to its steady state and recorded the asymptotic densities of susceptible and infected deer, denoted as $S_{ma}, S_{fa}, S_{ja}, I_{ma}, I_{fa}, I_{ja}$, asymptotic population density, D_a, and disease prevalence for males and females. Thus, the values we report for these outputs represent the long-term, equilibrium state.

If D_a<0.01D_0, we registered population collapse, otherwise we report disease prevalence for the whole population and separately for males and females. We calculated the asymptotic disease prevalence for different combinations of transmission mechanisms initially assuming equal susceptibility between sexes and then higher susceptibility of males. If the disease prevalence at equilibrium exceeded 0.1% both in males and females, we calculated the equilibrium prevalence ratio

$$r_{mf} = \frac{I_{ma}}{S_{ma} + I_{ma}} \frac{S_{fa} + I_{fa}}{I_{fa}} . \qquad (30)$$

We assessed all 127 possible combinations of the seven λ terms on the value of the ratio r_{mf} and repeated calculations for an increasing sequence of values of transmission coefficient β. Typically there are one or two thresholds for β values: 1)

persistence threshold, β_{per}, such that for $\beta<\beta_{per}$ the disease dies out with time, and 2) population collapse threshold β_{coll}, such that for $\beta>\beta_{coll}$ population collapses. The values of both thresholds depend on the specific transmission mechanisms used and on the harvest intensity. We calculated the value of $r_{mf}(\beta)$ for $\beta>\beta_{per}$, and we estimated the maximum possible male: female prevalence ratio

$$r_{\max} = \max_{\beta>\beta_{per}} r_{mf}(\beta). \quad (31)$$

The actual values of transmission coefficients (β) are unknown, and for this reason we used $r_{\max}$ for comparing different transmission mechanisms because as the maximum value it reflects the theoretical potential of the given mechanism, actual prevalence ratio most probably being lower. We searched for the single and combination of transmission mechanisms that were capable of providing $r_{\max}>2$ because the observed value of r_{mf} is close to 2 in nature.

Because values for $r_{\max}>2$ were observed for a number of combinations of transmission mechanisms, we used three aspects of the model outputs to assess the feasibility of mechanisms in driving the higher observed prevalence in males as reflected by $r_{\max} \geq 2$. 1) We followed the principle of parsimony: if the effect can be explained by action of 1-2 mechanisms and by a more complicated combination, the simpler one is more likely to occur. 2) We used the range of values of β where $r_{\max} \geq 2$ ($\Delta\beta$): the broader the range, the more likely that actual transmission coefficient falls into it. 3) We evaluated the sensitivities and elasticities of several model inputs to assess the effect of uncertainty or geographic variability in model parameters.

5. Numerical results

Under equal susceptibility of the sexes to CWD, within group environmental transmission (λ_6) alone produced $r_{\max} > 2$ when no transmission occurred during the rut and sexes were segregated either 50% or 90% of the year (Table 4). The high prevalence in males due to environmental transmission is due to a higher food consumption and associated prion intake by males than females, and these results were particularly sensitive to the actual ratio in male:female food consumption rate (Table 5). When males were infected by females during the rut, several basic mechanisms alone and in

combination with environmental transmission produced $r_{\max} > 2$ (Table 4). In contrast, direct within group fighting among males was sufficient for $r_{\max} > 2$ only when there was 90% duration segregation of the sexes, and $r_{\max}$ never exceeded 2 when there was male to female transmission during the rut. Increasing vertical transmission between females and juveniles at birth (p_V) decreased the value of $r_{\max}$, but did not alter these overall patterns, nor were the model results particularly sensitive to the range of values we tested in p_V (Table 5, see Appendix).

