# RISK, UNCERTAINTY AND DECISION-MAKING: ASSESSING CHRONIC WASTING DISEASE OCCURRENCE RISK ACROSS AN EMERGENCE SPECTRUM

By

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A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Fisheries and Wildlife–Doctor of Philosophy

2020

ABSTRACT

RISK, UNCERTAINTY AND DECISION-MAKING: ASSESSING CHRONIC WASTING DISEASE OCCURRENCE RISK ACROSS AN EMERGENCE SPECTRUM

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Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy that has spread in North American cervids for at least the last 50 years. Since its initial discovery in Colorado in 1967 (Williams and Young 1980), it has affected at least eight cervid species including white-tailed deer (*Odocoileus virginianus*), spread to at least 26 U.S. states (Rivera et al. 2019), and been called the greatest contemporary threat to free-ranging deer herds (Gillin and Mawdsley 2018). Once CWD is introduced, it is known to cause localized population declines that threaten the long-term sustainability of deer herds and associated hunting activities. As a result, state and federal agencies have allocated a large amount of financial and staff-time resources to manage CWD but have experienced limited success.

One of the most rational and effective ways to mitigate the effects of a persistent disease like CWD is to perform proactive surveillance efforts that can either prevent, or detect and eradicate, disease prior to its establishment. However, a combination of human activities that increase the risk of disease translocation, complex disease dynamics, and imperfect observation makes assessing the comprehensive risk of CWD introduction by empirical study prohibitive. Furthermore, once CWD is introduced and becomes established it has been difficult to maintain long-term monitoring programs at a level that produces accurate spatial predictions and improves our ability to understand the causal mechanisms that promote disease spread and persistence.

I developed several distinct modeling approaches to perform proactive and reactive CWD surveillance and monitoring given limitations in data availability, disease observation, and long-

term financial and staff-time resources. I determined that expert elicitation techniques are valuable tools to help inform comprehensive risk assessments given that appropriate methods are employed to limit expert biases. I determined that increasing the complexity of disease models can help predict the locations of CWD occurrence and may elucidate mechanisms that promote localized spread, long-distance spread, and persistence of disease. Finally, I utilized important covariate relationships that impact disease detection to help inform the strategic and efficient long-term use of resources.

Important findings from my dissertation include: 1) a comprehensive approach to estimate the spatially-explicit risk of disease exposure and amplification that is adaptable to localized disease hazards; 2) CWD extent estimates that are specific to the localized landscape and that include more disease detections than existing distance benchmark approaches; 3) a statistical modeling framework that incorporates more of the complex disease ecology and produces more accurate spatial estimates of disease occurrence; and finally, 4) the estimation of important covariate relationships that affect disease spread and persistence as well as disease detection. This dissertation and associated research findings will be broadly useful to disease management endeavors and contribute to improved decision making that maximizes the value of resources spent to acquire and learn from disease observation data.

# ACKNOWLEDGEMENTS

This work would not have been possible without the encouragement and support of my cherished family, friends, and colleagues. First and foremost, I thank my family who have sacrificed and supported me. I thank my beautiful wife, Megan, for her love and thoughtfulness. I thank my mother and father for providing me with a caring upbringing that promoted exploration and individual discovery. I thank my Aunt Marji for her encouragement, caring nature, and strong example of professional success. Finally, much love and gratitude to my sister, Natalie, and brother, Brian.

I acknowledge the contributions of my dissertation committee. I thank my doctoral advisors Bill Porter and David Williams for guiding, focusing, and increasing the impact of my research. I thank Kelly Straka for sharing her knowledge of wildlife diseases and management, and for being infectiously optimistic and thoughtful. I thank Kelly Robinson for critical insights and for exceeding my expectations at every opportunity. She has contributed to my success in ways she likely does not recognize. To my entire committee, I thank them for their expectations of rigor and for teaching me important skills that will have an enduring impact.

Funding and support were provided by the Michigan Department of Natural Resources, the Hal and Jean Glassen Memorial Foundation, the College of Agriculture and Natural Resources at Michigan State University (MSU), MSU Extension, MSU AgBioResearch, and the Boone and Crockett Quantitative Wildlife Center. Thanks to Chad Stewart, Steve Beyer, and Russ Mason for being champions of my research at times when I doubted its potential. Lastly, I thank my friends and lab mates in the Boone and Crockett Quantitative Wildlife Center and elsewhere for their support, encouragement, and good conversation. Special thanks to Sonja Christensen and Rose Stewart who contributed in more ways than can be articulated here.

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# CHAPTER 1: INTRODUCTION

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy that has spread among North American cervids for at least the last 50 years. Since the initial discovery of CWD in Colorado in 1967 (Williams and Young 1980), the disease has affected at least eight cervid species including white-tailed deer (*Odocoileus virginianus*), spread to at least 26 U.S. states (Rivera et al. 2019), and been called the greatest contemporary threat to free-ranging deer herds (Gillin and Mawdsley 2018). Many human- and disease-associated attributes have challenged the detection and management of CWD despite large resource expenditures and active interventions by managing agencies. First, CWD is difficult to detect in affected animals because of an apparent lack of observable symptoms; it takes months for diseased animals to manifest clinical indicators of infection (Tamgueney et al. 2009). Second, CWD results in a prolonged disease course that lasts months to years (Miller and Wild 2004), and likely results in many secondary infections. Current epidemiological evidence suggests that CWD is spread by multiple local routes of transmission (i.e., direct and indirect animal contact), and across long distances facilitated by human transport (Osterholm et al. 2019). Lastly, CWD is always fatal and has resulted in population declines in white-tailed deer (Edmunds et al. 2016) and mule deer (DeVivo et al. 2017).

Outside of the host, the pathogenic prion is highly stable, remaining infectious following treatments of desiccation, radiation, freezing, and incineration at temperatures exceeding 600˚C (Williams et al. 2002, Brown et al. 2004, Saunders et al. 2008). The prion is shed ubiquitously in secretions and excretions of diseased animals: urine, feces, saliva, and blood all include infectious prions (Haley et al. 2009, Tennant et al. 2020). Prion shedding represents a major

challenge to mitigation efforts because it can create hotspots of disease that persist for many years (Saunders et al. 2012, Plummer et al. 2018). Recent examples of states where environmental contamination is likely contributing to the persistence of CWD are Wisconsin, Illinois, and Arkansas; all three of which discovered CWD years after introduction, and none maintains that eradication remains an achievable goal. Broadly, once CWD becomes established, there has been little success in eradication despite sustained and aggressive actions by natural resource agencies (Rivera et al. 2019).

One of the most rational and effective ways to mitigate the effects of a persistent disease like CWD is to perform proactive surveillance efforts that can either prevent, or detect and eradicate, disease prior to establishment. Established disease can be characterized by localized disease transmission that results in sustained and persistent disease outbreaks without the need for additional introduction events. However, the combination of human interactions, complex disease dynamics, and imperfect observation makes assessing the comprehensive risk of CWD introduction by empirical study prohibitive. Hazards (i.e., factors that increase the likelihood of disease occurrence) implicated in CWD exposure differ in magnitude across space and time. For example, infectious deer carcasses are transported long-distances by hunters because of their popularity as a game species (Walsh et al. 2012). Live-animal transports occur across much of the United States as a result of an increasingly popular deer farming trade and sport hunting for large antlered individuals (Adams et al. 2016). Lastly, localized deer behaviors and disease transmission dynamics influence the spread of disease, but thus far, have been difficult to observe and quantify.

Once CWD is established it has been difficult to maintain monitoring at a level that matches the desired objectives of managing agencies without negatively affecting other

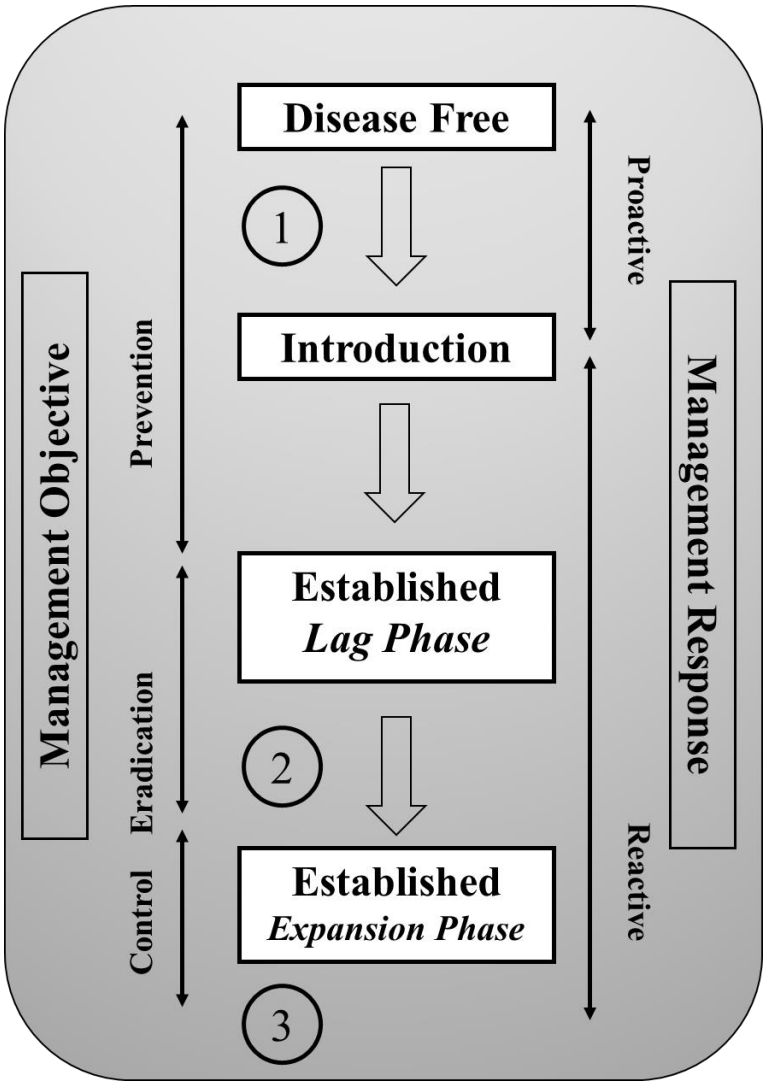
programs. As an example, since the discovery of CWD in Missouri in 2012, the state has spent more than $9 million U.S. dollars and 350,000 staff hours on disease surveillance and management; these expenditures have limited available resources for many other programs, such as habitat restoration and species recovery (Sumners 2019). Further exacerbating resource limitations is the persistence and spread of CWD that can lead to increases in resource allocations over time as geographic extent expands and disease intensity increases. Thus, the unique combination of disease ecology, human interactions, and localized persistence has identified a need for both proactive (i.e., prior to a known occurrence) and reactive (i.e., post occurrence) disease models that optimize decision-making and target locations at high risk of disease exposure or amplification.

My dissertation aims to develop analytical decision-making tools that help guide limited resources to high risk locations. I sought to design studies specific to a series of disease stages and associated decision-making Checkpoints that are linked to those stages (Fig. 1.1). I have defined 4 primary disease stages that include: disease free, disease introduction, lag phase of disease establishment, and expansion phase of disease establishment (Fig. 1.1). These stages are guided by prior work in disease epidemiology as well as the invasive species literature (e.g., Lodge 1993b, Kolar and Lodge 2001, Sakai et al. 2001).

I used these stages to guide my research and developed focused questions for 3 important decision-making Checkpoints (Fig. 1.1): Checkpoint 1 – What is the comprehensive pre-introduction risk of CWD based on a suite of locally relevant hazards?; Checkpoint 2 – Can an existing modeling framework be used to improve (i.e., incorporate more cases of existing disease) rapid estimates of disease extent when compared against current methods that rely on distance-based thresholds?; Checkpoint 3 – Can our understanding of the multiple drivers of

disease spread and persistence be improved if more of the ecological complexity inherent to CWD and host behaviors are explicitly considered? and, relatedly, can the disease testing burden be reduced by implementing a statistical framework that requires less data than has been collected in many locations? In the following sections I discuss and define the disease stages in more explicit detail.

Figure 1.1 Conceptual model of a disease emergence spectrum (modified from Lodge 1993b, Kolar and Lodge 2001, Sakai et al. 2001). Four stages are defined as disease free, disease introduction, disease establishment – lag phase, and disease establishment – expansion phase. On the left-hand side, disease stages are linked to commonly stated management objectives including prevention, eradication, and control. On the right-hand side are management responses ranging from proactive (i.e., prior to introduction) to reactive (i.e., post-exposure). Within each stage there are 3 decision-making Checkpoints that managing agencies commonly encounter. Checkpoint 1 – What is the comprehensive pre-introduction risk of CWD based on a suite of locally relevant hazards?; Checkpoint 2 – Can an existing modeling framework be used to improve (i.e., incorporate more cases of existing disease) rapid estimates of disease extent when compared against current methods that rely of distance-based thresholds?; Checkpoint 3 – Can our understanding of the multiple drivers of disease spread and persistence be improved if more of the ecological complexity inherent to CWD and host behaviors are explicitly considered? and, relatedly, can the disease testing burden be reduced by implementing a statistical framework that requires less data than has been collected in many locations?



## DISEASE EMERGENCE SPECTRUM

### *Disease Free*

The geographic distribution of CWD is discontinuous across space, and unlikely to be driven solely by diffusive spread of infectious hosts or pathogens. Disease free refers to a condition in which a CWD has yet to occur in location of interest (Fig. 1.1). It is at this stage where proactive CWD management is most effective at limiting disease impacts, and a stage where aggressive actions are the most difficult to justify. Effectuating action at a time when political motivation is low necessitates the availability of a proactive approach that is cost-effective, rigorous, and accurate.

Several papers have hypothesized about the role that human translocation plays in transporting infectious prions across the landscape, but most have been data-free thought pieces (e.g., Journal of Wildlife Management, Vol. 40, Issue 1, March 2016), and none have developed an integrative approach to hazard evaluation prior to disease introduction. Past efforts to quantify wildlife introduction risk have been accomplished by identifying and empirically estimating hazards individually (Gillette et al. 2004), or by convening expert panels to directly rank hazards through expert opinion (Oraby et al. 2016). There is a lack of guidance on appropriate methods to integrate multiple hazards in a way that supports proactive decision-making. Therefore, rigorous and cost-effective approaches need to be developed that allow state and federal agencies to quickly estimate the comprehensive risk of CWD introduction into novel areas not yet affected (Fig.1.1, Checkpoint 1). Chapter 2 develops and applies an expert-elicited methodology to estimate risk of CWD exposure and amplification.

*Disease Introduction*

Disease introduction is characterized by any exposure event (e.g., pathogen translocation) that occurs in a new area where emergent or established disease does not already exist. Often these introduction events fail to result in secondary infections. For surveillance and monitoring purposes, it is exceedingly unlikely and cost-prohibitive to detect introduction events as they occur, and thus, I have not explicitly linked this disease stage to a decision-making Checkpoint. Rather, I have reviewed past disease detections and the factors implicated in disease occurrence to inform Checkpoints designed to prevent introduction events from occurring.

One hypothesized mechanism of CWD introduction has been the movement of live animals and harvested carcasses by humans. The housing and transfer of CWD susceptible species on and between captive/privately owned cervid facilities increases the risk of spillover to free ranging white-tailed deer (Adams et al. 2016). Currently, at least 175 facilities in North America have tested positive for CWD (Richards 2019), often in close spatial proximity to disease detection in free-ranging animals. For example, Minnesota discovered its first positive case within ~5 km of a CWD infected captive elk facility. Missouri found CWD in a captive facility in February 2010 (Gerhold and Hickling 2016) and within one year, two free-ranging deer tested positive within three kilometers of the affected facility (Adams et al. 2016). Additionally, captive cervid facilities are frequently cited for noncompliance with regulations aimed to prevent disease spillover to free ranging animals (O'Brien et al 2005). During a 2002 Michigan state audit, it was documented that up to 37% of facilities did not comply with state regulations by failing to report escaped animals, fix fence faults, meet minimum fencing requirements, and submit the required animals for testing (O'Brien et al 2005).

Out-of-area hunting serves as a direct connection between CWD endemic locations and areas that are currently disease free. Many U.S. states have restricted out-of-state transport of game to deboned meat, antlers (attached and unattached to cleaned skullcap), and cleaned hides, and have thereby reduced the likelihood that these potentially contaminated tissues are transported. However, the regulation changes to restrict movement do not equate to a complete safeguard against CWD translocation as infectious prions remain viable in fat and muscle tissues (Race et al. 2009b) and may be transported via hunting gear (Wiggins 2009). Furthermore, hunting regulations are not subject to 100% compliance by hunters, making it probable that the transport of banned parts of harvested animals will continue.

