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# Chronic wasting disease model of genetic selection favoring prolonged survival in Rocky Mountain elk (*Cervus elaphus*)

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**Abstract.** As the area where chronic wasting disease (CWD) has been found continues to expand, there is concern over the impact it may have on elk (*Cervus elaphus*) populations that congregate on winter feedgrounds in Wyoming. A stochastic simulation model was created to determine the effect that genotype-specific CWD mortality rates had on a hypothetical free-ranging elk population. Life table data gathered from captive elk held in a CWD-contaminated facility was used to parameterize the model. Modeling the free-ranging elk herd without hunting or differences in survival by genotype resulted in a near extinction decrease in elk numbers over a 100-year period. However, incorporating differences in CWD-mortality by genotype into the model allowed the population to stabilize if hunting was modified to harvest only antlered elk. Our results indicate that, with flexible hunting management, elk populations could adapt to CWD through changes in the frequency of genotypes associated with the incubation time for CWD.

**Key words:** *Cervus elaphus*; chronic wasting disease; elk; feedgrounds; genetics; model; prion; Wyoming, USA.

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## INTRODUCTION

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) naturally found in elk (*Cervus elaphus*), mule deer (*Odocoileus hemionus*), white-tailed deer (*O. virginianus*), and moose (*Alces alces*) (Williams and Young 1980, 1982, Baeten et al. 2007). Prior mathematical models of CWD do not account for differences in survival by genotype and predict the disease will result in the eventual extinction of deer populations (Gross and Miller 2001, Almberg et al. 2011). Similar models have not been created for elk, but some wildlife managers speculate that CWD would have the same effect on elk populations (Schauber and Woolf 2003). Two factors suggest that an elk CWD model may differ significantly from a deer model. One is that CWD prevalence, for reasons unknown, are often an order of magnitude lower for elk than for deer (Miller et al. 2000). Secondly, there is an elk methionine/leucine (M/L) polymorphism at $PrP^{C}$ codon 132 that restricts propagation of $PrP^{CWD}$ resulting in a prolonged incubation time (O'Rourke et al. 1999, Hamir et al. 2006, O'Rourke et al. 2007, Green et al. 2008). A prolonged incubation time could allow for an extended reproductive life, and induce population-level increases in frequency of the associated allele similar to those predicted by Robinson et al. (2012) in white-tailed deer.

It has long been known that CWD prevalence in captive cervids can greatly exceed the proportion recorded in free-ranging populations (Keane et al. 2008). One explanation for this higher prevalence is the presumed accumulation of $PrP^{CWD}$ in the soil or water and the subsequent enhanced transmission in animals unable to avoid contact with the $PrP^{CWD}$. Much higher transmission coefficients are required to simulate epidemics in captive deer, suggesting more intensive transmission under confinement (Miller et al. 2000). It has been speculated that free-ranging cervids could experience similarly high prevalence in situations where they would concentrate for long periods of time in one location (Miller and Williams 2003) such as the supplemental winter feedgrounds located in western Wyoming.

Opponents of supplemental feeding of elk propose that the emergence of CWD in fed elk will eventually necessitate feedground closures to prevent local extinction of infected herd units (Smith 2011). We tested this assertion by using life table data, gathered from captive elk held in a CWD-contaminated facility, to parameterize a population model of free-ranging elk that use winter feedgrounds. We hypothesized that a model incorporating genotypic effects under severe selective conditions would predict a stable, elk population with prolonged CWD incubation times rather than extinction. Such extreme selection pressure approximates the worst-case effect that CWD could have on a free-ranging elk population. Predictions derived from this model may help determine what management options, if any, would prevent local extinction of fed elk.

## Methods

### *Captive elk data*

Thirty-nine female elk calves were captured on the National Elk Refuge in Jackson, Wyoming and transported to the Wyoming Game and Fish Department's (WGFD)

Thorne-Williams Wildlife Research Unit (TWWRU), Wheatland, Wyoming (41° 45.778′ N, 105° 22.605′ W) in March–May 2002. Surveillance had been conducted on the source herd for more than 10 years ($n = 3{,}284$ elk tested) and CWD has never been documented (WGFD, *unpublished data*). Chronic wasting disease has been documented at the TWWRU since 1979 (Williams and Young 1980, 1982) and several CWD inoculation studies have been conducted there. The TWWRU has eight, 0.2-ha elk holding pens, all of which held CWD-infected elk previous to and during this study. Elk were rotated randomly among all eight pens annually to maximize $PrP^{CWD}$ exposure, but were never intermingled with non-study, CWD-infected elk. Captive elk were fed alfalfa hay supplemented with a pelleted ration and provided water and a trace mineral block ad libitum. Husbandry, care, diagnostic techniques, and method of euthanasia were approved in 2002 by the WGFD Institutional Animal Care and Use Committee.

