

Advances in modeling highlight a tension between analytical accuracy and accessibility

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There is a persistent tension in ecological analysis between the call for increasingly accurate characterization of processes and the need for accessible models that provide both novel inference and valid forecasts (Clark et al. 2001, Hargreaves and Annan 2006, Keyl and Wolff 2008). Statistical and mathematical models are, by definition, designed to simplify a noisy reality in order to hone understanding. However, determining the relative trade-offs between simplicity and accuracy is not always straightforward. Ecological systems are complex and involve diverse communities that interact variably in space and time to influence ecosystem processes. Too much simplification can render model inference and predictions useless to the managers who need them. And yet, if model implementation is complicated and interpretation is not transparent, then even a well designed model may still not be used. Thus, a major goal of current ecological dialogue is to define the appropriate level of analytical complexity required to understand and forecast population, community, and ecosystem processes (Clark 2005, Bolker 2009, Cressie et al. 2009, de Valpine 2009). This dialogue is spurred on by an increasing number of citations that call for statistical frameworks more appropriate to ecological data than traditional, agriculturally derived methods (Gratzer et al. 2004, Clark 2005, Hobbs and Hilborn 2006), as well as through advances in computing that facilitate implementation of complex models (e.g., WinBUGS). The topic is also of critical importance as ecologists increasingly recognize the need (and answer the call) to both conduct research and transfer understanding in ways that can be used in policy and decision making. Here, I briefly review and discuss the evolution of recent modeling approaches in a wildlife disease system in order to better understand the complex Bayesian framework developed by Heisey et al. (2010).

Heisey et al. (2010) address a pervasive challenge in disease ecology: inferring transmission dynamics from observed patterns in disease prevalence data. Quantifying the latent transmission process is key to understand-

ing spatiotemporal progression of infectious diseases and devising management strategies (Anderson and May 1992, Schaubert and Woolf 2003, Wasserberg et al. 2009) but nearly impossible to observe directly (e.g., Cooper and Lipsitch 2004, Farnsworth et al. 2006, Wonham et al. 2006, Foley et al. 2007). This challenge is exacerbated in wildlife disease systems, where data limitations and sampling variation can effectively obscure real disease dynamics. Disease prevalence can vary geographically and temporally due to variation in host densities, age or gender structure, environmental characteristics, and time since introduction. Disease prevalence observations integrate across all of these considerations plus sampling mechanisms. Distinguishing the importance of any one in the transmission process requires careful analysis.

These challenges are especially prominent in the ongoing effort to manage the spread and impact of chronic wasting disease (CWD) among cervid populations in North America. CWD is caused by an infectious prion and was first documented in the 1960s in Colorado. The disease has since spread to captive and wild cervid populations in at least 14 other states and two Canadian provinces (Williams et al. 2002, USGS 2009). CWD infection eventually causes mortality, although the time from exposure to death is unknown and may vary significantly (USGS 2009). Despite considerable efforts to model CWD progression in both mule deer and white-tailed deer populations (e.g., Miller and Conner 2005, Farnsworth et al. 2006, Joly et al. 2006, Miller et al. 2006, Osnas et al. 2009, Song and Lawson 2009, Wasserberg et al. 2009), quantifying the relative importance of demography, spatial structure, and temporal trends in defining CWD prevalence remains an important research objective. The limited nature of the data that is often available to assess CWD dynamics (i.e., hunter-gathered) and the complexity of spatiotemporal epidemic processes in general make this objective a worthy target for diverse modeling approaches.

Deterministic models (i.e., SIR methods) have been instrumental in understanding epidemic progression in many infectious systems (e.g., Anderson and May 1992). However, the accuracy of these methods generally relies on how well researchers understand the process of

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infectious transmission. For example, these methods typically assume either density- or frequency-dependent transmission dynamics, a choice that is known to have direct implications on inferences (Schauber and Woolf 2003, Smith et al. 2009, Wasserberg et al. 2009). This is especially problematic in CWD, where the actual mode of transmission may be a mix of density-dependent and frequency-dependent interactions (Schauber and Woolf 2003, Miller et al. 2006, Wasserberg et al. 2009). Available management options to control CWD epidemics include selective and non-selective culling to remove infected individuals or decrease deer density, respectively. Effective management employing these options is intrinsically tied to the spatiotemporal transmission process (Schauber and Woolf 2003, Wasserberg et al. 2009). Mule deer and white-tailed deer herds are generally structured as small matrilineal units of females with relatively small seasonal home ranges and males that wander more broadly. Higher densities of deer within and among these units could lead to density-dependent opportunities for infectious transmission, although if the units remain separated for much of the year then the overall population prevalence of CWD infected deer could also be independent of overall abundance. If transmission is density-dependent then non-selective culling through hunting could be used to decrease deer density below the threshold needed to sustain the epidemic. If the transmission process is frequency-dependent then CWD eradication is contingent on host eradication (Wasserberg et al. 2009). To further complicate the issue, the infectious CWD prion can persist in soil and feces and infect deer indirectly over unknown temporal scales (Miller et al. 2004, Tamguney et al. 2009). Thus, environmental decontamination or local extirpation of all potential host species would also be necessary to eradicate CWD, regardless of more dominant forms of transmission. The relative importance of different modes of transmission remains an open question and a distinct challenge in managing the CWD epidemic.