*Established Disease – Lag Phase*

For the purposes of this dissertation, I have partitioned out established disease into two primary phases: a lag phase and an expansion phase. I have defined the lag phase as sustained occurrence of disease that leads to localized transmission in a geographic location (i.e., community spread in human health epidemiology), but not rapid expansion and localized growth (Marisco et al. 2010; invasive species theory). For CWD, it is at this stage that active management interventions are likely to be most effective at mitigating localized impacts. Thus, it is critical for state and federal agencies to have appropriate analytical tools that can direct management responses to the appropriate locations immediately upon a new detection (Fig. 1.1, Checkpoint 2). However, there is currently limited guidance on best practices and to my knowledge no approaches that utilize existing knowledge of disease processes to better understand and predict disease condition at locations of emergence or recent detection. Thus, I focused Chapter 3 on the application of an existing statistical model to estimate the spatial extent

of CWD using only data that are available immediately upon first detection (Fig. 1.1, Checkpoint 2).

*Established Disease – Expansion Phase*

During the expansion phase of disease establishment there are increased rates of disease transmission leading to a disease outbreak. In this stage there are persistent outbreaks without the need for additional translocation and introduction events. For wildlife diseases that are efficiently transmitted, the expansion phase may occur and decay quickly; however, for inefficiently transmitted and persistent diseases like CWD, disease clearance is rare and host-pathogen coexistence is the dominant state. Disease spread is characterized by an increasing geographic extent, whereas disease persistence represents the repeated occurrence of disease in the same geographic location.

The spread of wildlife disease results from complex ecological interactions between host, pathogen, and the habitat in which they co-occur. Common host behaviors, such as long-distance migration and dispersal, influence the ecological interactions of disease including the species and locations affected. Long distance movements may be particularly important to consider given their contribution to stochastic outbreaks and expansion of pathogens far-removed from locations of initial infection (Bar-David et al. 2006). Failure to explicitly consider the role of long-distance movements in the spread of wildlife diseases may lead to the underestimation of at-risk areas and may help explain past failures in wildlife disease control efforts (Gaughran et al. 2019). For example, Saiga antelope migrate hundreds of kilometers between wintering ranges and calving grounds transporting intestinal parasites (*Marshallagia*) that will eventually infect domesticated sheep (Morgan et al. 2006); similarly, the failure to account for additional dispersal that resulted from badger culling led to increased bovine tuberculosis spread and decreased efficacy of control

in Britain (Barlow 1996, Smith et al. 2001). Despite the documented prominence of long-distance movements and their effects on wildlife disease processes, they have rarely been incorporated directly into epidemiological modeling frameworks.

Past attempts to understand the spread and persistence of wildlife diseases have resulted in a suite of models. Diffusion-based models remain the option of choice because of their mathematical simplicity (Hosseini et al. 2006) and usefulness in predicting ecological dynamics that affect localized spread. Estimating wave-front velocities as they vary across distinct habitat types improves ecological understanding of complexities in disease dynamics, including the potential barriers to movement for diseases and hosts alike. Smith et al. (2002) reconstructed the spread of rabies in Connecticut by developing data-explicit models and found that barriers to animal movement, such as large rivers, were a barrier to disease spread. Hefley et al. (2017) developed a diffusion-based model using partial differential equations that identified river corridors and dense forest as locations that promote spread and growth of chronic wasting disease in white-tailed deer in Wisconsin. However, one limitation of these models has been their inability to consider multiple host movement behaviors. For many species, including those susceptible to CWD, their movements can be described by multiple modes. Common host behaviors, such as long-distance migration and dispersal, influence the ecological interactions of disease including the species and locations affected. Long distance movements may be particularly important to consider given their contribution to stochastic outbreaks and expansion of pathogens far-removed from locations of initial infection (Bar-David et al. 2006). Incorporating long-distance movements has been accomplished in rare instances by applying long-tailed contact kernels quantitatively defined by power laws or exponential relationships

(Filipe and Maule, 2004), or by using a small constant rate of global infection regardless of spatial proximity to prior cases of disease (Russell et al. 2005).

In addition to the quantitative complexity needed to incorporate different movement behaviors into epidemiological models, long-distance translocations of disease-affected wildlife are particularly difficult to observe and document (Macdonald and Voigt 1985). Indeed, long-distance spread often goes undetected early upon introduction because of rapid removal of morbid animals by scavengers or predators (McCallum and Dobson 1995), or simply because of the general difficulty in observing infrequent wildlife occurrences. A failure to detect emergence early precludes understanding because it is difficult to reconstruct conditions that led to the translocation of disease in the first place. Thus, I focused chapter 4 on developing a model structure that was well suited to account for difficulty in detection and was able to incorporate complex ecological dynamics of host, pathogen, and habitat. Specifically, chapter 4 presents a statistical model that incorporates multiple mechanisms for localized spread, long-distance spread, and disease persistence. In addition, I explicitly evaluated the effort necessary to detect disease given localized prevalence and past detection history.

The complete dissertation is intended to provide a holistic set of risk assessment approaches that are specific to each of the 4 primary disease stages (Fig. 1.1). However, I have crafted the original research chapters (Chapters 2 – 4) as stand-alone manuscript designed for independent submission to peer-review journals focused on disease ecology, wildlife management, and decision-making theory. As a result, I have provided additional framing and context to help guide the interpretation and application of my research findings to specific disease stages, as necessary.

# CHAPTER 2: AN EXPERT-ELICITED APPROACH TO INFORM RISK ASSESSMENTS FOR CHRONIC WASTING DISEASE

## INTRODUCTION

Chronic wasting disease (CWD) is a neurodegenerative prion disease that has been detected in eight cervid species across 26 U.S. states, Canada, Norway, Finland, and South Korea (Mysterud and Edmunds 2019). The disease has resulted in localized population declines in white-tailed and mule deer (Edmunds et al. 2016, DeVivo et al. 2017), driven concern in hunters who consume CWD-affected game meat (Osterholm et al. 2019), and challenged the availability of conservation funding because of a CWD-associated decline in hunter participation (Heberlein 2004, Uehlinger et al. 2016). Chronic wasting disease is transmitted by direct and indirect contact, typically mediated by social interactions of deer or by exposure to a prion contaminated environment. Furthermore, new detections of CWD have occurred repeatedly in new areas but have rarely been anticipated. Broadly, once CWD is introduced and becomes established, there has been little success in eradication despite sustained and aggressive actions by natural resource agencies (Rivera et al. 2019).

One of the most rational and effective ways to mitigate the effects of CWD is to perform proactive surveillance efforts that can either prevent disease prior to exposure or detect and eradicate disease prior to its establishment. Proactive surveillance and prevention efforts are often based on spatial risk assessments designed to identify and integrate multiple disease hazards (Walsh et al. 2012, OIE and IUCN 2014). Spatially accurate risk assessments are critical to effective disease interventions, particularly during the earlier stages of disease exposure when local, empirical data are not available.  In some narrowly defined wildlife disease systems,

hazard identification and risk estimation can be relatively straightforward process. For example, the spatial and temporal movement ecology of migratory bird species, combined with their affinity for spatially discrete wetland areas, can be used to accurately predict the risk of avian influenza outbreaks at migration stopover sites, such as Delaware Bay (Herrick et al. 2013, Sullivan et al. 2018). However, in most applications to CWD, estimating the risk of exposure and amplification is much more limited and difficult to quantify, particularly for wide-ranging species such as white-tailed deer.

White-tailed deer are habitat generalists (Long et al. 2005) that occur across broad regions of the United States. They are a popular game species, often pursued in the wild and captivity for meat and sport. Hazards implicated as causing CWD exposure and amplification differ in magnitude across space and time. For example, infectious white-tailed deer carcasses are transported long-distances by hunters because of their popularity as a game species (Walsh et al. 2012). Live-animal transports occur across much of the United States as a result of an increasingly popular deer farming trade and sport hunting for large antlered individuals (Adams et al. 2016). Lastly, deer behaviors and disease transmission dynamics influence the localized amplification of disease, but thus far, have been difficult to observe and quantify. The combination of human interactions, complex disease dynamics, and imperfect observation makes empirical assessments of the comprehensive risk of CWD prohibitive.

Given a lack of empirically-derived quantitative data to estimate the contribution of multiple CWD hazards to localized risk, there is a critical need to develop alternative approaches. One potential approach that is immediately available to guide risk assessments is the knowledge of experts. Expert-elicitation is a common technique that is used in a variety of decision-making contexts when alternative approaches are unavailable (Marcot et al. 2012).

Expert-elicitation exercises typically rely upon a small group of individuals (≤ 10) that have specialized and problem specific expertise that is useful to formally estimate causal relationships (Runge et al. 2011, McBride et al. 2012, Converse et al. 2013, Cannessa et al. 2015a, Johnson et al. 2017). Based on well-developed methodology designed to minimize individual biases and maximize estimation accuracy, expert elicitation has been successfully implemented in several environmental management contexts (Johnson et al. 2017, deLittle et al. 2018). Thus, assuming specific study design criteria are met (e.g., approaches to limit bias), expert-elicitation may provide accurate information (Lyons et al. 2015) useful in performing comprehensive wildlife disease risk assessments that lack empirical data.

In this chapter, I sought to evaluate whether an expert-elicited approach could be used to perform a comprehensive wildlife disease risk assessment. In particular, I was interested in evaluating the effect of multiple co-occurring CWD hazards that lacked numerical data necessary to perform quantitative assessments. In addition, I wanted to employ techniques that limited individual cognitive and motivational biases and that avoided group conflict that may challenge group consensus. As a motivating example, I applied my approach to Michigan, U.S., a location of recent CWD detection. I evaluated whether an expert elicited approach could produce coherent risk estimates across a team of agency experts that were spatially accurate based on CWD occurrence patterns.

## METHODS

### *General Approach*

To develop a generalizable protocol for risk assessment based on location specific CWD hazards, I followed general IUCN Guidelines for Wildlife Disease Risk Analysis and adapted expert-elicitation protocols previously developed in the environmental decision-making literature

(Cain 2001, OIE and IUCN 2014, deLittle et al. 2018). I found the IUCN protocol helpful as a guiding document, whereas, the methodology of deLittle et al. (2018) was critical to informing survey protocols that were specifically designed to control sources of expert bias. To perform my risk assessment, I formed a working group that consisted of selected agency personnel from the Michigan Department of Natural Resources (MDNR). Members were selected to participate based on their expertise in deer ecology (n = 4), deer management (n = 3), and disease ecology (n = 2). I guided the working group through two general steps, hazard identification and risk assessment.

*Hazard Identification*

The hazard identification stage was based on open group discussion amongst the experts to determine which hazards were most relevant to the ecology of white-tailed deer and human behaviors across Michigan. We began by tabulating a list based on a review of available literature and reports, such as Walsh et al. (2012). I allowed experts to add additional hazards that they viewed as relevant to localized conditions (e.g., deer wintering complexes [DWCs]). We then reviewed the complete list in a group setting and discussed each hazard individually. As part of the discussion, we evaluated the relevance to local deer populations and CWD; we classified hazards into two distinct categories: disease exposure (i.e., risk of introduction) and disease amplification (i.e., risk of increased disease growth); and finally, we discussed any available data that could provide a direct or indirect spatial estimate of each hazard. Experts ultimately identified five exposure and amplification hazards relevant to white-tailed deer in Michigan (Table 2.1).

Table 2.1 List of hazards, description, scale, and risk category identified by experts in Michigan for risk of chronic wasting disease exposure (i.e., risk of introduction) or amplification (i.e., risk of increased disease growth). For each hazard, I provided a description of the data, the proposed risk mechanism, the scale at which data were available and the general mechanism of risk. I included risk mechanisms that amplify disease and lead to disease exposure.

| Hazard | Description | Scale | Risk Mechanism |
|---|---|---|---|
| Deer Density | Buck harvest/area ($km^2$). Provides an index of relative deer density; higher density = higher risk of amplification | County | Amplification |
| Out-of-Area Hunting | Percent of hunters/county that hunt in other CWD positive counties. Out-of-area hunters = higher risk of exposure | County | Exposure |
| Captive Cervid Facilities | Locations of commercial cervid facilities (ranch and full registration only). Presence of facilities = higher risk of exposure. | Point Locations | Exposure |
| Taxidermists and Processors | More taxidermists and processors = higher risk of exposure | Point Locations | Exposure |
| Deer Wintering Complexes | Presence of deer wintering complexes = higher risk of exposure and amplification | Shapefile boundary layer. (Range of DWC areas: 21.4 – 691.1 $km^2$) | Amplification and Exposure |

Exposure hazards included point locations of captive cervid facilities, deer processors and taxidermists, and out-of-area hunting connectivity. In Michigan there were 4 types of captive cervid facilities: hobby, exhibition, ranch, and full registration. For my purposes, experts identified ranch and full-registration facilities as being the highest risk because they represented the majority of trade activity within the industry. Data for these facilities were summarized as presence/absence of facilities at the township scale based on 2018 data (Fig. 2.1). I combined deer processors and taxidermists into a single hazard defined by presence/absence within a township. Deer processor data were reported by MDNR in 2017, and deer taxidermist data were reported in 2015 (Fig. 2.2).

Figure 2.1 Point locations of captive cervid facilities in Michigan in 2018. Light gray symbols indicate point locations of full registration facilities, whereas, dark gray symbols indicate point locations of ranch facilities. Gridded background depicts the jurisdictional boundaries of all townships in Michigan.

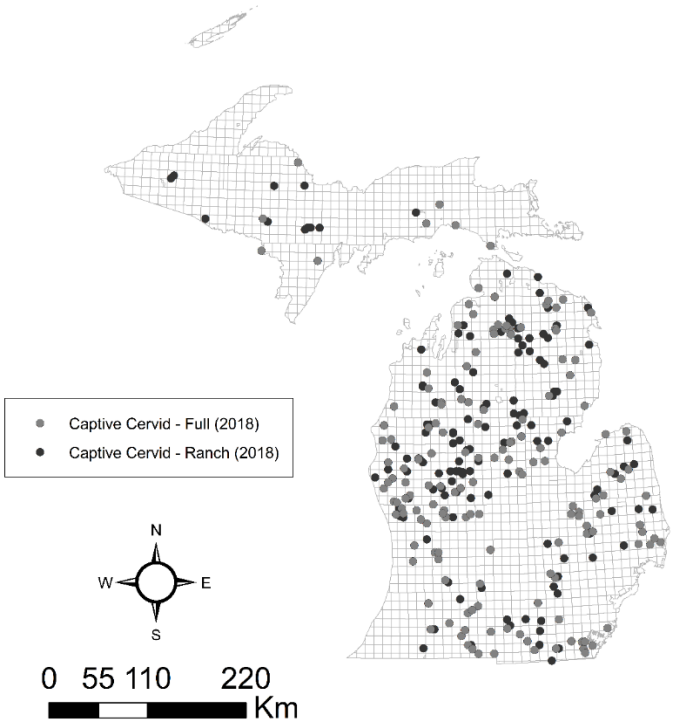
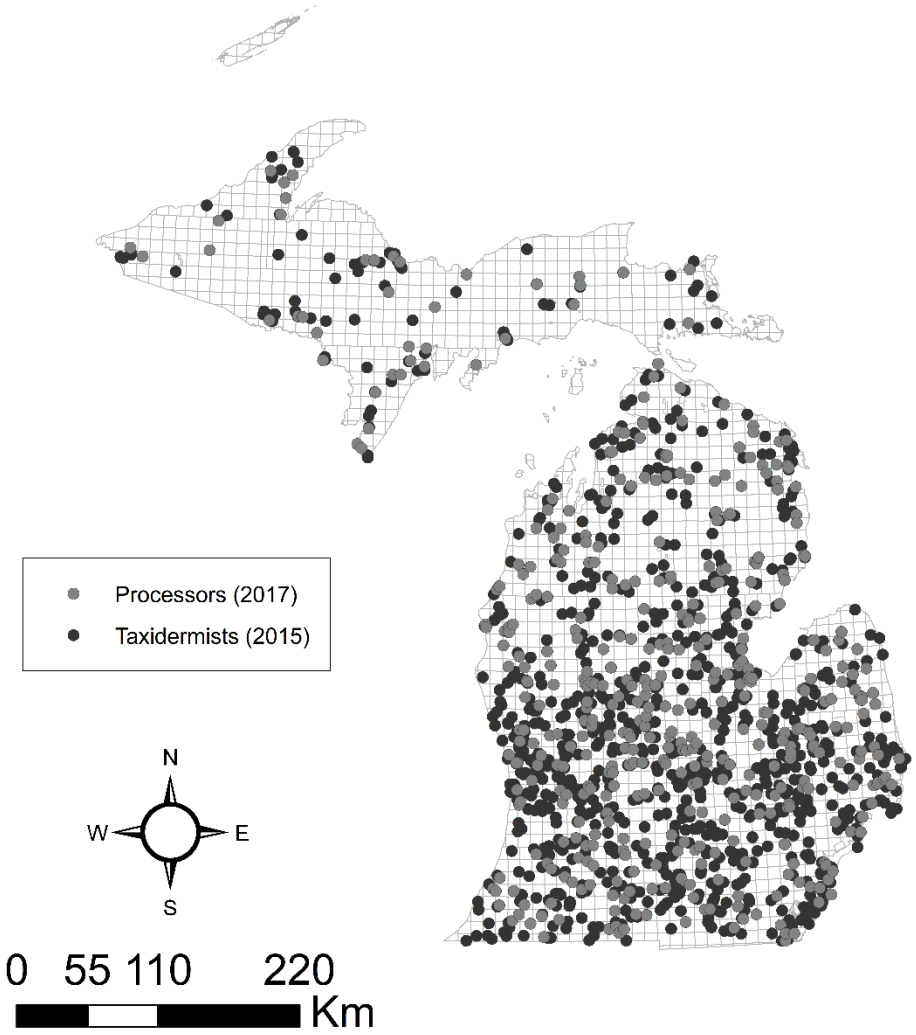


Figure 2.2 Point locations of processors and taxidermists in Michigan. Gray symbols represent the locations of deer processors. Black symbols represent the locations of deer taxidermists. Gridded background depicts the jurisdictional boundaries of all townships in Michigan.



