DISSERTATION

SPATIAL EPIDEMIOLOGY OF CHRONIC WASTING DISEASE IN COLORADO MULE DEER (*Odocoileus hemionus*)

Submitted by

Matthew Lee Farnsworth

Graduate Degree Program in Ecology

In partial fulfillment of the requirements

for the Degree of Doctor of Philosophy

Colorado State University

Fort Collins, Colorado

Fall 2004

COLORADO STATE UNIVERSITY

October 8, 2004

WE HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER OUR SUPERVISION BY MATTHEW LEE FARNSWORTH ENTITLED SPATIAL EPIDEMIOLOGY OF CHRONIC WASTING DISEASE IN COLORADO MULE DEER (*Odocoileus hemionus*), BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

Committee on Graduate Work

Advisor

Department Head

ABSTRACT OF DISSERTATION

SPATIAL EPIDEMIOLOGY OF CHRONIC WASTING DISEASE IN COLORADO MULE DEER (*Odocoileus hemionus*)

I conduct three separate studies using the spatial distribution of chronic wasting disease (CWD) in Colorado mule deer (*Odocoileus hemionous*) to examine the relationship between individual level infection probability and several biotic and abiotic components of the system. The models I develop are focused on: (1) examining the role of human induced land use change in exacerbating the disease; (2) the scales of mule deer seasonal movement patterns that correspond best to the observed distribution of CWD infection; and (3) the relationship between deer density and infection risk. These analyses address the known effects of age and sex, and in one study, I consider the effects of land ownership and habitat. All studies use contemporary information theoretic approaches; either Akaike's Information Criteria (AIC) or its Hierarchical Bayesian analogue, the Deviance Information Criteria (DIC), to determine the strength of support for candidate models representing various hypotheses about the proposed relationships.

The results suggest a positive relationship between human land use and land ownership patterns and infection risk. My analyses also suggest that the spatial distribution of CWD corresponds best to a highly localized infection process, however I am unable to detect a relationship between deer density and infection risk.

I conclude by addressing several issues associated with using the data as I have for retrospective analysis and provide management recommendations based on my findings. Finally, I extend the discussion to address future avenues of research that might benefit from the work presented in this dissertation.

Matthew Lee Farnsworth

Graduate Degree Program in Ecology

Colorado State University

Fort Collins, CO 80523

Fall 2004

ACKNOWLEDGEMENTS

The National Science Foundation-National Institutes of Health Grant DEB-0091961, and National Science Foundation grant DGE-0221595003 provided financial support. In addition, the University of Wyoming and the Colorado Division of Wildlife provided countless hours of human effort to amass the data used in my research.

The members of my committee made my graduate school experience one I will surely never forget. The guidance provided by Jennifer Hoeting in helping me to better understand and appreciate the complexities of Bayesian statistics and Hierarchical modeling will certainly stay with me, and benefit me, throughout my career. Mike Miller contributed extensively to the biological and epidemiological interpretations of model results, adding greatly to the substance of my research. Robin Reich spent many hours developing the Kriging algorithms and analysis used in my research. Ken Burnham, although not a committee member, contributed greatly to the material found between these covers, both implicitly and explicitly. My major professor, Tom Hobbs, provided many valuable ideas and insights along the way, along with fostering in me a greater appreciation for the challenges and rewards associated with outstanding scientific writing.

Finally, I owe the greatest thanks to my wife, Tiffany Rae Barnes, whose immense patience and constant support sustained me throughout the duration of my Ph.D. The sacrifices she made on a daily basis allowed me to focus much more energy on this body of work than would have ever been possible without her, thank you for seeing me through. I owe you one...no, make that two!

TABLE OF CONTENTS

INTRODUCTION

This dissertation focuses on the potential influence of anthropogenic land-use and biotic factors in shaping observed patterns of chronic wasting disease (CWD), a transmissable spongiform encephalopathy endemic to portions of Colorado and Wyoming. Specifically, I seek to understand differences in disease prevalence between urban and non-urban areas and its relationship to sex-specific infection rates in mule deer (*Odocoileus hemionus*) residing in North-central Colorado. Additionally, I examine the correspondence between relevant scales of mule deer movement patterns and the observed distribution of CWD across the landscape as well as developing a model that seeks to quantify the relationship between deer density and CWD. To accomplish this I develop three studies. The first study examines the effect of human land-use and deer gender on the presence of disease in three locations. The second study uses a Bayesian hierarchical framework to shed light on the most likely biological scale structuring the spatial heterogeneity of CWD. The final study relates estimates of mule deer density to the probability of infection in individual deer. The common thread linking these studies is a focus on the relationship between CWD and factors that may act to structure its distribution in mule deer across the landscape.

Because human alteration of landscapes can affect the distribution, abundance, and behavior of wildlife, in Chapter 1 I explore the effects of human land use on

prevalence of CWD in mule deer populations residing in north-central Colorado. I chose best approximating models estimating CWD prevalence in relation to differences in human land use, sex, and geographic location. Prevalence was higher in developed areas and among male deer, suggesting anthropogenic influences on the occurrence of disease. I also found a relatively high degree of variation in prevalence across the three study sites; suggesting that spatial patterns in disease may be influenced by other factors operating at a broader, landscape scale. These results suggest that multiple factors, including changes in land use, differences in exposure risk between sexes, and landscape-scaled heterogeneity, are associated with CWD prevalence in north-central Colorado.

Mule deer are highly mobile, gregarious ungulates that interact with one another over multiple temporal and spatial scales. These interactions provide an opportunity to transmit the disease and probably act as the primary biological driver of disease spread across the landscape. Therefore, the goal of Chapter 2 is to understand which scales of mule deer movement (individual, winter sub-population, or summer sub-population) have the greatest influence on the spatial pattern of CWD in north-central Colorado. I develop a fully Bayesian hierarchical model to compare the strength of evidence for each hypothesized scale along with individual-level sex and age effects and environmental predictors believed important in structuring this relationship. I found strong evidence that small-scale movement patterns were related to the distribution of CWD infection. There was also evidence that land ownership plays a role in exacerbating the disease, along with the known offsets of sex and age. This analysis demonstrates how information on the scales of spatial processes that generate observed patterns can be used to gain insight when process data are sparse or unavailable.

The third chapter focuses on understanding the relationship between mule deer density and CWD infection risk in individual deer. Understanding the controls of disease spread in natural and human dominated systems has emerged as a fundamental challenge in contemporary ecology. Models of disease dynamics often assume that increasing population density causes a proportionate increase in the per capita rate of contacts between infectious and susceptible individuals, causing transmission rates to increase with population density. Under this assumption, disease prevalence should be positively related to density. Although this assumption is widely invoked in modeling disease spread, there are few data for examining the role of density dependent disease transmission in structuring the dynamics of populations of long-lived, wide-ranging species. I use kriging to develop a surface of estimated deer density based on observations of abundance from 129 quadrats surveyed by helicopter over a four-year period. I then relate the kriged surface to the probability of CWD infection through a spatially structured hierarchical model that incorporated the uncertainty in deer density estimates that resulted from using interpolated values as a model covariate. I compared the strength of evidence for various forms of the density/disease relationship after adjusting for individual-level sex effects and found little evidence of a relationship between deer density and CWD. It is possible that the scale of analysis was inappropriate, the data were not adequate, or that other biological processes dominated the density/disease relationship at the scale of analysis. However, this analysis effectively demonstrates how data that are spatially disjoint can be aligned using spatial statistical models, and how the error from such models can be included in analysis to appropriately model estimation error using a hierarchical modeling framework.

I conclude the dissertation with a discussion of management recommendations based on my findings and suggest how my research might guide future work seeking a stronger mechanistic understanding of CWD dynamics in mule deer populations residing in north-central Colorado. My primary management recommendations are: (1) focus culling efforts on localized infection "hot spots" corresponding to the spatial scale and seasonal time period of individual deer winter home ranges; (2) continue to monitor and remove infected deer from urban areas using the "test and cull" program initiated by the CDOW, particularly adult males that may be a primary source for spreading CWD. I address the issue of using information from the statistical inferences I have made as a starting point for mechanistic models, such as network models based on mule deer movement patterns and mixing potential. Finally, I address several shortcomings of the data used in my retrospective analysis and suggest how future experimental research might be conducted to provide greater insight into CWD dynamics. Specifically, I address the issues of: (1) hunter killed deer as the primary source of data and the potential biases; (2) the lack of knowledge regarding the time since disease introduction into this population.

HUMAN LAND USE INFLUENCES CHRONIC WASTING DISEASE PREVALENCE IN MULE DEER

INTRODUCTION

In many areas of North America, alteration of landscapes by people has shaped the distribution and abundance of wildlife (Wiens et al. 1986, Turner 1989, McGarigal and McComb 1995, Crooks and Soule 1999, Dale et al. 2000) . Less attention has been paid to the ways human action influences ecological processes, for example, the dynamics of pathogens and hosts (Van Buskirk and Ostfeld 1995, Augustine 1998, Van Buskirk and Ostfeld 1998, Daszak et al. 2001, Wasserberg et al. 2003). A variety of emerging, infectious diseases affect wildlife populations (Dobson and Meagher 1996, Dobson and Foufopoulos 2001, Williams et al. 2002) and the dynamics of these pathogen-wildlife systems are potentially shaped by human action.

Chronic wasting disease (CWD) (Williams and Young 1980), a prion disease of mule deer (*Odocoileus hemionus*), white-tailed deer (*O. virginianus*), and Rocky Mountain elk (*Cervus elaphus nelsoni*), occurs naturally in free-ranging populations in several areas of North America, but the largest known outbreak occurs in a contiguous ~40,000 km^2 area of northeast Colorado and southeast Wyoming (Williams 1992, Miller et al. 2000, Williams and Miller 2002). CWD apparently has been endemic in this area for at least two decades, and field investigations and modeling suggest that the dynamics

of this emerging disease may be best viewed as an epidemic with a protracted time-scale (Miller et al. 2000, Gross and Miller 2001). More recent discoveries of other foci of CWD distant to this 40,000 km^2 "endemic area" have spawned interest in understanding spatial and temporal dynamics in order to develop management strategies for controlling CWD in affected populations and preventing or slowing its spread among unaffected populations.

The epidemic area also includes human communities that are growing more rapidly than almost any in the nation (Baron et al. 2000, Hansen et al. 2002). This population growth has caused dramatic change in mule deer habitat throughout the region. During 1970 to 2000, the area with housing density exceeding 1 per 20 ha more than doubled (40636 to 81836 ha) within game management units most affected by CWD (Theobald 2003). These trends are predicted to continue---by 2030, it is projected that 141732 ha will be developed, almost another doubling relative to 2000. Much of this development is occurring on winter ranges where deer populations concentrate seasonally. The effects of land use change on disease processes in mule deer populations are poorly understood, however two potential mechanisms affecting disease could exacerbate transmission in developed areas. First, if deer avoid areas of high human population density (Theobald et al. 1997, Theobald 2000) (because of fences, dogs, and other sources of disturbance), then development could compress the area of landscape used by deer, thereby increasing their density. It is plausible that increased density could accelerate rates of contact between infected and susceptible individuals. Second, development tends to reduce hunting pressure. As result, adults, particularly adult males, tend to live longer than in areas where hunting pressure is low. This might prolong the

average clinical course by eliminating a prominent, competing source cause of mortality, and in so doing, prolong the total time that infected animals are able to transmit the disease.

Here, I explore how patterns of human land use influence variation in CWD prevalence across north-central Colorado. Based on the logic outlined above and observations of relatively high CWD prevalence among mule deer captured and tested for CWD in urban areas (Wolfe et al. 2002), I hypothesized that human development of mule deer habitat could result in higher CWD prevalence in developed areas. I also examined influences of gender and geographic location on prevalence because earlier analyses (Miller et al. 2000, Wolfe et al. 2004) suggested that these factors may affect patterns of CWD prevalence and thereby could confound underlying influences of land use patterns.

METHODS

Study area

I studied the relationship between CWD infection and human land use using four free-ranging mule deer sub-populations (Conner and Miller 2004) located across three study sites spanning roughly 1200 km^2 in Larimer County, Colorado, USA. One sub-population resided in and around Estes Park (hereafter, EP), a second (Glacier View Meadows; GVM) was located west of Livermore, and the final two sub-populations were located west of Horsetooth Reservoir (HT). Deer habitat in the EP study area (elevation ~ 1850m – 2885m) included coniferous forest and mountain shrub communities interspersed with deciduous forest and grasslands at lower elevations. The GVM (elevation ~ 1825m – 2450m) and HT (elevation ~ 1580m – 2250m) sites were comprised of similar land cover and land use types as the EP site; however, the HT study

area had a higher proportion of privately owned land and grass/shrubland than either the EP or GVM areas. Based on empirical studies of local mule deer movement patterns (Conner and Miller 2004), there was minimal range overlap between the HT and EV subpopulations and essentially no overlap between either of these and the GVM subpopulation. Winter range sizes (~10 km^2 for individuals; ~100 km^2 for population units) were similar for these three subpopulations, but migratory behavior differed somewhat among them: about half of the EP and GVM subpopulations migrated seasonally to high-elevation summer ranges, while only ~20% of the HT deer migrated seasonally (Conner and Miller 2004).

I chose these sites because they were typical of rapidly growing development patterns found in historic mule deer habitat in north central Colorado where housing developments perforate the landscape (Theobald 2003). Each of the three study sites consisted of a developed zone nested within a larger undeveloped portion of the landscape (Figure 1). I separated land use into developed and undeveloped categories based on a housing density map (Theobald 2001, Theobald and Kneeland 2002). "Developed" zones were defined as having $\geq$ 1 dwelling per 20 acres, and "undeveloped" zones were remaining areas with < 1 dwelling per 20 acres. These zones were defined so that developed areas contained dense-urban, urban, and suburban housing density classes and undeveloped areas contained rural housing density classes (Theobald 2001). I limited the analysis to 2 categories because I was concerned that including more categories would increase the likelihood that home ranges of individual deer included more than one development type. In the remainder of this paper, I use the terms "developed" and "urban" interchangeably when referring to that land use class, and the

deer that were sampled from it, and the terms "undeveloped" and "non-urban" when referring to the other land use class and the deer sampled from it.

Data collection

During 1997-2002, the Colorado Division of Wildlife (CDOW) collected geo-referenced data on presence/absence of CWD infection in individual deer sampled from urban and non-urban areas in conjunction with ongoing surveillance. Survey and diagnostic methods have been described in detail elsewhere (Miller et al. 2000, Miller and Williams 2002, Wolfe et al. 2002, Hibler et al. 2003); sampled deer were classified as CWD-infected or uninfected based on immunohistochemistry of retropharyngeal lymph node or tonsil tissue (Miller and Williams 2002). All samples were geo-referenced using either a global positioning system unit or by identifying sampled locations on standardized maps. I used a geographic information system to assign each deer sample location to a land use class (Fig. 1). Deer sampled in or within 1 km of core developed areas in each study site were categorized as "urban" deer; deer sampled >1 km from developed areas were categorized as "non-urban" deer. I chose to use the binary classification of deer as being from either urban or non-urban areas, rather than the use of a continuous variable such as "distance to urbanization". Because land use practices within these two categories are distinctly different from one another (e.g., hunting is typically not permitted in "urban" areas), biologically it makes more sense to consider differences in disease prevalence between deer sampled from urban and non-urban areas, rather than as a function of distance from urban center. I labeled deer as being urban if they were nominally located 1 km beyond the developed boundary for two reasons. First, I wanted to reduce mapping errors associated with deer sampled near the boundary

between developed and undeveloped zones. Second, although deer sampled in developed zones undoubtedly spent time in these areas, some deer residing in developed zones also may spend time in the periphery of these areas, where they could have been sampled. Non-urban deer were sampled from locations > 1 km beyond the developed zone perimeter by using concentric rings extending out from the developed land use class in ½ kilometer increments (Fig. 2) until I obtained a sample size of non-urban deer that was similar to the number of urban deer collected from the corresponding developed zone at each study site. Small pockets of developed land that occurred within the matrix of undeveloped land were excluded from the analysis to minimize confounding effects.

Formulation of competing models

I evaluated support for competing models portraying the relationship between CWD prevalence and the three variables of interest: land use type, sex, and study site. I included these variables because 1) increasing development will likely increase deer density at local scales and reduce hunting mortality 2) previous observations (Wolfe et al. 2002) suggested that higher CWD prevalence may occur in developed locations, 3) male mule deer have been observed to have higher prevalence than females (Miller and Conner 2004, Wolfe et al. 2004), and 4) previous observations have revealed substantial local variation in prevalence across large geographic areas (Miller et al. 2000, Conner and Miller 2004). To assess the contribution made by each of these variables to predicting observed CWD prevalence, I developed a suite of 16 candidate models that incorporated these variables in different combinations. My primary hypothesis was that higher prevalence would be associated with developed areas as compared to nearby undeveloped areas. All models containing a land-use effect were represented by the

binary covariate "Use" indicating whether a deer was sampled from the developed or undeveloped land-use class. The influence of gender was coded as "Sex" in candidate models; similarly, site level effects were coded as EP, GVM, and HT to represent site effects considered alone or in various combinations. Based on differences in infection rates between males and females apparent from initial analyses, I separated the data by gender and developed candidate sets of models for each sex to investigate how the relative influence of land use and site effects on CWD prevalence differed between males and females. I determined relative support in the data for candidate models to assess the influence of each variable, both alone and in the presence of the other variables, on CWD prevalence.

Model selection

I used likelihood-based methods and information theoretics (Akaike's information criterion; AIC) (Burnham and Anderson 2002)to quantify the strength of evidence for alternative models and to estimate their parameters. Specifically, I used AIC adjusted for sample size (AIC_c) to assess the relative information content of the models. Because model parameters were estimated based on data, there was some uncertainty that the "best" model would emerge as superior if different data were used to compare alternatives. I quantified this uncertainty with Akaike weights, w_r (Burnham and Anderson 2002) ; in the context of this analyses, I regarded normalized w_r as "probabilities" that the estimated model r was the best Kullback-Leibler model for the data at hand, given the set of models considered (Burnham and Anderson 2002). The w_r can be used to estimate the likelihood of the model, given the data, and in so doing offer a way to compare the relative weight of evidence for each model considered.

All models contained only additive effects, with maximum likelihood estimates, confidence intervals on model parameters, and AIC_c values obtained through logistic regression model fitting using SAS PROC GENMOD (SAS 2000).