Figs. 3 and 4 show examples of the metrics that we use to characterize transmission mechanisms. The dependence of the asymptotic disease prevalence on transmission coefficient β is illustrated in Fig. 3. Population collapse at high β values is typical of FD transmission mechanisms. The dependence of the prevalence ratio $r_{mf}(\beta)$ (30) for these mechanisms shown in Fig. 4 demonstrates that addition of female to male transmission during the rut significantly increases the $\Delta\beta$ interval where $r_{mf}(\beta)>2$ for environmental transmission, but not for direct transmission. If we assume local variability of the transmission coefficient, e.g. due to differences related with landscape-dependent social group sizes, types of soil and vegetation, then it is more likely to observe $r_{mf} > 2$ (30) for a wide $\Delta\beta$ interval rather than for a narrow one. Therefore, transmission mechanisms or combinations with wider $\Delta\beta$ appear to be a more likely explanations of the observed pattern. Fig. 5 compares single transmission mechanisms and their pairwise combinations with $r_{\max} > 2$ in terms of $r_{\max}$ and $\Delta\beta$. Increasing the duration of sexual segregation (ratio of $w_{S6} / w_{M6} > 1$) and inclusion of transmission from females to males in the rut considerably increase the $\Delta\beta$ range (Fig. 5) for within group environmental transmission, but not for direct transmission. Biologically this means that a) the most plausible transmission mechanism should contain increased disease transmission to males, as occurs in environmental transmission (or by higher male susceptibility when exposed- see below) ; b) sexual segregation plays an important role in disease transmission; c) transmission during the rut may also be an important factor. Environmental transmission between groups (λ_7) combined with transmission from females to males in the rut (λ_3) also gives very wide $\Delta\beta$ range. However, intense

between group transmission implies an even more intense within group transmission, therefore λ_6 must be significant as well, which brings us back to the combination of $\lambda_6 + \lambda_3$ considered earlier.

When susceptibility of males and females is not equal, higher susceptibility of males to CWD than females also provided $r_{\max} > 2$, even without higher exposure through food intake in males or transmission to males during the rut, but seasonal grouping patterns still played an important role. High susceptibility in males at Y_m=2, however, provides $\Delta\beta = 0.16$, which increases to $\Delta\beta = 0.26$ after adding transmission during the rut from female to male; still it remains narrower than the environmental within group plus female to male rut transmission ($\lambda = \lambda_6 + \lambda_3$) at Y_m=1 with $\Delta\beta = 0.56$. Sensitivities of $r_{\max}$ to parameters in case of higher male susceptibility (Table 6) are greater than in Table 5, primarily because the value $r_{\max}$ is more than 1.5 times greater than in Table 5, though elasticities are similar in both tables. As in the previous analyses, increasing vertical transmission tends to diminish the male:female prevalence ratio, while disease-related mortality and the ratio of seasonal weights tend to increase it. However, the results are most sensitive to the ratio of male:female susceptibility.

6. Discussion and Conclusions

Our goal was to examine possible mechanisms of CWD transmission for producing a higher prevalence in males of both white-tailed and mule deer than females, which is a common observation across geographic regions (e.g., Miller and Conner 2005, Heisey et al. 2010, Rees et al. 2012, Alberta Fish and Wildlife CWD web site). We developed a simple model of CWD spread that included both animal-to-animal and environmental transmission of CWD, incorporating biological features deemed important in past modeling of CWD, such as population structure with density-dependent juvenile mortality. We built upon past models by adding seasonal changes in deer social structure and seasonality of disease transmission within deer social groups. By comparing various combinations of transmission mechanisms in a wide range of transmission coefficients

we were able to find several combinations providing male to female prevalence ratio of 2 and more.

Our modeling provided a number of insights. First, there are several potential mechanisms that may produce higher CWD prevalence in males, but all of these fall into the class of frequency dependent mechanisms. We found that due to their larger body size than females, if males have higher intake of food and prions from excreta-contaminated plant material, either directly or associated with soil intake (Miller et al. 2004), this could support higher prevalence in males than females. In our simulations, we assumed males consume about 20% more food than females (see Appendix D). But cervid males also are known to reduce feeding activity and food intake by 50-100% during the rut (e.g. Wallmo 1981), which may be related to mating-related behaviours, maintenance of the ingestion-rumination cycle, or to reduced parasite ingestion due to compromised or suppressed immune system (Willisch and Ingold 2007, Mysterud et al. 2008, Pelletier et al. 2009. Brivio et al. 2010). At the same time males may compensate for reduced intake during the rut by consuming greater amounts during the summer season than females (Alldredge et al, 1974), when males typically are in segregated male groups. We did not include such a seasonal reduction in food intake in our modeling, but the sensitivity of our model outcomes to differential rates of intake between males and females indicates its importance. For example, an increase in female to male body mass ratio from 0.78 to 0.82 can result in prevalence ratio in males:females < 2 when segregated and mixed groups contribute equally. The high sensitivity suggests environmental within-group transmission alone may be sufficient to explain the male-biased prevalence, especially when there are very high environmental reservoirs of prions (Almberg et al. 2011).