Elk were observed daily for signs of CWD through March 2012. Elk were either found dead or were humanely euthanized when demonstrating terminal signs of CWD. Elk were necropsied at the Wyoming State Veterinary Laboratory where retropharyngeal lymph nodes and obex were retained for CWD examination. Tissues were tested for $PrP^{CWD}$ both by enzyme-linked immunosorbent assay (ELISA; Idexx, Westbrook, Maine, USA) and by immunohistochemistry (Miller and Williams 2002). Elk were genotyped at $PrP^{C}$ codon 132 using methods previously reported (O'Rourke et al. 1999, Perucchini et al. 2008). Beginning in 2009, elk were examined annually for $PrP^{CWD}$ by rectal mucosa biopsy using ELISA (Spraker et al. 2009). During the analysis, 37 of 39 elk died, all of which were positive for CWD. Of those that had been examined for $PrP^{CWD}$ by rectal mucosa biopsy, all were positive ($n = 9$). Genotype frequencies for all elk were 27 $M/M_{132}$ (69.2%), 11 $M/L_{132}$ (28.2%), and 1 $L/L_{132}$ (2.6%). The genotypes of the last surviving elk were $M/L_{132}$ (which died in 2012) and $L/L_{132}$. In 2014, the $L/L_{132}$ is still alive and has remained negative for $PrP^{CWD}$ by rectal mucosa biopsy every year since 2009 and appears healthy, weighs 242 kg, and bore a healthy calf in May 2012. Over the course of the study, several elk were bred and their calves remained with the study population; no data were collected on these calves.

Kaplan-Meier survival estimates were created for the two cohorts, $M/M_{132}$ and $M/L_{132}$ (SigmaPlot, v. 12.3, Systat Software, San Jose, California, USA) (Fig. 1). The mean survival times were 1568

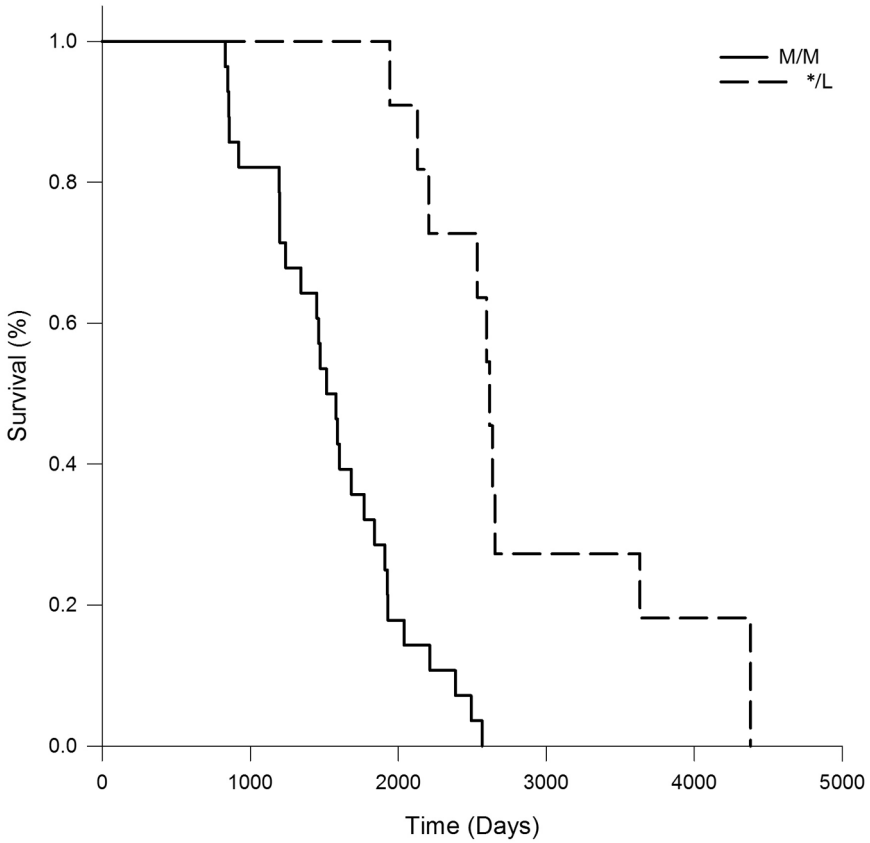


Fig. 1. Survival curves show the probability of death for the $M/M_{132}$ and $*/L_{132}$ cohorts given time in days. The solid line refers to the $M/M_{132}$ cohort, and the dashed line represents the cohorts which have at least one L allele. In this study, one or more copies of an L allele were considered a single cohort.

days (95% CI = 1383, 1754 days) for the $M/M_{132}$ and 2882 days (95% CI = 2376, 3389 days) for the $M/L_{132}$ and $L/L_{132}$. Using a log-rank test, there was a significant difference in the probability of survival between the two cohorts ($\chi^2_1 = 21.76$, $P \leq 0.0001$).