RESULTS

Of the 16 candidate models fit to the entire data set, the top two models (Table 1.1) suggested that sex, land use, and site effects all were important predictors of CWD prevalence. The combined w_r for the top two models indicated a 90% probability that the best approximating model for the field data contained all three covariates as additive effects, with the other 14 models sharing the remaining 10% of the support. Estimates of slope terms from the top model suggested that deer in developed areas were almost twice as likely to test positive for CWD than deer in undeveloped areas (odds ratio = 1.98, p = 0.011, 95% C.I. = 1.17, 3.34), and that males were nearly 2.5 times more likely to be infected than females (odds ratio = 2.35, p = 0.001, 95% C.I. = 1.39, 3.97). Deer sampled from the EP site were approximately one-fourth as likely to be infected with CWD as those sampled from the HT site (odds ratio = 0.27, $p < 0.001$, 95% C.I. = 0.14, 0.51) and deer from the GVM site were about one-half as likely to be infected as deer in the HT site (odds ratio = 0.55, p = 0.062, 95% C.I = 0.30, 1.03), although this comparison was not highly significant given a confidence interval coverage that included 1.00.

Modeling sexes separately (Tables 1.2 and 1.3) offered additional insight into the relative influences of land use and site-specific effects on CWD prevalence. Summing w_r values for the top male-only models (first two models in Table 1.2), each of which included both the EP site and land-use effects, showed that these models captured 75% of the total weight of evidence. Because I wished to account for model selection uncertainty

(Burnham and Anderson 2002) in the estimates of the effect of urban land use on CWD prevalence for each sex, I averaged the estimates of this effect across all models that included it. Based on the model averaged estimates, males in developed areas were more than twice as likely to be infected as males sampled from undeveloped areas (odds ratio = 2.27, 95% C.I. = 1.17, 4.42). Males in the EP site had approximately one-third the probability of testing positive for CWD relative to those at the HT site (odds ratio = 0.35, p = 0.011, 95% C.I. = 0.16, 0.78). When the EP and land use effect were uncoupled (last six models in Table 2) in male-only models, the support in the data diminished; for the next best model, w_r = 0.08 (Table 1.2).

The top four female-only models (Table 1.3) encompassed 95% of the support in the data with the EP covariate present in each of these models. Unlike the top male-only models, the EP and land-use effects did not always appear together in the top female-only models (first four models in Table 1.3), with the land-use effect appearing in two of the top four models. Based on model averaged estimates of the effect of land use on prevalence for the female-only models, female deer in developed areas showed a relatively insignificant difference in the probability of testing positive for CWD compared to females in undeveloped settings (odds ratio = 1.73, 95% C.I. = 0.75, 3.99). In the top female-only model containing an EP effect, I observed a more pronounced effect of site, with females sampled from the EP site being approximately one-sixth as likely to be infected as females sampled at the HT site (odds ratio = 0.17, p = 0.002, 95% C.I. = 0.05, 0.53). Overall, the site effect appeared to be the most informative predictor of CWD prevalence in females, while both land use and site effects contributed almost equally as predictors of prevalence in males.

DISCUSSION

CWD in north-central Colorado occurs in an environment undergoing marked human-induced changes (Hansen et al. 2002). The human population in this region grew by 68% during the last two decades, making it one of the fastest growing in the United States (Baron et al. 2000). Expanding human habitation has altered land cover as landscapes have been developed. These alterations in land use and land cover, in turn, have changed the amount and configuration of wildlife habitat in this region (Theobald et al. 1997), including specific habitats used by mule deer. My work suggests that changes in land use and land cover may play a role in spatial and temporal dynamics of CWD in mule deer.

Land use effects

Prevalence of CWD in deer sampled from developed areas was almost twice as high as prevalence in undeveloped areas (about 10% versus 6%), and models that included land use tended to be strongly support by the field data (Tables 1.1–1.3). Land use modifications that accelerate contact rates with the infectious agent might account for observed differences in prevalence between developed and undeveloped areas. Wolfe et al. (2002) suggested that higher prevalence observed in deer sampled from developed locations could be due to local factors such as artificial feeding around residences that concentrate deer at a few points on the landscape. Because CWD transmission can occur via exposure to infected animals or environments contaminated by excreta and carcasses from infected animals (Miller et al. 2004), changes in deer distribution or movements effected by human alteration of deer habitats could plausibly lead to higher local prevalence in developed areas. Consumable resources, including both vegetation and

artificial feed, are more likely to be replenished in urban areas than in non-urban areas, thereby allowing deer to meet foraging needs within smaller home ranges. It follows that land use effects may be more pronounced in populations where a higher proportion of deer are sedentary. Such a pattern is suggested in the data for female deer: land use effects appear to be most pronounced in the study area (HT) with the lowest seasonal migration rate (~16%; Conner and Miller 2004). Differences in the timing of data collection could have been partially responsible for observed differences in prevalence between land use types, but also may reflect underlying influences on CWD transmission: deer sampled in developed areas during the summer and early fall were more likely to be year-round residents than harvested deer sampled during the fall in undeveloped areas, and these year-round residents may have been subjected to greater exposure because their overall home ranges were smaller than those of migratory deer (Wolfe et al. 2002).

In addition to altering movements or habitat use, urbanized areas also may offer refuge from natural predators and human hunting, thereby allowing CWD-infected deer to survive and shed infectious agent longer than in areas where predators are more abundant. The relative paucity of predators in urban areas also could allow infected carcasses to persist longer in urban habitats.

Finally, elimination of suitable habitat by development might concentrate mule deer populations on smaller areas of undeveloped winter range, and in so doing, increase population density and accelerate transmission. All of these mechanisms could contribute to higher CWD prevalence in developed areas. Future work should focus on identifying which, if any of these mechanisms are responsible for the effects of land use I

observed.

Sex effects

Differences in CWD prevalence between sexes in the three study areas are consistent with patterns observed on a broader geographic scale throughout north-central Colorado (Miller and Conner 2005). Prevalence among male mule deer in this study was nearly twice as high as among females (about 10% versus 6%). Sex-specific analyses revealed that males sampled from developed locations were more than twice as likely to test positive for CWD as males in undeveloped settings, while females showed less difference between land use types. Model selection results also reflected this trend: support for land use effects on CWD prevalence was stronger in field data from males ($w_r = 0.84$) than from females ($w_r = 0.44$).

The relationship observed here between land use and sex effects may have arisen from differences in sex and age structure of mule deer populations in the two land use categories. Because CWD is always fatal (i.e., the infected class is an absorbing state), older age-classes will have more opportunity to be exposed to the infectious agent, and thus should exhibit higher prevalence. Comparisons of CWD prevalence among male and female deer (Miller et al. 2000) showed a pattern of increasing prevalence with age in both sexes, although this rise was much more dramatic in 4–6-year-old males than in females (Miller et al. 2000, Miller and Conner 2005). The mechanism driving this difference is unclear, but similarities to patterns observed in white-tailed deer (*O. virginianus*) infected with bovine tuberculosis (O'Brien et al. 2002) suggest that sex-specific social behavior may play an important role (Miller and Conner 2005). Hunting is virtually absent from developed areas, and in undeveloped areas hunting pressure on

male deer is much greater than on females. Consequently, land use may have had an additional effect on the composition of male herd segments in the study areas. Higher prevalence in male deer from urban areas could be a product of relatively light hunting pressure that preserves a larger proportion of middle-aged males than in more heavily hunted populations in undeveloped areas; because land use-associated differences in hunting pressure are smaller for females, this effect would be less evident among female subpopulations. It seems plausible that circumstances leading to differences in male mule deer subpopulations between developed and undeveloped areas could partially explain the patterns I observed. To test these biological hypotheses, data on age structures of mule deer residing in developed and undeveloped areas are needed, along with a better understanding of relationships between mule deer behavior and CWD exposure risk.

Site effects

Heterogeneous landscapes can give rise to spatial heterogeneity in disease prevalence (Barlow 1996). Observations of CWD prevalence across north-central Colorado show strong spatial heterogeneity (Miller et al. 2000), and the finer scale results are consistent with these observations. All of the supported models in this study included a site effect, with differences in prevalence among three study sites. Geographic heterogeneity in CWD prevalence may be structured in part by differences in the time since disease introduction (Miller et al. 2000), deer migration patterns (Conner and Miller 2004), demography (Miller and Conner 2005), harvest rates (Miller and Conner 2005), and habitat (this study) among infected mule deer subpopulations. Which factor or combination of factors gave rise to the differences observed among the three study areas

cannot be determined with certainty. The size, duration, and intensity of human development do differ somewhat among the GVM, HT, and EP areas, and these may have produced differential effects on deer habitats and deer use of altered habitats. Among females, differences in migration rates among these subpopulations (HT < EP or GVM; Conner and Miller 2004) may have contributed to observed site effects; among males, differences in harvest pressure (EP < HT < GVM) and resulting male age structure (Miller et al. 2000, Miller and Conner 2005) may have contributed. In addition, the "site" effect may have been influenced in part by sampling artifact associated with the EP study area: the undeveloped EP area covered a much larger geographic area then either the HT or GVM sites (Fig. 1), and EP had relatively imbalanced sampling between land use classes within each sex. Additional work will be needed to understand the interactions and relative importance of these various factors in affecting CWD prevalence across north-central Colorado.

MANAGEMENT IMPLICATIONS

Based on these findings, it appears that mule deer wintering in developed locations need to be included in control efforts intended to reduce overall CWD prevalence in north-central Colorado. Modification of land use practices and other human activities that foster congregation or sedentary behavior in urban mule deer populations could have beneficial effects on reducing opportunities for CWD transmission. Because urban areas may serve as refugia from hunting, alternative management strategies like the "test-and-cull" program under evaluation by the Colorado Division of Wildlife (Wolfe et al. 2004) may be necessary adjuncts to more traditional population management approaches (Williams et al. 2002) in such areas. A better

understanding of the specific features of urban landscapes that have the greatest potential influence on CWD transmission among mule deer should aid in further refining landscape-level control strategies.

CONCLUSIONS

I offer strong evidence that land use influences prevalence of CWD in north-central Colorado mule deer populations. Future work needs to resolve mechanisms responsible for the phenomena I observed, in particular the relative importance of land use on 1) frequency of local contact with infectious material, 2) difference in exposure due to differences in population sex and age structures and 3) mixing of subpopulations with different levels of prevalence.

LITERATURE CITED

Augustine, D. J. 1998. Modelling Chlamydia-Koala Interactions: Coexistence, Population Dynamics and Conservation Implications. Journal of Applied Ecology **35**:261-272.

Barlow, N. D. 1996. The ecology of wildlife disease control: Simple models revisited. Journal of Applied Ecology **33**:303-314.

Baron, J. S., D. M. Theobald, and D. B. Fagre. 2000. Management of land use conflicts in the United States Rocky Mountains. Mountain Research and Development **20**:24-27.

Burnham, K. P., and D. R. Anderson. 2002. Model selection and multimodel inference : a practical information-theoretic approach, 2nd edition. Springer, New York.

Conner, M. M., and M. W. Miller. 2004. Movement patterns and spatial epidemiology of a prion disease in mule deer population units. Ecological Applications **15**.

Crooks, K. R., and M. E. Soule. 1999. Mesopredator release and avifaunal extinctions in a fragmented system. Nature **400**:563-566.

Dale, V. H., S. Brown, R. A. Haeuber, N. T. Hobbs, N. Huntly, R. J. Naiman, W. E. Riebsame, M. G. Turner, and T. J. Valone. 2000. Ecological principles and guidelines for managing the use of land. Ecological Applications **10**:639-670.

Daszak, P., A. A. Cunningham, and A. D. Hyatt. 2001. Anthropogenic environmental change and the emergence of infectious diseases in wildlife. Acta Tropica **78**:103-116.

Dobson, A., and J. Foufopoulos. 2001. Emerging infectious pathogens of wildlife. Philosophical Transactions of the Royal Society of London Series B-Biological Sciences **356**:1001-1012.

Dobson, A., and M. Meagher. 1996. The population dynamics of brucellosis in the Yellowstone National Park. Ecology **77**:1026-1036.

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.

Hansen, A. J., R. Rasker, B. Maxwell, J. J. Rotella, J. D. Johnson, A. W. Parmenter, L. Langner, W. B. Cohen, R. L. Lawrence, and M. P. V. Kraska. 2002. Ecological causes and consequences of demographic change in the new west. Bioscience **52**:151-162.

Hibler, C. P., K. L. Wilson, T. R. Spraker, M. W. Miller, R. R. Zink, L. L. DeBuse, E. Andersen, D. Schweitzer, J. A. Kennedy, L. A. Baeten, J. E. Smeltzer, M. D. Salman, and B. E. Powers. 2003. Field validation and assessment of an enzyme-linked immunosorbent assay for detecting chronic wasting disease in mule deer

(Odocoileus hemionus), white-tailed deer (Odocoileus virginianus), and Rocky Mountain elk (Cervus elaphus nelsoni). Journal of Veterinary Diagnostic Investigation **15**:311-319.

McGarigal, K., and W. C. McComb. 1995. Relationships between landscape structure and breeding birds in the Oregon coast range. Ecological Monographs **65**:235-260.

Miller, M. W., and M. M. Conner. 2005. Epidemiology of chronic wasting disease in free ranging mule deer; spatial, temporal, and demographic influences on observed prevalence patterns. *in press* Journal of Wildlife Diseases

Miller, M. W., and E. S. Williams. 2002. Detection of PrPCWD in mule deer by immunohistochemistry of lymphoid tissues. Veterinary Record **151**:610-612.

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'Brien, D. J., S. M. Schmitt, J. S. Fierke, S. A. Hogle, S. R. Winterstein, T. M. Cooley, W. E. Moritz, K. L. Diegel, S. D. Fitzgerald, D. E. Berry, and J. B. Kaneene. 2002. Epidemiology of Mycobacterium bovis in free-ranging white-tailed deer, Michigan, USA, 1995-2000. Preventive Veterinary Medicine **54**:47-63.

SAS. 2000. SAS statistics users guide. *in*. SAS Institute, Cary, North Carolina, USA.

Theobald, D. M. 2000. Fragmentation by inholdings in exurban development. Pages 155-174 *in* F. W. S. R.L. Knight, S.W. Buskirk, W.H. Romme, and W.L. Baker, editor. Forest fragmentation in the southern Rocky Mountains. University Press of Colorado, Boulder, Colorado.

Theobald, D. M. 2001. Land use dynamics beyond the American urban fringe. Geographical Review **91**:544-564.

Theobald, D. M. 2003. Targeting conservation action through assessment of protection and exurban threats. Conservation Biology **17**:1624-1637.

Theobald, D. M., and M. Kneeland. 2002. Mapping housing density for prioritization of urban/forest wildfire hazards in Colorado. Unpublished Report, Natural Resources Ecology Lab, Colorado State University., Fort Collins.

Theobald, D. M., J. R. Miller, and N. T. Hobbs. 1997. Estimating the cumulative effects of development on wildlife habitat. Landscape and Urban Planning **39**:25-36.

Turner, M. G. 1989. Landscape ecology: the effect of pattern on process. Annual Review of Ecology and Systematics **20**:171-197.

Van Buskirk, J., and R. S. Ostfeld. 1995. Controlling Lyme disease by modifying the density and species composition of tick hosts. Ecological Applications **5**:1133-1140.

Van Buskirk, J., and R. S. Ostfeld. 1998. Habitat heterogeneity, dispersal, and local risk of exposure to Lyme disease. Ecological Applications **8**:365-378.

Wasserberg, G., Z. Abramsky, B. P. Kotler, R. S. Ostfeld, I. Yarom, and A. Warburg. 2003. Anthropogenic disturbances enhance occurrence of cutaneous leishmaniasis in Israel deserts: patterns and mechanisms. Ecological Applications **13**:868-881.

Wiens, J. A., J. T. Rotenberry, and B. Vanhorne. 1986. A Lesson in the Limitations of Field Experiments - Shrubsteppe Birds and Habitat Alteration. Ecology **67**:365-376.

Williams, E. S., and S. Young. 1992. Spongiform encephalopathies of Cervidae. Scientific and Technical Review Office of International Epizootics **11**:551-567.

Williams, E. S., and M. W. Miller. 2002. Chronic wasting disease in deer and elk in North America. O I E Revue Scientifique et Technique **21**:305-316.

Williams, E. S., and S. Young. 1980. Chronic Wasting Disease of Captive Mule Deer - Spongiform Encephalopathy. Journal of Wildlife Diseases **16**:89-98.

Williams, E. S., T. Yuill, M. Artois, J. Fischer, and S. A. Haigh. 2002. Emerging infectious diseases in wildlife. Scientific and Technical Review Office of International Epizootics **21**:139-157.

Wolfe, L. L., M. M. Conner, T. H. Baker, V. J. Dreitz, K. P. Burnham, E. S. Williams, N. T. Hobbs, and M. W. Miller. 2002. Evaluation of antemortem sampling to estimate chronic wasting disease prevalence in free-ranging mule deer. Journal of Wildlife Management **66**:564-573.

Wolfe, L. L., M. W. Miller, and E. S. Williams. 2004. Feasibility of "test and cull" as a strategy for managing chronic wasting disease in urban mule deer populations. Wildlife Society Bulletin **32**.

Table 1.1: Candidate sets of models used to understand the relative influence of covariates on the probability that an individual mule deer tested positive for CWD. Only the top five models are shown for clarity

Model (all deer)	K	Log-lik	ΔAICc	w_r
Sex Use EP GVM	5	-224.359	0.000	0.601
Sex Use EP	4	-226.063	1.385	0.301
Sex EP GVM	4	-227.742	4.743	0.056
Sex EP	3	-229.516	6.273	0.026
Use EP GVM	4	-229.581	8.420	0.009

1.2: Candidate set of models used to understand the relative influence of covariates on the probability that an individual male deer tested positive for CWD.

Model (males only)	K	Log-lik	ΔAICc	w_r
Use EP	3	-125.615	0.000	0.458
Use EP GVM	4	-125.026	0.863	0.297
Use	2	-128.343	3.425	0.083
EP	2	-128.530	3.800	0.068
EP GVM	3	-127.876	4.522	0.048
Use GVM	3	-128.155	5.080	0.036
Intercept	1	-131.891	8.501	0.007
GVM	2	-131.607	9.955	0.003

Table 1.3: Candidate set of models used to understand the relative influence of covariates on the probability that an individual female deer tested positive for CWD.