Alternatively, our assumption that environmental prion exposure was related to food intake, in reality, may simply reflect the higher risk overall of males to contracting the disease when exposed to it in the environment. Indeed, when we modeled the differential susceptibility of males to CWD we also found that to reliably reproduce the higher male prevalence, males would need to be less than twice as susceptible than females. However, potential physiological mechanisms for higher male susceptibility are not clear. Parasite loads have been shown to be male-biased and this pattern has been

attributed to either the immunosuppressive effect of testosterone and/or sex-specific host behaviour or space use favouring exposure (Zuk & McKean, 1996; Ferrari et al., 2010). Recent evidence also suggests that in some cases the susceptibility of males to parasitism might solely reflect their greater body size and skin area (Moore & Wilson, 2002, Kiffner et al. 2011). On the other hand, to our knowledge there are no data that the deer immune system can distinguish between cell prion protein PrP^{C} and infective prion PrP^{CWD} and that prions can induce an immune response (e.g. Aguzzi et al. 2003). Determining sex-related differences in CWD susceptibility may be a key to improving our understanding of CWD transmission.

Second, we also found support for the importance of CWD transmission during the rut when males and females are directly interacting (Silbernagel et al. 2011), but only when transmission was largely from females to males (Miller and Conner 2005). The transmission of the disease from females to males again could be interpreted as the higher risk of acquiring the disease for males. Thus, transmission during the rut may augment the likelihood of male-biased prevalence resulting from both food-based environmental transmission (Table 4), and higher male susceptibility during direct contacts (Fig. 6). In reality only some males may participate in mating whereas our model assumes all males participate; therefore, the model may overestimate the influence of transmission during the rut. Because we did not find that transmission from males to females during breeding led to higher prevalence in males, wide-ranging movement of males hypothesized result in contacting many females (Silbernagel et al. 2011) may not be important in producing a male-biased prevalence unless males are more the susceptible sex.

Thus, our current modeling leads us to believe that higher risk of males to contracting the disease, whether through environmental exposure in feeding, during the rut, or across all types of contacts, may be the major factor contributing to the male-biased prevalence. If exposure to prions in food consumption is important, the most intensive disease transmission in male groups should occur in summer, when food consumption is high. Alternatively, if males are more likely to become infected during the rut than females, similar or even fewer direct within-group contacts than females may result in higher disease transmission due to a higher likelihood of a group member being infected. On the other hand, if social contact rates within bachelor groups are more

frequent than in female groups due to behaviours like sparring (e.g., 2 times in Table 4 at the original density), this also may cause differences in prevalence between males and females similar to what we observe for environmental transmission. From the viewpoint of our model this means that coefficients ψ_{uv} (Table 3), which characterize direct contacts and are assumed equal to 1 above, may have similarity to ϕ_{uv} of environmental transmission and also reflect higher male risk of getting the disease. Therefore, even if species-specific susceptibility of male cervids does not vary across geographic areas, patterns in understanding mixed group contact rates remain important for understanding disease dynamics.

The results of our modeling reflect observed differences between male and female CWD prevalence that might occur at equilibrium. It is possible that these are not the driving mechanisms at the beginning of a disease outbreak. However, in our model we show the ratio of asymptotic male and female prevalence is approximately proportional to the ratio of force of infection terms for males and females, and the difference in force of infection provides similar prevalence differences not only at equilibrium, but on the way to it as well. To demonstrate this, we started calculations with small (0.01%) but equal disease prevalence in males and females and estimated maximum transient prevalence ratio $r_{\max,t}$ and maximum asymptotic prevalence ratio $r_{\max,a}$ for the cases listed in Table 4. On average, $r_{\max,t} \approx 1.2 r_{\max,a}$, and the condition $r_{\max,t} > 2$ corresponds to $r_{\max,a} > 1.72$. In other words, for our model transient effect implies an asymptotic effect and vice versa.