### *Modeled elk population*

We modeled a free-ranging fed elk herd hypothetically exposed to the high levels of CWD prions found at TWWRU. Demographic information for this population came from the Pinedale elk herd unit located in western Wyoming. The herd unit occupies approximately 2,474 square miles and includes three supplemental elk winter feedgrounds. From 2000 to 2009, this population ranged from 1,698 to 1,983 elk with an average of 28 males and 28 calves for every 100 females. The number of elk using feedgrounds in the Pinedale elk herd unit varies from 81.4% to 98.7% of the elk counted during the course of a typical winter (Wyoming Game and Fish Department 2009). All elk ($n = 66$) tested for CWD between 2003 and 2010 from the Pinedale elk herd unit were test negative. The carrying capacity of feedground elk is based on supplemental feeding practices, not by the amount of winter forage as is the case of elk on native winter range (Stewart et al. 2005). Additionally, this elk population experiences low nonhunting mortality (Table 1) which is on the order of mortality estimated for elk in a comparable herd unit with supplemental feeding (Lubow and Smith 2004).

### *Model structure*

An epidemiologic stochastic simulation modeling framework was developed in a spreadsheet

Table 1. Number of days to death for elk held at TWWRU based on reported genotypes.

| Genotype | No. days to death | | |
|---|---|---|---|
| | Minimum | Maximum | Median |
| $M/M_{132}$ | 830 | 2568 | 1514 |
| $M/L_{132}$ | 1589 | 3633 | 2607 |
| $L/L_{132}$ | NA | NA | NA |

format (Excel, v. 14.0.6112.5000, Microsoft, Redmond, Washington, USA; @Risk, v. 5.7.1, Palisade, Ithaca, New York, USA). A series of models were created to forecast population trends through a 100-year period in the elk herd hypothetically infected with CWD. The population was recalculated yearly after accounting for hunting, non-hunting, and CWD losses. Ages were advanced at the start of the biological year. Because the herd of interest consisted largely of elk that received supplemental feeding, density-dependent effects were not considered relevant to this population.

Annual age-specific survival was given by the following equation:

$$n_{ijk} = n_{i(j-1)(k-1)} \times (1 - (m_{\mathrm{h}} + m_{\mathrm{nh}} + m_{\mathrm{CWD}}))_{i(j-1)(k-1)}$$

where the number of individuals of the *i*th sex, of age *j* in the *k*th year is a function of the number of individuals of the same sex in the previous age class and year that survive mortality ($m$) from hunting (h), non-hunting (nh), and CWD (CWD).

Estimates for initial genotype frequencies and time from CWD exposure to death came from TWWRU data (Table 1). The beginning population size for the model was determined using WGFD elk classification data for 2006–2009 from the Pinedale elk herd unit (Table 1). Population sizes from these years were averaged and divided among age classes based on elk aged during WGFD trapping efforts ($n = 1{,}027$ females $\geq 1$ year old; WGFD, *unpublished data*), assuming that the proportion of age classes trapped was representative of the whole elk herd unit. Age estimates were based on incisor wear , and elk were assigned to groups (Quimby and Gaab 1957) (juvenile, yearling, 2–5, 6–9, or 10+ years). Elk in groups with multiple ages were divided equally among individual age classes.

The number of calves in a given year was based on reported calf:cow ratios over a 10-year period, 2000–2010 (Wyoming Game and Fish Department 2009), and fitted to a logistic distribution (@Risk; Table 2). The calf:cow ratios were truncated between minimum and maximum values (Table 2) and the probabilities of outcomes were proportionally redistributed within the acceptable range. This forced the simulation model to select a value from within our given ranges for each iteration, while maintaining the relative frequencies of each acceptable value. The calf:cow ratios were obtained from post-hunt classification efforts and reflect calfhood hunting mortality and fecundity. Additional non-hunting mortality ($m_{\mathrm{nh}}$) was applied to the first year of life to account for losses in the spring. Hunting mortality ($m_{\mathrm{h}}$) was deterministic and included in three models based on the 2006–2009 WGFD averages for adult males (51%) and females (7%). A uniform distribution for non-hunting mortality was fitted to data on WGFD reported elk mortalities on and off elk feedgrounds (WGFD, *unpublished data*) and incorporated into each model (Table 2). The uniform distribution was a weighted average of data on unknown, management-related, and feedground deaths.

Rather than simulate a changing CWD prevalence or modeling disease transmission, we assumed that each elk had a constant high level of exposure to $PrP^{CWD}$ prions similar to that at

Table 2. Parameter estimates for modeling population trends for the Pinedale elk herd unit.

| Parameter | Value | Source |
|---|---|---|
| Elk estimated in Pinedale herd unit | 1752 | WDFD (2009) |
| Male harvest rate | 51% | WGFD (2009) |
| Female harvest rate | 7% | WGFD (2009) |
| Cow:calf ratio | Logistic: (0.27812, 0.02397), Median = 0.282, SD = 0.0287, Truncated at min. = 0.23, max. = 0.35 | WGFD (2009) |
| Non-hunting mortality | Uniform: (0.00055, 0.01686), Median = 0.00862, SD = 0.00466 | WGFD, *unpublished data* |

