Hierarchical Bayesian Modeling of Disease Dynamics:
A Case Example Using Chronic Wasting Disease

CWD Annual Report – 2009-2010

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Partners
Colorado Division of Wildlife
City of Fort Collins
Larimer County, Colorado
Colorado State University Research Foundation
The Nature Conservancy
Landowners Association for Phantom Canyon Ranches
Colorado State University Veterinary Diagnostic Laboratories

Overview of research

Aims

Portraying dynamics of infectious disease offers a fundamental challenge in population and community ecology. Rising to this challenge often provides immediate application to assuring the health of people and animals. Traditionally, models of infectious disease have not dealt with uncertainty in a sophisticated way---there are few examples of dynamic models of disease systems that have estimated uncertainty arising from variance in processes, errors in observations, and random effects in a statistically coherent way. Forecasting the spread of diseases depends on partitioning uncertainty into these components. Our primary goal is to demonstrate the use of Bayesian hierarchical methods to model the dynamics of an infectious disease, to estimate associated uncertainties, and to provide forecasts. Our secondary goal is to advance understanding of a particular disease system, chronic wasting disease of the deer family (CWD). These goals motivate the following specific aims:

Aim 1: Provide a case example of a novel, general approach for assimilating data with dynamics of populations infected with a emerging infectious disease.
Aim 2: Evaluate support in data for competing models of transmission of CWD and estimate the basic reproductive rate of the disease.
Aim 3: Reveal demographic, genetic, and environmental sources of heterogeneity in disease transmission.
Aim 4: Use the models developed under Aim 1 and 2 to evaluate the consequences of disease for the trajectories of populations infected with proteinase resistant prions.

Research Approach

Stage structured, discrete time models of population dynamics provide widely used methods for representing and analyzing dynamics of populations, but these models have rarely been applied to infectious diseases. We will represent a population of mule deer infected with chronic wasting disease using two sexes, two ages, and two disease states (Eq 1).

To parameterize this model and estimate uncertainties, we will combine data from historic time series of monitoring data on population size, sex and age composition, and disease prevalence with data from multi-state capture-mark-recapture studies that we are conducting during the five years of the project

See Figure 1 for a heuristic formulation of the model.

Activities in Year One

Community Outreach and Landowner Participation

We are working in Northern Larimer county, CO, an area where prevalence of CWD is high and where we can exploit an extensive history of earlier research. The area includes a complex mosaic of land ownerships, including six different land management agencies and hundreds of private landowners.

Gaining permission and permits to work on this landscape required extensive outreach to the community and to local governments. We began the project with a mailing to all landowners in the project study area informing them of the project and inviting them to a public information meeting, attended by about 100 community members, held in November 2009. We will have these public meetings twice a year in order to keep the community involved in the project. Additionally, we have a contact list of about 200 interested community members and partners who receive periodic project updates. We have obtained permission from sixteen private landowners in the study area to use their land for research, as well as from a number of public land managers.

We have formed a citizen's advisory committee that includes landowners and land managers in the area where we work. We meet quarterly with the committee to update them on progress on the project, to seek their advice, and to hear concerns.

Animal Capture, Sampling, and Monitoring

During January and February of 2010 we captured, using helicopter net gunning, 125 adult females and 15 fawns from seven sampling locations within our study area. Animals were transported to a processing site within each sampling location where we fit them with radio collars (60 GPS, 80 VHF) and collected blood, fecal, and tissue samples. There were no major injuries or mortalities during capture.

We attempted to locate all individuals at least once weekly to monitor for mortality signals, using standard ground and aerial telemetry homing techniques. Mortalities were investigated by ground teams to determine cause of death and secure samples for infection biopsy.

Blood samples were obtained and stored for all deer and DNA has been extracted from these samples. We will use a PCR-based assay to determine 225S/F genotypes of female deer in our study area, and relate SS/SF genotype frequencies to collection areas, age of deer, and rates of disease-related mortality. Additional genotyping of a series of microsatellite markers will allow us to test how relatedness within deer groups (a measure of contact between female deer) influences disease status and mortality of deer.