Most notable is that in all cases the seasonal segregation of the sexes reinforces the likelihood of male-biased prevalence. In modeling host-parasite interactions in alpine ibex (*Capra ibex*), Ferrari et al. (2010) also showed that when females were less susceptible and segregated (infected with parasites only from females), and males were more susceptible and randomly distributed in space (infected with parasites equally likely from either sex), the mean numbers of parasites per individual (to a certain extent an analog of disease prevalence) were lowest in both sexes. The highest parasite load per individuals in males occurred when both species were segregated, which resembled our results. Genetic studies of mule deer in Alberta and Saskatchewan have shown that

CWD-infected deer are more closely related to other infected deer than uninfected deer, which stresses the importance of deer social organization (Cullingham et al. 2011).

Despite realistic assumptions in our model, there remain important gaps in our knowledge of CWD transmission, which has limited our parameterization of the model and our evaluation. For example, Dulberger at al. (2010) reported a 71% decrease in fecundity or fawn viability from infected females based on observations of about a dozen infected females. We evaluated the effects of lower fecundity in infected animals in our model by reducing it to 50% of the healthy females, and found it did not change our conclusion concerning the major transmission mechanisms, but a 50% lower fecundity narrowed the range of transmission coefficients for which the population remained viable. In comparing models of penned deer, Miller et al. (2006) found the best model was one without a latent stage (when an individual has the disease but does not spread it yet), thus we did not explicitly include a latent stage in our disease modeling. In Appendix D, we compare models with (SLI) and without (SI) latent stage, and show that both types of models behave similarly (see also e.g. Keeling and Rohani 2008), especially at low disease prevalence, but that transmission coefficients in different models have a different meaning. For the SI model the transmission coefficient characterizes newly infected individuals while for SLI model it characterizes new cases with latent infection. If mortality in the latent class is significant, not all latent individuals become infective and spread the disease. Therefore, the models with an explicit latent stage typically should have larger values of transmission coefficients. This makes it difficult to compare of the values of transmission coefficients between different models. In our model the presence of a 6-8 months latent period provides about 6% decrease of r_{max}, but all conclusions concerning transmission mechanisms remain the same.

Validity of our model outcomes also depends on the dynamics of prions in the environment, for example, how long they remain infectious and available for deer consumption. Almberg at al. (2011) showed that the outcome of their model strongly depends on the duration of environmental prion persistence. Our approach stems from the deer studies of Miller et al. (2006) and assumes that prions become inaccessible to deer faster than the disease prevalence grows (see Potapov et al. 2012 as well). If this assumption is valid, the actual rate at which prions become inaccessible determines only

the value of the effective transmission coefficient, see paragraph after Eq. (22). Alternatively, the amount of accessible prions in the environment and deer exposure to them could be explicitly modelled, but this would bring considerable complexity with little supporting data. Our parameterization is based on data from a penned-deer study (Miller et al. 2006), which may correspond to a comparatively high level of prion contamination. Potentially, it may be possible that at lower contamination levels, corresponding to free-ranging deer, the dynamics of prion accessibility may be different, e.g. stochasticity may become important.

Even a model of moderate complexity like ours shows that more detailed data on deer behaviour and CWD epidemiology are necessary for creating reliable management models of CWD spread. Nevertheless, our results point to frequency-dependent disease transmission given that almost all transmission mechanisms which predicted higher male prevalence belong to that class. To date, there remains considerable debate over whether reducing deer density is an effective management strategy given FD transmission (McCallum et al. 2001, Schauber and Woolf 2003), and considerable effort has been directed on distinguishing whether CWD is DD or FD (Wasserberg et al. 2009). Frequency-dependent transmission creates a challenge for CWD management because FD-force of infection depends on disease prevalence, and the latter cannot be lowered by nonselective population reduction. This has two important consequences: 1) most likely CWD eradication is impossible without vaccination of deer, and 2) disease management by nonselective population harvest may be based only upon density-dependent juvenile survival in deer (Potapov et al. 2012). Sufficiently intensive harvest can reduce the lifespan of infected individuals and hence the number of secondary cases, while at the same time density reduction increases the recruitment of new healthy adults. Presently it is not clear whether intensive harvest management is practical because modeling efforts to assess the approach require more accurate knowledge of deer recruitment potential and prion dynamics in the environment. Selective harvest, when infected deer are harvested more intensely than susceptible ones, would be a more efficient management tool: it is equivalent to an increase of disease-related mortality μ, which in turn decreases the disease basic reproduction number R_0 (Potapov et al. 2012). Selective harvest also