For out-of-area hunting connectivity (i.e., carcass risk), the group identified two sources: intrastate and interstate connectivity. Intrastate hunting connectivity was quantified using hunter survey data administered by MDNR that linked the home residence of hunters to hunting activity in CWD positive counties (Years 2015 – 2018). The percentage of respondents that travelled from one county to another was scaled up to the total number of hunters that resided in a county. CWD positive counties included Clinton, Dickinson, Eaton, Gratiot, Ingham, Ionia, Jackson, Kent and Montcalm counties. Interstate hunting was quantified as the number of Michigan resident hunters who purchased an out-of-state license in Wisconsin between years 2013 – 2017 (i.e., nonresident license). Wisconsin was chosen to represent interstate hunting connectivity because it was the only neighboring state endemic for CWD at the time of this study. Based on the distribution of connectivity values by county, connectivity was summarized at two levels: low and high (Fig. 2.3 and Fig. 2.4). The levels were identified by natural breaks on normalized data at the county scale, according to methods described by Jenks (1967).

Figure 2.3 Intrastate connectivity of hunters by county, quantified as the percent of hunters per county that hunted in counties with cases of CWD from 2015 – 2018 (red outline). Experts considered areas with greater connectivity to CWD positive counties as presenting a greater risk of CWD introduction.

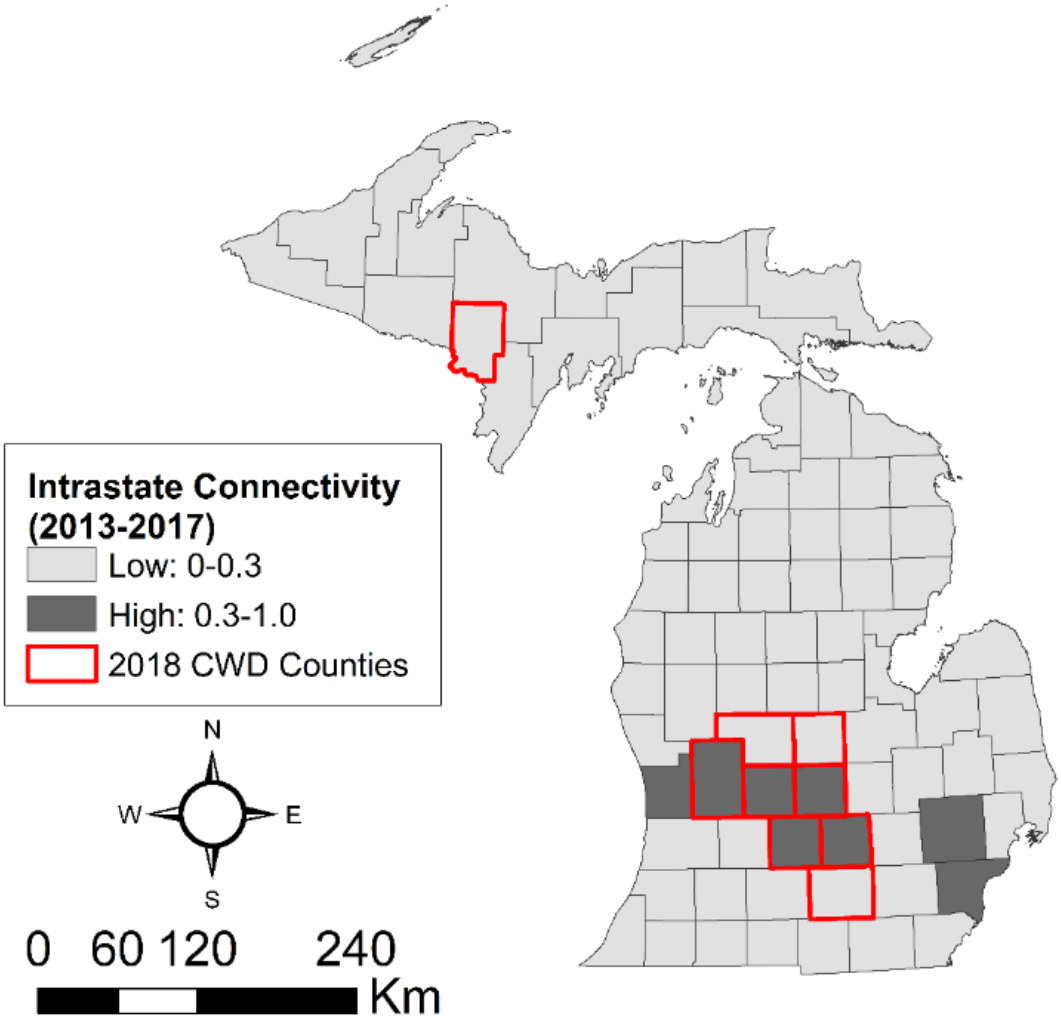
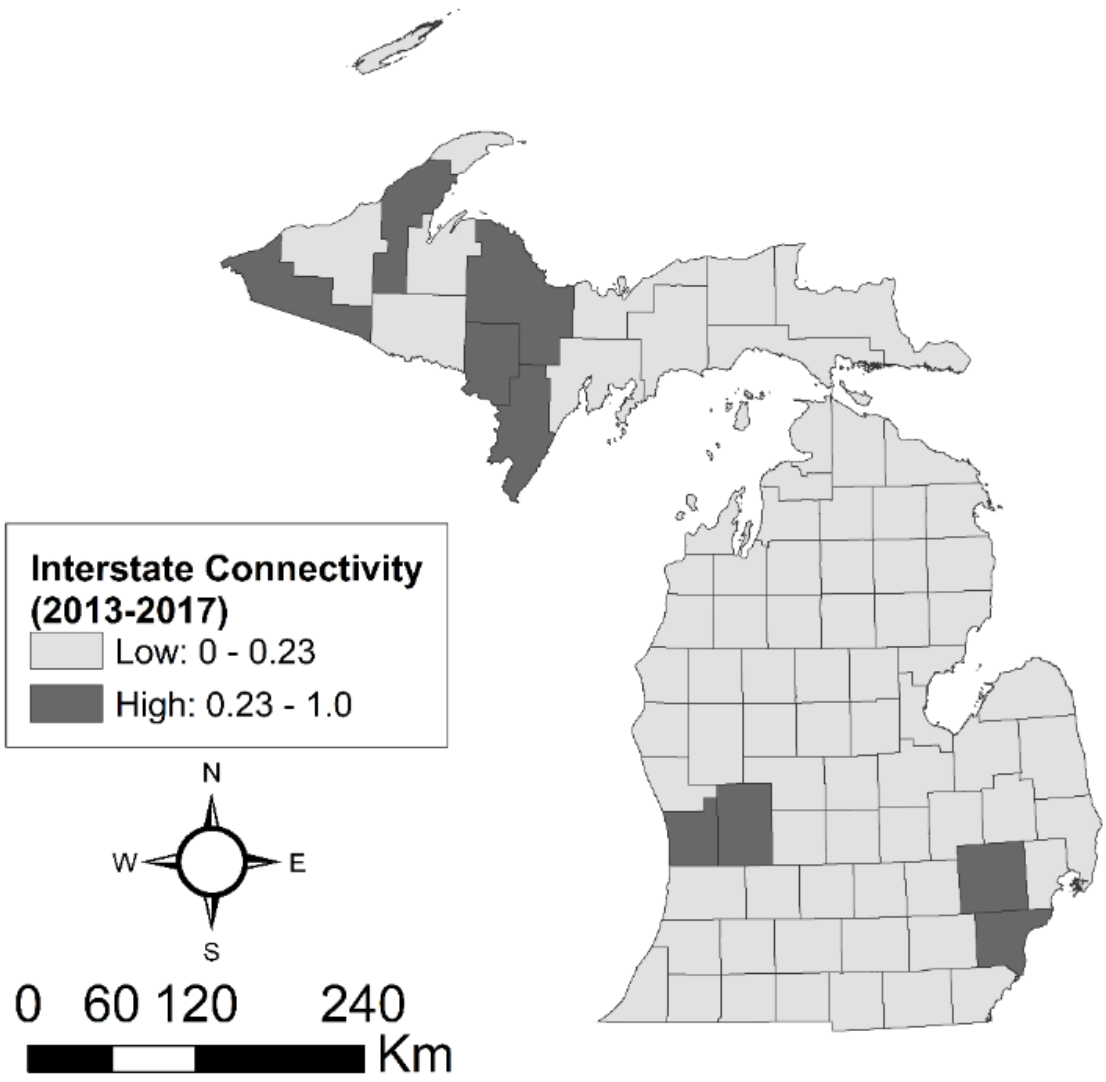


Figure 2.4 Interstate connectivity by county to Wisconsin, the only CWD endemic state that shares a border with Michigan. Values are based on the normalized average number of Michigan residents from each county that travelled to Wisconsin to hunt from 2013 – 2017.



For amplification hazards, the experts selected deer density and deer wintering complexes (DWCs) as hazards that promote locally elevated disease transmission. Deer density was quantified as the average number of harvested bucks/km$^2$ per county during years 2013 – 2017 (Fig. 2.5). Deer wintering complexes were summarized as presence/absence within each township in Michigan's upper peninsula (Fig. 2.6).

Figure 2.5 Deer density by county in Michigan. Metric is based on the average harvested bucks/km$^2$ from 2013 – 2017. Red outlined counties were adjusted to higher density levels based on the opinion of the experts.

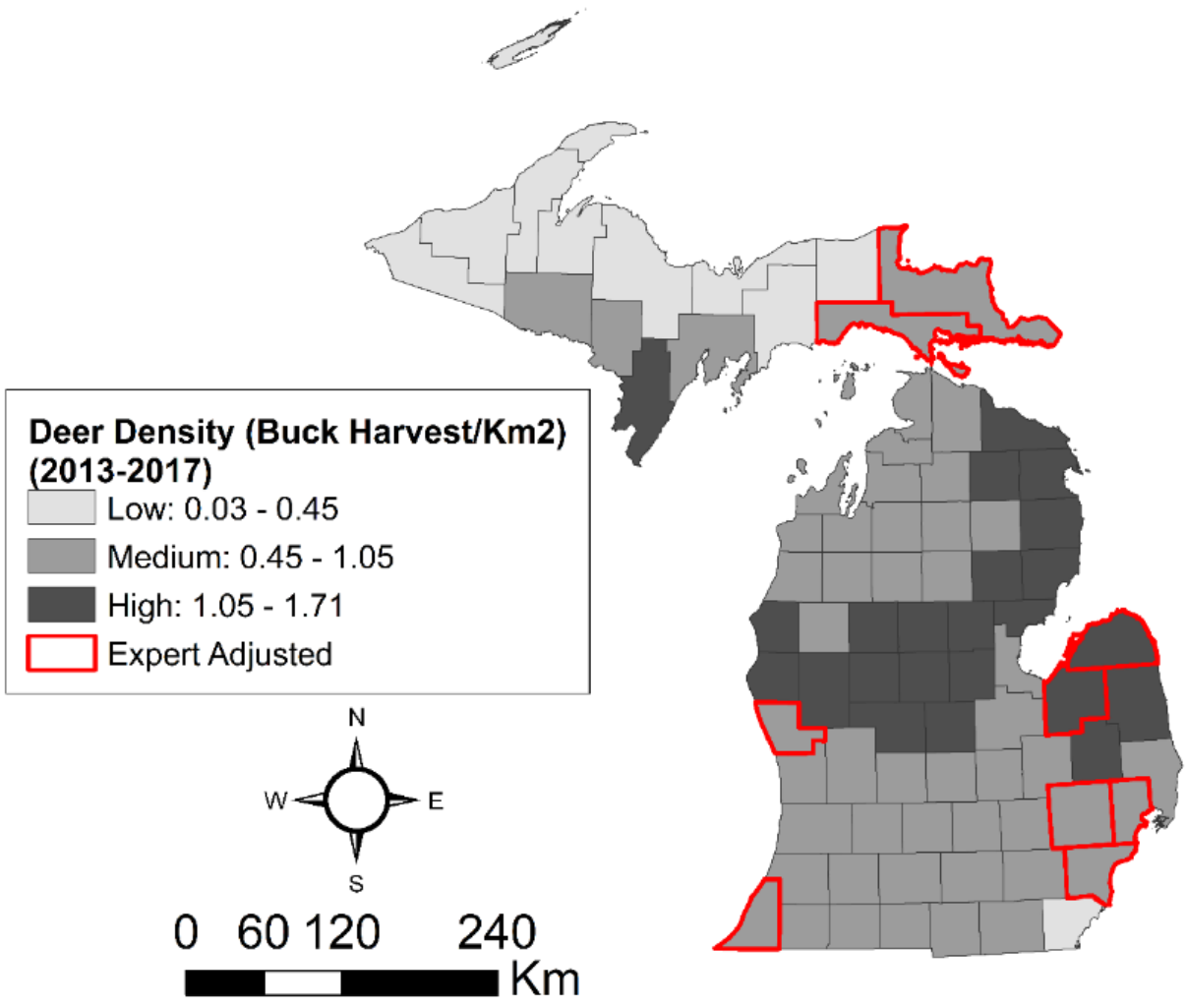
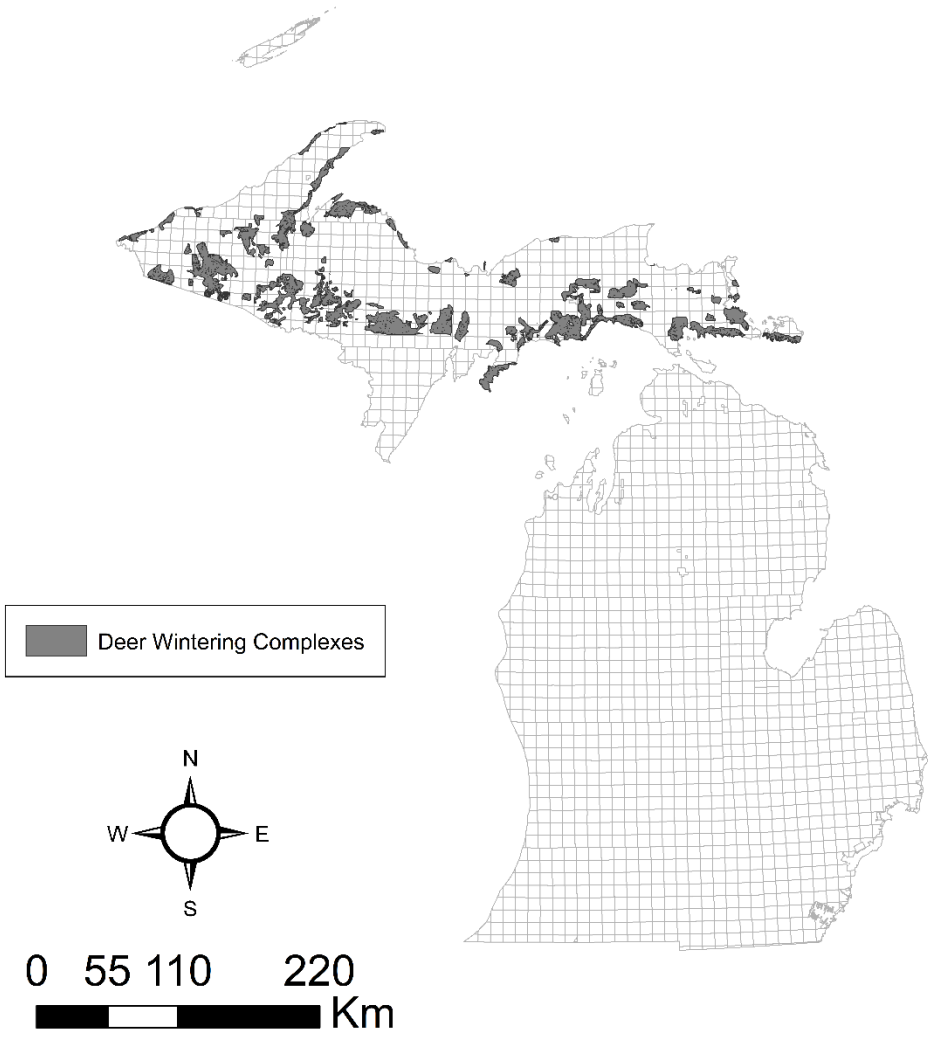