Model (females only)	K	Log-lik	ΔAICc	w_r
EP GVM	3	-99.580	0.000	0.288
Use EP GVM	4	-98.679	0.240	0.255
EP	2	-100.865	0.540	0.220
Use EP	3	-100.014	0.869	0.186
Intercept	1	-104.104	4.997	0.024
Use	2	-103.711	6.231	0.013
GVM	2	-103.999	6.808	0.010
Use GVM	3	-103.554	7.949	0.005

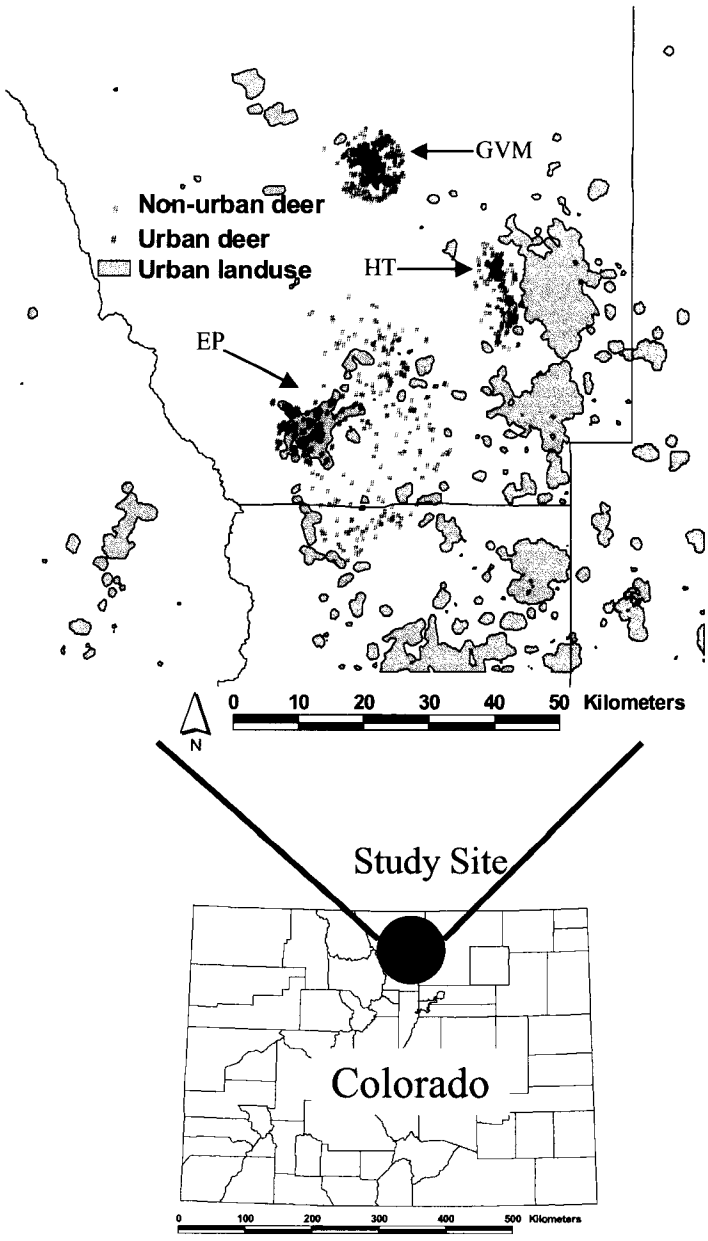

Figure 1.1. Locations of the three study sites, Estes Park (EP), Glacier View Meadows (GVM), and Horsetooth Reservoir (HT), in north-central Colorado.

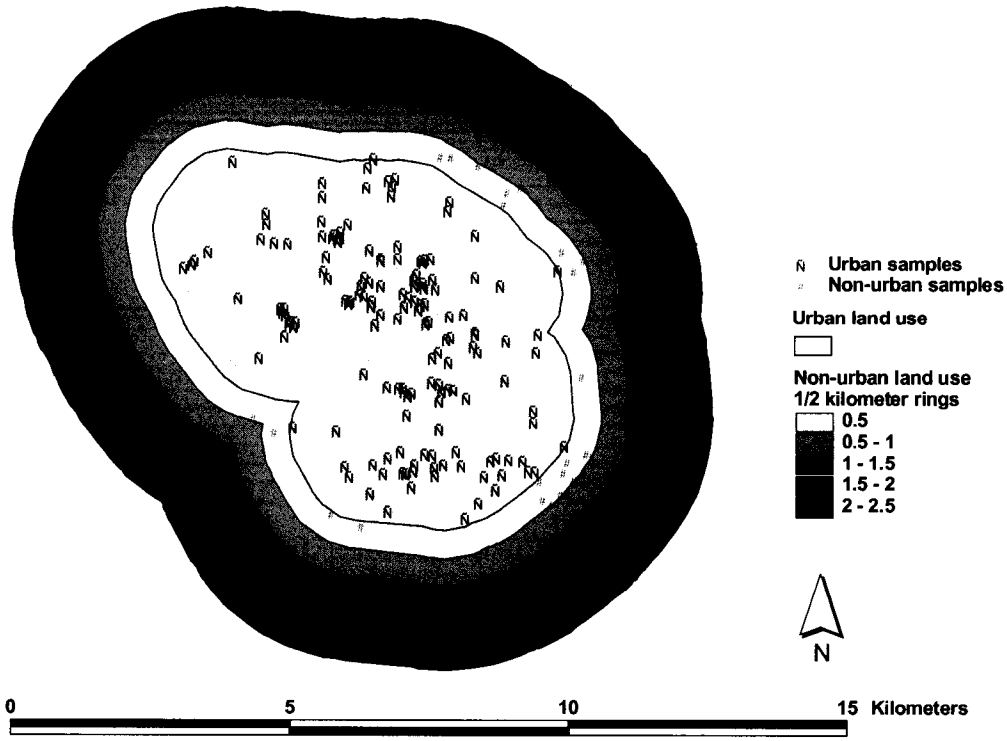

Figure 1.2. Mule deer samples for the GVM site, showing the area defined as "developed" along with the half-kilometer annuli used for allocating deer to "undeveloped" land use class.

LINKING MULE DEER MOVEMENT SCALES TO THE SPATIAL DISTRIBUTION OF CHRONIC WASTING DISEASE: A HIERARCHICAL BAYESIAN APPROACH

INTRODUCTION

Linking spatial patterns to the processes that generate them offers a fundamental challenge in contemporary ecology (Levin 1992, Sarnelle 1994, Pascual and Levin 1999). This problem is particularly difficult to solve when processes operate over large spatial and temporal scales. When this is the case, it is possible that emergent patterns reflect the outcome of processes operating at more than one, nested scale. Hierarchical models provide a natural, unified framework for comparing spatial and temporal processes that operate across a range of scales. Here, I use hierarchical modeling to investigate the spatial distribution of an emerging infectious disease of wildlife in North America.

Chronic wasting disease (CWD) (Williams and Young 1980), a prion disease of North American cervids, is the only prion disease known to occur in free-ranging populations (Williams and Miller 2002). The largest known outbreak occurs in a contiguous ~80,000 km^2 area of northeastern Colorado, southeastern Wyoming, and western Nebraska, USA (Williams 1992, Miller et al. 2000, Williams and Miller 2002). CWD may have been present in free-ranging deer within this area since the 1960s or

earlier (Miller et al. 2000). Although the infectious agent causing CWD is contagious in its natural setting (Williams and Young 1993, Miller and Williams 2003), relatively little is known about transmission mechanisms among infected mule deer populations (Williams and Miller 2002). Possible routes of transmission include animal-animal and animal-environment-animal pathways (Miller and Williams 2003, Miller et al. 2004). Recent discoveries of CWD foci distant to this 80,000 km^2 endemic area have spawned interest in understanding spatial and temporal dynamics in order to develop management strategies for controlling CWD in affected populations and prevent or slow its spread among unaffected populations.

The distribution of CWD in northeastern Colorado appears heterogeneous at both small (≤50 km^2) (Wolfe et al. 2002) and large (>38,000 km^2) (Miller et al. 2000) scales (fig. 1). Small-scale heterogeneity may result from highly localized contact processes, such as interactions among individuals within matrilineal groups, which are tightly clustered and patchily distributed across their winter home range (Conner and Miller 2004, Miller and Conner 2005). Recent investigations suggest that once the infectious agent is shed into the environment it may persist there for several years (Miller et al. 2004); consequently, large quantities of agent deposited in a relatively small geographic area could result in "hot-spots" of infection scattered across natural landscapes.

The process of mule deer movement in north-central Colorado can be divided into three categories, reflecting the geographic scales of seasonally dependent movement patterns (Conner and Miller 2004). At the largest scale, the summer subpopulation home range, mule deer home range sizes average approximately 310 km^2 and exhibit greater overlap (about 22%) than at any other time of year (Conner and Miller 2004). At the

winter subpopulation home range scale, deer live in larger groups with average home range size of approximately 80 km^2 and exhibit little overlap (<1%) among wintering groups (Conner and Miller 2004). Finally, individual mule deer have a characteristic home range size that averages about 9 km^2 during the winter when deer are more sedentary (Conner and Miller 2004).

High fidelity to seasonal use areas and temporally consistent movement patterns of subpopulations (Conner and Miller 2004), and presumably the resulting home range scales, suggest the importance of local, small-scale contact processes in structuring CWD spatial heterogeneity. At the same time, large-scale movement patterns, such as those that occur when subpopulations expand their home range between winter and summer locations, could result in a greater number of contacts among deer that do not interact during the winter months. If large-scale movement were primarily responsible for structuring the host-pathogen relationship, then the spatial distribution of infected deer should exhibit greater homogeneity at large geographic scales than would be expected if disease transmission occurs predominately at local winter subpopulation or individual movement scales. Heterogeneity in CWD prevalence also may result from different times since disease introduction into the various subpopulations (Miller et al. 2000); unfortunately, time since introduction will remain unknown for most or all infected subpopulations.

To understand the potential relative contribution of different movement scales to structuring observed spatial heterogeneity of CWD, I specified a set of candidate models reflecting the different scales, combinations of predictor variables, and spatial dependencies affecting the probability of CWD infection in individuals. I then used

contemporary model selection techniques to identify those scales and predictors corresponding best to the observed spatial structure of CWD infection across the landscape. In addition to gaining insights into the spatial epidemiology of CWD, I demonstrate how hierarchical modeling can be used to understand the relative contribution of hypothesized generating processes to observed patterns of disease prevalence.

Hierarchical models

Statistical models frequently include multiple parameters that can be regarded as related or connected in some manner by the structure of the problem, implying that a joint probability model for these parameters should reflect the dependence among them (Gelman et al. 2004). For example, consider a vector of infection probabilities, $\pi = (\pi_1 .. \pi_n)$, where π_j is the infection probability of the *jth* subpopulation. It might be biologically reasonable to expect that estimates of the π_j's may be related to one another since each π_j is a member of the same "super population". A hierarchical model provides a formal mechanism for describing these relationships. The model consists of a series of hierarchically connected strata, where some relationship connecting the strata can be specified. Thus, a hierarchical parameterization allows individuals within a group to be related at one level while the groups themselves are related at another level. In addition, the hierarchical model allows for between group comparisons, without the typical concerns about multiple comparisons. For example, if there were little evidence of variation between the sub-populations, then the estimates of π_j would be automatically shrunk towards one another. In essence, the hierarchical model structure allows the data to determine the necessary level of dependence among model parameters,

thus providing an objective analysis approach for determining the appropriate degree of smoothing towards or away from a common mean.

Recent advances in methods for data collection and analysis have increased the potential for study of natural populations distributed over geographic regions. The advent of remote sensing and geographic information systems allow collection of large quantities of high resolution, geo-referenced data on locations of individual organisms, as well as features of the landscape that may control their spatial distribution (Beck et al. 1994, Hay et al. 2000). At the same time, computer intensive methods such as Markov chain Monte Carlo have offered a feasible approach for analyzing these spatial data (Brooks 2003). It is now possible, for example, to estimate the joint distribution of a high dimensional parameter space that includes spatial dependency across scales, where classical models cannot (Wikle 2003). Hierarchical models are well suited for addressing questions regarding how individual-level responses change with the spatial context (Clark 2003). For disease modeling, hierarchical models allow investigation of how individual-level disease risk responds to population level processes operating across a range of spatial or temporal scales.

Although some studies of natural populations have examined correlations between the spatial distribution of disease and environmental variables (Van Buskirk and Ostfeld 1998, Giraudoux et al. 2003), and others have proposed biological explanations for the spatial patterns they observe (Jolles et al. 2002, Aylor 2003), few if any have identified the scales over which population level processes act to shape the spatial distribution of disease in wildlife populations. Hierarchical models provide a natural way to address this problem.

METHODS

Study Area

The study area included 6,500 km^2 in north-central Colorado (fig. 1) where CWD is endemic in free-ranging cervids (Miller et al. 2000). Elevation ranged from 1,500 m to 3,500 m, rising from east to west. The northeastern quarter of the study area, from Fort Collins north, was rolling foothills and high prairie where livestock grazing was the main land use. Vegetation was primarily sagebrush-steppe habitat with big sagebrush (*Artemesia tridentata*), antelope bitterbrush (*Purshia tridentata*), mountain mahogany (*Cercocarpus montanus*), and mixed grasses. The southeastern quarter of the study area, from Fort Collins south, consisted of urban centers separated by rural areas with numerous small ranches, agricultural fields, natural areas, and more scattered suburban areas. Vegetation communities in the western half of the study area followed the east-west elevation gradient. Lower elevations were mostly dense mountain mahogany interspersed with grassland openings and small patches of ponderosa pine (*Pinus ponderosa*) that transitioned to mountain shrub habitat with a primarily mixed conifer overstory at higher in elevations. The highest elevations were mainly alpine tundra habitat.

Data

The Colorado Division of Wildlife (CDOW) provided georeferenced data for 3,855 mule deer tested for CWD infection between 1997 and 2003 within the approximately 6,500 km^2 study area. All samples were geo-referenced using either a global positioning system unit or by identifying sample source locations on standardized maps. Sampling methods included deer that were killed by hunters, culled by wildlife

managers, or captured and tonsil biopsied; survey and diagnostic methods have been described in detail elsewhere (Miller et al. 2000, Miller and Williams 2002, Wolfe et al. 2002, Hibler et al. 2003). Sampled deer were classified as CWD positive or negative based on immunohistochemistry of retropharyngeal lymph node or tonsil tissue (Miller and Williams 2002). For the current analysis, I partitioned the study area into three grids, where each grid had a resolution representing one of the scales of mule deer movement; $9km^2$, $81km^2$, and $324km^2$ overlaid on the map of deer samples. Because CWD prevalence remained relatively constant within the study area between 1996 and 2001 (Miller et al. 2000, Miller and Conner 2005), I combined data across all years.

Along with locations, data on sex and age class (juvenile or adult), which are known to influence infection probability (Miller and Conner 2005), were recorded for each deer. In addition to these individual-level demographic (Demo) covariates offsets, three environmental (Env) covariates were calculated using a geographic information system containing data grids representing land ownership and vegetation patterns across the study area at a 90-meter resolution. The covariate values were simple measures of proportions and landscape configuration, as described below, calculated for each of the three movement scales used in the model. Each environmental covariate was assumed to exert the same influence on all individuals sampled from the same grid cell. Thus, these covariates were scaled to the map resolution considered in each model.

There is evidence of anthropogenic influences on CWD prevalence in mule deer (Wolfe et al. 2002, Farnsworth et al. 2005); consequently, I considered an environmental covariate, %PRIV, that represented the proportion of private land in a grid-cell. Because not only the proportion of private land but also its configuration may be important, I

developed a second environmental covariate, DISP, which was a landscape index measuring the degree of patchiness and isolation of each patch of private land within a grid-cell (McGarigal and Marks 1995). A final environmental covariate, %HAB, measuring the proportion of low-elevation grassland habitat in each grid cell, was used to represent the amount of wintering habitat to capture the potential influence of deer winter range concentration on CWD prevalence.

Hierarchical model of CWD infection

Two aspects of the data made it difficult to relate movement scales to CWD infection probability. First, mule deer wintering subpopulation distributions had been delineated for only about 12% of the study area (Conner and Miller 2004). Although data on movement patterns were unavailable across much of the area, I wanted to use information from previous research where available to shed light on potential transmission scales. Second, since deer were only sampled for CWD one time and their movement was not followed over time, there was no way to incorporate estimates of the area traversed by an individual deer before it was sampled. I addressed these challenges by partitioning the study region into aerial units (i.e., grid cells) reflecting the various scales of seasonally dependent mule deer movement patterns. This specification allowed me to compare different movement scales in the face of limited information on the spatial structure of this process across the study area. The hierarchical structure accommodated uncertainties in the point-based CWD data by treating all individuals sampled from within the same grid cell as having an identical exposure risk to the infectious agent after adjusting for individual-level sex and age effects.

I consider a generalized linear model for disease presence/absence. For each individual deer, I model the probability of being CWD-positive as a function of the covariates and two random effect terms, which account for any unobserved covariates as well as the spatial pattern in the probability of disease presence.

This generalized linear model can be described in three stages: the data model, or likelihood linking the data to the model parameters; the process model relating the covariates and random effects to the parameters, and the prior distributions for all model parameters (Wikle 2003). My interest focused on the distribution of the process and parameters after being informed by the data. To arrive at this posterior distribution, I used Bayes theorem:

$$f(\text{process, parameters}|\text{data}) \propto f(\text{data}|\text{ process, parameters}) \times f(\text{process}|\text{ parameters}) f(\text{parameters}) \quad (1)$$

where $f(x_1)$ denotes the probability distribution of x_1 and $f(x_1|x_2)$ is the conditional distribution of x_1 given x_2. The posterior distribution is simple to understand in terms of basic probability, but it can be difficult to derive in closed form. For many ecological problems, the high dimensionality of the model can prohibit the use of standard methods. However, Markov Chain Monte Carlo (MCMC) (Geman and Geman 1984, Gelfand and Smith 1990, Gilks et al. 1998) techniques allowed me to estimate the posterior distribution in (1).

Data model

The data model relates the known infection status for each deer to the probability of infection. Let Y_{ij} be the known infection status for deer $i = 1,\ldots,n$ in cell $j = 1,\ldots,k$. Then let infection status be Bernoulli distributed with parameter π_{ij}:

$$Y_{ij} \mid \pi_{ij} \sim \text{Bernoulli}(\pi_{ij}), \qquad (2)$$

where π_{ij} is the probability of infection for individual i in cell j. All observations are assumed conditionally independent given this parameter.

Process model

The process component of the model relates the probability of infection for each deer, π_{ij}, to the individual and environmental covariates. I include two random effect terms to account for variability that is not accounted for by the covariates. To constrain the Bernoulli distributed infection probability to the range 0-1, I use a standard logit transform. Thus I model the probability that an individual is infected as:

$$\text{logit}(\pi_{ij}) = \mu + x_{ij}^T \beta + \gamma_j + \delta_j, \qquad (3)$$

where μ was the background infection rate- common to all deer, β was an m x 1 vector of regression coefficients corresponding to the x_{ij}^T, the transpose of the m x 1 vector of individual and scale-dependent environmental covariates associated with each deer; γ_j was the scale-dependent spatial random effect term for the jth grid cell; and δ_j was the independent random effect term associated with the jth grid cell. The independent random effects varied with the scale of analysis, but exhibited no spatial dependency. The random effect terms are described further below.

Prior and posterior distributions

Because the analysis is fully Bayesian, prior distributions for all model parameters in the hierarchy are specified. The spatial component, modeled by γ_j, is a key parameter of interest because it models the latent, or unobserved, process of mule deer movement.