potentially could target specific species, age, or sex criteria. Development of such harvest techniques may be another way to overcome the effects of FD disease transmission.

Acknowledgements

This work has been supported by Alberta Prion Research Institute and Alberta Innovation through grants (E.Merrill: RES0004230) and (D.Coltman G22420004), Natural Sciences and Engineering Research Council of Canada Discovery Grants (EM, MAL) and a Canada Research Chair to MAL.

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Table 1. Notation for model variables and parameters.

	Variable or subscript	Symbol	Units
1	Deer age and sex classes: males, females, juveniles	f, m, j	
2	Disease classes: infected, susceptible but uninfected	I,S	
3	Deer population density	D	deer/km^2
4	Density at disease-free equilibrium	D_0	deer/km^2
5	Equilibrium (asymptotic) density after the disease introduction	D_a	deer/km^2
6	Density of susceptible males, females, juveniles	S_m, S_f, S_j	deer/km^2
7	Density of infected males, females, juveniles	I_m, I_f, I_j	deer/km^2
8	Fertility rate of healthy females	B	year^{-1}
9	Probability of vertical transmission	p_V	
10	Fertility rate of infected females for bringing healthy and infected fawns	$B_{IS}=(1-p_V)B$, $B_{II}=p_VB$	year^{-1}
11	Fawns maturation rate (inverse of juvenile stage duration τ,)		year^{-1}
12	Per capita mortality rate	$m_{S,m}$, $m_{S,f}$, $m_{S,j}$, $m_{I,m}$, $m_{I,f}$, $m_{I,j}$,	year^{-1}
13	Density-independent portion of mortality rate	$m_{0S,m}$, $m_{0S,f}$, $m_{0S,j}$, $m_{0I,m}$, $m_{0I,f}$, $m_{0I,j}$	year^{-1}
14	Starvation index	V	
15	Density-dependent portion of mortality rate of juveniles only	$Vm_{0S,j}$, $Vm_{0I,j}$,	year^{-1}
16	Per capita hunting rate (equal for S and I)	h_m, h_f, h_j	year^{-1}
17	Overall harvest rate	$h=\max\{h_m, h_f, h\}$	year^{-1}
18	Hunter's preferences	h_{Pm}, h_{Pf}, h_{Pj} ($h_x=h\times h_{Px}$, $x=m, f, j$)	
19	Per capita food consumption	$F_{S,m}$, $F_{S,f}$, $F_{S,j}$, $F_{I,m}$, $F_{I,f}$, $F_{I,j}$,	kg/day
20	Total force of infection (per susceptible capita disease transmission rate)	λ_m, λ_f, λ_j	year^{-1}
21	Partial force of infection, corresponding to i-th transmission mechanism	λ_{mi}, λ_{fi}, λ_{ji}	year^{-1}
22	Area occupied by population	A	km^2
23	Total number of deer	N	
24	Mean group size	k	
25	Rate of getting the disease in pairwise contacts between deer of categories u and v	b_{uv}	year^{-1} or km^2/year
26	Rate of getting the disease in contacts with the	b_u	(year×kg^2/d

	environment		$ay^2)^{-1}$
27	Transmission rate between deer of categories *u* and *v*	β_{uv}	$year^{-1}$ or $km^2/year$
28	Relative transmission rate between two deer categories for direct and indirect transmission	ψ_{uv}, ϕ_{uv}	
29	Transmission rate for contact of type *i*, *i*= *m,f,j*	β_i	$year^{-1}$ or $km^2/year$
30	Seasonal weights	w	
31	Rate of soil contamination by prions from infected deer	ε_m, ε_f, ε_j	prions/deer/ year
32	Rate of prions decay or becoming inaccessible to deer	τ_W	$year^{-1}$
33	Environmental contamination by prions	E	$prions/km^2$
34	Relative susceptibility to CWD for different deer categories normalized by female susceptibility Y_m	$Y_m, Y_f = 1, Y_j$	