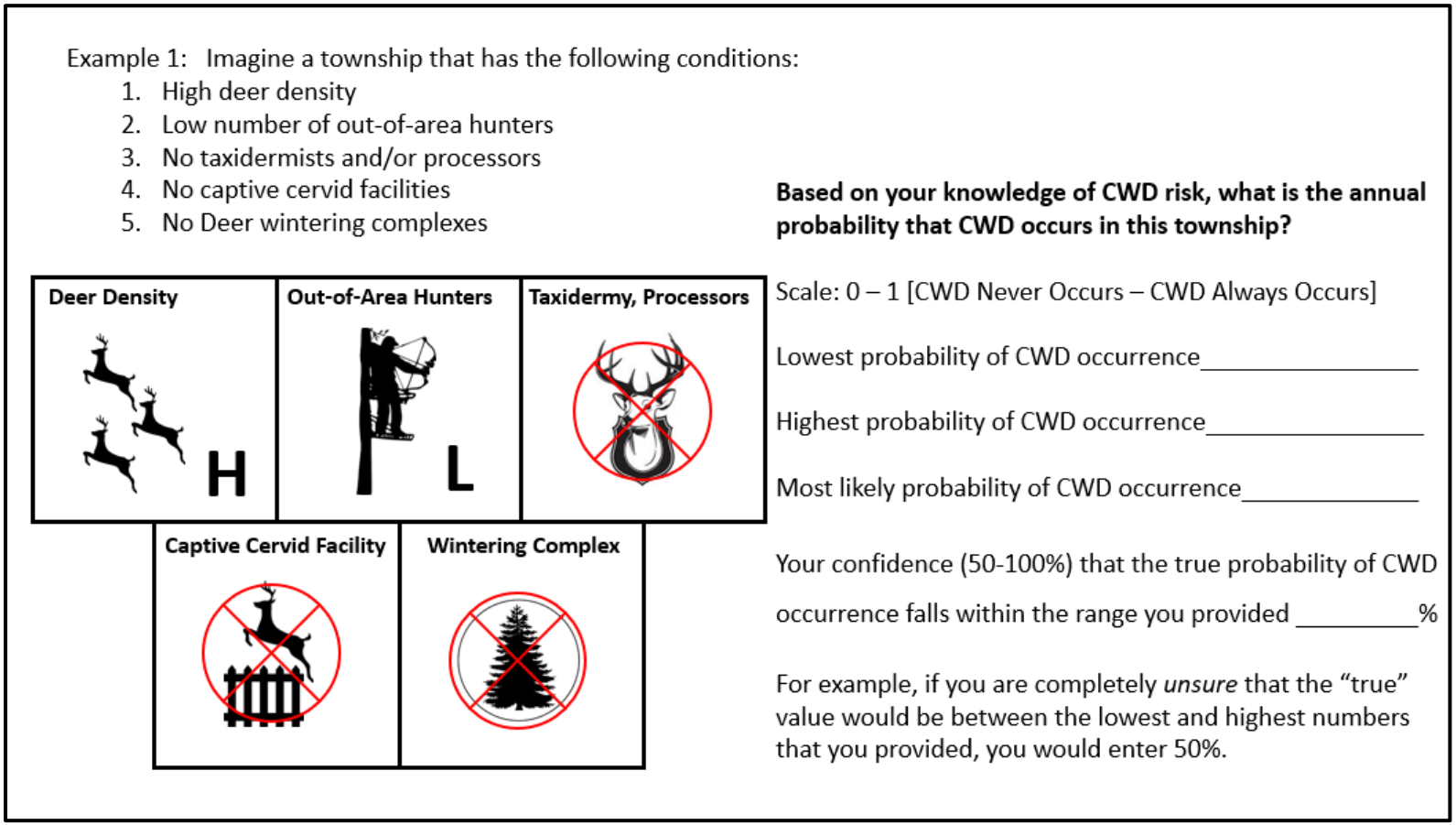
Figure 2.6 The geographic boundaries of deer wintering complexes (DWC) in year 2018. All DWCs occur in the upper peninsula of Michigan where wintering conditions are extreme enough to trigger deer migratory behaviors. Gridded background depicts the jurisdictional boundaries of all townships in Michigan.



*Risk Assessment*

Using the complete and summarized list of hazards identified by the expert working group, I developed a questionnaire that required experts to estimate the annual probability of CWD occurrence under a range of relevant scenarios (Fig. 2.7). Each question included a suite of co-occurring hazards that was described in text and using pictures (deLittle et al. 2018). Elicited response fields were structured using the four-point method designed to limit expert bias by minimizing overconfidence and to quantify expert uncertainty (Speirs-Bridge 2010). In addition, the indirect scenario design limited motivational bias by obscuring the tractable linkage between individual hazards and risk (Hetes et al. 2011). In total, my questionnaire included 18 out of a total of 48 unique combinations (Fig. 2.7) to limit expert fatigue. I elicited a section to explain rationale and to provide direct relative rankings useful in evaluating internal consistency of expert response.

Figure 2.7 Example of a Michigan-specific scenario that I presented as part of the expert elicitation exercise. The left side described the scenario in text and included a pictorial description. On the right side was a description of the problem followed by questions that followed the four-point method of elicitation (Speirs-Bridge et al. 2010). I bounded confidence at 50% and assumed that confidence less than 50% was complete uncertainty.



I convened the working group to formally assess the risk (i.e., risk of exposure or amplification) using the 18 scenarios. To limit potential availability and anchoring bias in estimation, I included 4 new participants at the elicitation stage that were not privy to prior working group discussions (Hetes et al. 2011). These newcomers allowed us to assess whether existing experts informed and adjusted elicited responses based on prior risk reference values (i.e., anchoring bias), or knowledge of hazards gained from other previous group discussions (i.e., availability bias). If either source of bias existed, I expected to see deviations between the two groups (i.e., existing and new experts) that may result in an overall bias of risk assessment values (Hetes et al. 2011). To initiate the elicitation exercise, I described project goals to new attendees (n = 4), the scenarios and format of response fields, and the expected use of the elicited data. I avoided any group discussion on specific risk valuations at this stage to prevent anchoring bias. Once there was group clarity, we proceeded to individual assessments.

I fit unique beta distributions to each expert and scenario using their estimates of uncertainty, and their the lowest, highest, and most likely annual probability of disease occurrence (Fig. 2.7; Speirs-Bridge et al. 2010). The use of a principled beta distribution allowed for direct comparison of responses across experts using standard measures of uncertainty that was critical for review and re-evaluation (i.e., range of values in 95% confidence interval). Based on my generated statistical summaries, I used a modified Delphi method (Kuhnert et al. 2010) for expert review and adjustment (Delbecq et al. 1975). Once there was group consensus on individual responses, I combined individual estimates with simple averaging to create a single unifying group distribution for each elicited scenario (Clemen and Winkler 2007, deLittle et al. 2018).

Based on these results, I used linear interpolation to estimate a unique probability distribution for each of the remaining 30 scenarios that were not included in the elicitation exercise (Cain 2001, deLittle et al. 2018). For each hazard, I calculated a unique interpolation factor defined by the magnitude change in effect size when a hazard switched from one state to another. Typically, state change (i.e., interpolation factor) has been quantified as a change from negative to positive; however, in my specific application, I applied an inverse state change (i.e., from positive to negative effect) because a low probability of disease occurrence was the desirable state. The interpolation factors were then used as a scalar to interpolate across the entire set of unelicited scenarios (Cain et al. 2001, deLittle et al. 2018).

Based on the results of my interpolation, I used the unique values for the 48 scenarios to quantify comprehensive risk at Michigan township and county scales. To categorize risk into discrete levels and to facilitate decision-making, I used natural breaks in ArcGIS v.10.6 to identify: high, medium, and low risk areas (ESRI 2018). I evaluated the quality of my risk assessment by visually assessing the spatial agreement between my risk estimates and the locations of CWD detection from 2015 – 2018. Spatial agreement was evaluated visually using two risk maps, one that evaluated the comprehensive risk ("comprehensive map") using all selected hazards and another that excluded hazards that relied upon knowledge of CWD occurrence in Michigan ("simplified map"). My goal was to identify the surveillance value of my approach with and without the knowledge of CWD occurrence in Michigan.

Lastly, I verified whether my indirect approach altered the behaviors and expectations of experts by assessing the agreement between direct and indirect scenario responses. To facilitate this comparison, I generated relative ranks from my indirect probability estimates using minimum cross entropy comparisons calculated within a Bayesian Belief Network ("BBN";

Norsys Software Corp. 2010). Bayesian Networks are based on graphical relationships that use conditional probability relationships to link a set of explanatory variables (i.e., CWD hazards in this study) to a response (i.e., probability of CWD occurrence; Korb and Nicholson 2010, deLittle et al. 2018). To inform these linkages I discretized the elicited probability estimates based on 3 risk levels across a five-year time horizon: low risk (probability of occurrence < 0.5), medium risk (probability of occurrence: 0.5 – 0.75), and high risk (probability of occurrence: 0.75 – 1). I used minimum cross entropy to measure the magnitude change of the risk of CWD occurrence with respective changes in the magnitude of each of the chosen CWD hazards. A larger minimum cross entropy value represents a more influential linkage between variables.

## RESULTS

### *Hazard Quantification*

Exposure hazards included point locations of captive cervid facilities, deer processors and taxidermists, and out-of-area hunting connectivity. As of 2018, there were a total of 296 ranch and full-registration facilities in Michigan. In terms of their spatial distribution, there were facilities in 196 out of 1240 townships, and 71 out of 83 counties (Fig. 2.1). There were 468 registered deer processors and taxidermists in 2017, the year for which data were available. Processors and taxidermists occurred in 696 out of 1240 townships, and 82 out of 83 counties (Fig. 2.2). Lastly, out-of-area hunting was based on both intrastate and interstate metrics. For intrastate hunting, the percentage of respondents that travelled from one county to another was scaled up to the total number of hunters that reside in a county. CWD positive counties included Clinton, Dickinson, Eaton, Gratiot, Ingham, Ionia, Jackson, Kent and Montcalm counties. The average number of hunters per resident county from 2013 – 2017 who travelled to a CWD positive county ranged from 0 – 3832 per year (Fig. 2.3). A low number (i.e., low connectivity)

of interstate hunters ranged from 0 – 1059 for the 5-year average, whereas a high number ranged from 1060 – 3832 (Fig. 2.3). Interstate hunting was quantified as the number of Michigan resident hunters who purchased an out-of-state license in Wisconsin between years 2013 – 2017 (i.e., nonresident license). For interstate connectivity, I found that average annual number of Michigan county residents that traveled to Wisconsin between 2013 –2017 was 0 – 170 per year (Fig. 2.4). A low number (i.e., low connectivity) of interstate hunters ranged from 0 – 39 for the 5-year average, whereas a high number ranged from 40 – 170 (Fig. 2.4).

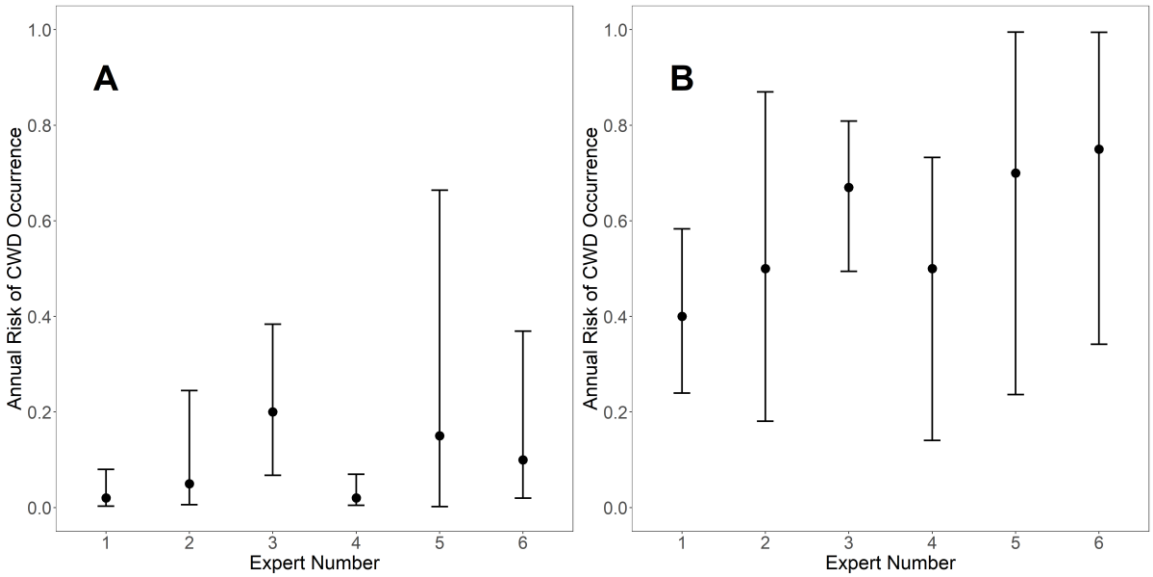
For amplification, the experts selected deer density and deer wintering complexes (DWCs) as hazards that lead to locally elevated disease transmission risk. Estimates for deer density ranged from 0.04 – 1.71 harvested bucks/km$^2$ and were binned into three levels (low: 0.04 – 0.44 harvest bucks/km$^2$; medium: 0.45 – 1.04 harvested bucks/km$^2$, high: 1.05 – 1.71 harvested bucks/km$^2$) identified by natural breaks at the county scale: low, medium, and high values. In addition, based on the belief that deer density estimates were underestimated in some locations, I adjusted the values in 9 counties (Fig. 2.5, red outline). The majority of adjusted counties were in urban areas and lacked hunting opportunity, and thus, reliable harvest-based density estimates (Fig. 2.5, red outline). Lastly, DWCs were present in 98 out of 151 upper peninsula townships (Fig. 2.6, 98 out of 1240 total Michigan townships), and 14 out of 15 upper peninsula counties (14 out of 83 total Michigan counties).