Recall that γ_j is the extra variation not accounted for by the covariates in grid cell j. I specify the spatially structured variation in infection probability, γ_j, via an Intrinsic Gaussian Conditional Autoregressive (ICAR) model (Besag et al. 1991). For a grid cell j in the problem, the ICAR model states that γ_j is related to the γ terms for the neighboring grid cells; and, given the γ terms for the neighboring grid cells, each grid cell is independent of all other grid cells outside the local neighborhood. Specifically, let the set of neighbors contributing to γ_j be denoted by γ_{j+}. Then, for each grid cell j, I assume the conditional relationship

$$\gamma_j \,|\, \gamma_{j+} \sim \text{Normal}\left(\frac{1}{n_{j+}}\sum \gamma_{j+}, \frac{\sigma_\gamma^2}{n_{j+}}\right) \qquad (4)$$

where n_{j+} is the number of neighbors of grid cell j and σ_γ^2 is the variance for all grid cells. Thus the conditional mean of γ_j is simply the average value of its neighbors γ_{j+}, with conditional variance σ_γ^2 proportional to the number of neighbors. In the conditional mean in (4), the neighboring grid cells are equally weighted so that all neighbors of cell j influence it equally. Spatial variation in the model is limited to cells sharing a border; however there are no *a priori* restrictions on specifying the neighborhood structure or cell weights. I use second-order neighborhoods, meaning only cells sharing a border with the focal cell are considered in modeling spatial dependency, because I wish to maintain a sharp distinction between local dependency and global unstructured heterogeneity, which becomes increasingly blurred as the local neighborhood is extended.

The unstructured heterogeneity term, δ_j, corresponds to a latent process operating independently in each grid cell at the chosen scale (e.g., home range scale). I

let $\delta_j \sim i.i.d.\ N(0, \sigma_\delta^2 \mathbf{I})$ for $j = 1,\ldots, J$. This component models the overall, unstructured heterogeneity in the data by assuming no relationship among neighboring grid cells, but with a variance that was common to all grid cells. In the following section I describe the parameter values for the probability distributions governing the behavior of each of the process model components.

The following distributions applied to the remaining model parameters: baseline disease risk, $\mu \sim$ flat() and normalized covariates $\beta \sim N(0, \sigma_\beta^2 \mathrm{I})$ where I is the indicator matrix. In addition, I specified non-informative hyperparameter distributions for all the variance parameters: $\sigma^2 \sim Uniform(0,10)$ for σ_β^2, σ_γ^2 and σ_δ^2. Note that $\mu \sim$ flat() corresponds to an improper (flat) prior on the whole real line. This prior distribution, along with a sum-to-zero constraint placed on the spatial random effects, is necessary to assure identifiability because the model contains ICAR random effects (Besag and Kooperberg 1995). These restrictions result from defining the spatial random effect component conditionally rather than jointly. I considered a final quantity, $\lambda = \frac{\sigma_\gamma^2}{\sigma_\gamma^2 + \sigma_\delta^2}$, which measured the contribution from the spatial random effect component of variance to the overall variance due to the random effects. This parameter allowed me to understand the relative contributions of spatially structured and unstructured variation in models containing both.

Finally, the joint posterior distribution of all model parameters given the field data was fit at the three scales of interest (grid cells of 9 km^2, 81 km^2, and 324 km^2) for various combinations of predictors selected *a priori*. Thus, the models contained various combinations of demographic (Demo), environmental (Env), spatially structured (Space),

and unstructured (Het) variation. All models were fit using WinBUGS software (Speigelhalter et al. 2002). The MCMC procedure for these models was run for 50,000 iterations after a burn-in period of 500,000 iterations to ensure convergence of all model parameters.

Model comparisons

I used a Deviance Information Criteria (DIC), a generalization of the Akaike Information Criteria (AIC), to compare the set of candidate models (Spiegelhalter et al. 2002). These criteria are based on the deviance, $D(\theta) = -2\ln L$, where L is the likelihood and θ is the vector of model parameters, and a penalty for model complexity. For AIC, the penalty is two times the number of parameters in the model. The complexity of a hierarchical model is measured by the effective number of parameters, p_D, which is often smaller than the total number of parameters due to the borrowing of strength property of hierarchical models described earlier. This complexity is defined as $p_D = \overline{D(\theta)} - D(\bar{\theta})$, where $\overline{D(\theta)}$ is the expected deviance over the posterior distribution of parameter vector θ taken across all MCMC samples, and $D(\bar{\theta})$ is the deviance evaluated at the posterior mean of the parameter vector. Finally, $\mathrm{DIC} = \overline{D(\theta)} + p_D = 2\overline{D(\theta)} - D(\bar{\theta})$. Smaller values of DIC indicate a better-fitting model. As with other penalized likelihood criteria, DIC is a method for comparing a collection of alternative models (Carlin and Louis 2000).

Burnham and Anderson (2002) derived Akaike weights that, when normalized, can be interpreted as a set of weights that sum to one and estimate the probability that model r is the best Kullback-Leibler model for the data at hand, given the set of models considered. This approach provides a method for assessing model selection uncertainty.

It has been suggested as an analogous approach for estimating model selection uncertainty within a Bayesian modeling context (Spiegelhalter et al. 2002). I used DIC weights (w_{DIC}) to estimate model selection uncertainty for each model r in the candidate set, calculated using the formula for Akaike weights

$$w_{DIC} = \frac{\exp(-\frac{1}{2}\Delta DIC)}{\sum \exp(-\frac{1}{2}\Delta DIC)} \quad (5)$$

where ΔDIC was the difference between the minimum DIC value in the candidate set and model r, and the denominator was the sum over all models in the set under consideration. The DIC weights are an informal measure and allow easier comparison between models than the DIC value itself.

RESULTS

The analyses revealed strong support for local influences on observed spatial patterns of CWD prevalence in mule deer. For clarity, only results for the top 10 out of 22 models fit are shown in Table 2.1. Based on the w_{DIC} shown in Table 1, the individual home range scale of 9 km^2 is the only one that merits consideration as the process scale corresponding to the spatial structure of the CWD data. The combined weights for Models 1-4 (Table 2.1), $w_{DIC} = 0.997$, indicated nearly exclusive support for models at the individual-home range scale. Within this set, Models 1 and 2 did not contain any environmental covariates, although all four contained a spatial random effect for estimating the probability of CWD infection.

Table 2.2 shows the posterior means, standard deviations, and 95% credible intervals, all on the logit scale, for the univariate parameters from Models 1 and 3. The individual-level offsets of SEX and AGE, which were known a priori to be important predictors of CWD infection probability, show that infection probability is higher in

males (odds-ratio = 2.04, 95% C.I. = 1.57, 2.65) and in animals at least 2 years old (odds-ratio = 3.46, 95% C.I. = 2.16, 5.75). Estimates of environmental covariate effects from Model 3 show that only %PRIV significantly influenced infection probability (odds-ratio = 2.17, 95% C.I. = 1.14, 4.10), however its credible intervals appear relatively wide, reflecting a high degree of uncertainty in this estimate.

Lambda (λ), which is the ratio of spatial to unstructured variability, was 0.88 with a 95% credible interval ranging from 0.71 to 0.99 for Model 1. Thus, across the landscape, the spatial random effect accounted for between 71% and 99% of the variability attributed to the random effects in that model, strengthening the argument that the contact process resulting in landscape-scaled disease heterogeneity is local in nature; influenced more by small-scale spatial structure than by overall unstructured heterogeneity. These results make sense considering that across the entire study area CWD prevalence was about 9% for all deer sampled, making overall infection probabilities relatively low. However, within a single 9 km^2 aerial unit, prevalence rates were estimated as high as 35%, emphasizing that locally dependent processes scale with the spatial distribution CWD infection.

The weight of evidence for the top model, containing both spatially structured and unstructured heterogeneity was relatively high at 0.88. Examination of p_D provides insight into the contribution made by both sources of heterogeneity to model fit. A decrease in p_D of two in Model 1 compared to Model 2, which did not contain unstructured heterogeneity effects and which had a w_{DIC} of approximately 0.08, illustrates the counterintuitive nature of hierarchical analysis; adding random effect terms can reduce the number of effective parameters in a model. It is likely that this reduction

occurred because including unstructured heterogeneity reduced the range of variability necessary for modeling local spatial structure in the top model. Because these two random effects are not uniquely identifiable, it is not possible to measure the number of effective parameters contributed by each. However, the high w_{DIC} value and reduced p_D for the top model relative to the second best model, suggests that the unstructured heterogeneity has "shrunk" the spatial random effect towards an overall mean, thus reducing the number of effective parameters in the model

A visual comparison (Figs. 2.1 and 2.2) of the top model without environmental effects (Model 1 in Table 2.1) to the best model that included them (Model 4 in Table 2.1), shows that Model 1 had a more concentrated distribution of spatial random effects across the landscape, while Model 4, which contained these covariates, had a more diffuse distribution and lower overall intensity for the spatial random effects. It is not surprising that including environmental covariates in the model has diminished the strength of the local spatial process. This effect can be demonstrated quantitatively by examining the difference in the number of effective parameters, p_D, between the top models with and without this effect (Table 2.1). Adding the three environmental covariates, each contributing a single parameter, to the top model reduces p_D by more than 25 in the resulting second best model. This reduction in p_D with the addition of three covariate parameters occurred because including the environmental covariates reduced the effective number of parameters necessary for modeling the spatial variation in CWD infection probability. By "shrinking" the variability in the spatial random effect towards an overall mean effect, the intensity of the local spatial process component of variation was diminished, suggesting the usefulness of the environmental covariates. For

models that included the landscape covariates, the spatial random effects had 95% credible intervals that overlapped zero for all grid cells, while models without environmental covariates had spatial random effects that were significantly different from zero for 11% of the grid cells. However, the environmental covariates produced a poorer fitting model that was less consistent with the observed spatial distribution of CWD, as measured by DIC.

DISCUSSION

An important first step towards understanding host-pathogen dynamics in spatially structured populations is to understand the scales over which population processes and landscape features shape the host-pathogen relationship. The dynamics of CWD transmission in mule deer are potentially structured by interactions that occur across a range of nested spatial scales in a heterogeneous environment (Miller et al. 2000). Unfortunately, little empirical data exist for relating transmission dynamics, and the resulting spatial distribution of CWD infection, to the scales of seasonal movements that likely help shape observed prevalence patterns. Previous research on the ecology of CWD in mule deer populations identified plausible natural transmission mechanisms (Miller et al. 2004), as well as apparent influences of demography (Miller and Conner 2005), seasonal movement patterns (Conner and Miller 2004), and land use (Farnsworth et al. 2005) on spatial epidemiology; however, quantitative analyses comparing potential movement scales structuring the spatial distribution of CWD have not been addressed until now.

The results of this study provide evidence that the spatial structure of CWD results from small-scale, local contact processes, which likely occur primarily during the

winter season when subpopulation home ranges are reduced in size and the potential for infectious contacts among sympatric individuals is possibly increased (Miller and Williams 2003, Conner and Miller 2004, Miller and Conner 2005, Miller et al. 2004). The key to arriving at this conclusion was the use of information about the scales over which the structuring process of movement occurs. Because I specified analysis scales to correspond to the crucial epidemiological process of seasonal movements, I was able to better understand which type of movement pattern (wintering individual, winter subpopulation, or summer subpopulation) appears to be the most plausible process scale underlying observed spatial patterns of CWD prevalence. This result, in turn, provides critical information for further process-based investigations. This work demonstrates how scientific hypotheses regarding potential generating processes can be tested even in the face of sparse empirical data. Enumerating the relative contributions from each of these process scales was made possible by the hierarchical modeling framework.

There are biological explanations for the effects of covariates that emerged as important influences on CWD infection probability. Because the clinical course of CWD is protracted, lasting about two years on average (Williams and Miller 2002), I expected an effect of age such that animals older than two years were more likely to test positive for CWD (Miller et al. 2000, Miller and Conner 2005); this highly significant effect is reflected by the models. Private land ownership and developed areas of the landscape often restrict hunter access to deer populations and may encourage their use as refugia (Farnsworth et al. 2005); this restriction possibly leads to populations with larger numbers of males and an older age distribution, both of which are associated with an elevated probability of infection (Miller and Conner 2005). Also, because CWD

transmission can occur via exposure to infected animals or environments contaminated by excreta and carcasses from infected animals (Miller et al. 2004), changes in deer distribution or movements effected by land ownership patterns and human alteration of deer habitats could possibly lead to higher local prevalence in these areas (Wolfe et al. 2002, Farnsworth et al. 2005). The sex effect, per se, is more difficult to explain, but could be due to the polygamous mating structure of deer populations combined with effects of predominantly male hunting (Miller and Conner 2005); in this situation, a sex ratio skewed toward females coupled with the polygamous mating system in which individual males contact groups of females may act to increase the contact rate of males relative to females, thereby increasing their probability of infection.

My research differs fundamentally from previous pattern-based analyses used in the few wildlife landscape epidemiological investigations that have been undertaken to date. Unlike other studies, I incorporated both host endogenous correlates (sex and age) of the disease and exogenous features of the environment thought *a priori* to be important predictors of CWD spatial heterogeneity. More importantly, by formulating my approach in terms of a hierarchical model I was able to simultaneously consider the contributions made by these covariates as well as from local spatial structure and overall landscape heterogeneity to the risk of disease occurrence at each of the three movement scales.

Unlike earlier landscape epidemiological investigations in natural systems, I show how an exploration of disease patterns across multiple, process-based, spatial scales can lead to important epidemiological inference regarding plausible biological scales and mechanisms of disease spread. This provides a spatial perspective for further research into the etiology of disease. To fully understand the interrelationship between host,

pathogen, and environment requires in-depth knowledge about host population dynamics and movement patterns, disease etiology, interactions between host and pathogen, and the effects of environmental variation on host and pathogen distributions and dynamics. Achieving this level of understanding requires process-based, biological investigations, informed by statistical analyses that identify relevant scales and correlations among the system's components.

The hierarchical method I have demonstrated provides a powerful approach for a difficult problem in ecology; linking spatial patterns to the scales over which generating processes operate. By maintaining a constant data structure at the lowest (e.g., individual) level in the hierarchy, while varying the scale of the spatial process component of the model, a hierarchical approach allows for direct comparisons of the effect of various process scales on the spatial structure of host-pathogen relationships. In contrast, classical approaches to multi-scaled spatial analysis can suffer from what is known as ecological fallacy; where inference at one level is based on data collected at a different level (Schwartz 1994, Diez-Roux 1998). Ecological fallacy frequently occurs when the data structure is altered to accommodate multiple scales of analysis, obviating any direct comparison of how different process scales are related to the spatial structure of disease.

My approach is applicable to many ecological questions where georeferenced data are available; for example presence/absence data or counts of individuals that can be tied to specific locations on the landscape. Further, although the data were in the form of discrete individuals, the hierarchical model structure is readily applied to continuous spatial processes such as the distribution of nutrients in soils or hydrologic systems.

Thus, the generality of this approach is applicable across a wide range of ecological questions framed within a spatial context.

Within the Bayesian paradigm there are numerous possible ways to examine the hierarchical model results, and these estimates are accompanied by standard error that provide for a complete assessment of model uncertainty. For example, in addition to the results considered here, I can construct maps of the mean and standard deviation of cell-level prevalence over the landscape to obtain an aerial estimate of disease prevalence, I can also compare the posterior distribution of disease prevalence over a larger region such as the management units that are used in developing strategies for managing the disease. With additional analysis, I can also compare the spatial cumulative distribution function (Lahiri et al. 1999) for prevalence for two or more regions to determine which areas have the greatest concentration of CWD infected deer.

Determining the processes that give rise to patterns in nature is difficult in any ecological system. This problem is particularly challenging when we seek to understand processes that act over large geographical or temporal scales. In such cases, data are often limited, and several plausible mechanisms can be identified as potential causes for observed patterns -- consequently, it is not always clear how to proceed with testing scientific hypotheses about generating mechanisms. By casting hypotheses regarding scale-dependent processes in terms of models that can be quantitatively compared, hierarchical analyses provide a powerful tool for gaining insight in this context, even when data are limited.

LITERATURE CITED

Aylor, D. E. 2003. Spread of plant disease on a continental scale: Role of aerial dispersal of pathogens. Ecology **84:**1989-1997.

Beck, L. R., M. H. Rodriguez, S. W. Dister, A. D. Rodriguez, E. Rejmankova, A. Ulloa, R. A. Meza, D. R. Roberts, J. F. Paris, M. A. Spanner, R. K. Washino, C. Hacker, and L. J. Legters. 1994. Remote-Sensing as a Landscape Epidemiologic Tool to Identify Villages at High-Risk for Malaria Transmission. American Journal of Tropical Medicine and Hygiene **51**:271-280

Besag, J., and C. Kooperberg. 1995. On conditional and intrinsic autoregressions. Biometrika **82**:733-746.

Besag, J., J. York, and A. Mollie. 1991. Bayesian Image-Restoration, with 2 Applications in Spatial Statistics. Annals of the Institute of Statistical Mathematics **43**:1-20.

Brooks, S. P. 2003. Bayesian computation: a statistical revolution. Philosophical Transactions of the Royal Society of London Series a-Mathematical Physical and Engineering Sciences **361**:2681-2697

Carlin, B. P., and T. A. Louis. 2000. Bayes and Empirical Bayes methods for data analysis. Chapman & Hall/CRC, Boca Raton, Florida, USA.

Clark, J. S. 2003. Uncertainty and variability in demography and population growth: A hierarchical approach. Ecology **84**:1370-1381.

Conner, M. M., and M. W. Miller. 2004. Movement patterns and spatial epidemiology of a prion disease in mule deer population units. Ecological Applications **15**.

Diez-Roux, A. V. 1998. Bringing context back into epidemiology: Variables and fallacies in multilevel analysis. American Journal of Public Health **88**:216-222.

Farnsworth, M. L., L. L. Wolfe, N. T. Hobbs, K. P. Burnham, E. S. Williams, D. M. Theobald, M. M. Conner, and M. W. Miller. 2005. Human land use influences chronic wasting disease prevalence in mule deer. *in press*, Ecological Applications **16**:1.

Gelfand, A. E., and A. F. M. Smith. 1990. Sampling-Based Approaches to Calculating Marginal Densities. Journal of the American Statistical Association **85**:398-409

Gelman, A., J. B. Carlin, H. S. Stern, and D. B. Rubin. 2004. Bayesian data analysis, 2nd edition. Chapman & Hall/CRC, Boca Raton, Florida, USA.

Geman, S., and D. Geman. 1984. Stochastic relaxation, Gibbs distributions and the Bayesian restoration of images. IEEE Transactions on Pattern Analysis and Machine Intelligence **6**:721-741

Gilks, W. R., S. Richardson, and D. J. Spiegelhalter. 1998. Markov chain Monte Carlo in practice. Chapman & Hall, Boca Raton, Florida, USA.