Table 2. Parameter values used in modeling deer population dynamics		
Parameter	Mule Deer	Comment
Birth rate for healthy females B (fawns per adult female)	1.65	Merrill et al. (2011)
Maturation time τ	1.5 years	
Food consumption by healthy adult male, female, fawn air dry food kg/day $F_{S,m}$, $F_{S,f}$, $F_{S,j}$. (estimates in Appendix)	1.40, 1.09, 1.03	Appendix C
Food consumption by infected adult male, kg/day $F_{I,m}$	$=0.7F_{S,m}$	
Food consumption by infected adult female, kg/day $F_{I,f}$	$=0.7F_{S,f}$	
Food consumption by infected fawn, kg/day $F_{I,j}$	$=F_{S,j}$	
Equilibrium deer density for WMU 234, deer per km^2, D_0	1.58	Alberta Fish & Wildlife, unpublished data, Edmonton, AB Habib et al. (2010)
Equilibrium proportions of healthy population S_{0m}/D_0, S_{0f}/D_0, S_{0j}/D_0 (estimates in Appendix)	0.44, 0.18, 0.38	Appendix A
Adult female mortality m_{0f}	0.15	Appendix A
Adult male mortality m_{0m}	0.29	Appendix A
Juvenile mortality $m_{0j}+Vm_{1j}$	$0.30+12.3V$	Appendix A
Mortality coefficient for infected adult males, years^{-1}, $m_{0I,m}$	$m_{0S,m}+0.57$	Miller et al. (2006)
Mortality coefficient for infected adult females, years^{-1}, $m_{0I,f}$	$m_{0S,f}+0.57$	Miller et al. (2006)
Mortality coefficient for infected fawns, years^{-1}, $m_{0I,j}$	$=m_{0S,j}$	[a]
Density-dependent mortality coefficient for infected adult males, years^{-1}, $m_{1I,m}$	0	Miller et al. (2006) [a]
Density-dependent mortality coefficient for infected adult females, years^{-1}, $m_{1I,f}$	0	Miller et al. (2006) [a]
Density-dependent mortality coefficient for infected fawns, years^{-1}, $m_{1I,j}$	$=m_{1xj}$	[a]
Hunters' preference for males, h_{Pm}, h_{Pf}, h_{Pj}	1.00, 0.33, 0.23	Appendix A

[a]No known evidence on difference with healthy deer

Table 3. Expressions for the force of infection (λ) for males (*m*) and family groups (*x*) consisting of females (*f*) and juveniles (*j*) from seven transmission mechanisms hypothesized to drive CWD spread and whose combinations are used in simulations to produce results corresponding to the observed patterns of sex-specific prevalence rates in deer in Alberta.