Statistical models can be used to explore and identify generating forces behind patterns of disease prevalence without explicitly assuming density- or frequency-dependent transmission. In this manner, more precise understanding of the causes of spatial and temporal heterogeneity in CWD prevalence can provide insight into the transmission process. Miller and Conner (2005) used model selection criterion (AIC; Burnham and Anderson 2002) to compare 16 logistic regression models to evaluate the influence of age, gender, year, and spatial location on CWD prevalence in mule deer and found all to be important causes of heterogeneity in disease prevalence. While susceptibility to CWD infection is similar between genders and across age classes (see references in Miller and Conner 2005), observed prevalence was highest in mid-aged males and increased over time within local deer populations. The analysis by Miller and Conner (2005) did not differentiate between

uncertainties in the process model vs. uncertainties due to the sampling protocol, as they assumed CWD detection and prevalence to be equal. If not completely valid, this key assumption may bias Miller and Conner's (2005) age and gender structured results. In their conclusions, Miller and Conner (2005) proposed a framework for local-scale, predominantly independent, CWD epidemics within the "endemic CWD" range. They hypothesized that male deer are responsible for spreading the disease among the relatively isolated matrilineal clans, resulting in spatial heterogeneity of local CWD introductions and variable prevalence rates that are dependent on time since introduction. However, a paucity of data on disease prevalence sampled (with error) over multiple years from an age-structured population make this a difficult hypothesis to test.

The collection of CWD models published in recent years, regardless of statistical philosophy, have generally employed approaches that compare multiple alternative or nested models to explore CWD dynamics, rather than rely on more traditional hypothesis testing procedures (sensu Hobbs and Hilborn 2005, Plowright et al. 2008) and there is a logical progression of models, inference, and interpretation that runs throughout much of this work (e.g., Miller and Conner 2005, Miller et al. 2006, Osnas et al. 2009, Song and Lawson 2009, Heisey et al. 2010). A majority of recent models use a hierarchical Bayesian framework, which can coherently estimate the latent spatiotemporal transmission process and account for uncertainty in the data generating process (Clark 2005, Cressie et al. 2009). Regardless of the modeling framework, most analyses consistently support increased infection among male deer and increasing risk of infection with age after two years (Farnsworth et al. 2006, Grear et al. 2006, Osnas et al. 2009, Song and Lawson 2009). Several analyses also found that observed prevalence declined in the oldest age classes (Miller and Conner 2005, Osnas et al. 2009). Furthermore, studies consistently report that disease prevalence is spatially heterogeneous (Osnas et al. 2009, Song and Lawson 2009) and may be influenced by habitat characteristics (Farnsworth et al. 2005, Joly et al. 2006), time since introduction (Miller and Conner 2005, Wasserberg et al. 2009), differences in demography (Miller and Conner 2005, Osnas et al. 2009) and localized "hotspots" of high transmission (Farnsworth et al. 2006). In 2006, Farnsworth and colleagues used a Bayesian hierarchical model to link CWD prevalence among mule deer in Colorado to known scales of mule deer movement. In the ongoing effort to understand how CWD transmission leads to the observed spatial heterogeneity in disease prevalence, Farnsworth et al. (2006) looked to define the scale at which deer interactions (which occur at known and divergent spatial scales) were most likely to generate the observed patterns of prevalence. In addition to deer age and gender effects, Farnsworth et al. (2006) identified local-scale contacts, particularly those that occur during the winter season, as a key generating force behind the

observed spatial patterns of CWD prevalence among Colorado's mule deer.