Giraudoux, P., P. S. Craig, P. Delattre, G. Bao, B. Bartholomot, S. Harraga, J. P. Quere, F. Raoul, Y. Wang, D. Shi, and D. A. Vuitton. 2003. Interactions between landscape changes and host communities can regulate Echinococcus multilocularis transmission. Parasitology **127**:S121-S131.

Hay, S. I., S. E. Randolph, D. J. Rogers, and (Eds.). 2000. Remote sensing and geographical information systems in epidemiology. Academic Press, London.

Hibler, C. P., K. L. Wilson, T. R. Spraker, M. W. Miller, R. R. Zink, L. L. DeBuse, E. Andersen, D. Schweitzer, J. A. Kennedy, L. A. Baeten, J. E. Smeltzer, M. D. Salman, and B. E. Powers. 2003. Field validation and assessment of an enzyme-linked immunosorbent assay for detecting chronic wasting disease in mule deer

(Odocoileus hemionus), white-tailed deer (Odocoileus virginianus), and Rocky Mountain elk (Cervus elaphus nelsoni). Journal of Veterinary Diagnostic Investigation **15**:311-319.

Jolles, A. E., P. Sullivan, A. P. Alker, and C. D. Harvell. 2002. Disease transmission of aspergillosis in sea fans: Inferring process from spatial pattern. Ecology **83**:2373-2378

Lahiri, S. N., M. S. Kaiser, N. Cressie, and N. J. Hsu. 1999. Prediction of spatial cumulative distribution functions using subsampling. Journal of the American Statistical Association **94**:86-97.

Levin, S. A. 1992. The Problem of Pattern and Scale in Ecology. Ecology **73**:1943-1967

McGarigal, K., and B. J. Marks. 1995. FRAGSTATS: spatial pattern analysis program for quantifying landscape structure. USDA Forest Service General Technical Report PNW-351.

Miller, M. W., and M. M. Conner. 2005. Epidemiology of chronic wasting disease in free ranging mule deer; spatial, temporal, and demographic influences on observed prevalence patterns. *in press,* Journal of Wildlife Diseases.

Miller, M. W., and E. S. Williams. 2002. Detection of PrPCWD 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, N. T. Hobbs, and L. L. Wolfe. 2004. Environmental sources of prion transmission in mule deer. Emerging Infectious Diseases **10**:1003-1006.

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.

Pascual, M., and S. A. Levin. 1999. From individuals to population densities: Searching for the intermediate scale of nontrivial determinism. Ecology **80**:2225-2236.

Sarnelle, O. 1994. Inferring Process from Pattern - Trophic Level Abundances and Imbedded Interactions. Ecology **75**:1835-1841.

Schwartz, S. 1994. The Fallacy of the Ecological Fallacy - the Potential Misuse of a Concept and the Consequences. American Journal of Public Health **84**:819-824

Speigelhalter, D. J., A. Thomas, and N. G. Best. 2002. WinBUGS version 1.4 user manual. MRC Biostatistics Unit.

Spiegelhalter, D. J., N. G. Best, B. R. Carlin, and A. van der Linde. 2002. Bayesian measures of model complexity and fit. Journal of the Royal Statistical Society Series B-Statistical Methodology **64**:583-616.

Van Buskirk, J., and R. S. Ostfeld. 1998. Habitat heterogeneity, dispersal, and local risk of exposure to Lyme disease. Ecological Applications **8**:365-378.

Wikle, C. K. 2003. Hierarchical Bayesian models for predicting the spread of ecological processes. Ecology **84**:1382-1394.

Williams, E. S., and S. Young. 1992. Spongiform encephalopathies of Cervidae. Scientific and Technical Review Office of International Epizootics **11**:551-567.

Williams, E. S., and M. W. Miller. 2002. Chronic wasting disease in deer and elk in North America. Scientific and Technical Review Office of International Epizootics **21**:305-316.

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. 1993. Neuropathology of chronic wasting disease of mule deer (Odocoileus hemionus) and elk (Cervus elaphus nelsoni). Veterinary Pathology **30**:36-45.

Wolfe, L. L., M. M. Conner, T. H. Baker, V. J. Dreitz, K. P. Burnham, E. S. Williams, N. T. Hobbs, and M. W. Miller. 2002. Evaluation of antemortem sampling to estimate chronic wasting disease prevalence in free-ranging mule deer. Journal of Wildlife Management **66**:564-573.

Table 2.1. Model selection results to identify the candidate models best explaining observed spatial patterns of chronic wasting disease (CWD) prevalence in mule deer. I examined three analysis scales (grid cells of 9 km^2, 81 km^2, and 324 km^2), using models that incorporated various combinations of demographic (Demo), environmental (Env), spatial (Space), and unstructured heterogeneous (Het) variation. Demo = Age + Sex; Env = %HAB + %PRIV + DISP (see Methods for details), Space is the spatial random effect, and Het is the unstructured variation in the model, pD = effective number of parameters, DIC = Deviance Information Criteria, DIC weight informally quantifies model selection uncertainty.

Model	Scale (km^2)	Model	pD	DIC	w_{DIC}
1	9	Demo + Space + Het	69.8	2178.33	0.879
2	9	Demo + Space	71.7	2183.23	0.076
3	9	Demo + Env + Space	46.4	2185.13	0.029
4	9	Demo + Env + Space + Het	53.7	2186.74	0.013
5	81	Demo + Env + Space	16.6	2191.56	0.001
6	81	Demo + Env + Space + Het	17.1	2192.96	0.001
7	81	Demo + Env + Het	14.5	2193.13	0.001
8	9	Demo + Env + Het	52.3	2193.71	0.000
9	81	Demo + Env	6.1	2197.76	0.000
10	81	Demo + Space + Het	32.4	2199.95	0.000

Table 2.2: Univariate parameter estimates from Model 1 and Model 4. Estimates for individual-level covariates SEX and AGE are from Model 1, the top DIC model, which did not contain environmental covariates, with environmental covariate effects from Model 3, the best model containing these effects.

Variable	Model rank	Mean	Std.dev.	2.5% C.I.	97.5% C.I.
SEX	1	0.71	0.13	0.46	0.97
AGE	1	1.23	0.24	0.79	1.73
%PRIV	3	0.77	0.33	0.13	1.41
%HAB	3	0.67	0.39	-0.08	1.40
DISP	3	0.04	0.07	-0.11	0.18

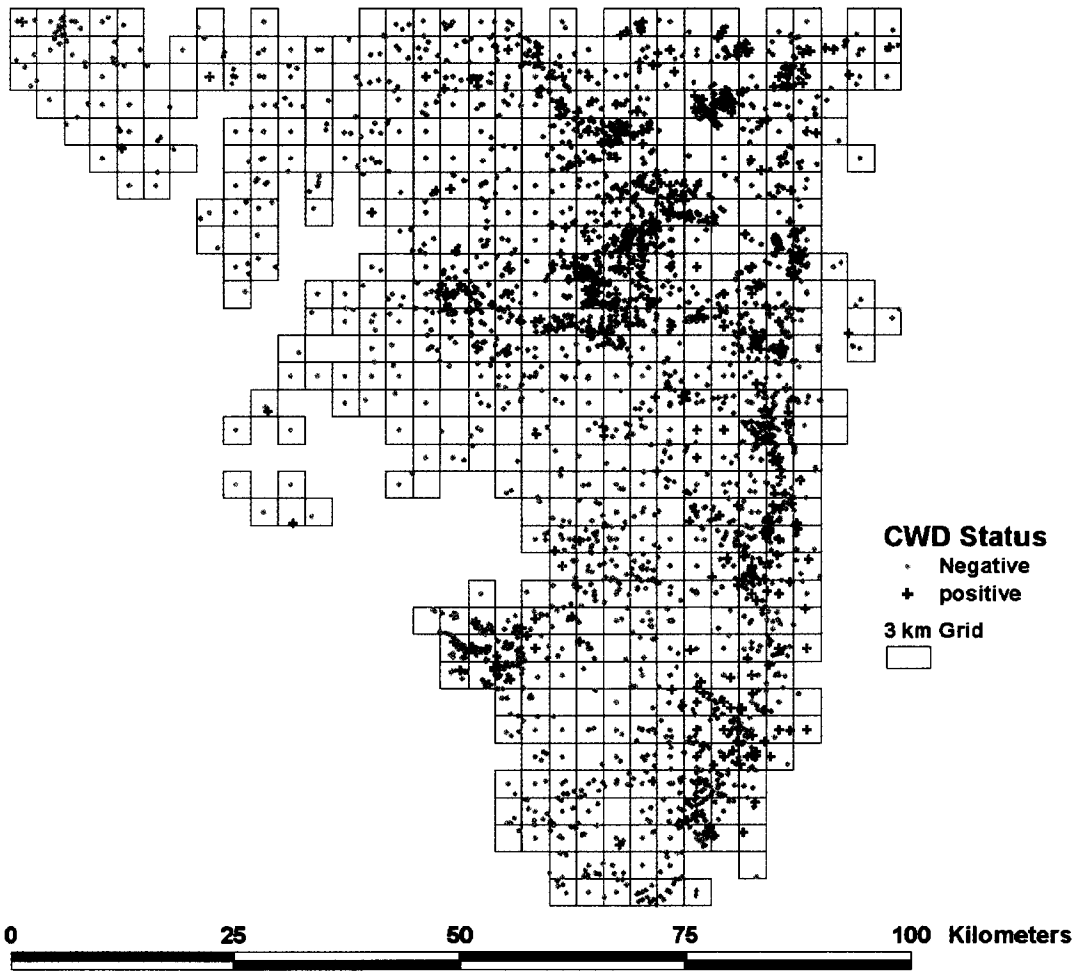

Figure 2.1 - Study site in north-central Colorado overlaid with with the spatial distribution of chronic wasting disease (CWD) data and the 540, 9 km^2 grid cells used in modeling individual-level infection probability ath finests analysis scale.

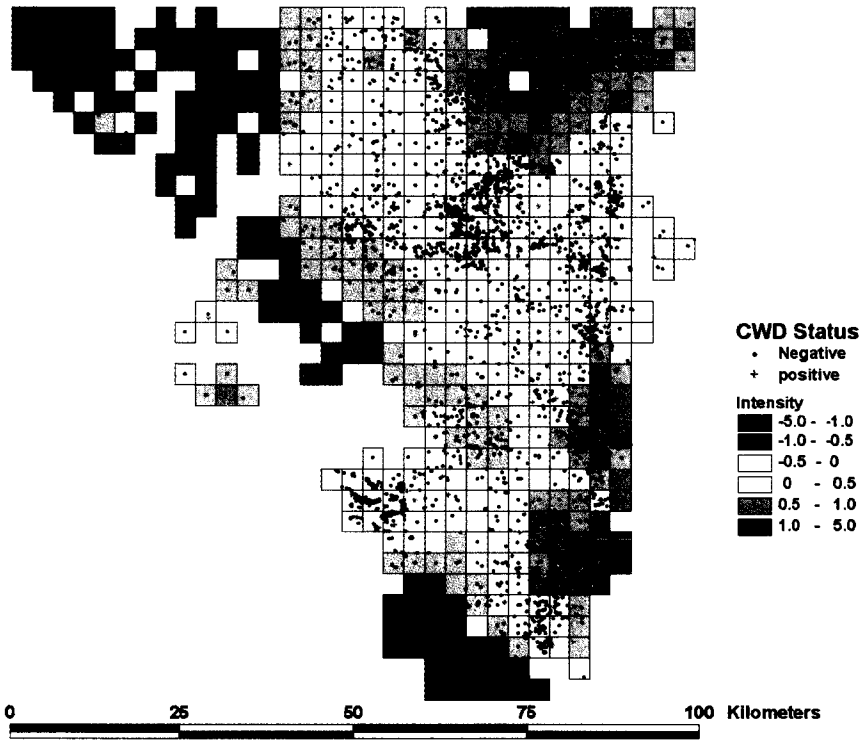

Figure 2.2 – Posterior estimates of mean spatial random effects for Model 1, the best approximating model of the probability that an individual deer was infected with CWD. The model was fit at a 9 km^2 analysis scale and used the demographic (Demo), spatial random effects (Space), and unstructured heterogeneity (Het) resulting in a concentrated distribution of infection probabilities.

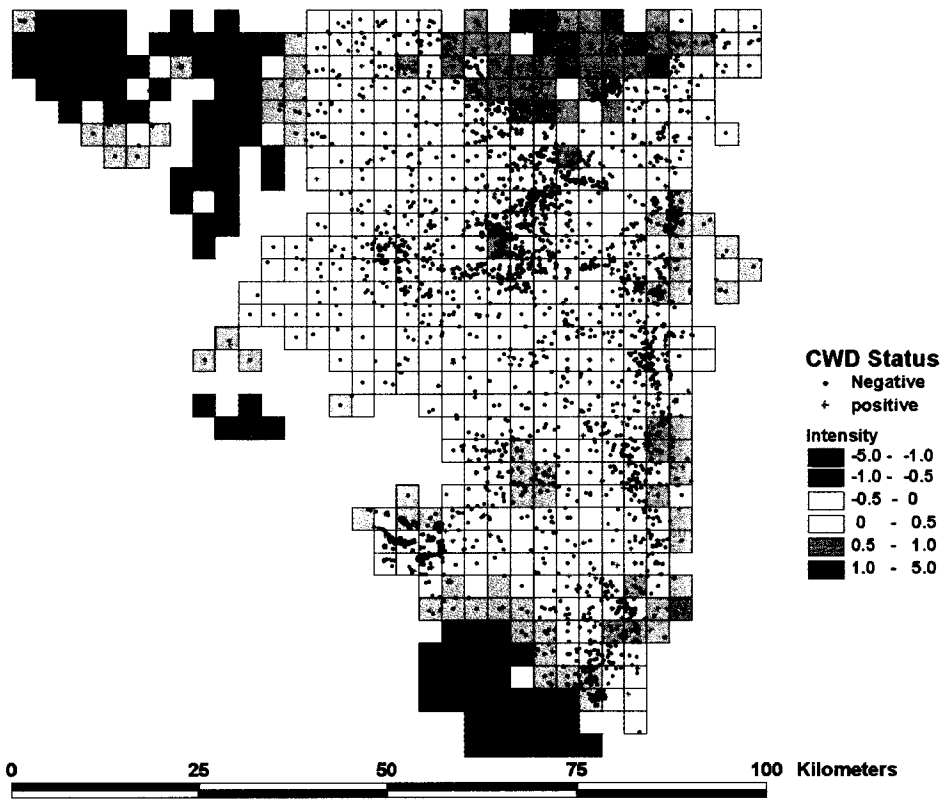

Figure 2.3 – Posterior estimates of mean spatial random effects for Model 4 of the probability that an individual deer was infected with CWD. The model was fit at a 9 km^2 analysis scale and used the demographic (Demo) and environmental (Env) covariates and spatial random effects (Space), resulting in a more diffuse distribution of infection probability than in Model

RELATING MULE DEER DENSITY TO CHRONIC WASTING DISEASE OCCURRENCE IN NORTHERN COLORADO

INTRODUCTION

Epidemiological models typically assume that increases in host population density result in an increase in the per capita contact rate among conspecifics inhabiting a fixed area (Diekmann et al. 1990, Heesterbeek and Metz 1993). Under this assumption, transmission rates, and hence disease prevalence, are positively related to increases in the density of individuals (Anderson and May 1979, Grenfell 1988, de Jong et al. 1995). Unfortunately, studies examining the relationship between host density and the transmission and prevalence of infectious diseases in free-ranging populations at landscape scales are rarely undertaken (Hudson 2002). Determining the role of density dependent disease transmission in structuring the dynamics of populations of long-lived, wide-ranging species has been difficult, with few published studies (but see Dobson 1996), possibly due in part to the difficult task of collecting the necessary data (Hudson 2002). Understanding the role that variations in density play in shaping prevalence of infectious diseases is important both from a management perspective and for improving models that incorporate such relationships.

Chronic wasting disease (CWD) (Williams and Young 1980), is the only prion disease known to occur in free-ranging populations (Williams and Miller 2002). The largest known outbreak occurs in a contiguous ~80,000 km^2 area of northeastern

Colorado, southeastern Wyoming, and western Nebraska, USA (Williams 1992, Miller et al. 2000, Williams and Miller 2002). CWD may have been present in free-ranging deer within this area since the 1960s or earlier (Miller et al. 2000). Although the infectious agent causing CWD is contagious in its natural setting (Williams and Young 1993, Miller and Williams 2003), relatively little is known about transmission mechanisms among infected mule deer (*Odocoileus hemionus*) populations (Williams and Miller 2002). Possible routes of transmission include animal-animal and animal-environment-animal pathways (Miller and Williams 2003, Miller et al. 2004). Recent discoveries of CWD foci distant to this 80,000 km^2 endemic area have spawned interest in understanding spatial and temporal dynamics in order to develop management strategies for controlling CWD in affected populations and prevent or slow its spread among unaffected populations. It has been suggested that the distribution of CWD in North-central Colorado results from a highly localized contact process, such as interactions among individuals within matrilineal groups that are tightly clustered and patchily distributed across their winter home range (Conner and Miller 2004, Miller and Conner 2005). High fidelity to seasonal use areas and temporally consistent movement patterns of subpopulations (Conner and Miller 2004), and presumably the resulting home range scales, suggest the importance of local, small-scale contact processes in structuring CWD spatial heterogeneity; these local scales appear to best explain observed patterns in CWD prevalence across the north-central Colorado landscape (Farnsworth et al. 2005a). Further, recent investigations suggest that infectious agent may persist in the environment for several years (Miller et al. 2004); consequently, large quantities of agent deposited over a relatively small geographic area could result in "hot-spots" of infectious agent

across the landscape. It follows that a highly localized contact process occurring within such areas might result in an elevated risk of disease exposure, possibly exacerbated by high deer densities. Understanding whether a relationship exists between mule deer density and CWD is of interest since culling deer that occur in high-density locations may provide a management tool for reducing disease intensity and spread.

A common problem in ecological studies involving multiple sources of spatial data is a failure of the data sources to align properly for analysis (Zhu and Carlin 2000, Zhu et al. 2000). This misalignment problem is particularly acute in studies involving point-based data and data collected over a small area relative to the analysis extent (Banerjee et al 2004). I provide an example, and illustrate a solution, for this problem by aligning point data on the locations of deer tested for CWD with estimates of deer density collected over a relatively small area to arrive at a model that reflects the relationship between density and infection probabilities. I used an interpolation technique known as kriging (Matheron 1963, Cressie 1993) to develop a surface of estimated deer density based on the spatial structure of survey data. I then overlaid the point-based CWD data and examined the disease/density relationship by specifying a set of generalized linear mixed-models (McCullagh and Nelder 1998) reflecting various hypotheses about the form of this relationship while accounting for the spatial dependency and sex effects (Conner and Miller 2004, Farnsworth et al. 2005b) thought to influence the probability of infection. I used the predicted variance in density from the kriged surface to adjust the models for the estimation error associated with each grid cell of the surface.