TWWRU. The annual CWD-mortality probability was directly parameterized from the data seen in the observation of captive elk at TWWRU. The prevalence of CWD never changed and the probability of dying was considered constant through the duration of the study. We assumed that the annual mortality in free-ranging elk could be no higher than that observed in the captive population. The first CWD-associated deaths occurred in year two, based on data from the long-term CWD elk study. Age classes 1–12 plus juveniles were included in the model, but only ages 2–12 were subjected to CWD-associated death. All 12-year-old elk were removed from the model due to the low number of >10-year-old individuals recorded during WGFD trapping efforts. Models that included hunting experienced high losses of mature males. It was assumed that the calf:cow ratio was not impacted by a reduced number of mature bull elk. It was also assumed that there were no differences in susceptibility or exposure between males and females. Fluctuations in population in the Pinedale elk herd unit associated with emigration and immigration is less than 10% (Dean et al. 2004). While immigration may have slowed the rate of population decline in some of the models, we assumed a closed herd.

Five different scenarios were derived from a single general model, incorporating increasing complexity. The scenarios modeled were: (1) crude age-specific CWD mortality without hunting; (2) crude age-specific CWD mortality with current hunting harvest; (3) genotype-specific CWD mortality without hunting; (4) genotype-specific CWD mortality with current hunting harvest; and (5) genotype-specific CWD mortality with antlered-only hunting. The probability of dying from CWD ($m_{CWD}$) was derived from the observations of captive elk at TWWRU. The nine best distributions (beta, logistic, etc.) were fit to observed days to death data based on $\chi^2$ goodness-of-fit testing. The age-specific expected values from these days to death distributions were used to bootstrap a logistic distribution that would estimate the annual probability of dying from CWD in each age class of the population. Scenarios 3–5 incorporated genotype-specific estimates for age-specific CWD mortality. This allowed for genetic selection for genotypes with varying incubation times based on Hardy-Weinberg predictions.

The model assumed random assortment of individuals and that no other fitness differences were associated with exchanging amino acids at codon 132. To verify this assumption, we created a model with our initial genotypic frequencies without selection pressure (i.e., no CWD mortality) and observed the population over 100 years. In the absence of selection pressure, all genotype frequencies, including the rare $L/L_{132}$ genotype frequency, remained within 1% of its starting value.

After ensuring the appropriate starting values for the model, genotype-specific CWD mortalities were incorporated. The CWD mortalities for the groups of elk with $M/L_{132}$ and $L/L_{132}$ genotypes were pooled so that the single $L/L_{132}$ elk held at TWWRU would not overly influence the model outcomes. Elk were initially distributed into genotype groupings based on the frequency of occurrence in the population held at TWWRU, which were similar to those sampled from other populations (Perucchini et al. 2008). For subsequent years, offspring were assigned a genotype based on predicted Mendelian frequencies. Each scenario was iterated 5,000 times. The median population at years 25, 50, 75, and 100 was recorded along with the median population growth ($\lambda$) for the 100-year period or for those years which had at least one elk.

### *Sensitivity analysis*

The parameters hunting mortality ($m_h$), non-hunting mortality ($m_{nh}$), CWD mortality ($m_{CWD}$), and calf:cow ratio were allowed to diverge by ±10% using the @Risk Advanced Sensitivity Analysis tool (@Risk, v. 5.7.1). The genotype-specific CWD mortality with current hunting harvest scenario was used for the analysis since it was the most complex. Each age class was changed during the analysis rather than only changing the yearly output. Year 25 was chosen as the output to monitor changes to the population. Each simulation was iterated 100 times.

## Results

### *Model*

Modeling the Pinedale elk herd unit without consideration for genotypic variation resulted in a substantial decrease in elk numbers over a 100-

year period. Without hunting, this population slightly increased in numbers initially followed by a gradual decrease until the 100th year, which ended with a median of 140 elk (SD = 22.4; 95% PI = 108–181; Fig. 2A) and a median λ of 0.975 (SD = 0.002; 95% PI = 0.972–0.976). The addition of current hunting harvest caused this population to decline sharply. By year 50, the population decreased by 98.5% and reached extinction by year 100 with a median λ of 0.917 (SD = 0.92; 95% PI = 0.913–0.920; Fig. 2B) for those years that had at least one elk.

Incorporating the genotype data into a model without hunting resulted in a population that increased after an initial decline. After 100 years, the population had a median of 5,733 elk (SD = 1,142.01; 95% PI = 4,234–7,886), a 32.5% increase from the initial starting population (Fig. 2C). We observed a change in genotype frequencies with the formerly predominate $M/M_{132}$ genotype reduced by 89% and $L/L_{132}$ genotype over 18.5 times higher than their respective starting frequencies by year 100 (Table 3).