	Effect	Defined in equations	Force of infection terms
λ_1	Direct within groups	17, 18	$\lambda_{m1} = \beta_1\left[w_{S1} \frac{\psi_{mm} I_m}{S_m + I_m} + w_{M1} \frac{\psi_{mm} I_m + \psi_{mf} I_f + \psi_{mj} I_j}{D} \right],$ $\lambda_{x1} = \beta_1\left[w_{S1} \frac{\psi_{xf} I_f + \psi_{xj} I_j}{S_f + I_f + S_j + I_j} + w_{M1} \frac{\psi_{xm} I_m + \psi_{xf} I_f + \psi_{xj} I_j}{D} \right], \quad x = f, j\,.$ $\psi_{xu} = 1$ (Section 3.2.1) or $\psi_{xu} = Y_x$ (Section 3.4).
λ_2	Direct between groups	23	$\lambda_{x2} = \beta_2\left(\psi_{xm} I_m + \psi_{xf} I_f + \psi_{xj} I_j\right), \quad \psi_{xu} = 1$ (Section 3.2.2) or $\psi_{xu} = Y_x$ (Section 3.4).
λ_3	Mating females→males	25	$\lambda_{m3} = \beta_3 \frac{I_f}{S_m + I_m}$
λ_4	Mating males→females	26	$\lambda_{f4} = \beta_4 \frac{I_m}{S_m + I_m}$
λ_5	Male fights	27	$\lambda_{m5} = \beta_5 I_m$
λ_6	Environmental within groups	36, 37	$\lambda_{m6} = \beta_6\left[w_{S6} \frac{\phi_{mm} I_m}{S_m + I_m} + w_{M6} \frac{\phi_{mm} I_m + \phi_{mf} I_f + \phi_{mj} I_j}{D} \right], \quad w_{M6} + w_{S6} = 2\,,$ $\lambda_{x6} = \beta_6\left[w_{S6} \frac{\phi_{sf} I_f + \phi_{sj} I_j}{S_f + I_f + S_j + I_j} + w_{M6} \frac{\phi_{sm} I_m + \phi_{sf} I_f + \phi_{sj} I_j}{D} \right], \quad x = f, j$
λ_7	Environmental between groups	38	$\lambda_{x7} = \beta_7\left[\phi_{xm} I_m + \phi_{xf} I_f + \phi_{xj} I_j\right]$

Table 4. Ratio of asymptotic male to female prevalence, r_{max}, for basic, transmission mechanisms (λ_1, λ_2, λ_6 to λ_7, Table 3), rut-related mechanisms (λ_3,λ_4 or λ_5), and combinations of basic and rut mechanisms. The values $r_{max}>2$ are shown in bold. The results are given no vertical transmission (p_V=0) and for no hunting (h=0). Weights of 90:10, 50:50, and 10:90 reflect the duration of seasonal segregation of sexes.

Mechanism and w_S:w_M,	Basic only	Basic + mating f to m ($+\lambda_3$)	Basic + mating m to f ($+\lambda_4$)	Basic + mating m fights ($+\lambda_5$)
Single basic mechanisms				
Environmental within groups, 90:10	**13.3**	**15.3**	1.01	**17.0**
Environmental within groups, 50:50	**2.11**[a]	**3.69**	0.92	**2.85**
Environmental within groups, 10:90	1.16	**2.23**	0.84	1.44
Direct within groups, 90:10	1.94	**5.13**	0.89	**4.23**
Direct within groups, 50:50	1.04	**2.21**	0.87	1.29
Direct within groups, 10:90	0.97	1.66	0.85	1.04
Environmental between groups	1.07	**2.71**	0.72	1.55
Direct between groups	0.97	**2.09**	0.78	1.14
Combinations of 2 basic mechanisms, $r_{max}>2$				
Direct within groups(90:10)+environmental within groups(90:10)	**6.34**	**7.98**	1.11	**7.83**
Environ within group(90:10)+environmental between groups	**2.68**	**3.89**	1.01	**3.29**
Direct within groups(90:10)+environmental within groups(50:50)	**2.09**	**3.30**	0.99	**2.63**
Direct within groups(50:50)+environmental within groups(90:10)	**2.08**	**3.14**	1.02	**2.53**
Direct between groups+environmental within groups(90:10)	1.89	**2.97**	1.00	**2.30**
Environ within groups(50:50)+environmental between groups	1.52	**2.47**	0.95	1.81
Direct within groups(90:10)+environmental between groups	1.33	**2.54**	0.92	1.69
Direct within groups(90:10)+environmental within groups(10:90)	1.33	**2.21**	0.95	1.55
Direct within groups(50:50)+environmental within groups(50:50)	1.38	**2.19**	0.97	1.60
Direct within groups(10:90)+environmental within groups(90:10)	1.43	**2.18**	0.98	1.63
Direct between groups+ environmental within groups(50:50)	1.28	**2.10**	0.94	1.48

[a]Sensitivity in Table 5 is given for this case

Table 5. Sensitivity of $r_{\max}$ to changes in model parameters for indirect within-group environmentally mediated transmission with $w_{S6} / w_{M6} = 50:50$. Parameters correspond to $r_{\max}$=2.10 (see Table 4).