Of three CWD modeling papers published in 2009, all used some subset of the Wisconsin white-tailed deer harvest data detailed in Heisey et al. (2010), and two used Bayesian hierarchical modeling frameworks to quantify spatiotemporal patterns in disease prevalence (Osnas et al. 2009, Song and Lawson 2009). CWD has been monitored in Wisconsin since 2002, largely through hunter-harvested samples. Despite aggressive management of deer densities, disease prevalence has increased (especially in recent years) and spread beyond the initial detection zone (data from Wisconsin Department of Natural Resources, *available online*).² Following patterns seen in Colorado's mule deer, observed CWD prevalence in white-tailed deer in Wisconsin is higher in males (10% vs. 4–5% in females), spatially variable, and may decline in older age classes (e.g., Grear et al. 2006, Osnas et al. 2009). Understanding the causes of the spatial heterogeneity and determining whether or not the epidemic is increasing over time remain important considerations.

Wasserberg et al. (2009) used a deterministic multistate matrix model to explicitly evaluate the consequences of density- and frequency-dependent transmission assumptions on estimates of time since introduction, epidemic duration, and management outcomes. The model characterizes four infection stages for 20 age classes and two genders, for a 160-by-160-cell transition matrix and is nonspatial but does incorporate seasonality. The authors fit the Wisconsin data to density- and frequency-dependent models using maximum likelihood techniques with a somewhat indecisive outcome. Although the AIC value was slightly lower for the frequency-dependent model, both transmission models fit to a subset of the data predicted 2006 prevalence data equally well. Furthermore, while the estimate for time since introduction using the frequency-dependent model was 188 years, the density-dependent transmission model estimated a more realistic 36 years. The authors also compared the simulated effects of culling on frequency- and density-dependent disease progression and reaffirmed that culling is only effective at managing CWD if transmission is density-dependent. Wasserberg et al. (2009) argue that management (i.e., culling) experiments could be used to identify the driving mode of transmission: density-dependent transmission will eventually produce an epidemic wave, while frequency-dependent transmission will result in asymptotic epidemic growth.

The hierarchical Bayesian model published by Osnas et al. (2009) defines a Bernoulli observation model where the probability of CWD infection increases with age according to a cumulative hazard function informed by the age and gender of the deer sampled. They used a model selection criterion similar to AIC (DIC; Spiegel-

halter et al. 2002) to select a fully saturated model with age, age², gender, a latent spatial effect, and a spatially varying linear time trend. Osnas et al. (2009) again confirmed that males are more likely to be positive for CWD and that risk of infection, especially in males, increases with age and decreases among older deer. They concluded that the observed spatial heterogeneity in CWD prevalence is due to sampling variation and deer demography and not to spatial differences (i.e., hot-spots) in transmission. Still, the analysis of Osnas et al. (2009) was insufficient to prove or disprove the notion that patterns of high prevalence might result from differences in epidemic growth rates or variable timing of local introductions. Osnas et al. (2009) also stressed that the temporal duration of the available data was insufficient to fully deduce spatiotemporal CWD epidemic processes.

Song and Lawson (2009) also used data from deer harvests in Wisconsin to fit a hierarchical Bayesian survival model where risk of infection is a power function of deer age. Unlike the models discussed above, their model is explicitly structured to account for the fact that harvest age does not equal age of infection and that the data are censored depending on infection status. Additionally, the authors explored the degree of infectious clustering in space and time through covariates representing (spatial and temporal) distances between harvested deer and all other CWD positive deer sampled. Like the other studies, the authors concluded that males are at higher risk of infection, although they did not find evidence to support changing CWD prevalence with age. This may be due to the absence of an age–sex interaction (*sensu* Osnas et al. 2009). Covariates defining temporal and spatial clusters of CWD infections were also significant. Unfortunately, the interpretation of what causes the spatial, temporal, and spatiotemporal clustering of CWD infected deer remains unclear. Indeed, the authors noted that a negative temporal clustering effect may suggest increasing temporal trend in infection hazard (i.e., a growing epidemic) but could also result from insufficient accommodation of the difference between harvest age and actual infection age.

So, by the end of 2009, we knew that male deer over 2 years old are roughly twice as likely to be CWD positive than females and that infection risk increases initially with age but then is reduced in both genders among the oldest age classes. It remains unclear how important CWD-related mortality is to the non-linear relationship between prevalence and deer age (Osnas et al. 2009). Additionally, spatial structure in CWD prevalence is evident, although conclusions are mixed as to the relative importance of time since CWD introduction, environmental characteristics, and deer demography. Likewise, the importance of the censoring mechanism in the hunted deer samples remains an open question. The censored survival analysis by Song and Lawson (2009) performed only slightly better by DIC comparison than

² (<http://dnr.wi.gov/org/land/wildlife/whealth/issues/CWD/maps.htm>)

a simpler logistic regression. All of this sets the stage for the presentation by Heisey et al. (2010), which describes a complicated model that attempts to coherently accommodate many of the shortcomings in each of its predecessors.