Findings

Four adult females tested positive for CWD (3.2%). We used a Bayesian random effects model to estimate prevalence within the study population.

There have been sixteen mortalities (10 adults, 6 fawns). Seven adults were killed by mountain lions, one died from chronic wasting disease, one from a motor vehicle accident, and one from an unknown cause. One fawn mortality is probably related to capture, one fawn was killed by winter kill and four fawns had unknown causes of death. Diagnostic samples were available on seven of the ten adult mortalities, and one of the six fawn mortalities. In the adult mortalities for which diagnostic samples were available, four CWD tests were negative, one was positive, and three are pending. There were no conversions from non-infected to infected among the adult mortalities.

Graduate Education and Training

We have recruited four graduate students, two in ecology and biology, one in statistics, and one in mathematics. These students are receiving interdisciplinary training throughout working closely together to implement project goals. Biology and ecology students are participating in field work and math and statistics students are doing mathematical and statistical modeling.

Undergraduate Research Experience

First-year Honors Undergraduate Research Scholars Emily Dommermuth, Katharine Fielding, Nicholas Bartush, and Stephanie Richert worked with Co-PI Boone throughout the academic year. In the fall semester the students learned about the scientific method, what it means to be a scientist, and the nature of data. In the spring semester, students learned introductory concepts to geographic information science. The students have learned about the projects they wished to be most closely associated with (this project tracking mule deer, EF-0914489, PI: Hobbs, and DEB-0919383 tracking migratory wildebeest, PI: Boone), and each has gained experience in using the equipment helping our team track mule deer. The students on the Laramie Foothills Mule Deer Project, Nicholas Bartush and Emily Dommermuth, participated in capture activities, and in addition to gaining extraordinary experiences, helped the larger team greatly.

In the spring semester, the students began a larger research effort, testing the accuracy of a Global Positioning System (GPS) collar used on mule deer. Over several months the students moved a collar to 15 locations, recording the true position of the location using a hand-held GPS unit. The students worked with Boone to analyze the results, then prepared a poster that was displayed at the 'Celebrate Undergraduate Research and Creativity' Symposium on the CSU campus in April 2010. The students received positive comments on their poster. The testing of the collar is somewhat informative to the larger project. But most importantly, the students learned about project design, GIS, simple statistical analyses, and the presentation of information to audiences. The students will continue to work with Dr. Boone throughout their undergraduate education.

Outreach

Hobbs led a training session on CWD for interpretive staff at Rocky Mountain National Park as well as for Master Naturalists at the City of Fort Collins. We have contributed educational materials and interpretive signage regarding CWD and the study to the City of Fort Collins and Larimer County. We have initiated a collaboration with four high school teachers who will help us with field investigations and with outreach to the local community. They will participate in all project meetings and will become familiar with all aspects of the research with the ultimate goal of developing curriculum for biology and statistics classes using the research.

Publications

Journals

Dulberger, J., N. T. Hobbs, H. M. Swanson, C. J. Bishop, and M. W. Miller. In press. Estimating Chronic Wasting Disease Effects on Mule Deer Recruitment and Population Growth. Journal of Wildlife Disease.

Hobbs, N. T. and K. Ogle. In press. Introducing model data assimilation to students of ecology. Ecological Applications.

LaDeau, S. L., G. E. Glass, N. T. Hobbs, A. Latimer, R. S. Ostfeld. In press. Data-model fusion to better understand emerging pathogens and improve infectious disease forecasting. Ecological Applications.

Webb, C.T., J. A. Hoeting. G. M. Ames, M. I. Pyne, N. L. Po. 2010. A structured and dynamic framework to advance traits-based theory and prediction in ecology. Ecology Letters, 13: 267-283.

Books and other One Time Publications

Schmidt, A., J. A. Hoeting, J. B. M. Pereira, P. P. Vieira. 2010. Mapping Malaria in the Amazon Rain Forest: a Spatio-Temporal Mixture Model. To appear in The Handbook of Bayesian Analysis, editors Tony O'Hagan and Mike West.