*Risk Quantification*

Six of the eight experts successfully completed the elicitation exercise in an average elapsed time of approximately 30 minutes. One expert failed to return their exercise, and a second expert was excluded because their responses had no informational value (i.e., uncertainty estimate encompassed the entire probability range 0 – 1). Based on the submitted responses, I fit unique

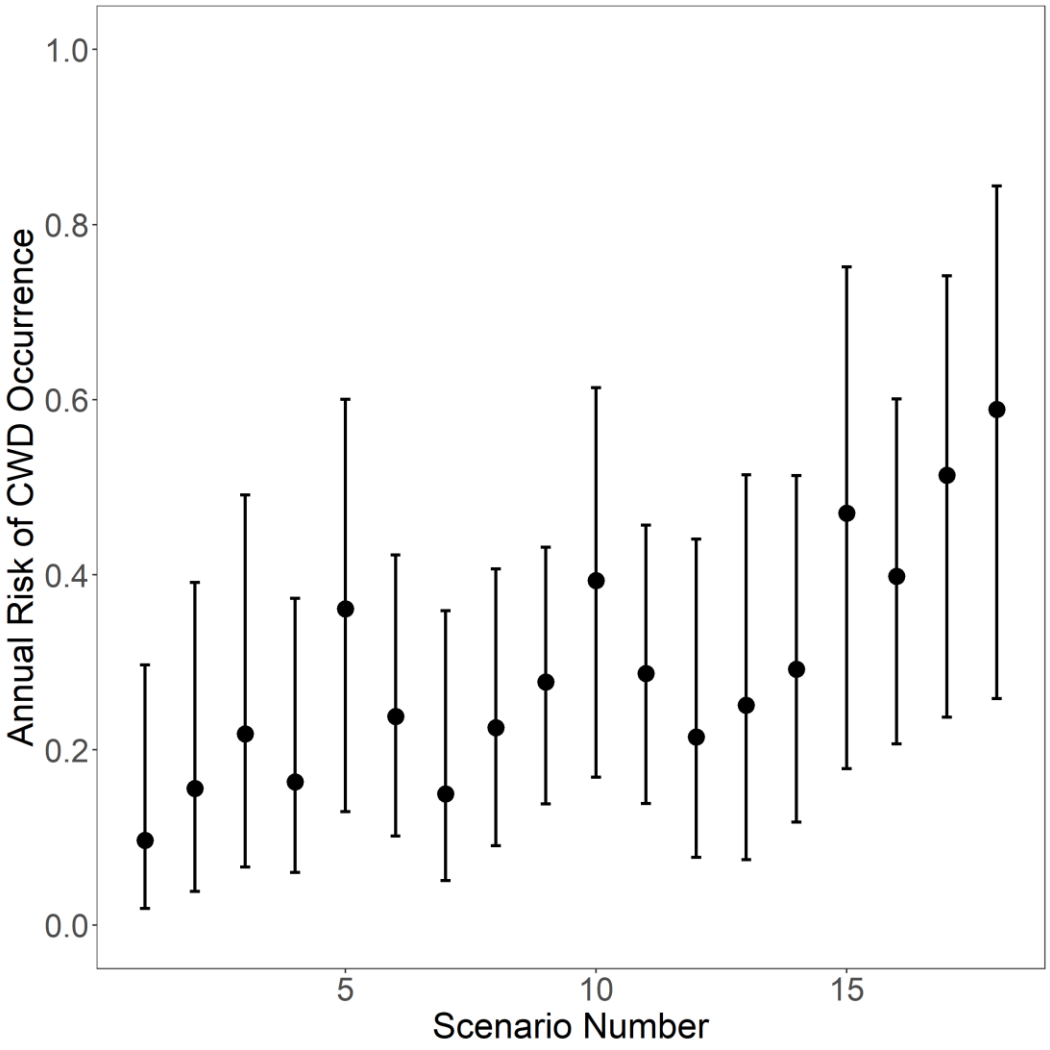
beta distributions to each expert and scenario, summarized the results and distributed them anonymously by email (Fig. 2.8). After summarizing and distributing the results, one out of the six experts changed their response for a single scenario.

Figure 2.8 Panels A and B Examples for scenarios 1 (panel A) and 18 (panel B) of individual Beta probability distributions for each of the 6 experts. There was general agreement within questions and between questions on the magnitude of risk that each co-occurring set of hazards introduced. Points describe the most likely probability estimate from each scenario and lines, the 95% confidence interval.




I used these finalized data to evaluate the coherence in responses within scenarios and consistency in responses among scenarios. I found overlapping uncertainty bounds across most of the individual responses. The exception was expert 5, who consistently estimated narrow uncertainty bounds that differed from the large uncertainty that was typical of the other experts. Between scenarios, we found that the magnitude of risk changed similarly amongst experts (Fig. 2.8). Furthermore, across group-averaged distributions and scenarios, there was an increase in risk estimates as factor levels increased in risk (e.g., higher deer density) (Fig. 2.9).

Figure 2.9 Group results from simple averaging across the 18 scenarios included in the expert elicitation packet. In general, probablity of CWD occurrence estimates increased as more hazards co-occurred at higher factor levels.




I found that group coherence for direct estimation of hazards was low (Table 2.2). Several individual direct estimates of risk fell outside of the 95% confidence interval defined by the group (Table 2.2). This was particularly true for deer density and deer wintering complexes, factors that may be assessed differently according to the location where an individual expert gained their knowledge and expertise. I considered the differences in direct estimation of hazards

across experts as representative of a potential barrier to achieving group consensus, if not for my indirect scenario design.

Both spatial risk representations (i.e., comprehensive and simplified maps) indicated several regions of Michigan that were at elevated risk of CWD emergence and amplification. I found that areas where CWD detections occurred from 2015 – 2018 were consistently ranked as high risk in both the comprehensive and simplified maps (Fig. 2.10 and Fig. 2.11). For the simplified map, 59% of the positives fell in high risk townships (69/117), 23% fell in medium risk townships (23/117), and 18% fell in low risk townships (18/117; Fig. 2.11). For the comprehensive risk map, 62% were in high risk townships, 31% in medium risk, and only 7% fell in low risk townships (Fig. 2.10). In addition to areas where positives were detected, my method identified several other high-risk areas, one in the northeastern region of the state, one in the eastern lower peninsula, and a third in the upper peninsula immediately adjacent to Wisconsin.

Figure 2.10 Comprehensive risk map by township according to 3 risk levels: high, medium and low. The comprehensive map included all hazards, including intrastate connectivity, which relied on prior knowledge of CWD occurrence in Michgian. There was high spatial agreement between locations of CWD positives and high risk townships.

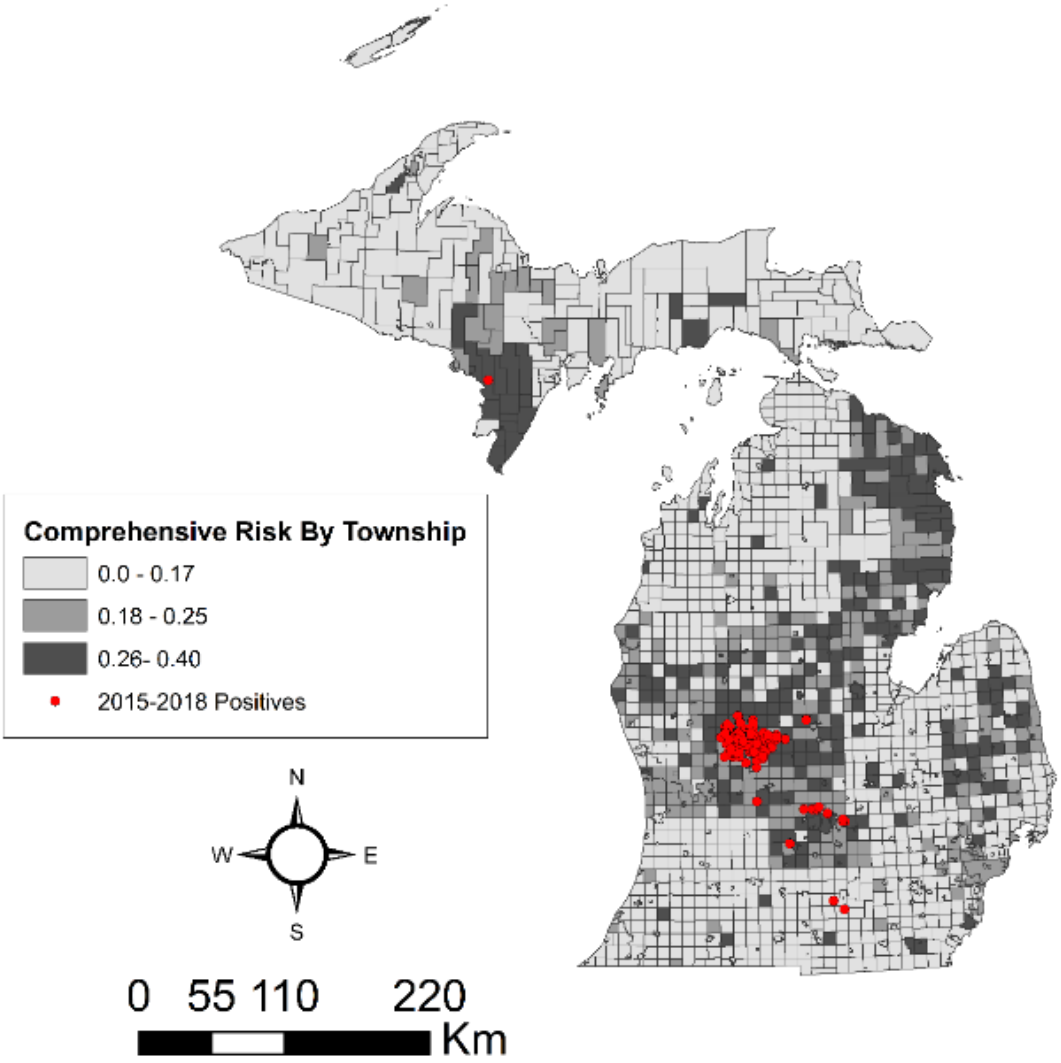
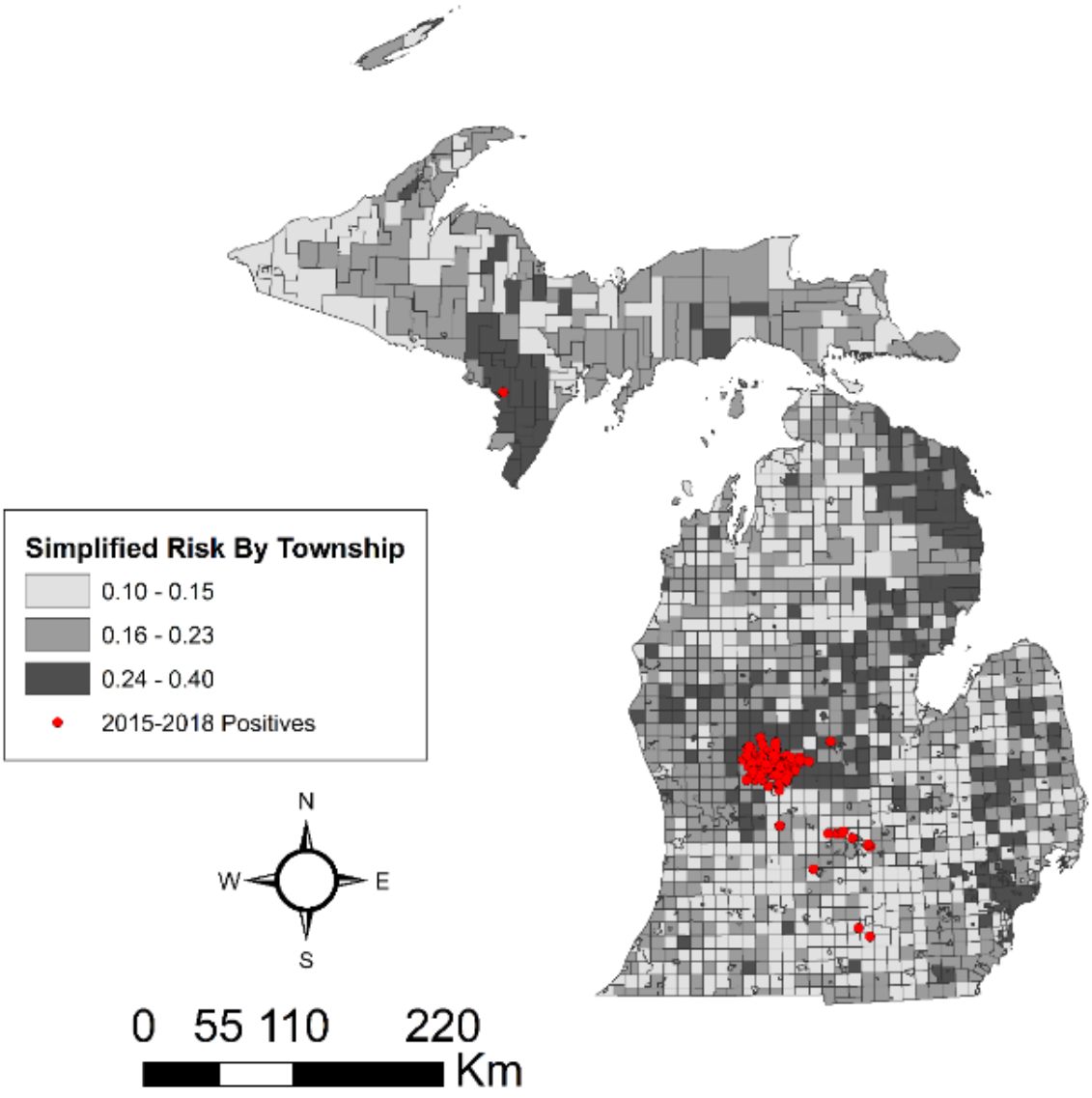


Figure 2.11 Simpified risk map by township according to 3 risk levels: high, medium and low. The simplified map included a subset of hazards, excluding intrastate connectivity, which relied on prior knowledge of CWD occurrence in Michigan. There was high spatial agreement between locations of CWD positives and high risk townships.



In comparisons between my direct and indirect ranks calculated by entropy reduction, I found consistent rank ordering between the two methods (Table 2.2). There were minor discrepancies between the risk of out-of-area hunting and captive cervid facilities. The largest discrepancy was in the importance of deer density. For the direct ranking, deer density was evaluated to be the 4$^{th}$ most risky hazard, whereas in the indirect ranking approach it was estimated to be the hazard that presented the most risk to CWD occurrence.

Table 2.2 Comparison of direct ranking and indirect ranking of CWD hazards. Direct rankings are the mean (± standard deviation) of estimates from the six expert participants. Indirect ranking estimates are calculated as entropy reduction based on a Bayesian Belief Network parameterized in Netica (Norsys Software Corp. 2010).

| Hazard | Direct Ranking (1 = Least; 5 = Most Risky) | Indirect Ranking (Smaller=Lower Risk; Larger = Higher Risk) |
|---|---|---|
| Deer Density | 2.5 ± 1.38 | 0.05403 |
| Out-of-Area Hunting | 4.0 ± 1.10 | 0.01205 |
| Captive Cervid Facilities | 3.7 ± 1.03 | 0.01533 |
| Taxidermists and Processors | 3.0 ± 1.67 | 0.0049 |
| Deer Wintering Complexes | 1.8 ± 1.17 | 0.00099 |

**DISCUSSION**

I developed an expert-elicitation approach that accurately estimated locations of CWD occurrence despite an apparent lack of data necessary to perform a quantitative assessment. Spatially accurate risk assessments are critical to effective disease interventions, particularly during the earlier stages of disease exposure when local, empirical data are not available. I relied on local experts to estimate risk based on a suite of co-occurring hazards, while explicitly controlling for multiple sources of cognitive and motivational biases (deLittle et al. 2018). My results indicated coherence within and among expert evaluations that resulted in accurate identification of high-risk areas based on CWD detections in Michigan from 2015 – 2018. The spatial agreement held even when hazards that were dependent on the knowledge of CWD

occurrence were excluded. I measured expert uncertainty using the four-point method (Speirs-Bridge et al. 2010) and combined individual responses into a simple-averaged group distribution. Furthermore, my indirect ranking approach was consistent with direct rankings while avoiding the uncertainty amongst experts in relative risk contributions that may have challenged group consensus. Taken together, my findings support my application of expert-elicitation to inform wildlife disease risk assessments, particularly in situations where proactive decision-making is necessary but linkages between hazards and risk remain unclear.

Spatial alignment between risk estimates and disease occurrence is a fundamental attribute of useful risk assessments because it ensures that limited resources are allocated to appropriate areas. However, in my case identifying high-risk locations was challenged by complex human-wildlife interactions that varied spatially and temporally, primarily as a result of the high intrinsic and economic value of white-tailed deer (VerCauteren et al. 2011). Chronic wasting disease occurs in asymptomatic animals that can be distributed far removed from prior positive detections (Belay et al. 2004). New disease foci are frequently discovered only after disease is established, effectively limiting the ability to reconstruct the events that led to the initial exposure (Miller and Fischer 2016). The combination of human interactions, natural spread dynamics, and imperfect detection make quantitative risk assessments for CWD particularly difficult. Despite these inherent limitations and uncertainties, my approach provided a viable alternative that is useful to decision-makers and is based on a rigorous and reproducible data collection process.