The models were developed using a hierarchical structure that allowed me to include the density estimates and their error. This approach also provided a method for

quantitatively comparing models using contemporary model selection techniques to assess the strength of evidence supporting the relationship between deer density and CWD at an epidemiologically important scale. Thus, this approach allowed me to identify the combination of predictor variables and the functional form of the relationship between estimated mule deer density and the distribution of CWD infection that were best supported by the data while properly accounting for multiple sources of observed and unobserved variation in the models.

METHODS

Study Area

The study included 1,250 km^2 in north-central Colorado (Fig. 3.1) where CWD is endemic in free-ranging cervids (Miller et al. 2000). Elevation ranged from 1,600 m to 2,600 m, rising from east to west. The northeastern quarter of the study area, from Fort Collins north, is rolling foothills and high prairie where livestock grazing was the main land use. Vegetation is primarily sagebrush-steppe habitat with big sagebrush (*Artemesia tridentata*), antelope bitterbrush (*Purshia tridentata*), mountain mahogany (*Cercocarpus montanus*), and mixed grasses. The southeastern quarter of the study area, from Fort Collins south, consists of urban centers separated by rural areas with numerous small ranches, agricultural fields, natural areas, and more scattered suburban areas. Vegetation communities in the western half of the study area follow the east-west elevation gradient. Lower elevations are mostly dense mountain mahogany interspersed with grassland openings and small patches of ponderosa pine (*Pinus ponderosa*) that transitioned to mountain shrub habitat with a primarily mixed conifer overstory at higher in elevations.

Data

The Colorado Division of Wildlife provided geo-referenced data for 1,679 mule deer tested for CWD between 1997 and 2003 within the study area. All samples were geo-referenced using either a global positioning system unit or by identifying sample locations on standardized maps. Sampling methods included deer that were killed by hunters, culled by wildlife managers, or captured and tonsil biopsied. Survey and diagnostic methods have been described in detail elsewhere (Miller et al. 2000, Miller and Williams 2002, Wolfe et al. 2002, Hibler et al. 2003). Sampled deer were classified as CWD positive or negative based on immunohistochemistry of retropharyngeal lymph node or tonsil tissue (Miller and Williams 2002). Because CWD prevalence remained relatively constant within the study area between 1996 and 2001 (Miller et al. 2000, Conner and Miller 2004), I combined samples across all years. Along with locations, data on the sex of each deer, which is known to influence infection probability (Conner and Miller 2004, Farnsworth et al. 2005) was recorded. Specific ages of deer were unavailable; however only adult deer were used in the analysis to reduce the effect of age.

Interpolating deer counts

During 1998-2002, the Colorado Division of Wildlife counted mule deer in 0.64 km^2 quadrats distributed randomly along north-south and east-west section lines throughout the study area as part of its population estimation program (Fig. 3.1). Quadrats were surveyed one time between January and February of each year using a helicopter that flew in a systematic grid pattern across the study area. Survey teams were a minimum of three people, including a pilot and two observers. A more detailed description of the survey protocol can be found in Kufeld et al. 1980. Because the CWD

data were combined across the years of the study to increase the sample size, I also combined the count data across years. The number of quadrats surveyed varied over the four years and were as follows, 87 in 1999, 112 in 2001, 130 in 2002, and 126 in 2003. Missing counts were assumed to be the average of the observed counts for each quadrat. The total area surveyed was approximately 72 km^2, which was less than 1% of the study region.

Data on the distribution of deer tested for CWD and on the estimates of deer density are a classic example of misaligned point data (Fig. 3.1). Since the aerial coverage of the count data was sparse, the CWD and quadrat locations rarely coincided. Thus, to relate deer density to the presence of CWD in individual deer I interpolated the mule deer density data across the entire study region and related the interpolated density to CWD point locations.

The density data were sparse and spatially variable. In addition, I wanted to use a grid-based analysis of the relationship between estimated density in a grid cell and the CWD status of each deer harvested from that cell. To accomplish this I used a median polish estimator (Tukey 1977, Cressie 1993), which is robust to outliers, followed by kriging of the median polish residuals to interpolate the counts across the study area based on a grid that had a resolution of 800 meters (0.64 km^2) corresponding to the size of each quadrat. Before developing the interpolated surface of deer density, I summed the counts in each quadrat across the years covered by the study to correspond to the structure of the CWD data, the latter data had been combined across the years of the study to maintain an adequate sample size for analysis. Because I summed the CWD data across years, it followed that summing deer counts across years would be more

appropriate than using a measure such as a simple average for developing the models relating deer density to CWD prevalence. The relatively stable population size and prevalence observed across the study area for the period I considered allowed me to structure the data in this manner.

The final deer density surface was scaled such that each grid cell had a resolution of 9 km^2 that matched the estimated scale of an individual winter home range (Conner and Miller 2004). To change scale I summed the estimates from all 0.64 km^2 cells that fell within the area covered by a single 9 km^2 grid cell. Similarly, I estimated the variance in each 9 km^2 grid cell as the sum of predicted variances in each of the 0.64 km^2 grid cells that fell within it. Thus, I assumed independence among all estimated deer counts at the 0.64 km^2 that fell within the same 9 km^2 cell. I did not use the original 0.64km^2 resolution of the interpolated density surface because this scale was too small to be biologically relevant to the relationship between density and CWD.

The interpolated surface of deer density could be broken into two parts; the median polish surface that accounted for large-scale trends in counts, followed by kriged residuals from that surface that modeled small-scale, or local, spatial variability in the data. Although the factors generating this structure remained unknown, determinants of large-scale variability could include elevation gradients and the corresponding large-scale distribution of habitat types, while small-scale variability might be structured by local features such as small areas of highly suitable habitat and those that provided refugia from predation and hunting (Farnsworth et al. 2005).

Projected onto an analysis grid, the density data could be considered as a two-way table similar to those used in analysis of variance (ANOVA). Thus, heuristically

speaking, the density data could be decomposed into the following components of an additive model,

$$\text{Data} = \text{all} + \text{row} + \text{column} + \text{residual} \qquad (1)$$

Letting there be i rows and j columns, the count in each grid cell, Z_{ij}, is estimated using the decomposition in (1) as,

$$Z_{ij} = Z_{..} + (Z_{i.} - Z_{..}) + (Z_{.j} - Z_{..}) + (Z_{ij} - Z_{i.} - Z_{.j} + Z_{..}) \qquad (2)$$

where the dot (•) represents averaging over that subscripts of the rows and columns. The median polish algorithm successively "sweeps" medians out of the rows, then the columns, accumulating them in the marginal cells of the grid, analogous to the margins of an ANOVA table, leaving behind a grid of residuals. The "sweeping" was repeated until there were no discernable changes in the marginal cell values. The resulting marginal cell values were equivalent to the "all", "row", and "column" values shown in (1) and (2), and constituted the large–scale spatial variability, while the residuals that were left behind in the grid represented the small-scale spatial variability. The spatially dependent residuals were then modeled using kriging, after which they were added back to the median polish surface. Thus, the final estimated surface of deer density was a function of large and small-scale spatial variability.

Kriging the residuals from the median polish algorithm required an estimator of the spatial covariance function, often called the variogram model (Cressie 1993). This model, which quantifies the small-scale spatial dependence in the residuals, was used to interpolate the spatial variability in the residuals across the grid assuming a stationary and isotropic process (Cressie 1993). Under these assumptions, the spatial dependency was modeled as a function of the separation distance between pairs of quadrats, independent

of the locations of the quadrats themselves, and this dependency was assumed to have a constant mean across the study area. I initially fit three different parametric variogram models to the median polish residuals: Spherical, Exponential, and Gaussian models. Using AIC_c (Burnham and Anderson 2002) I determined that the Gaussian model had the best support for interpolating the small-scale spatial variability in the residuals. Specifically, I modeled the spatial structure of the residuals using a Gaussian variogram model, which under the assumptions noted above is given by;

$$\gamma(h;\theta) = \begin{cases} 0, & \text{h} = 0, \\ c_0 + c_1\left\{1 - \exp\left(-3h^2 / a^2\right)\right\}, & \text{h} \neq 0, \end{cases} \qquad (3)$$

$$\theta = \left(c_0, c_1, a\right)', \text{ where } c_0 \geq 0,\ c_1 \geq 0, \text{ and } a \geq 0$$

where h is the "spatial lag" and measures the Euclidean distance between all pairs of points in the data set, c_0 is known as the nugget effect, which captures the discontinuity at the origin of this function. The nugget effect is typically attributed to microscale variations that occur at distances smaller than the minimum distance between any two pair of points in the data set used to estimate the variogram. c_1 is the sill which estimates the variance of the spatial process when the components of the process (data) become spatially independent, which occurs at a spatial lag distance that is known as the "range", given by a. I used non-linear least squares to estimate the parameters of the variogram model, which were then used to carry out the interpolation, resulting in a grid of spatially modeled "residuals" that captured the small-scale variation in spatial structure that was not modeled by the corresponding median polish algorithm. The interpolated values from each cell in this grid were added back to each corresponding cell of the median

polish surface that captured the large-scale trend in the data to arrive at the final surface of estimated deer density that I used to model the relationship between density and CWD.

The estimated variance in deer density for each grid cell was obtained from the empirical variogram model as;

$$\hat{\sigma}_i^2\left(\hat{z}_i\right) = c_1 - \sum_{i=1}^{k} w_i d_i \qquad (4)$$

where $\hat{z}_i$ is the estimated density in grid-cell i, c_1 is the "sill" from (3), w_i is the n x 1vector of kriging weights obtained by non-linear optimization of the spatial covariance matrix for the sample data and is used in predicting deer densities in cell i, and d_i is the vector of covariances for the cell whose density is being estimated. Thus, as the data approach spatial independence, as estimated by the "sill" of the variogram, the covariances, d_i, approach 0, and the estimated variance, $\hat{\sigma}_i^2$, approaches the value of the "sill". This uncertainty was incorporated into models reflecting the relationship between deer density and disease incidence in individual deer.

Density model evaluation

I used 10-fold cross-validation (Efron and Tibshirani 1993) to assess the prediction error of the kriged surface. The cross-validation entails removing 10% of the quadrat data, re-fitting the model to the remainder of the data as described above, and assessing the predictive accuracy for the 10% of the data removed.

To evaluate the effectiveness of the model, I computed various measures of prediction error based on the 10-fold cross validation. Prediction bias (Williams 1997) was calculated for each validation dataset as a percentage of observed deer density. Accuracy was measured by the mean absolute error (MAE), which is a measure of the

sum of absolute residuals (i.e., actual minus predicted values) and the root mean squared error (RMSE), which is the square root of the mean of sum of squared residuals (Kravchenko and Bullock 1999, Schloeder et al. 2001). MAE indicates the overall error for all locations with data, while RMSE indicates the level of prediction accuracy on a cell-by-cell basis since it is more sensitive to extreme values that might occur in an individual grid cell (Schloeder et al. 2001). The consistency between the observed estimation errors (i.e., true error) based on the variogram, $e_i^* = (Z_i - Z_i^*)$, where Z_i is the observed density in quadrat *i* and Z_i^* is the modeled density from the median polish kriging, and the prediction variance based on the 10-fold cross validation, σ_{i*}^2, was measured using the standard mean squared error (SMSE) (Hevesi et al. 1992);

$$\text{SMSE} = \frac{1}{n}\sum_{i=1}^{n}\frac{(e_i^*)^2}{\sigma_{i*}^2} \qquad (5)$$

for all *n* quadrats. SMSE values close to one reflect good agreement between observed and predicted errors, thereby providing a method for gauging the agreement between true and predicted errors for grid-cells without data. The σ_{i*}^2 were also used to construct 95% confidence intervals around individual estimates. Coverage rates were calculated as the proportion of individual confidence intervals that contained the true value.

Hierarchical model of the density-disease relationship

There exists a growing recognition of the need to incorporate uncertainty into model covariates that are estimated with error (Haining 2003). The approach to this problem is frequently termed "errors in variables modeling" (Fuller 1987, Richardson and Gilks 1993, Best et al. 2000). The need for errors in variables modeling typically arises

under two circumstances; when data are recorded with error and when estimated values are used as input into a model. This research provides an example of the latter, where it would be inappropriate to treat estimates from the interpolated density surface as though they were actual data. Therefore, to arrive at appropriate inference regarding the relationship between CWD and deer density it was necessary to incorporate estimation uncertainty into the models. To accomplish this, I adopted a hierarchical modeling approach that included estimation error by allowing the density estimates to vary during model fitting. Specifically, I use the empirical variogram model to estimate the variance in density within each grid cell of the interpolated surface. I then used the density estimates from each grid cell as the covariate relating density to infection probability and added error based on the estimated variance for that cell.

I considered a set of generalized linear models for disease presence/absence. The global model estimated the probability that a deer is CWD-positive as an additive function of its sex, estimated density and density^2 and associated error in the grid cell it was sampled from, and two random effect terms, which account for unobserved covariates as well as the spatial dependency in the probability of disease presence. All other models in the candidate set were variations on this global model. Additionally, the grid structure accommodated uncertainties in the point-based CWD data by treating all individuals sampled from within the same grid cell as having an identical exposure risk to the infectious agent after adjusting for individual-level sex effects.

This hierarchical, generalized linear model, has three components: the data model, or likelihood linking the data to the model parameters; the process model relating the covariates and random effects to the parameters, and the prior distributions for all model

parameters (Wikle 2003). My interest focused on the distribution of the process and parameters after being informed by the data. To arrive at this posterior distribution, I used Bayes theorem:

$$f(\text{process, parameters}|\text{data}) \propto f(\text{data}|\text{ process, parameters}) \times f(\text{process}|\text{ parameters}) f(\text{parameters}) \quad (6)$$

where, in general, $f(x_1)$ denotes the probability distribution of x_1 and $f(x_1|x_2)$ is the conditional distribution of x_1 given x_2. For many ecological problems, the high dimensionality of the model can prohibit the use of standard methods for estimating the posterior distribution. However, Markov Chain Monte Carlo (MCMC) (Geman and Geman 1984, Gelfand and Smith 1990, Gilks et al. 1998) techniques allowed me to estimate the posterior distribution in (6).

Data model

The data model relates the known infection status for each deer to the probability of infection. Let Y_{ij} be the known infection status for deer $i = 1,\ldots,n$ in cell $j = 1,\ldots,k$. I assume that infection status is Bernoulli distributed with parameter π_{ij}:

$$Y_{ij} \mid \pi_{ij} \sim \text{Bernoulli}(\pi_{ij}) \quad (7)$$

where π_{ij} is the probability of infection for individual i in cell j. All observations are assumed conditionally independent given this parameter.

Process model

The process component of the model relates the probability of infection for each deer, π_{ij}, to the Sex and Density covariates. I include two random effect terms to model

variability that is not accounted for by these covariates. To constrain the Bernoulli distributed infection probability to the range 0-1, I use a standard logit transform. Thus, I model the probability that an individual is infected as:

$$\text{logit}(\pi_{ij}) = \mu + x_{ij}^T \beta + \gamma_j + \delta_j, \qquad (8)$$

where μ is the background infection rate- common to all deer, β is an m x 1 vector of regression coefficients corresponding to the x_{ij}^T, the transpose of the m x 1 vector of the Sex and Density covariates associated with each deer; γ_j is the spatial random effect term for the jth grid cell; and δ_j is the independent random effect term associated with the jth grid cell that exhibits no spatial dependency. The random effect terms are described further below.

Prior and posterior distributions

Because the analysis is fully Bayesian, I specify prior distributions for all model parameters in the hierarchy. I specify the spatially structured variation in infection probability, γ_j, via an Intrinsic Gaussian Conditional Autoregressive (ICAR) model (Besag et al. 1991). For a grid cell j in the problem, the ICAR model states that γ_j is related to the γ terms for the neighboring grid cells; and, given the γ terms for the neighboring grid cells, each grid cell is independent of all other grid cells outside the local neighborhood. Specifically, let the set of neighbors contributing to γ_j be denoted by γ_{j+}. Then, for each grid cell j, I assume the conditional relationship

$$\gamma_j \mid \gamma_{j+} \sim \text{Normal}\left(\frac{1}{n_{j+}}\sum \gamma_{j+}, \frac{\sigma_\gamma^2}{n_{j+}}\right) \qquad (9)$$

where n_{j+} is the number of neighbors of grid cell j and σ_γ^2 is the variance for all grid cells. Thus, the conditional mean of γ_j is simply the average value of its neighbors γ_{j+}, with conditional variance σ_γ^2 proportional to the number of neighbors. In the conditional mean in (9), the neighboring grid cells are equally weighted so that all neighbors of cell j influence it equally. Spatial variation in the model is limited to cells sharing a border; however there are no *a priori* restrictions on specifying the neighborhood structure or cell weights. I use second-order neighborhoods, meaning only cells sharing a border with the focal cell are considered in modeling spatial dependency, because I wish to maintain a sharp distinction between local dependency and global unstructured heterogeneity, which becomes increasingly blurred as the local neighborhood is extended.

The unstructured heterogeneity term, δ_j, corresponds to a latent process operating independently in each grid cell. I let $\delta_j \sim i.i.d.\ N(0, \sigma_\delta^2 \mathrm{I})$ for $j = 1, \ldots, J$. This component models the overall, unstructured heterogeneity in the data by assuming no relationship among neighboring grid cells, but with a variance that was common to all grid cells. In the following section, I describe the parameter values for the probability distributions governing the behavior of each of the process model components.

The following distributions apply to the remaining model parameters: baseline disease risk, $\mu \sim$ flat() and Sex and Density covariates $\beta \sim N(0, \sigma_\beta^2 \mathrm{I})$ where I is the indicator matrix. In addition, I add error to the density estimates by specifying an additional additive term in each cell as $\varepsilon \sim N(0, \sigma_\varepsilon^2 \mathrm{I})$, where σ_ε^2 is the estimated variance from the variogram model. This component of the model is the "errors in variables" portion that allows for the modeling of the uncertainty in the density estimates. I specify

non-informative hyperparameter distributions for all the variance parameters: $\sigma^2 \sim U(0,10)$ for σ_β^2, σ_γ^2 and σ_δ^2. Note that $\mu \sim$ flat() corresponds to an improper (flat) prior on the whole real line. This prior distribution, along with a sum-to-zero constraint placed on the spatial random effects, is necessary to assure identifiability because the model contains ICAR random effects (Besag and Kooperberg 1995). These restrictions result from defining the spatial random effect component conditionally rather than jointly. I consider a final quantity, $\lambda = \frac{\sigma_\gamma^2}{\sigma_\gamma^2 + \sigma_\delta^2}$, which measures the contribution from the spatial random effect component of variance to the overall variance due to the random effects. This parameter allows me to understand the relative contributions of spatially structured and unstructured variation in models containing both.