Maintaining current levels of hunter harvest in the genotype model caused the population to decrease by 84.6% by year 25 with zero elk remaining by year 100 (Fig. 2D). This population also saw changes in genotypes with frequencies of $M/M_{132}$ decreased by 72% and $L/L_{132}$ increased by 10.8 times at year 50. Population growth was higher for the group not subjected to hunting with a median λ of 1.012 (SD = 0.002; 95% PI = 1.009–1.016). The median λ for the scenario with hunting for the years which had at least one elk was 0.934 (SD = 0.002; 95% PI = 0.930–0.937).

The third genotype-specific scenario included hunting of only antlered elk. In this scenario the population declined and stabilized. Years 90–100 had a median λ of 1.01 (SD = 0.005; 95% PI = 0.990–1.010) with a median population of 666 elk (SD = 118.28; 95% PI = 504–881; Fig. 2E) at year 100. The median λ for the full 100 years was 0.991 (SD = 0.002; 95% PI = 0.988–0.993). This population saw similar changes to the distribution of genotypes as the no hunting scenario with frequencies of $M/M_{132}$ decreased by 91% and $L/L_{132}$ genotype 20 times higher by year 100.

### *Sensitivity analysis*

At year 25, changes in CWD mortality proportion had the greatest effect on the population. The change in population size was indirectly related to the incremental percent changes in CWD mortality. A 25% decrease in population size was caused by a 10% increase in CWD mortality probability. Hunting mortality had a similar but less pronounced effect on population size. As the second most influential parameter in the model, population size changed by 17% at year 25 when the hunting mortality parameter was increased by 10%. The output at year 25 was not highly sensitive to non-hunting mortality with only a 3% change in population size after a 10% increase. Incremental changes in calf:cow ratios had no change on the population size output at year 25.

## Discussion

The purpose of this study was to model population-level impacts of CWD in a free-ranging elk herd. We parameterized life expectancies and genotype frequencies using observations from a cohort of captive elk naturally exposed to $PrP^{CWD}$. Unlike free-ranging elk, the captive elk were unable to avoid $PrP^{CWD}$ exposure and it is unlikely that any natural setting, even feedgrounds, could reproduce this degree and duration of $PrP^{CWD}$ exposure. However, by modeling higher than expected CWD exposure and subsequent mortality, an upper bound is created which can be used to estimate worst-case population-level impacts. This additive CWD-mortality was superimposed over population data from an elk herd using winter feedgrounds to assess the impact CWD could have under these circumstances.

The genotype-specific models showed selection for the $L_{132}$ allele. By year 100, the $M/L_{132}$ and $L/L_{132}$ alleles were found at much higher frequencies than $M/M_{132}$. In the model without hunting, this switch in genotypic frequencies increased the number of days to death and allowed for population growth, suggesting that this population could respond to the emergence of CWD.

For the modeled population, it was assumed that no non-CWD associated fitness differences existed between M and L alleles at codon 132. While it is unknown what consequences a major switch in genotype frequencies would have, the $M/L_{132}$ and $L/L_{132}$ elk in captivity at the TWWRU