In comparisons of direct and indirect ranking results, I found that experts generally assessed hazards similarly with few inconsistencies. The similarity suggests that my indirect approach allowed experts to provide data that were consistent with their gained expertise, despite

the unclear linkage between individual hazards and risk created by my indirect approach. The greatest disagreement occurred in method comparisons for deer density (Table 2). These differing evaluations for deer density are likely associated with cognitive biases derived from an expert's geographic reference area. Because of Michigan's large north-south gradient in winter severity, deer behavior is highly variable between upper and lower peninsulas (Beyer et al. 2010). White-tailed deer in the upper peninsula have lower densities as a result of harsh winter conditions and lower quality habitat. In contrast, deer residing in the lower peninsula experience higher quality habitats, fewer predators, milder winters, and reduced hunting-caused mortality in more urbanized areas where hunting access is limited. These differing ecologies presumably contribute to disparity in relative importance that may have challenged an approach based on direct ranking. In my application, however, it is likely that these different perspectives improved the quality of my indirectly elicited data because they expanded the range of judgement of the group (Torrance 1957).

Expert-elicited data for use in decision-making has been criticized because of a lack of objective, empirically based observation. Experts are commonly hesitant to adopt these methods because of their lack of perceived knowledge, the complexity of the problem, or, because these methods are outside of norms of traditional scientific inquiry (Conroy and Peterson 2013). In this study, I had to remove the responses of one of our experts because of a perceived lack of knowledge that affected their ability to provide useful estimates of disease risk. In addition to the hesitancy of some experts, there are many opportunities for introduced bias and group conflict to affect expert elicitation (Clark et al. 2006). My study avoided group conflict because of the individually based elicitation exercise and modified Delphi review process (Kynn 2008). I applied simple averaging with a principled statistical distribution to propagate and, in many

cases, reduce the overall group uncertainty of experts. As a result, my study supported other mounting evidence on the value of expert opinion given the application of appropriate methods to address expert hesitancy, control sources of bias, and limit preconceptions (McBride et al. 2012).

There have been many calls for proactive disease management, such as Grant et al. (2017), which supports the use of decision-making tools to improve the success of disease intervention. However, system variability and critical sources of unresolved uncertainty (e.g., empirical relationship between hazard magnitude and risk) often preclude proactive approaches. Furthermore, past efforts to quantify wildlife disease risk have mostly been accomplished in piecemeal by identifying and evaluating hazards individually (Gillette et al. 2004, Oraby et al. 2016). While this approach provides some guidance on spatial risk assessments, it is often insufficient to integrate multiple risk factors in a way that supports decision-making. My approach improved on past efforts by comprehensively evaluating risk across space in a way that is customizable to the unique attributes of disease systems, and that aligned with known cases of disease in my application. As a result, my comprehensive protocol is being implemented in at least two other states in the Midwestern, U.S.

# CHAPTER 3: USING MODEL PROJECTION TO IMPROVE THE RAPID RESPONSE TO A CHRONIC WASTING DISEASE OUTBREAK

## INTRODUCTION

Infectious wildlife diseases in novel wildlife hosts or geographic regions have increased globally over the past several decades (Jones et al. 2008, Cunningham et al. 2017). When wildlife diseases are first detected, natural resource agencies are compelled to act quickly to prevent further spread of disease, reduce impacts to wildlife populations and ecosystems, and, if necessary, mitigate zoonotic potential. One of the priority actions upon detecting wildlife disease is to estimate and map the area currently affected by disease and to identify areas at high risk in the near future (Langwig et al. 2015). Quickly delineating accurate boundaries for wildlife disease is challenging because most locations lack data necessary to define boundaries directly or to use in predictive disease models. Furthermore, many wildlife diseases continuously change in their spatial extent and intensity, causing spatial estimates based on current observation to be subject to a high degree of uncertainty (James et al. 2009). As a standard regulatory response, managers often adopt generic distance benchmarks for management zones that encircle positives by a predetermined distance based on movement patterns or known geographic ranges of affected hosts. However, these benchmarks may fail to consider the unique landscape context surrounding disease detections and may underestimate or overestimate the geographic areas affected by disease.

An alternative approach to using distance benchmarks for estimating and mapping wildlife disease extent is to project spread patterns based on model results from endemic locations to other locations with similar conditions. For wildlife diseases, model projection may

be particularly useful because diseases often occur repeatedly across space and time in locations that share ecological conditions. Given a modeling framework and fitted values appropriate to the ecological context, projection may allow for: 1) explicit and immediate incorporation of landscape-specific estimates of disease risk critical to mapping disease extent; and, 2) a potential mechanism to predict and forecast locations at highest risk for disease exposure. Thus, projection is likely an important, yet underutilized, approach for the early management response of wildlife diseases.

One disease that could immediately benefit from model projection is chronic wasting disease (CWD). CWD is a fatal neurodegenerative disease affecting deer, elk and moose that has repeatedly emerged globally, including many times within the same ecoregion. New detections are attributed to natural movements of affected animals and human-mediated transport of infectious carcasses and live animals. Currently, upon detection of CWD, natural resource agencies prioritize surveillance and implement management actions in areas typically defined by distance benchmarks consistent with movement ecology of affected deer species (e.g., Michigan Department of Natural Resources [MDNR] and Michigan Department of Agriculture and Rural Development [MDARD] 2012, Pennsylvania Game Commission [PGC] 2020). For white-tailed deer (*Odocoileus virginianus*) in the Midwestern U.S., juvenile dispersals range from 0 km – 35.8 km (Peterson et al. 2017), and thus, common distance benchmarks are often set to 8.05km, 16.09km, 19.31km, or 40.23km radii (5, 10, 12, or 25 miles) surrounding detection sites (MDNR 2019). While distance benchmarks are often useful as immediate disease response criteria, these benchmarks treat all landscapes surrounding a CWD detection as homogenous and thus ignore important relationships that may drive disease progression. Landscape heterogeneity is known to

influence dispersal rates and distance (Long et al. 2005), spatial distribution of deer (Walter et al. 2009), and transmission of CWD (Conner and Miller 2004).

In 2017, the Michigan Department of Natural Resources (MDNR) detected CWD in a 3-year-old white-tailed doe submitted during an early season youth hunt (MDNR 2017). Additional surveillance in the area during 2017 identified 45 total CWD-positive animals in a concentrated disease focus in the west-central Lower Peninsula of Michigan within Kent and Montcalm counties. Nine previous CWD detections had occurred in the state in 2015 and 2016; however, the 2017 detections were the first evidence that CWD might be widespread and established within Michigan. Based on a single year of observation, predicting the area affected by the cluster of disease with distance benchmarks would likely fail to fully encapsulate the affected area. Furthermore, based on the sparsity of data, fitting complex disease models was not possible. Thus, there was an immediate need for an alternative approach that could more appropriately estimate the extent of CWD and identify locations at high risk using limited available information

In other locations where CWD occurs, such as Wisconsin, U.S., extensive data have been collected and used to develop disease models. Based on the similarity of the landscape across much of the Midwestern U.S., and the repeated occurrence of CWD, these results may be useful in estimating disease extent elsewhere. Hefley et al. (2017) created a mechanistic disease model using partial differential equations (PDEs; Hefley et al. 2017). PDEs address many of the statistical challenges of spatio-temporal disease data, such as locally unique autocorrelation effects, while providing principled predictions and forecasts of CWD dynamics that are reliable for application elsewhere.

My objective was to estimate disease extent in a region in west-central Lower Peninsula of Michigan based on PDE-based modeled results projected from similar habitats in Wisconsin. As part of my evaluation, I sought to: 1) use existing data to estimate an apparent origin of CWD given a single year of disease observations and limited historical data; 2) use the apparent origin to initiate a dynamic PDE to project disease extent in Michigan; 3) evaluate uncertainty in estimates of disease extent; and 4) retrospectively compare the performance of projection relative to distance benchmarks. My intent was to inform rapid disease response in Michigan by incorporating knowledge gained studying a CWD outbreak in another Midwestern state that had sufficient longitudinal data for statistical model fitting and prediction.

**STUDY AREA**

The study area in Michigan was selected to include a large portion of the lower peninsula (LP) that surrounded CWD detections in free-ranging white-tailed deer (Fig. 1). The LP is part of the upper midwestern region of the United States and is encircled by 3 of the 5 Great Lakes: Lake Michigan, Lake Huron, and Lake Erie. It has a 4-season, temperate continental climate that is characterized by warm summers and moderately long winters with frequent lake effect snowfalls. Average temperatures range from approximately -3.8°C in January to 23.3°C in July. The topography is primarily low-lying and hilly (elevation range: 176m – 256m), having been shaped by previous glaciation. Landscape cover is a mix of agriculture and hardwood forest cover types in the western LP and central LP regions where this study occurred. Dominant tree species include sugar maple (*Acer* spp.), red and white oaks (*Quercus* spp.), white pine (*Pinus strobus*), eastern cottonwood (*Populus* spp.), beech (*Fagus* spp.), and birch (*Betula* spp.). Agriculture is primarily sugar beet, corn, and soybean varieties.

## METHODS

Across the Midwestern U.S. white-tailed deer exhibit similarities in habitat preference, space use, and estimated home range size (Walter et al. 2009), which are factors important to the geographic distribution of CWD (Evans et al. 2016, Edmunds et al. 2018). To estimate the spatial extent of CWD using only a single year of disease observations, I projected a hierarchical model developed in one state, Wisconsin, and applied it to another, Michigan.

The probabilistic model generated spatiotemporal predictions and forecasts of CWD infection based on Bayesian inference. It used a cell-based, mechanistic PDE for disease growth and diffusion processes, and regression-based relationships to incorporate habitat and demographic covariates relevant to deer behavior and disease dynamics (Hefley et al. 2017). The parameterization of the original hierarchical model used to estimate CWD growth and spread dynamics was:

$$y_i \sim Bernoulli(p_i), \tag{1}$$

$$g(p_i) = u(s_i, t_i)e^{x_i'\beta}, \tag{2}$$

$$\frac{\partial}{\partial_t}u(s,t) = \left(\frac{\partial^2}{\partial s_1^2} + \frac{\partial^2}{\partial s_2^2}\right)[\mu(s)u(s,t)] + \lambda(s)u(s,t), \tag{3}$$

$$\log\big(\mu(s)\big) = \alpha_0 + z(s)'\alpha, \tag{4}$$

$$\lambda(s) = \gamma_0 + w(s)'\gamma, \tag{5}$$

where, $y_i$, was the disease status of a sampled deer and, $p_i$, was the probability of infection. A unique site-, *s*, and time-specific, *t*, estimate of the probability of infection was generated using the PDE in equation 3. Covariates for the probability of infection were estimated by a vector that included the sex and age of tested animals, $x^i$, effect size, β, and scaled according to the

relationship $e^{x_i'\beta}$. The age and sex of individual animals tested were considered in the PDE framework because of the strong age-specific pattern of CWD infection that exists (Samuel and Storm 2016, Mysterud et al. 2019). Age classes of deer were defined in 3 categories based on age at the time of harvest: fawn (<1 year of age), yearling (1 – 2 years of age), and adult (>2 years of age). Lastly, because the probability of infection ranges from 0 – 1, a truncated normal distribution link function was applied as notated by g(.) (Hefley et al. 2017). For growth, $\lambda(s)$ across space, *s*, (i.e,, site specific increase in probability of infection) and spread, $\mu(s)$ across space, (i.e., diffusion), unique landscape relationships, γ and α, respectively, were estimated for each site using vectors *z(s)* and *w(s)* in equations 4 and 5. Landscape factors included hardwood forest, human development, and large river corridors. For additional detail on model development and parameterization, I refer the interested reader to Hefley et al. (2017).

To project the results of the PDE developed in Wisconsin, I first required a reasonable assumption of ecological similarity between locations of application. Thus, I compared landscape composition between study regions as relevant to my analyses. I used the 2011 National Land Cover Database to calculate percent cover of hardwood forest and human development within a 2.6 $km^2$ grid cell, (section-level, Public Land Survey System), and publicly available flowline data from Michigan Department of Natural Resources to calculate the presence/absence of river corridors within a cell. At a broad scale, these landscape features (i.e., percentage hardwood forest and human development, presence/absence of large rivers) are frequently reported for their effects on white-tailed deer movements and CWD dynamics (Joly et al. 2006, Blanchong et al. 2008, Robinson et al. 2013, Evans et al. 2016). Further, similar landscape composition has resulted in consistent white-tailed deer behaviors across the Midwestern and Eastern U.S. (Long et al. 2005, Walter et al. 2009). Based on the sparsity of

available data to fit spatiotemporal disease dynamics unique to Michigan, I used reported values estimated from 103,526 individual testing records collected from 2002 – 2016 across a 15,539 $km^2$ area of south-central Wisconsin that were reported in Hefley et al. (2017) (Table 3.1).

Table 3.1 Parameter estimates and 95% Bayesian credible interval for the spread and growth of CWD as reported in Hefley et al. (2017). Included are estimates for the intercept term (α) and landscape covariates of rivers, percent forest, and percent development in a 2.6 $km^2$ grid cell.

| Spread Covariates | Median (α) | Lower 95% CRI | Upper 95% CRI |
|---|---|---|---|
| $\alpha_0$ | $1.72\times10^{1}$ | $1.70\times10^{1}$ | $1.74\times10^{1}$ |
| River | $6.25\times10^{-1}$ | $1.89\times10^{-1}$ | 1.11 |
| Forest | $-1.92\times10^{-1}$ | $-2.95\times10^{-1}$ | $-8.88\times10^{-2}$ |
| Development | $-1.30\times10^{-1}$ | $-3.44\times10^{-1}$ | $1.40\times10^{-1}$ |
| **Growth Covariates** | **Median (γ)** | **Lower 95% CRI** | **Upper 95% CRI** |
| $\gamma_0$ | $6.91\times10^{-2}$ | $-1.76\times10^{-2}$ | $1.43\times10^{-1}$ |
| River | $2.19\times10^{-1}$ | $-4.03\times10^{-1}$ | $8.01\times10^{-1}$ |
| Forest | $2.09\times10^{-1}$ | $1.20\times10^{-1}$ | $3.21\times10^{-1}$ |
| Development | $7.01\times10^{-2}$ | $-8.23\times10^{-2}$ | $2.97\times10^{-1}$ |

The next step was to initiate model projection; thus, I required an estimate of the apparent date and location of first occurrence of CWD in free-ranging white-tailed deer. I approximated an apparent date of first occurrence as the earliest surveillance year where sampling was insufficient to detect CWD at an apparent prevalence below 0.01 in adult male deer (reference class). I used a detection threshold probability of 95% (Jennelle et al. 2018). I verified the date of first occurrence by examining a range of dates from 1 – 20 years from first detection. I assessed fit by examining the agreement between locations of detection and the maximum probability of infection estimates at those locations (Fig. B.1).