The research presented in Heisey et al. (2010) further examines the spatial heterogeneity in CWD prevalence and specifically asks: (1) Do areas of high CWD prevalence reflect high transmission rates? and (2) Are there hotspots in local CWD cases? If high prevalence is not the result of epidemic growth, the authors consider the alternative explanation that heterogeneous infection prevalence results from differences in local introductions (e.g., Miller and Conner 2005). A key advance in the analysis presented by Heisey et al. (2010) is simultaneous consideration of several issues important in disease ecology within a common model framework. They detail a logical path through some complicated model components that accommodate the data censoring mechanism, address the challenge in discerning age vs. time influences when interpreting temporal changes (in transmission) in an age-structured host population, and simultaneously, examine potential causes of the spatial patterns in disease prevalence. The authors are careful to point out that their analysis models the force-of-infection and is not a model of the time of initial infection. This is important to the interpretation of their results. The specific model components include a hierarchical Bayesian survival or hazard model for cumulative risk of infection, a smoothing function to model the dependence structure between deer age and time, and a spatial component. The authors perform detailed model selection on each component. They acknowledge two primary assumptions in their model structure: (1) that time of death is not associated with infection status and, (2) that conditional on gender, age, and location, deer samples are independent of CWD infection status. Both assumptions are likely violated (by their admission). Whether or not hunters are more or less likely to shoot CWD positive deer and whether or not that changes with time remains unclear (but see Grear et al. 2006)—and is potentially a source of bias in this and all previous models. The model presented by Heisey et al. (2010) certainly advances understanding of the spatiotemporal structure in CWD prevalence beyond the capacity of the logistic regression model in Miller and Conner (2005), but both models are fundamentally dependent on the information available in the fitted data.

The model by Heisey et al. (2010) supports Miller and Conner's (2005) scenario of temporally distinct local introductions and does not support differences in the rate of increase of CWD prevalence or the existence of spatial "hotspots." Furthermore, Heisey et al. (2010) found that while CWD infection rates are higher in male deer, prevalence is more spatially clustered in female deer. Their results further support the idea that both density-dependent and density-independent mechanisms

are important in CWD transmission. Is this enough new information to warrant such an extensive model? Heisey et al.'s (2010) model requires a lot of data and some advanced statistical savvy. And like all models, this one is still vulnerable to critical assumptions and data limitations. Still, CWD is a complicated emergent system and simple models are unlikely to render accurate characterization of the spatiotemporal transmission process. In light of the complexities of the system and the shortcomings of preceding models, the complex and thoughtful approach by Heisey et al. (2010) seems warranted. Their model is not perfect but it is clearly structured to address limitations in previous models. Heisey et al. (2010) articulated a coherent modeling framework that addresses an important question, with full acknowledgement of assumptions made. It then becomes the purview of the next user to either build up from this framework or start anew to test other assumptions and hypotheses.

Heisey et al. (2010) characterize a gender-specific spatial structure in CWD prevalence that could inform more effective strategies for managing the CWD epidemic. But as they admit, defining gender-specific culling perimeters around CWD positive samples might be beyond the practical capacity of management resources. Are the efforts of designing models to more accurately characterize our understanding of processes and data mechanisms wasted if they cannot be used to manage the epidemic? The models mentioned here are undoubtedly important contributions to a growing body of research being used to understand and manage CWD. However, the very thoroughness of Heisey et al.'s (2010) approach raises important questions regarding the role of big statistical models in advancing ecological understanding and when necessary, guiding action. The question of how big or complex a model needs to be has been and will continue to be a popular target for critique, but most will agree that the answer depends on the research goals. Is the model designed to generate inference about key process or disturbance parameters? Is it important to test assumptions (Schauber and Woolf 2003, Wasserberg et al. 2009), generate forecasts (Clark et al. 2001), or evaluate management actions (Keeling et al. 2003, Lipsitch et al. 2003, Tildesley et al. 2006)? Models (statistical or mathematical) should be precisely as complex as necessary to address the relevant research questions and goals. Still, every model has key assumptions and limitations, regardless of its complexity. Standardizing protocols for testing assumptions, representing limitations, and validating model output in contemporary ecological analyses remains a critical task for the research community (Craigmile et al. 2009).

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