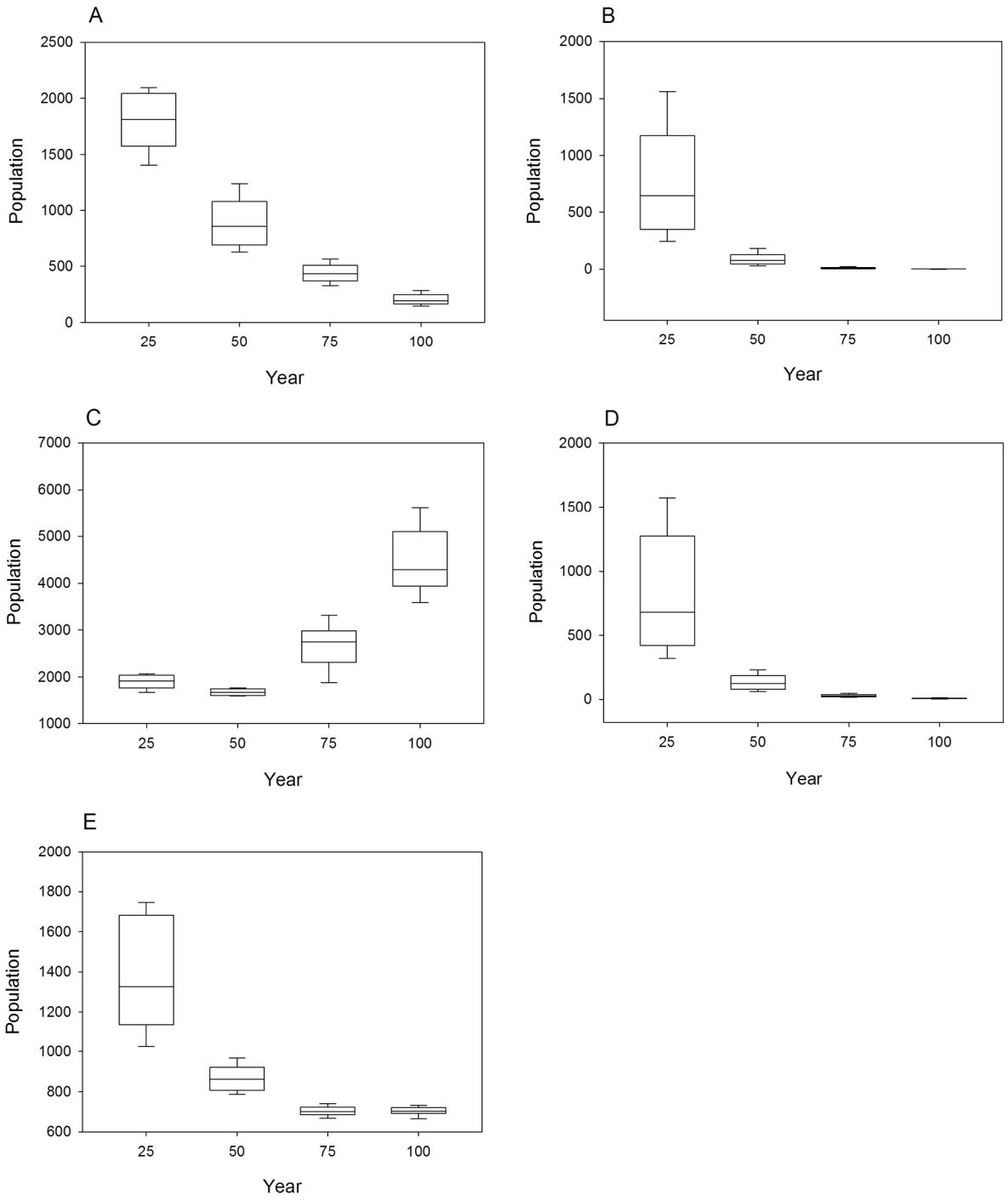


Fig. 2. Box and whisker plots representing population trends for the different scenarios modeled for the Pinedale, Wyoming elk herd unit. Plots (A) and (B) are modeled populations with crude age-specific CWD mortality, plot (B) includes current hunting harvest. Plots (C), (D), and (E) incorporate genotype-specific CWD mortality; B and D include current hunting harvest; C was modeled with no hunting; and E was modeled with antlered only hunting. The middle bar of the boxes represents the median values, the 25th and 75th percentiles are shown by the box borders, and the whiskers of each box are the maximum and minimum values of the data.

Table 3. Genotype frequencies (%) for model scenarios listed in order for no hunting, current harvest, and antlered hunting only.

| Genotype | Year 25 | Year 50 | Year 100 |
|---|---|---|---|
| M/M | 46.5, 42.1, 44.9 | 27.0, 19.3, 22.6 | 7.5, †, 6.0 |
| M/L | 44.8, 47.6, 46.0 | 57.5, 52.7, 52.8 | 44.4, †, 42.0 |
| L/L | 8.7, 10.3, 9.1 | 23.4, 28.1, 24.5 | 48.1, †, 52.0 |

† Current hunting harvest resulted in no elk by year 100 so genotype frequencies were not reported for that time period.

did not display a noticeable fitness disadvantage. Additionally, fitness disadvantages have not been seen in research in scrapie-resistant domestic sheep (Sweeney and Hanrahan 2008).

If all elk have equal CWD incubation times, the model predicts infection could exert a more negative impact, similar to previous models without genetic factors (Miller et al. 2006). However, research with sheep (*Ovis aries*), mule deer (*Odocoileus hemionus*), white-tailed deer (*Odocoileus virginianus*), and humans (*Homo sapiens*) has shown that different genotypes alter an individual's response to TSEs (Elsen et al. 1999, Jewell et al. 2005, Johnson et al. 2006, Mead et al. 2009). In Colorado, mule deer with serine and phenylalanine at codon 225 were observed at lower than expected frequencies within groups that tested positive for CWD (Jewell et al. 2005). These results indicated the 225SF genotype may offer prolonged incubation after CWD exposure. This genotype was found at low frequencies in free ranging mule deer herds located within CWD endemic areas in Colorado implying that genetic selection toward the prolonged incubation genotype had not occurred. A similar scenario was described in a CWD endemic area in white-tailed deer populations in Wisconsin. Chronic wasting disease genotypes consisting of combinations of serine at codon 96 were underrepresented in infected deer populations (Johnson et al. 2006). These genotypes were found at comparable frequencies in areas with and without CWD. A switch towards higher frequencies of genotypes that provide prolonged survival has not yet been documented in any of the CWD endemic areas. The slow progression of disease associated with CWD infection may not exert enough selective pressure to cause a dramatic genotypic shift similar to the one presented in our model. However, as demonstrated by Robinson et al. (2012), if the timescale is drawn out to several hundred years, progression of CWD likely will cause a switch to higher frequencies of slower disease progression genotypes in wild populations.