Apparent prevalence was estimated using a web application (https://popr.cfc.umt.edu/CWD/) that applied weighted surveillance methodology to historical CWD testing data collected from 2008 – 2016 across 12 townships (Cato, Douglass, Fairplain, Ferris, Maple Valley, Montcalm, Oakfield, Pine, Reynolds, Sidney, Spencer, and Winfield) in

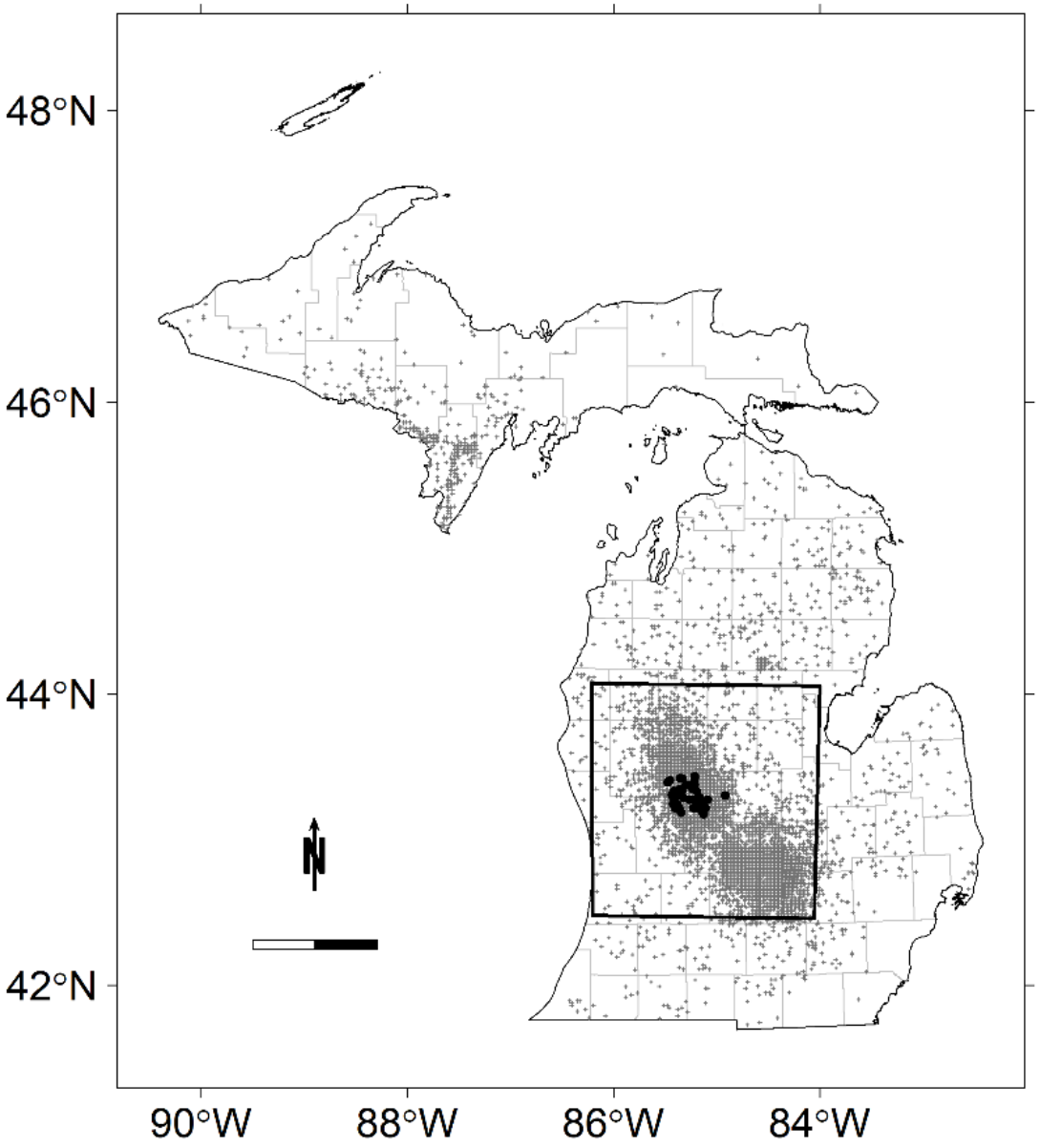
Michigan that coincided with the location where CWD was detected in 2017 (Table 3.2). The total number of animals tested during that period was 484, with males and females across all age classes represented. Weighted surveillance uses hazard weight estimates for 16 distinct sample types related to the sex, age, and method of collection (e.g., hunter-harvest, targeted removal) to estimate the maximum apparent prevalence that could exist in an area based on existing or planned sampling effort. Risk of infection generally increases with the age of the animal and is higher in males than in females (Walsh and Miller 2010, Heisey et al. 2014, Jennelle et al. 2018). While the differences between infection risk between adults and younger age classes are generally attributed to shorter time of exposure risk for younger age classes, it is possible that at least some of the elevated risk results from limitations in test sensitivity that biases results to older individuals with higher pathogen loads (Vijugrein et al. 2019). Whether the positive association between age and infection risk is a result of behavioral aspects of deer, or simply an artefact of testing diagnostics, it was important to consider in my application because of the change in spatial extent estimates that resulted from younger age classes versus older age classes.

Table 3.2 Total number of individual animals that were tested for CWD from 2008 – 2016. Prevalence column is the potential adult male apparent prevalence estimates that could exist in the population but remain undetected based on the total number of samples. Data from 12-township area (includes Cato, Douglass, Fairplain, Ferris, Maple Valley, Montcalm, Oakfield, Pine, Reynolds, Sidney, Spencer, Winfield) in Michigan where CWD was discovered in 2017. Data source: Michigan Department of Natural Resources.

| Year | Fawn Male | Yearling Male | Adult Male | Fawn Female | Yearling Female | Adult Female | Total | Prevalence ± St. Dev. |
|---|---|---|---|---|---|---|---|---|
| 2008 | 3 | 115 | 18 | 12 | 37 | 98 | 283 | 0.0097 ± 0.00969 |
| 2009 | 5 | 13 | 6 | 1 | 8 | 25 | 58 | 0.04273 ± 0.0414 |
| 2010 | 2 | 9 | 4 | 3 | 5 | 19 | 42 | 0.05909 ± 0.0565 |
| 2011 | 1 | 15 | 3 | 1 | 14 | 36 | 70 | 0.03716 ± 0.0363 |
| 2012 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — |
| 2013 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — |
| 2014 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — |
| 2015 | 0 | 2 | 1 | 0 | 3 | 0 | 6 | 0.273 ± 0.209 |
| 2016 | 0 | 6 | 1 | 0 | 7 | 11 | 25 | 0.097 ± 0.089 |

I estimated the apparent location of first occurrence using a grid search technique that evaluated each of 12,100 cells (cell area: 2.6 $km^2$; total area: $3.13\times10^4$ $km^2$) for their ability to maximize the probability of infection at each location within the disease cluster where CWD was observed in 2017 (Fig. 3.1 depicts study area). I excluded prior detections from 2015 – 2016 that were geographically distant (>50 km away) from the cluster because they presumably resulted from a different spatial spread process than diffusion. Each cell matched the total area and approximate configuration of public land survey system section-level data and MDNR deer harvest records. To generate cell-specific estimates, I initiated the model at each cell centroid and produced a spatially explicit probability of infection across the entire area. I then calculated the sum of the estimated log probability of infection derived from each location where disease was observed in 2017. I assumed that the most likely location of first occurrence for model initiation purposes was the cell with the maximum joint log-probability of infection (i.e., maximum[$log\text{-}likelihood(\theta|x1,\ldots,xn)$], where, $\theta$ = proposed cell centroid (i.e., location of first occurrence) and $xn$ = Probability of Infection) given the distribution of the 45 clustered positive animals detected.

Figure 3.1 2017 CWD monitoring record in Michigan. Black box indicates the study area. Gray symbols indicate locations where CWD was not detected in deer whereas black symbols indicate a positive detection (n = 45). The total number of animals tested in 2017 was 17,414.



To validate my origin identification approach, I conducted simulations to assess the accuracy and precision of the grid search technique by reconstructing a disease outbreak with a known starting location and subsequently attempting to estimate its origin. I quantified uncertainty by calculating the distance between the known point of introduction and the estimated point of introduction dependent of the number of disease detections available. The number of disease detections was varied between 5 different levels: 5, 10, 25, 45, 100. Each level was repeated 20 times. Thus, the steps in the procedure were to: 1) select a known point of first occurrence; 2) generate a disease outbreak with varying number of positives; and 3) estimate the location of first occurrence using joint log-probability of infection.

Using estimates of the date and location of first occurrence, I initiated the model based on empirical relationships from Wisconsin's CWD outbreak and transferred them to Michigan's landscape. I projected at each grid cell across all years starting from the estimated date of first occurrence through year 2018. I selected adult male deer for my estimates because this class of animal has the highest estimated risk of infection (Jenelle et al. 2018), and thus would represent the most conservative estimate for disease extent predictions. To incorporate potential differences in deer movement behavior between Wisconsin and Michigan, I analyzed variation across posterior distributions for its effect on projected disease extent. I used only the posterior distributions of fitted values for landscape-based risk factors (i.e., hardwood forest, human development, rivers) to evaluate variability in projected findings because sex and age were modeled as scalars in the original parameterization (Hefley et al. 2017).

I summarized model variability in 3 ways. First, because the goal of the analysis was to provide an estimate of the spatial extent of disease for decision-makers, I was interested in the effect that varying fitted values for landscape risk factors reported in Hefley et al. (2017) had on

the estimated geographic extent of disease. Thus, I extracted the maximum and minimum spatial extents across all variations of fitted values attempted. Second, I generated spatially explicit estimates of the coefficient of variation to provide a visual assessment of variability in probability of infection. My third measure of variability was a non-spatial evaluation of probability of infection estimates in distinct landscape types of hardwood forest, human development, and river corridors. For each of these 3 metrics of variability, I performed repeated runs (n = 88) with varied estimates of fitted values (Δ 10%) across the 95% credible interval of posterior distributions from Hefley et al. (2017) (Morris 1991). The number of runs was determined as the product of the number of Δ10% bins (total = 11) across the 8 covariate posterior distributions. While searching the parameter space of one covariate, I held other estimates at mean values. Across all scenarios, I removed estimates of probability of infection that were less than 0.001, a value corresponding to < 0.1% prevalence.

To evaluate the performance of projection relative to distance benchmarks, I performed 2 separate retrospective analyses on disease monitoring data collected in 2018 and 2019 after management zones were established. There was a total of 180 positive animals detected between those years in Michigan's lower peninsula. The first analysis was a comparison between the maximum model-based estimate of disease extent with an area that would result from using a distance benchmark of 16.09 km surrounding all 2017 positives. I selected a 16.09 km radius to match the distance benchmark chosen by MDNR (MDNR and MDARD 2012). To compare the effectiveness of both approaches I evaluated the ability to encompass all disease detections (2015 – 2019). I considered the zone that was able to encompass more positives to be superior for management efforts.

The second retrospective analysis was designed to evaluate the predictive capacity of my model-based projection method. To perform this evaluation, I compared probability of infection estimates at all locations where CWD was detected in Michigan (2015 – 2019) to probability of infection estimates at randomly selected and clustered disease detections (n=180) generated by a multi-variate gaussian distribution described by a mean (i.e., my empirical point of introduction), and a covariance matrix. The covariance was informed by the correlation between latitude and longitude of observed disease detections and was calculated as [$5.6\times10^8$, 0, 0, $5.6\times10^8$]. To facilitate a quasi-statistical comparison, I performed 999 repeated simulations of my multivariate point processes and compared each against my observed monitoring dataset. I selected 999 simulations such that any deviation of the observed probability of infection estimates from the random gaussian process represented a p-value approximation at that site of $< 0.001$. All analyses were performed in Program R version 3.5.2 (R Core Development Team 2018).

**RESULTS**

I found similar landscape composition between Wisconsin and Michigan study areas. Percentage hardwood forest in Michigan and Wisconsin study areas was 38%, percentage urban development was slightly higher in Michigan (6% versus 3%, respectively), and each area was bisected by one major river corridor. For apparent prevalence based on historical surveillance, I found that the first year of surveillance in the region, 2008, was the best estimate of date of origin. In 2008, the apparent prevalence rate using weighted surveillance was $0.0097 \pm 0.00969$ (mean ± standard deviation). All subsequent years, 2009 – 2016, had insufficient testing to detect CWD at a prevalence rate of $< 0.0371 \pm 0.0363$ (Table 3.1). Based on the surveillance record and mean apparent prevalence rate of 0.0097 in 2008, I adopted 2008 as a reasonable date of first occurrence in Michigan for model projection purposes. I presumed that if CWD was introduced

prior to 2008, it would have been detected during sampling that year or would have been at a low prevalence in a relatively confined geographic space.

Informed by the time since introduction estimate of 10 years derived from historical surveillance records, I ran the full hierarchical disease model and estimated a joint log-probability value for the centroid of each grid cell given 45 CWD positive locations (Fig. 3.1). The point location with the highest joint log-probability of generating the observed cases of disease was near the geographic center of the disease focus, at 85.29°W, 43.29N (Fig. 3.2). Based on the smooth decay in log-probability estimates across the study region, I was interested in evaluating the performance of the technique given the probability surface (i.e., model validation; Fig. 3.2). For the smallest number of CWD detections considered (n = 5 positives) and using the same time since introduction, the average distance between the known point of first occurrence and the estimated point of first occurrence was 12.6 ± 9.4 km after 10 years (mean ± standard deviation; Fig. 3.3). With 45 disease detections and 10 years of disease presence, the distance was 7.6 ± 3.6 km. Over the entire range of values considered, 5 to 100 positive detections, the accuracy and precision of the grid search technique generally improved with additional cases of disease; however, there was no improvement when detections increased from 45 to 100 (Fig. 3.3).

Figure 3.2 Joint log-probability of infection using the grid search method. Gray symbols indicate locations of 2017 positive detections; black cross indicates point of maximum joint log-probability (Geographic coordinate: 85.29°W, 43.29N).

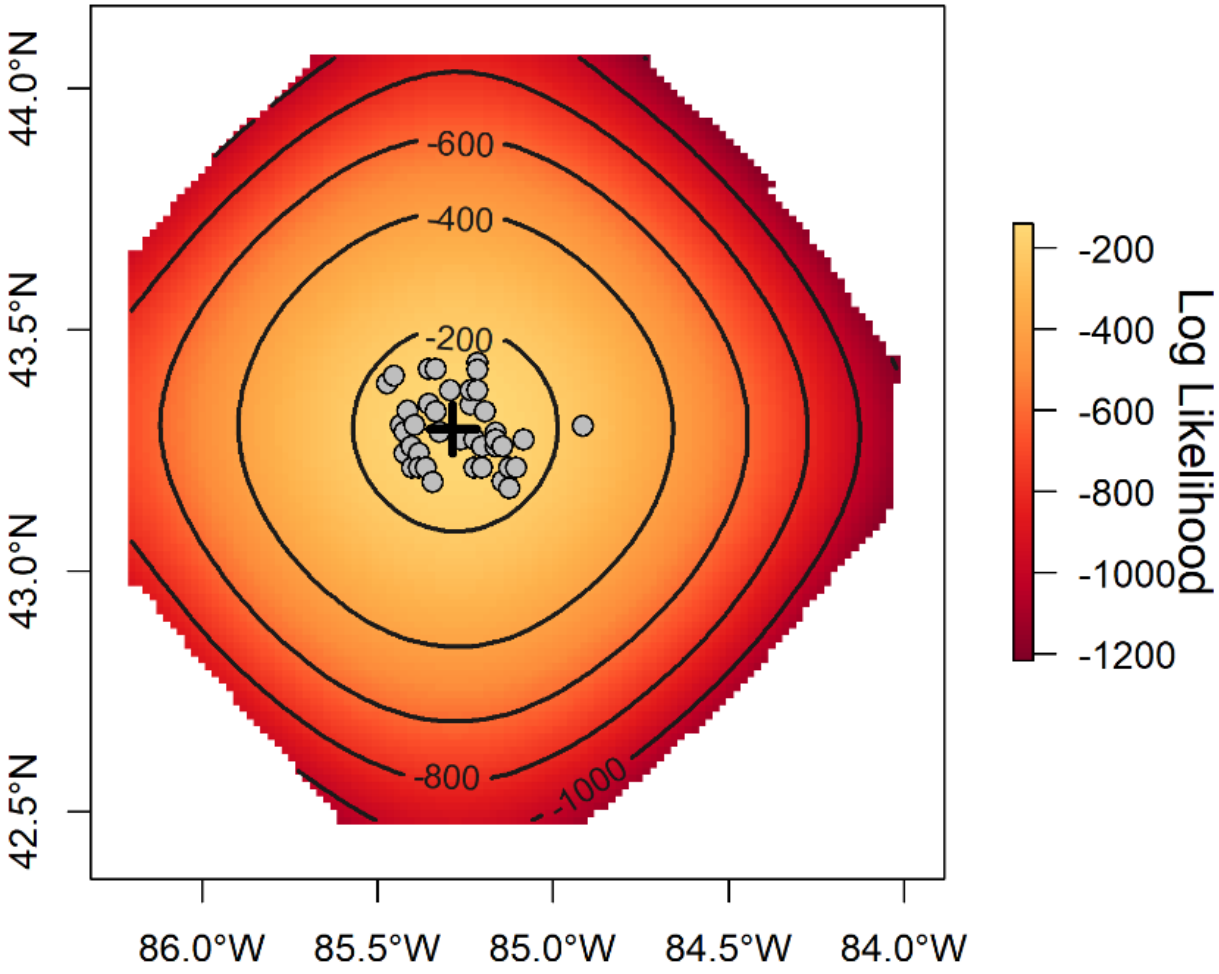
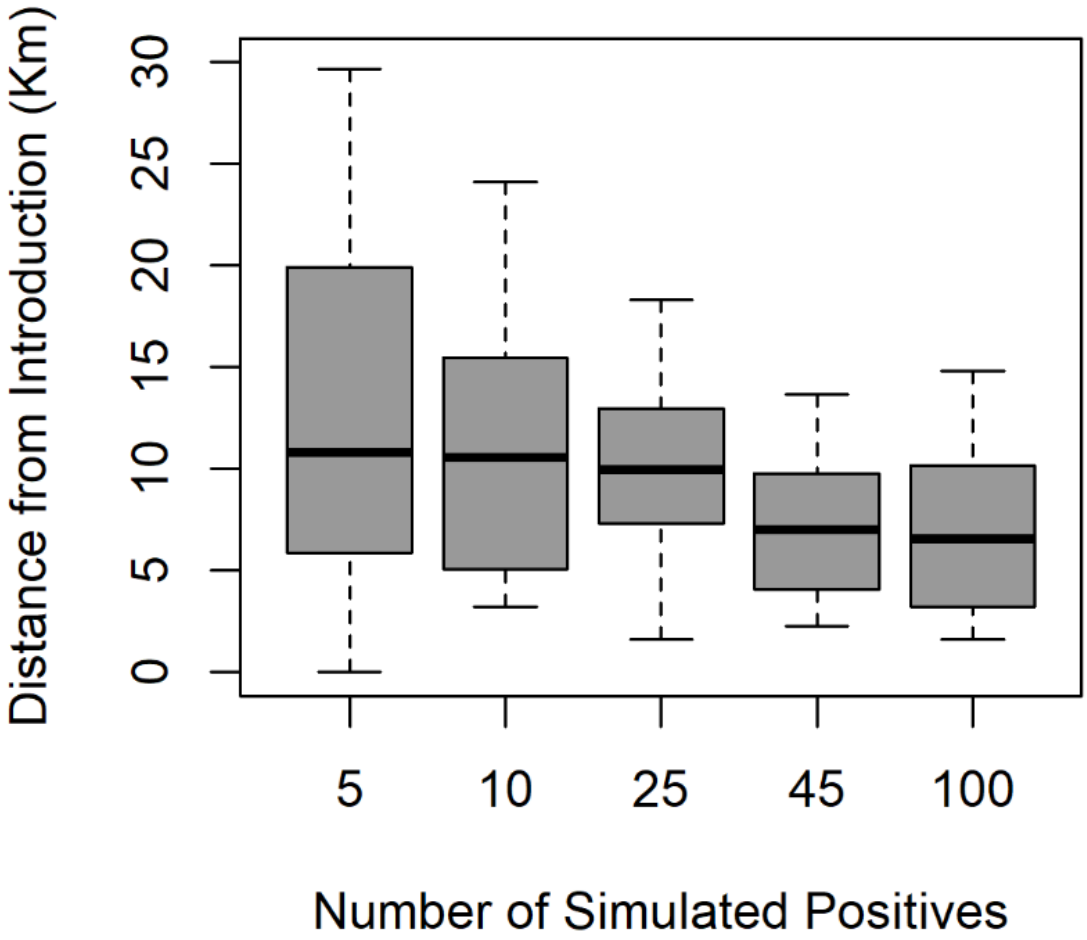