Finally, the joint posterior distribution of all model parameters given the field data was fit for various combinations of predictors selected *a priori*. The models contained various combinations of sex, density, density^2 to capture non-linear effects, and spatially structured (Space) and unstructured (Het) variation. All models were fit using WinBUGS software (Speigelhalter et al. 2002). The MCMC procedure for these models was run for 50,000 iterations after a burn-in period of 250,000 iterations to ensure convergence of all model parameters.

Model comparisons

I used a Deviance Information Criteria (DIC), a generalization of the Akaike Information Criteria (AIC), to compare the set of candidate models (Spiegelhalter et al. 2002). These criteria are based on the deviance, $D(\theta) = -2 \ln L$, where L is the likelihood and θ is the vector of model parameters, and a penalty for model complexity.

For AIC, the penalty is two times the number of parameters in the model. The complexity of a hierarchical model is measured by the effective number of parameters, p_D, which is often smaller than the total number of parameters due to the borrowing of strength property of hierarchical models described earlier. This complexity is defined as $p_D = \overline{D(\theta)} - D(\bar{\theta})$, where $\overline{D(\theta)}$ is the expected deviance over the posterior distribution of parameter vector θ taken across all MCMC samples, and $D(\bar{\theta})$ is the deviance evaluated at the posterior mean of the parameter vector. Finally, $\text{DIC} = \overline{D(\theta)} + p_D = 2\overline{D(\theta)} - D(\bar{\theta})$. Smaller values of DIC indicate a better-fitting model. As with other penalized likelihood criteria, DIC is a method for comparing a collection of alternative models (Carlin and Louis 2000).

Burnham and Anderson (2002) derived Akaike weights that, when normalized, can be interpreted as a set of weights that sum to one and estimate the probability that model r is the best Kullback-Leibler model for the data at hand, given the set of models considered. This approach provides a method for assessing model selection uncertainty. It has been suggested as an analogous approach for estimating model selection uncertainty within a Bayesian modeling context (Spiegelhalter et al. 2002). I used DIC weights (w_{DIC}) to estimate model selection uncertainty for each model r in the candidate set, calculated using the formula for Akaike weights

$$w_{DIC} = \frac{\exp(-\frac{1}{2}\Delta DIC)}{\sum \exp(-\frac{1}{2}\Delta DIC)} \qquad (10)$$

where ΔDIC was the difference between the minimum DIC value in the candidate set and model r, and the denominator was the sum over all models in the set under

consideration. The DIC weights are an informal measure and allow easier comparison between models than the DIC value itself.

RESULTS

Interpolation of deer density

The following parameter estimates resulted from fitting the Gaussian variogram model to the residuals from the median polish surface; nugget = 0, sill = 498.62, and range = 10.94km. Table 3.1, which compares basic statistics from the observed deer densities to the surface of median polish kriged estimates, shows that the interpolated surface of estimated deer density (Fig. 3.1) was an accurate and relatively unbiased estimator of the observed deer count data. Table 3.2 reflects measures of model fit based on the 10-fold cross validation. In particular, the agreement between the model-based MAE and RMSE with the observed standard error from the data, shown in Table 3.1, suggests good agreement between observed and estimated errors. The MAE was smaller than the RMSE indicating, in general, that the model was more accurate in predicting global means rather than on a cell-by-cell basis. The SMSE value, which is the ratio of observed to predicted errors averaged across all quadrats, was 1.29, which suggested that the prediction errors were somewhat smaller than, but consistent with, the true errors. Finally, the coverage rate, based on the prediction error, $\hat{\sigma}_{i^*}$, was 90%, suggesting that the prediction variance slightly underestimated the true variance from the data, which is in agreement with the SMSE value of 1.29.

Figure 3.2 shows the interpolated surface of density with the observed quadrat counts overlaid suggesting good agreement between observed and modeled densities for the quadrat locations. The portions of the surface with density estimates of zero

correspond to cells that fell outside the study area shown in Figure 3.1. The standard deviation surface (Fig. 3.3) resulted directly from the Gaussian variogram model. Based on the quadrat locations shown in Figure 3.2, it can be seen that standard deviations increased as a function of the separation distance between quadrats and for cells that were relatively isolated from the quadrat locations, which is an underlying assumption of the variogram model. The strong agreement between the observed and model-based statistics, including the low bias, shown in table 3.1, and the results from the 10-fold cross validation shown in table 3.2 suggest that the surface of deer counts adequately reflected the spatial variability present in the observed densities based on the survey data.

Relationship between CWD and estimated density

Based on the results shown in Table 3.3, there was weak support for models containing a density effect. The Sex covariate was included in all models since it was known *a priori* to be related to CWD incidence. The best approximating model only included the covariates of Sex and the Space, with the spatial random effect modeling unobserved covariates that correspond to the distribution of CWD prevalence. Models that did not contain the spatial random effect had virtually no support in the data, emphasizing the importance of local spatial processes in structuring the distribution of CWD. Based on the distribution of w_{DIC} across Models 1-6, no single model included the majority of support, as measured by this criterion, suggesting a high degree of similarity among the models with respect to fit. Because Models 1-6 had the covariates of Sex and Space in common, it follows that this combination of predictors were responsible for explaining the majority of the variance in each of these models, with the other covariates apparently adding noise to the base model and possibly detracting from its fit. The top

model containing a mixture of structured and unstructured heterogeneity (Model 4) allowed for an estimate of Lambda, which is the proportion of variability attributed to these two random effects, of 0.769 with a 95% Credible Interval ranging from 0.438 to 0.988, highlighting the dominant role of spatially structured heterogeneity in modeling infection probabilities.

The parameter estimate for the Density covariate from the top model (Model 3) containing this effect was 0.248 with 95% Credible Intervals ranging from -0.335 to 0.922, suggesting that the relationship between estimated density and the probability of infection was not significant and contributed little to the spatial heterogeneity in disease incidence. I refit this top model without including the density estimation error from the variogram model. This resulted in similar estimates, showing that even if the density estimates were considered "fixed", there was little evidence of a relationship between estimated density and infection probability.

DISCUSSION

Disease transmission models typically invoke either a frequency dependent (De Palma and Lefevre 1988) or density dependent (Anderson and May 1979, Begon et al. 2002) assumption in modeling the conversion from susceptible to infectious states. Frequency dependent transmission implies that the number of contacts per unit time between susceptible and infected deer increases linearly with population density (de Jong et al. 1995) for a fixed area. Density dependent transmission assumes that the number of contacts per unit time between susceptible and infected deer is proportionate to the number of infected individuals in the population. As the population size increases over a fixed area, density, and hence contact rate, increases, however this increase is non-linear

for a fixed proportion of infectious individuals. Modeling density dependent CWD infection rates in the manner I presented assumed that the area used by an individual deer was fixed (i.e., a 9 km^2 grid cell), and that contact rate, and hence infection rates, should increase with increases in estimated deer density. Because I did not want to assume *a priori* which form of disease transmission was operating in the study area I included linear and non-linear density effects in the candidate set of models.

There are circumstances under which the assumption of a positive relationship between increased density and disease prevalence does not hold. For a disease operating under frequency dependent transmission this relationship will not be observed if R_0, the number of new infections needed to allow the infection to be maintained within the population, is less than one (de jong 1995). This same principal holds true for diseases operating under density dependent transmission, with the additional constraint of a threshold density below which the positive relationship between prevalence and density, even when $R_0 > 1$, cannot occur (Anderson and May 1979). Therefore, it is plausible that I failed to observe a positive relationship between prevalence and density for this enzootic, or more appropriately, protracted epizootic (Miller 2000), if the value for R_0 occurs outside of the range for which this relationship is expected to hold. Alternatively, structuring the model in terms of local relationships (i.e. 9 km^2 grid cells) could have masked the existence of a positive relationship between prevalence and density, even in the presence of R_0 values operating within a range that should result in such a relationship, if this scale of analysis does not include the biologically relevant range of scales over which this relationship occurs.

A second possible explanation for the apparent lack of a relationship between CWD and deer density may be the social contact structure of the populations used in this study. For example, if the contact rate among individuals is relatively constant across the study area, independent of variations in deer density at the scale used here, then I would not detect a relationship between disease occurrence and deer density.

Under either form of disease transmission, it becomes crucial to identify the relationship between density and disease rates at epidemiologically relevant scales, as I have attempted here, if one assumes that the area of interaction is fixed as population levels fluctuate. The fact that I was unable to demonstrate a relationship between mule deer density and the probability of CWD infection in individual deer does not rule out the presence of such a relationship. I modeled the relationship at a scale that made sense biologically and that was feasible given the resolution and extent of the mule deer survey data, which may not coincide with the scale of an existing relationship. Although a previous analysis (Farnsworth et al. 2005) in this area identified that the most likely scale, among three scales examined, of spatial dependence in the probability of CWD infection occurred at the individual home range scale of 9 km^2, it remains possible that the relationship between CWD and mule deer density differs from that scale. Additionally, it is likely that if density affects infection probability it is only one of several processes influencing the spatial heterogeneity in disease incidence. Further, irrespective of the scale at which density exerts its greatest influence on disease transmission, other processes operating at the individual home range scale of 9km^2, for which data are unavailable, may dominate density in structuring the distribution of the disease.

Densities are relatively low in this area and mule deer are gregarious. Thus, in the presence of threshold densities necessary for disease transmission and the detection of a density/prevalence relationship, infection rates may remain relatively constant even as populations fluctuate. Therefore, the modeled, and even measured, density may not accurately reflect the dynamics underlying the estimated density when a quadrat was sampled. Thus, the failure of density to predict prevalence may simply reflect that the survey data were inadequate for the questions I asked. Despite this inadequacy, I emphasize that these survey data come from an expensive, well designed, and spatially intensive effort, largely unmatched anywhere in the world for ungulate species. This illustrates that relating density to prevalence in large, mobile wildlife remains a formidable sampling challenge.

Although the survey design used in this study was intended to allow managers to estimate population size under a mean field assumption (i.e., no spatial heterogeneity), it is likely among the best available survey data for an ungulate species for use in developing a surface of estimated density for modeling the density/disease relationship. Despite the relatively low densities in the study area, there exists substantial spatial heterogeneity in the observed distribution of densities. This research demonstrates the challenge of using data intended for estimation under a mean field assumption in spatial analyses that seek to model and estimate the effects of spatial heterogeneity on the process or pattern of interest. The relatively large coefficients of variation for both the data and interpolated surface (116% for both) highlights the potentially prohibitive level of survey effort needed to examine this relationship to obtain a greater level of

confidence in the estimated values, and hence in the estimated relationships that may exist between mule deer density and infection rates in Northern Colorado.

Although I found little difference in results whether I considered mule deer density estimates to be fixed or variable, this research illustrates how hierarchical analysis can be used to include appropriate levels of uncertainty when covariates are estimated rather than observed without error, an issue that arises frequently in ecological analysis (Haining, 2003). Past studies have largely ignored such errors; however, in many ecological studies error propagation can play a large role in determining research results and thus should not be ignored, but rather explicitly incorporated into models that admit appropriate levels of estimation uncertainty in the model fitting process.

LITERATURE CITED

Anderson, R. M., and R. M. May. 1979. Population Biology of Infectious-Diseases .1. Nature 280:361-367.

Begon, M., M. Bennett, R. G. Bowers, N. P. French, S. M. Hazel, and J. Turner. 2002. A clarification of transmission terms in host-microparasite models: numbers, densities and areas. Epidemiology and Infection 129:147-153

Besag, J., and C. Kooperberg. 1995. On conditional and intrinsic autoregressions. Biometrika 82:733-746.

Besag, J., J. York, and A. Mollie. 1991. Bayesian Image-Restoration, with two Applications in Spatial Statistics. Annals of the Institute of Statistical Mathematics 43:1-20.

Best, N. G., K. Ickstadt, and R. L. Wolpert. 2000. Spatial Poisson regression for health and exposure data measured at disparate resolutions. Journal of the American Statistical Association 95:1076-1088.

Burnham, K. P., and D. R. Anderson. 2002. Model selection and multimodel inference : a practical information-theoretic approach, 2nd edition. Springer, New York.

Carlin, B. P., and T. A. Louis. 2000. Bayes and Empirical Bayes methods for data analysis. Pages xvii, 419 p. *in*. Chapman & Hall/CRC, Boca Raton.

Conner, M. M., and M. W. Miller. 2004. Movement patterns and spatial epidemiology of a prion disease in mule deer population units. Ecological Applications 15.

Cressie, N. A. C. 1993. Statistics for spatial data, Rev. edition. Wiley, New York.

de Jong, M. C. M., O. Diekmann, and H. Heesterbeek. 1995. How does transmission of infection depend on population size. Pages 84-94 *in* D. Mollison, editor. Epidemic models : their structure and relation to data. New York Cambridge University Press, Cambridge, England.

De Palma, A., and C. Lefevre. 1988. Population systems with (non)-extensive interaction rates. Mathematical and Computer Modeling 10:359-365.

Diekmann, O., J. A. P. Heesterbeek, and J. A. J. Metz. 1990. On the Definition and the Computation of the Basic Reproduction Ratio R0 in Models for Infectious-Diseases in Heterogeneous Populations. Journal of Mathematical Biology 28:365-382.

Efron, B., and R. Tibshirani. 1993. An Introduction to the bootstrap. Chapman & Hall, New York.

Farnsworth, M. L., J. A. Hoeting, N. T. Hobbs, and M. W. Miller. 2005a. Linking mule deer movement scales to the spatial distribution of chronic wasting disease: a hierarchical Bayesian approach. *in review.*

Farnsworth, M. L., L. L. Wolfe, N. T. Hobbs, K. P. Burnham, E. W. Williams, D. M. Theobald, M. M. Conner, and M. W. Miller. 2005b. Human land use influences chronic wasting disease prevalence in mule deer. Ecological Applications 15:1.

Fuller, W. A. 1987. Measurement error models. Wiley, New York.

Gelfand, A. E., and A. F. M. Smith. 1990. Sampling-Based Approaches to Calculating Marginal Densities. Pages 398-409 *in* Journal of the American Statistical Association.

Geman, S., and D. Geman. 1984. Stochastic relaxation, Gibbs distributions and the Bayesian restoration of images. Pages 721-741 *in* IEEE Transactions on Pattern Analysis and Machine Intelligence.

Gilks, W. R., S. Richardson, and D. J. Spiegelhalter. 1998. Markov chain Monte Carlo in practice. Pages xvii, 486 p. *in.* Chapman & Hall, Boca Raton, Fla.

Grenfell, B. T. 1988. Gastrointestinal Nematode Parasites and the Stability and Productivity of Intensive Ruminant Grazing Systems. Philosophical Transactions of the Royal Society of London Series B-Biological Sciences 321:541-563.

Haining, R. P. 2003. Spatial data analysis : theory and practice. Cambridge University Press, Cambridge, UK ; New York.

Heesterbeek, J. A. P., and J. A. J. Metz. 1993. The Saturating Contact Rate in Marriage and Epidemic Models. Journal of Mathematical Biology 31:529-539.

Hevesi, J. A., J. D. Istok, and A. L. Flint. 1992. Precipitation Estimation in Mountainous Terrain Using Multivariate Geostatistics .1. Structural-Analysis. Journal of Applied Meteorology 31:661-676.

Hibler, C. P., K. L. Wilson, T. R. Spraker, M. W. Miller, R. R. Zink, L. L. DeBuse, E. Andersen, D. Schweitzer, J. A. Kennedy, L. A. Baeten, J. E. Smeltzer, M. D. Salman, and B. E. Powers. 2003. Field validation and assessment of an enzyme-linked immunosorbent assay for detecting chronic wasting disease in mule deer (Odocoileus hemionus), white-tailed deer (Odocoileus virginianus), and Rocky Mountain elk (Cervus elaphus nelsoni). Journal of Veterinary Diagnostic Investigation 15:311-319.

Hudson, P. J. 2002. The ecology of wildlife diseases. Oxford University Press, New York.

Kravchenko, A., and D. G. Bullock. 1999. A comparative study of interpolation methods for mapping soil properties. Agronomy Journal 91:393-400.

Kufeld, R. C., J. H. Olterman, and D. C. Bowden. 1980. A Helicopter Quadrat Census for Mule Deer on Uncompahgre Plateau, Colorado. Journal of Wildlife Management 44:632-639.

Matheron, G. 1963. Principles of geostatistics. Economic Geology 58:1246-1266.

McCullagh, P., and J. A. Nelder. 1998. Generalized linear models, 2nd edition. Chapman & Hall/CRC, Boca Raton.

Miller, M. W., and M. M. Conner. 2005. Epidemiology of chronic wasting disease in free ranging mule deer; spatial, temporal, and demographic influences on observed prevalence patterns. *in press* Journal of Wildlife Diseases.

Miller, M. W., and E. S. Williams. 2002. Detection of PrPCWD 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.

Miller, M. W., E. S. Williams, N. T. Hobbs, and L. L. Wolfe. 2004. Environmental sources of prion transmission in mule deer. Emerging Infectious Diseases **10**:1003-1006.

Richardson, S., and W. R. Gilks. 1993. Conditional-Independence Models for Epidemiologic Studies with Covariate Measurement Error. Statistics in Medicine 12:1703-1722.

Schloeder, C. A., N. E. Zimmerman, and M. J. Jacobs. 2001. Comparison of methods for interpolating soil properties using limited data. Soil Science Society of America Journal 65:470-479.

Speigelhalter, D. J., A. Thomas, and N. G. Best. 2002. WinBUGS version 1.4 user manual. *in*. MRC Biostatistics Unit.

Spiegelhalter, D. J., N. G. Best, B. R. Carlin, and A. van der Linde. 2002. Bayesian measures of model complexity and fit. Pages 583-616 *in* Journal of the Royal Statistical Society Series B-Statistical Methodology.

Tukey, J. W. 1977. Exploratory data analysis. Addison-Wesley Pub. Co., Reading, Mass.

Wikle, C. K. 2003. Hierarchical Bayesian models for predicting the spread of ecological processes. Ecology 84:1382-1394.

Williams, E. S., and S. Young. 1992. Spongiform encephalopathies of Cervidae. Scientific and Technical Review Office of International Epizootics 11:551-567.

Williams, E. S., and M. W. Miller. 2002. Chronic wasting disease in deer and elk in North America. O I E Revue Scientifique et Technique 21:305-316.

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. 1993. NEUROPATHOLOGY OF CHRONIC WASTING DISEASE OF MULE DEER (ODOCOILEUS HEMIONUS) AND ELK (CERVUS ELAPHUS NELSONI). Veterinary Pathology 30:36-45.

Williams, M. S. 1997. A regression technique accounting for heteroscedastic and asymmetric error. Journal of Agricultural, Biological, and Environmental Statistics 2:108-129.