Website

http://www.nrel.colostate.edu/projects/modelingCWD/

Contributions

To principle disciplines

We are developing modeling approaches that we believe will become standard in many studies of infectious disease, particularly diseases of wildlife.

To human resource development

We have engaged graduate and undergraduate students and provided unusual opportunities to participate in an interdisciplinary project.

Figures and Equations

$$\mathbf{N_{t+1} = MN_t} \qquad (1)$$

$$\mathbf{M} = \begin{bmatrix} 0 & \alpha F_2 & \alpha F_3 & 0 & 0 & 0 \\ \varphi_1 g_{2,1} & \varphi_2 g_{2,2} & 0 & 0 & 0 & 0 \\ \varphi_1 g_{3,1} & \varphi_2 g_{3,2} & \varphi_3 & 0 & 0 & 0 \\ 0 & (1-\alpha)F_2 & (1-\alpha)F_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & \varphi_5 g_{5,4} & \varphi_5 g_{5,5} & 0 \\ 0 & 0 & 0 & \varphi_4 g_{6,4} & \varphi_5 g_{6,5} & \varphi_6 \end{bmatrix}, \quad \mathbf{N}\begin{bmatrix} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \end{bmatrix} = \begin{bmatrix} \text{juvenile female susceptibles} \\ \text{adult female susceptibles} \\ \text{adult female infecteds} \\ \text{juvenile male susceptibles} \\ \text{adult male susceptibles} \\ \text{adult male infecteds} \end{bmatrix}$$

Nt is a vector of numbers of individuals in six possible states characterized by age, sex, and disease status. The *F's* are state specific fertilities, α is the sex ratio of offspring, the φ's give survival probabilities for state *i* during time *t* to *t + 1* and the *gjk*'s give the probability of transition from state *k* to state *j*. Hierarchical Bayesian models allow us to embed equation 1 in a composite likelihood that also includes a data model for capture-mark-recapture estimating φ and **g**. We can also incorporate historic, landscape level data on disease prevalence (supporting estimates of **g)**, observations of sex and age structure (supporting estimates of **F** and φ) and estimates of total population size into the model.

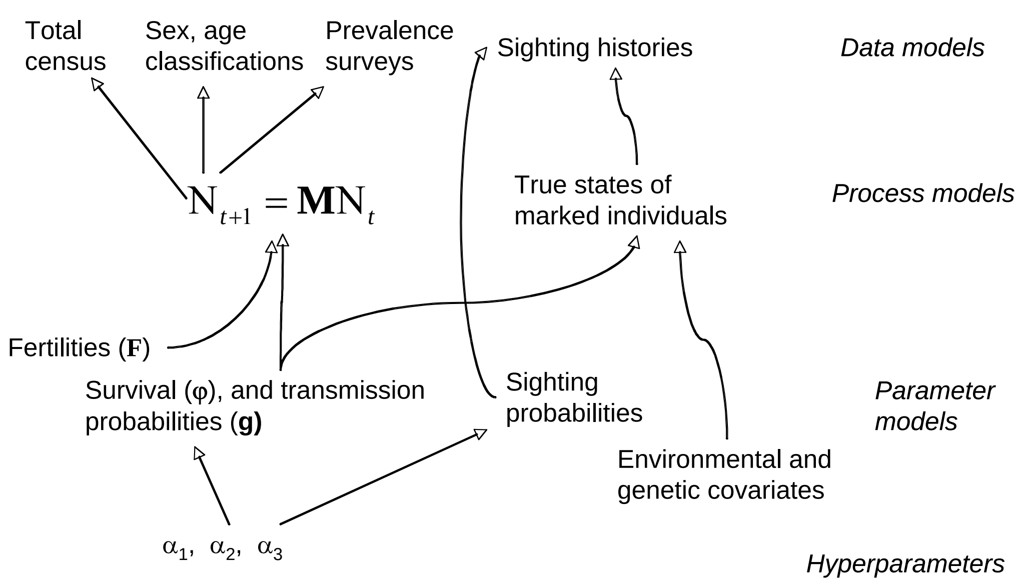

Figure 1. Schematic of relationships among data, models, and parameters in studies of chronic wasting disease.