Genotypic frequencies of the captive elk used to parameterize the model closely agreed with previous findings in free-ranging elk (Perucchini et al. 2008), suggesting that the captive animals were an accurate representation of the source elk population. The prolonged survival of elk having either $M/L_{132}$ or $L/L_{132}$ also agreed with previous findings where the presence of leucine at codon 132 severely restricted propagation of $PrP^{CWD}$ and reduced the probability of CWD by more than half (O'Rourke et al. 1999, Hamir et al. 2006, Green et al. 2008, White et al. 2010).

Manipulating hunting in our models greatly influenced elk population trends and genetic frequencies. After comparing three management strategies, the models indicated that, with genetic selection, a level of hunting existed that would not cause a local extinction of elk populations. All possible levels of hunting were not analyzed. An antlered-only management option that maintained current high levels of bull harvest caused a decrease in the population well below the population objective. However, the downward trend stabilized and suggested that if the time frame was drawn out, the population may begin to rebound. The antlered only strategy was included because it is one method that is highly likely to be incorporated in an area where the population is a concern to managers who want to continue hunting (Wyoming Game and Fish Department 2009). The model showed that in an environment without harvest, CWD was not limiting enough to keep this population from rising to higher than desired numbers (i.e., three times the proposed population objective of 1,900 elk; Wyoming Game and Fish Department 2012).

Our models indicated that elk populations exposed to $PrP^{CWD}$ could respond through changes in frequency of genotypes with varying

incubation times. Also, changes in hunting strategies of elk populations could help maintain numbers through these transitional periods. A reduction in hunting would likely be necessary; however, eliminating harvest of all elk would allow this population to exceed population objectives over time. Experimentation with hunting levels likely would be required to determine what level of elk harvest is most likely to maintain desired numbers. Additionally, monitoring genotypic frequencies in conjunction with fecundity and recruitment are highly warranted. According to our models and assumptions and considering prolonged incubation times associated with certain genotypes, CWD alone was not enough to cause extinction of elk herds that congregate on winter feedgrounds. While CWD can negatively impact wildlife populations (Miller et al. 2008), our results indicated that, with flexible management, elk populations could adapt to CWD through increases in the frequency of genotypes over 100-year modeled timeframes.

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## Literature Cited

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

Baeten, L. A., B. E. Powers, J. E. Jewell, T. R. Spraker, and M. W. Miller. 2007. A natural case of chronic wasting disease in free-ranging moose (*Alces alces shirasi*). Journal of Wildlife Diseases 43:309–314.

Dean, R., M. Gocke, B. Holz, S. Kilpatrick, T. J. Kreeger, B. M. Scurlock, S. Smith, E. T. Thorne, and S. Werbelow. 2004. Elk feedgrounds in Wyoming. Wyoming Department of Game and Fish, Jackson, Wyoming, USA.

Elsen, J.-M., Y. Amigues, F. Schelcher, V. Ducrocq, O. Andreoletti, F. Eychenne, J. V. Tien Khang, J.-P. Poivey, F. Lantier, and J.-L. Laplanche. 1999. Genetic susceptibility and transmission factors in scrapie: detailed analysis of an epidemic in a closed flock of Romanov. Archives of Virology 144:431–445.

Green, K. M., S. R. Browning, T. S. Seward, J. E. Jewell, D. L. Ross, M. A. Green, E. S. Williams, E. A. Hoover, and G. C. Telling. 2008. The elk PRNP codon 132 polymorphism controls cervid and scrapie prion propagation. Journal of General Virology 89:598–608.

Gross, J. E., and M. W. Miller. 2001. Chronic wasting disease in mule deer: disease dynamics and control. Journal of Wildlife Management 65:205–215.

Hamir, A. N., T. E. Gidlewski, T. R. Spraker, J. M. Miller, L. Creekmore, M. Crocheck, T. F. Cline, and K. I. O'Rourke. 2006. Preliminary observations of genetic susceptibility of elk (*Cervus elaphus nelsoni*) to chronic wasting disease by experimental oral inoculation. Journal of Veterinary Diagnostic Investigation 18:110–114.

Jewell, J. E., M. M. Conner, L. L. Wolfe, M. M. Miller, and E. S. Williams. 2005. Low frequency of PrP genotype 225SF among free-ranging mule deer (*Odocoileus hemionus*) with chronic wastsing disease. Journal of General Virology 86:2127–2134.

Johnson, C., J. Johnson, J. P. Vanderloo, D. Keane, J. M. Aiken, and D. McKenzie. 2006. Prion protein polymorphisms in white-tailed deer influence susceptibility to chronic wasting disease. Journal of General Virology 87:2109–2114.

Keane, D. P., D. J. Barr, P. N. Bochsler, S. M. Hall, T. E. Gidlewski, K. I. O'Rourke, T. R. Spraker, and M. D. Samuel. 2008. Chronic wasting disease in a Wisconsin white-tailed deer farm. Journal of Veterinary Diagnostic Investigation 20:698–703.