Wolfe, L. L., M. M. Conner, T. H. Baker, V. J. Dreitz, K. P. Burnham, E. S. Williams, N. T. Hobbs, and M. W. Miller. 2002. Evaluation of antemortem sampling to estimate chronic wasting disease prevalence in free-ranging mule deer. Journal of Wildlife Management 66:564-573.

Zhu, L. and B. P. Carlin. 2000. Comparing hierarchical models for spatio-temporally misaligned data using the deviance information criterion. Statistics in Medicine 19:2265-2278.

Zhu, L., B. P. Carlin, P. English, and R. Scalf. 2000. Hierarchical modeling of spatio-temporally misaligned data: Relating traffic density to pediatric asthma hospitalizations. Environmetrics 11:43-61

Table 3.1. Comparison of statistics for Observed and Modeled deer counts in 800 meter grid cells based on summing the four years of deer counts for years 1998, 1999, 2000, and 2002 . The low bias and good agreement between observed and modeled deer counts suggests the ability of the model to reflect the data and its spatial structure.

	Observed	Modeled
Mean	20.9	20.5
Std. Dev.	22.5	21.8
CV%	106.8	106.5
Minimum	0.0	0.0
First quantile	4.0	5.4
Median	12.0	14.1
Third quantile	32.0	28.7
Maximum	110.0	124.4
Bias%		1.9

Table 3.2. Statistics from cross-validation of the median polish kriged (MPK) surface. The Agreement between the model-based MAE and RMSE with the observed standard error from the data, suggests good agreement between observed and estimated errors. The SMSE, which is the ratio of observed to predicted errors averaged across all quadrats, shows that the prediction errors were smaller than, but consistent with, the true errors. The coverage rate, based on the prediction error, σ_{i^*}, was 90%, suggesting that the prediction variance slightly underestimated the true variance from the data, which is consistent with the SMSE value.

Statistic [1]	MPK
Mean error	0.4
IQR	36.0
MAE	22.7
RMSE	30.3
SMSE	1.24
0.95 coverage rate	0.90

[1] IQR = interquartile range, MAE = mean absolute error, RMSE = root mean square error, SMSE = standardized mean square error.

Table 3.3. Model selection results identifying each candidate model's ability to explain the observed spatial patterns of chronic wasting disease (CWD) prevalence in mule deer. All models were fit at the individual winter home range scale of 9 km^2 and incorporated various combinations of deer sex (Sex), estimated density (Dens), spatial (Space), and unstructured heterogeneous (Het) variation. Space and Het are random effects, pD = effective number of parameters, DIC = Deviance Information Criteria, DIC weight, w_{DIC}, informally quantifies model selection uncertainty.

Model	pD	DIC	w_{DIC}
Sex + Space	10.	930.	0.256
Sex + Space + Het	11.	930.	0.203
Sex + Dens + Space	12.	930.	0.175
Sex + Dens + Space + Het	12.	931.	0.164
Sex + Dens + $Dens^2$ + Space	13.	931.	0.105
Sex + Dens + $Dens^2$ + Space +	13.	932.	0.096
Sex	2.0	941.	0.001
Sex + Dens	2.7	942.	0.001
Sex + Dens + $Dens^2$	3.4	943.	0.000
Sex + Het	28.	962.	0.000
Sex + Dens + Het	30.	964.	0.000
Sex + Dens + $Dens^2$ + Het	31.	966.	0.000

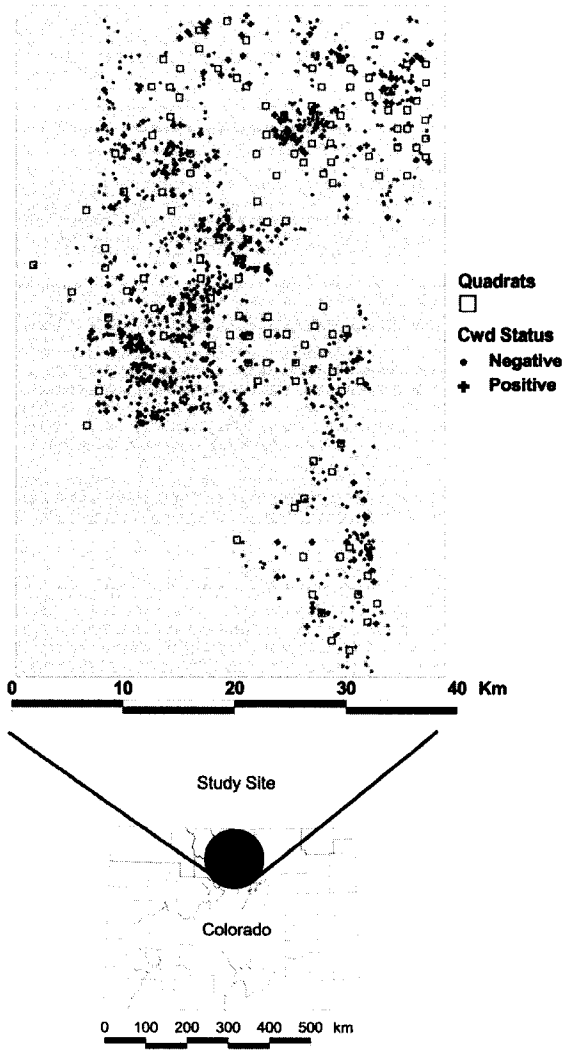

Figure 3.1 – Study area in North-central Colorado with the 129, 0.64 km^2 survey quadrats of deer densities shown as squares. CWD sample locations are shown as "+" for deer that tested positive and "-" for deer that tested negative for the disease.

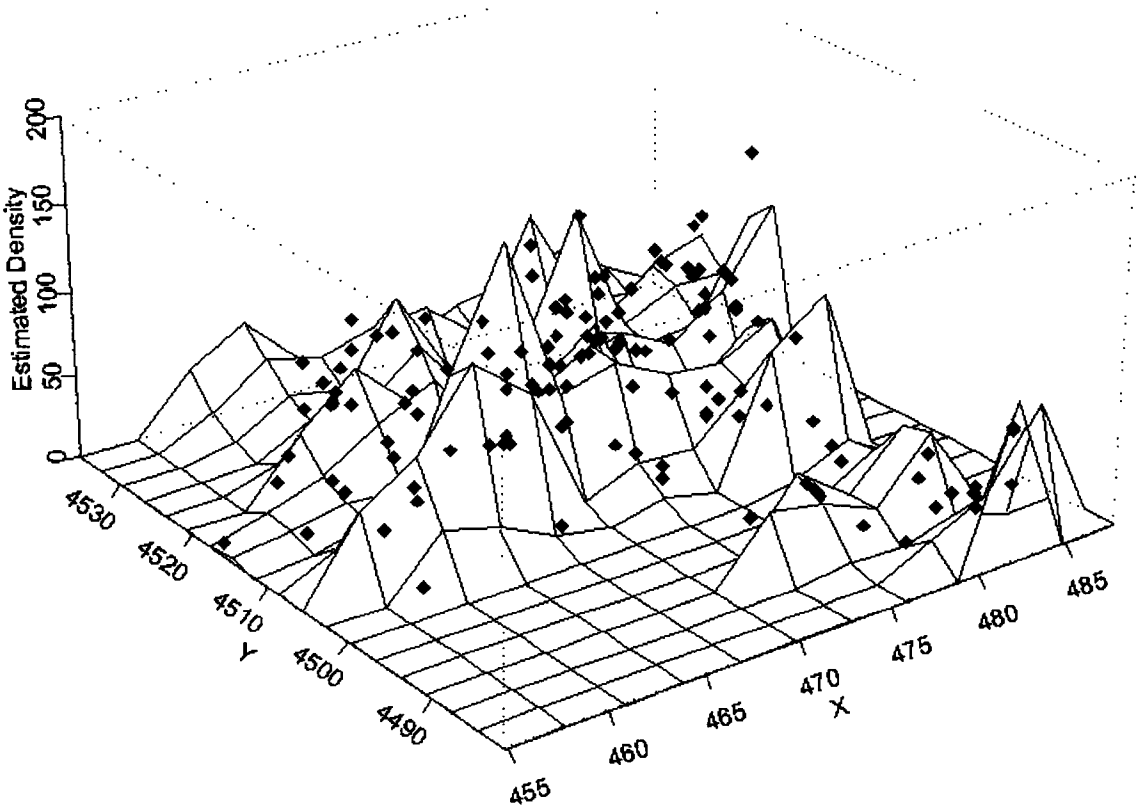

Figure 3.2 – Perspective plot of 9km^2 grid of estimated deer/km^2 based on median polish kriging. The surface is based on the sum of deer counts, shown here as points, in each quadrat during the four years covered by the study. Note the good agreement between observed densities and those estimated by the underlying surface

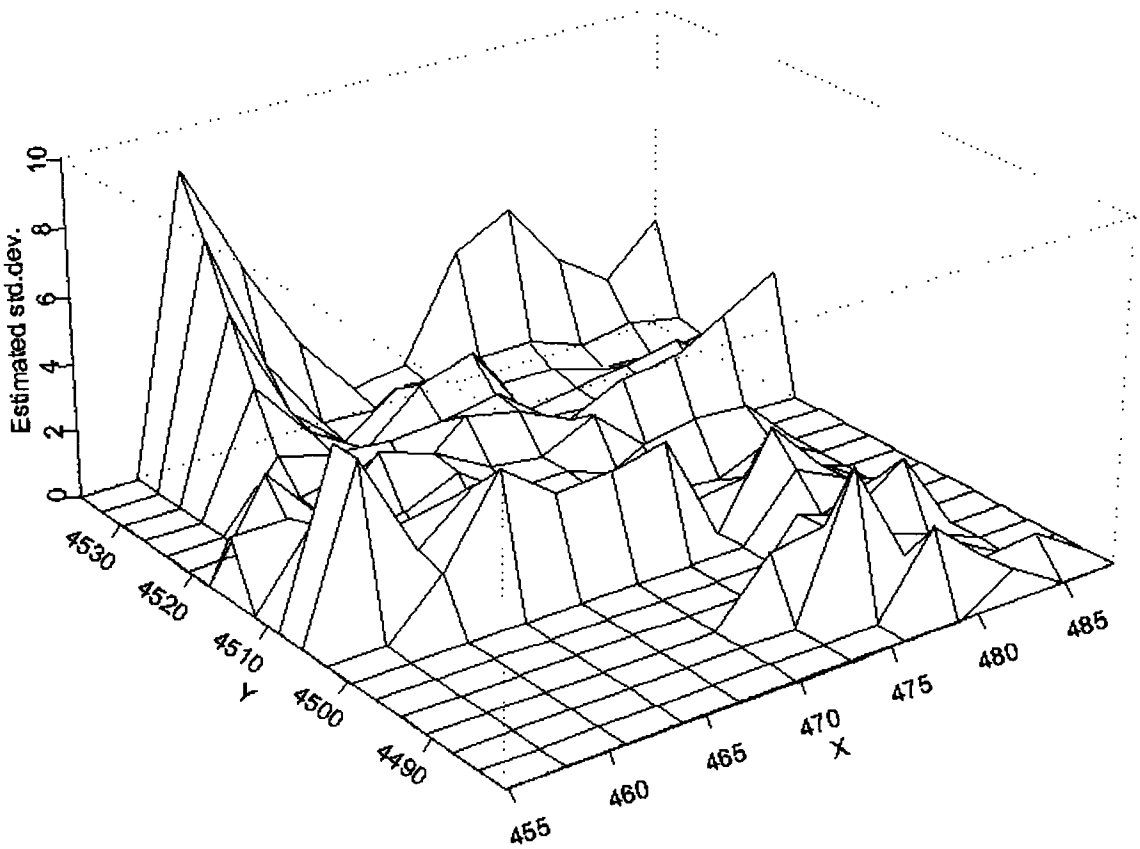

Figure 3.3 – Perspective plot of 9km^2 grid of estimated standard deviations in deer/km^2 based on median polish kriging. Standard deviations were obtained from the variogram model fit to the survey data of deer counts. Note the increase in estimation uncertainty in cells that are furthest from the quadrat locations, resulting from an assumption of the variogram model. The standard deviations were used to model the estimation error during the fitting of the surface of estimated density to the CWD data

CONCLUSION

MANAGEMENT RECOMMENDATIONS AND RESEARCH EXTENSIONS

Managing Urban Deer Populations

The effects of human land use on disease dynamics rarely have been quantified for natural populations. Because mule deer sampled from urban locations, as defined in the first chapter, exhibited prevalence rates that were nearly double those of deer located in non-urban areas, management efforts that target urban populations for culling of diseased individuals may aid in reducing CWD transmission and overall prevalence. Further, because males appear to contribute disproportionately to infection rates in urban areas, culling activities might focus on them, however females should not be ignored since they are more abundant than males. While this research suggests that a disparity in age distributions between males and females could explain the difference in prevalence, there are currently no data available to confirm or reject this hypothesis. Future research should seek to quantify differences in the age structure of males and females in urban and non-urban settings to test this hypothesis. Such an assessment could lead to stronger public support for managing deer populations for CWD in urban areas.

Scaling management to mule deer biology

Because CWD infection risk corresponds strongly with the scale of an individual deer winter home range of 9 km^2, disease management efforts targeted at this biological scale may be most effective in reducing disease transmission. Specifically, targeted reductions of deer belonging to populations that occur in the areas of high disease prevalence shown in Figure 2.2 might aid in reduction of overall prevalence in northern Colorado. Coupling results from chapter one, which suggest that older males are disproportionately responsible for elevated prevalence in urban settings, with the highly localized contact process structuring the distribution of CWD suggested by the results of chapter 2, leads to the conclusion that culling of mature males in the geographic "hot spots" identified in Figure 2.2 may provide a highly focused approach for slowing the spread of CWD. The development of simulation models exploring various culling strategies could potentially be used to determine which management approaches are most likely to reduce disease transmission and prevalence.

Density and CWD Epidemiology

Because there was no strong relationship between deer density and prevalence at the individual winter home range scale of 9 km^2, large scale density reduction may not be as effective at reducing transmission and prevalence as local, and perhaps more intensive, culling of known "hot spots" of infection. Following this line of reasoning also suggests that deer removal might be most effective if it is targeted at the component of the population that has the greatest number of potential contacts with other deer, irrespective of local density. Specifically, targeting older males, even in areas where CWD prevalence is relatively low, may reduce the overall number of potential transmission

events since this is the component of the population that appears to have the greatest number of potential contacts, particularly during the breeding season.

Research Extensions

As noted above, the results of chapter one suggest that research efforts focused on elucidating the age structure of urban and non-urban deer populations could provide evidence for the mechanism that is primarily responsible for the elevated prevalence seen in urban males.

The results from chapter two suggest that the distribution of CWD corresponds to a highly localized contact process occurring on mule deer winter home ranges. This information could aid in the development of mechanistic models of disease transmission. For example, modeling the transmission process as occurring primarily during the winter season, when deer are aggregated into discrete and relatively non-interacting sub-populations, using a seasonal forcing component could add realism to such models. This could result in a better mechanistic approximation of the process leading to the heterogeneity in infection probabilities illustrated in chapter two. When coupled with a demographic model, this information could result in a more realistic representation of the interrelationship between mule deer and disease population dynamics than previous efforts. Extending this to a spatially explicit framework, the grid-based representation of disease intensity shown in Figure 2.2 could be used to specify infection probabilities in a dynamic model that includes deer movement patterns between the cells. One particularly attractive approach for this system would be to model transmission probabilities using the temporal and spatial variations suggested from the results of chapter two within an

individual based demographic model that includes deer movement patterns and contact probabilities within a network specification of the interaction potential among deer.

Finally, the model I developed to explore the relationship between the probability a deer is infected with CWD and estimated density showed no relationship based on the spatial modeling approach I chose applied to the large-scale field data. If such a relationship exists, it is possibly better elucidated using an experimental approach. For example, captive deer could be maintained at various densities for a period that is sufficient to ensure the absence of infection. CWD could then be introduced and the rate of infection measured to estimate the relationship. This type of experimental approach might be the most feasible way to understand the density/disease relationship for a wide-ranging ungulate species like mule deer. Two main caveats to such an experiment are the recognition that deer may not interact with each other in the same manner in a captive setting and that achieving the scale and densities seen in natural settings may not be feasible. However, it may still prove useful in shedding light on the relationship between mule deer density and infection risk.

Data considerations

For all of the analyses in this dissertation, deer location data were represented by a single point on the landscape. Treating these highly mobile animals as static points potentially introduces confounding in the geographic representation of the disease. This may be the greatest potential criticism of the use of these data for spatial analysis. Another issue, although probably not of as great a concern, is the method by which most of the spatially referenced deer locations were mapped. Locations of individual deer were typically mapped by hunters, often using 7.5" topographic maps to identify harvest

locations. This method obviously suffers from an unknowable amount of error associated with each location. For the purposes of landscape-scaled analysis, targeted at identifying broad spatial patterns in relative disease prevalence, both of these issues may be negligible. However, these data illustrate one of the primary dilemmas faced by applied landscape ecologists; amassing data for spatial analysis across large geographic extents often requires a sacrifice in data representation and collection rigor. The most often highlighted example of this dilemma that is often cited is the North American Breeding Bird Survey, where voluminous amounts of data on bird counts across North America are available, however these data are often criticized because they are collected only along roads and thus are not representative of the entire population. Similar criticisms of the CWD data can be made, therefore use of these data for local analysis over small extents should be carefully considered.

I was unable to address the issue of temporal bias in the spatial patterns of disease prevalence because all analyses used in this dissertation were retrospective. Thus, all analyses implicitly assumed that the disease had been present on all parts of the landscape long enough for differences in the time since CWD introduction to be negligible, i.e. that the disease had previously reached a state of equilibrium everywhere. It is possible, however, that areas of the landscape with high prevalence resulted from the disease being present longer in these areas than in low prevalence locations (Miller et al. 2000, Miller and Conner 2005). It would be difficult to design a prospective study that is unlikely to be confounded by this temporal effect. For example, baseline estimates of landscape variation in prevalence from this study could be used to measure future changes in prevalence. While monitoring the rate of change in prevalence across the landscape in

this manner might allow for stronger inference about the biotic and abiotic factors that act to shape CWD spatial heterogeneity, this type of study cannot rule out the potentially confounding effect of different times since disease introduction into different parts of the landscape if equilibrium levels have not been reached everywhere. Without the knowledge of where the disease first appeared on the landscape and its subsequent spread, it will be impossible to entirely refute the notion of temporal confounding. One could assume that the disease has been present in all areas long enough to reach equilibrium based on the assumption that CWD may have been present in free-ranging deer within this area since the 1960s or earlier. However, even if there exists an equilibrium that would be achieved after a sufficient period, which is unknown, there is no way to determine the time needed to achieve such equilibrium.