Variable x	Value	Possible range min—max	Sensitivity $(dr_{\max} / dx)$	Elasticity $(d \ln r_{\max} / d \ln x)$
$F_{S,f} / F_{S,m}$	0.78	0.68—0.82[a]	–6.97	–2.57
$F_{S,j} / F_{S,m}$	0.37	?—0.74[b]	–0.30	–0.05
p_V	0	0—0.05[c]	–0.63	N/A
h	0	0—1	–0.92	N/A
w_{S6} / w_{M6}	1	0—∞	1.25	0.59
μ[d]	0.57	0—?	0.90	0.24

[a] estimated from available data on ratio of body masses, see Appendix C
[b] maximum value corresponding to autumn food consumption, not year average
[c] Most likely range according to (Miller et al. 2000)
[d] $\mu = m_{0I,m} - m_{0S,m} = m_{0I,f} - m_{0S,f}$, increase in adult mortality due to infection, estimate from (Miller et al., 2006)

Table 6. Sensitivity of $r_{\max}$ to changes in model parameters for direct within-group transmission with $w_{S6} / w_{M6} = 50:50$ when male susceptibility is twice greater than female and juvenile, $Y_m = 2, Y_f = Y_j = 1$.

Variable x	Value	Possible range min—max	Sensitivity $(dr_{\max} / dx)$	Elasticity $(d \ln r_{\max} / d \ln x)$
Y_m	2	1—?	2.91	1.72
p_V	0	0—0.05	–1.92	N/A
h	0	0—1	–1.70	N/A
w_{S1} / w_{M1}	1	0—∞	2.08	0.61
μ	0.57	0—?	1.96	0.33

Figure captions

Fig. 1. Sketch of minimum structured deer population model and spread of CWD.

Fig. 2. Possible mechanisms of direct and environmental CWD transmission.

Fig. 3. Equilibrium relative population density (density divided by that of healthy population) and disease prevalence as a function of transmission coefficient β for environmental within-group transmission (a) and direct within-group transmission (b) combined with female to male mating transmission ($\lambda = \lambda_6 + \lambda_3$ with equal $\beta_6 = \beta_3 = \beta$ and $\lambda = \lambda_1 + \lambda_3$ with $\beta_1 = \beta_3 = \beta$). Seasonal weights are 50:50 reflecting the duration of seasonal segregation of the sexes.

Fig. 4. The ratio of male to female prevalence, r_{mf} (30) typically reaches its maximum $r_{\max}$ at low values of transmission coefficient β and then decreases. Adding female to male rut transmission increases both $r_{\max}$ and the range of β values where $r_{mf} > 2$ ($\Delta\beta$). a) within-group environmentally-mediated transmission $\lambda = \lambda_6$ and $\lambda = \lambda_6 + \lambda_3$; b) direct transmission $\lambda = \lambda_1$ and $\lambda = \lambda_1 + \lambda_3$. Seasonal weights are 50:50.

Fig. 5. (a) Definition of the values $r_{\max}$ and $\Delta\beta$ for a plot similar to ones in Fig. 4: $r_{\max}$ is the maximum prevalence ratio for the given combination of transmission mechanisms and $\Delta\beta$ characterizes reliability in observation of the ratio equal to or exceeding 2 e.g. in case of spatial variability of β. (b) Comparison of single transmission mechanisms and pairwise combinations (dots) from Table 4 in terms of $r_{\max}$ and $\Delta\beta$ (only with $r_{\max} > 2$). Both $\Delta\beta$ and $r_{\max}$ increase when the contribution of separate groups $W_S : W_M$ increases, compare λ_6 for 50:50 and 90:10, or when the rut female to male transmission (λ_3) is added. See discussion in the text and Fig A4 and Table A5 in Appendix for more details on $\Delta\beta$ values for each combination of transmission mechanisms.

Fig. 6. The plots of $r_{\max}$ for sex-related susceptibility difference with $Y_m \geq Y_f = 1$. a) Directs within group transmission λ_1 with three seasonality ratios $w_S : w_M$ and no harvest. b) Direct within group transmission and rut female to male transmission ($\lambda_1 + \lambda_3$). The circle shows the point where the sensitivity analysis is done (Table 6).