Lubow, B. C., and B. L. Smith. 2004. Population dynamics of the Jackson elk herd. Journal of Wildlife Management 68:810–829.

Mead, S., M. Poulter, J. Uphill, J. Beck, J. Whitfield, T. E. F. Webb, T. Campbell, G. Adamson, P. Deriziotis, S. J. Tabrisi, H. Hummerich, C. Verzilli, M. P. Alpers, J. C. Whittaker, and J. Collinge. 2009. Genetic risk factors for variant Creutzfeldt-Jakob disease: a genome-wide association study. Lancet Neurology 8:57–66.

Miller, M. W., N. T. Hobbs, and S. J. Tavener. 2006. Dynamics of prion disease transmission in mule deer. Ecological Applications 6:2208–2214.

Miller, M. W., H. M. Swanson, L. L. Wolfe, F. G. Quartarone, S. L. Huwer, C. H. Southwick, and P. M. Lukacs. 2008. Lions and prions and deer demise. PLoS ONE 3:e4019.

Miller, M. W., and E. S. Williams. 2002. Detection of $PrP^{CWD}$ in mule deer by immunohistochemistry of lymphoid tissues. Veterinary Record 151:610–612.

Miller, M. W., and E. S. Williams. 2003. Horizontal prion transmission in mule deer. Nature 425:35–36.

Miller, M. W., E. S. Williams, C. W. McCarty, T. R. Spraker, T. J. Kreeger, C. T. Larsen, and E. T. Thorne. 2000. Epizootiology of chronic wasting disease in free-ranging cervids in Colorado and Wyoming. Journal of Wildlife Diseases 36:676–690.

O'Rourke, K. I., T. E. Besser, M. W. Miller, T. F. Cline, T. R. Spraker, A. L. Jenny, M. A. Wild, G. L. Zebarth, and E. S. Williams. 1999. PrP genotypes of captive and free-ranging Rocky Mountain elk (*Cervus elaphus nelsoni*) with chronic wasting disease. Journal of General Virology 80:2765–2679.

O'Rourke, K. I., T. R. Spraker, D. Zhuang, J. J. Greenlee, T. E. Gidlewski, and A. N. Hamir. 2007. Elk with a long incubation prion disease phenotype have a unique PrPd profile. Neuroreport 18:1935–1938.

Perucchini, M., K. Griffin, M. W. Miller, and W. Goldmann. 2008. PrP genotypes of free-ranging wapiti (*Cervus elaphus nelsoni*) with chronic wasting disease. Journal of General Virology 89:1324–1328.

Quimby, D. C., and J. E. Gaab. 1957. Mandibular dentition as an age indicator in Rocky Mountain elk. Journal of Wildlife Management 21:435–451.

Robinson, S. J., M. D. Samuel, C. J. Johnson, M. Adams, and D. I. McKenzie. 2012. Emerging prion disease drives host selection in a wildlife population. Ecological Applications 22:1050–1059.

Schauber, E. M., and A. Woolf. 2003. Chronic wasting disease in deer and elk: a critique of current models and their application. Wildlife Society Bulletin 31:610–616.

Smith, B. L. 2001. Winter feeding of elk in Western North America. Journal of Wildlife Management 65:173–190.

Spraker, T. R., K. C. VerCauteren, T. E. Gidlewski, D. A. Schneider, R. Munger, A. Balachandran, and K. I. O'Rourke. 2009. Antemortem detection of $PrP^{CWD}$ in preclinical, ranch-raised Rocky Mountain elk (*Cervus elaphus nelsoni*) by biopsy of rectal mucosa. Journal of Veterinary Diagnostic Investigation 21:15–24.

Stewart, K. M., R. T. Bowyer, B. L. Dick, B. K. Johnson, and J. G. Kie. 2005. Density-dependent effects on physical condition and reproduction in North American elk: An experimental test. Population Ecology 143:85–93.

Sweeney, T., and J. P. Hanrahan. 2008. The evidence of association between prion protein genotype and production, reproduction, and health in sheep. Veterinary Research 39:28.

White, S. N., T. R. Spraker, J. O. Reynolds, and K. I. O'Rourke. 2010. Association analysis of PRNP gene region with chronic wasting disease in Rocky Mountain elk. BMC Research Notes 3:314.

Williams, E. S., and S. Young. 1980. Chronic wasting disease of captive mule deer: a spongiform encephalopathy. Journal of Wildlife Diseases 16:89–98.

Williams, E. S., and S. Young. 1982. Spongiform encephalopathy of Rocky Mountain elk. Journal of Wildlife Diseases 18:465–471.

Wyoming Game and Fish Department. 2009. Job completion report. Wyoming Game and Fish Department, Cheyenne, Wyoming, USA.

Wyoming Game and Fish Department. 2012. Job Completion Report. Wyoming Game and Fish Department, Cheyenne, Wyoming, USA.