Figure 3.3 Boxplot of uncertainty in the grid search technique after 10 years of disease presence. Uncertainty was measured as the Euclidean distance (in km) between the estimated point of first occurrence and a known point of first occurrence.




The geographic extent ranged from a minimum of $3.93\times10^3$ km$^2$ total area to a maximum of $9.91\times10^3$ km$^2$ (Fig. 3.4A). The spatially explicit coefficient of variation ranged from 18.26% to 24.23%, with the majority of variation occurring in a heavily forested region along the Muskegon River in the northwest part of the study area. Variability in projected probability of infection was higher in the southern part of the study area along the Grand River (Fig. 3.4B). These findings corresponded with large coefficients of variation in distinct landscape features of

hardwood forest and river corridors, albeit results in areas of high human development exhibited a wide range of variation.

Figure 3.4 Panels A – C Panel A is the mean probability of infection in adult male white-tailed deer based on projected model fit from Hefley et al. (2017). Panel B is the coefficient of variation across 88 model runs exploring the sensitivity in probability of infection estimates across the 95% Bayesian credible interval of fitted values from Wisconsin. Darker black colors indicate greater variation, whereas lighter gray colors indicate less variation. Panel C is a comparison of a projected zone generated from maximum estimated probability of infection across a range of fitted values (gray line with black boundary) to a simple zone created from a 16.09 km buffer surrounding 2017 positive detections (black line).

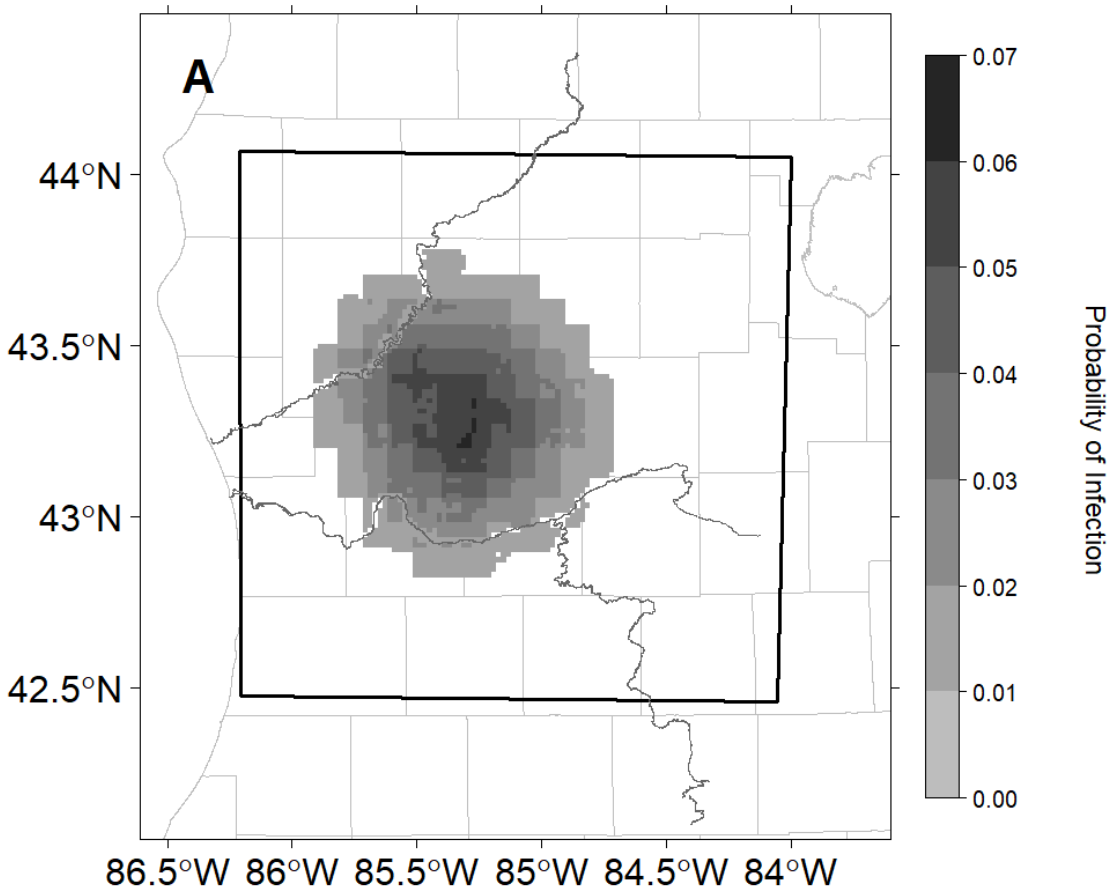
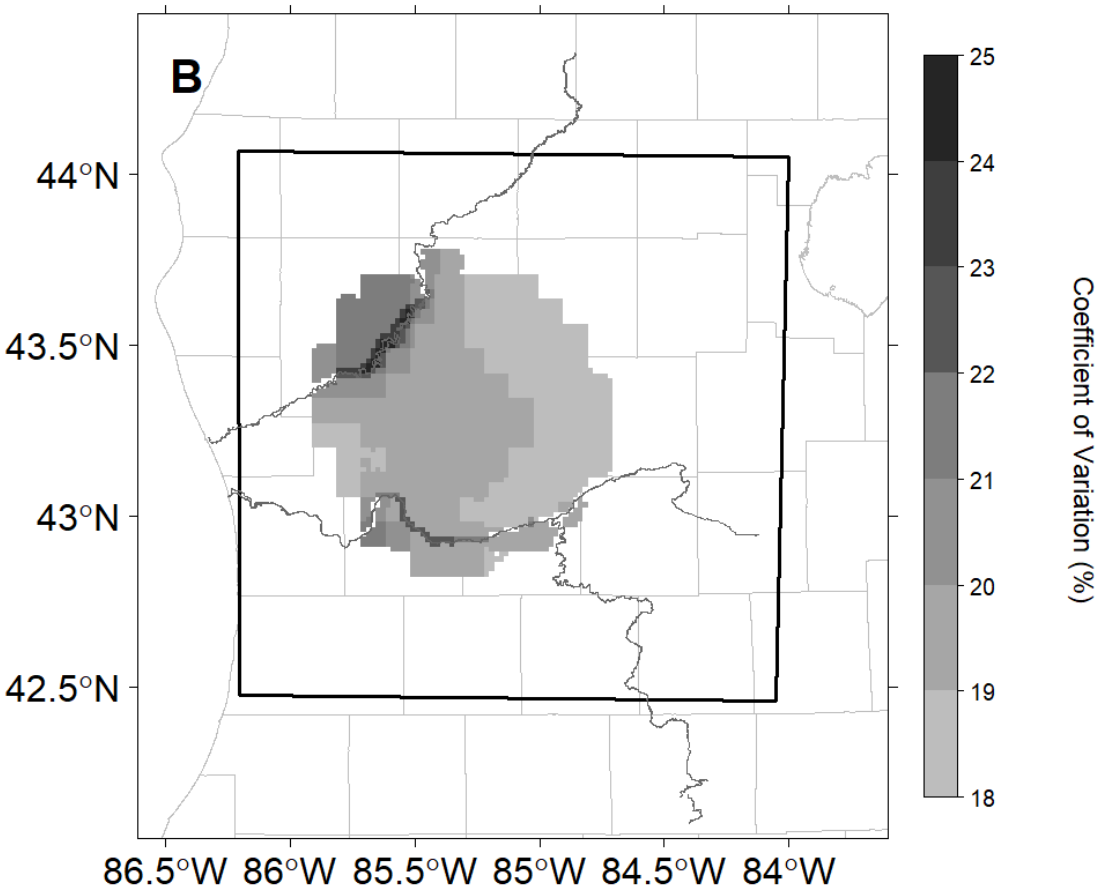


Figure 3.4 (cont'd)



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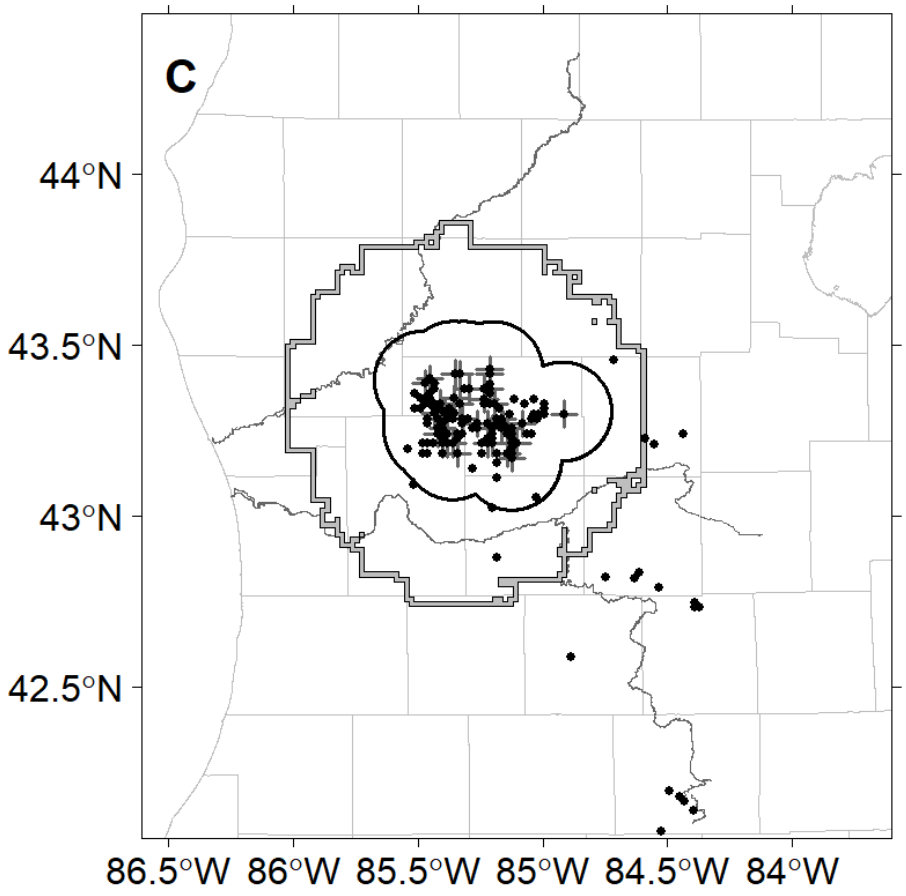
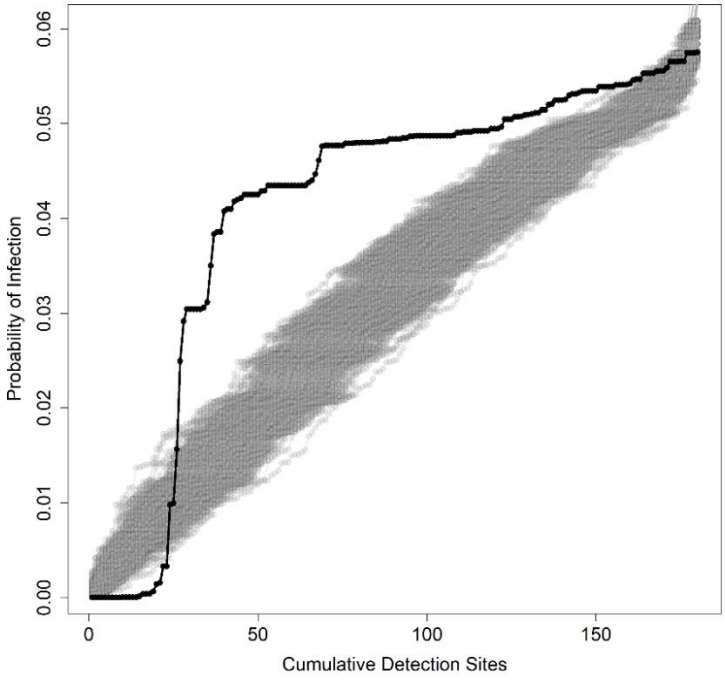



Variability across the range of fitted values necessitated the use of maximum projected values for comparisons with distance benchmarks. I compared a management zone established using a radius of 16.09 km surrounding all 45 of the 2017 positives ("simple zone," total area: $3.46 \times 10^3 km^2$) to a management zone established using the maximum extent ("projected zone," total area: $9.91 \times 10^3$ $km^2$). Based simply on raw number of positives, the projected zone included 5 additional positives within its boundaries compared to the simple zone. Both zones were insufficient in size to encompass 17 distant detections, and the projected zone was 186% larger than the simple zone (Fig. 3.4C).

For model performance, I found that my projection outperformed a random gaussian process model across the majority of locations where CWD was observed in Michigan (Fig. 3.5). In the majority of cases my observed CWD detection sites had higher probability of infection estimates than a random realizations, with the only areas of underperformance occurring at disease detections sites that were > 60 km away from the focus of disease in Kent and Montcalm counties. The superior performance of my projected model compared against repeated random realizations indicated that empirically derived CWD spread and growth relationships estimated in Wisconsin were predictive in Michigan.

Figure 3.5 Probability of infection estimates at observed CWD detection locations (black line) and at simulated CWD detection locations (gray lines) that were estimated by a multivariate normal distribution. I considered disease detections whose probability of infection estimates were either higher or lower than the 999 repeated simulations to be a statistically significant deviation. The majority of those deviations indicated that my projected model had predictive capacity at locations of CWD detection (2015 – 2019).



## DISCUSSION

I sought to improve the rapid response to a CWD outbreak by developing methodology for rapidly estimating disease extent given data that are typically only used to estimate distance benchmarks. For my estimates, I used a combination of locations of current-year positive animals identified through surveillance, historical surveillance records and projected results from another location within the same ecoregion. I found that management zones based on my estimate of CWD affected areas were better at encompassing future detections of disease and were larger compared to distance benchmarks ($9.91 \times 10^3$ km$^2$ versus $3.46 \times 10^3$ km$^2$, respectively). In addition, I was able to generate spatial estimates of the probability of infection that were unique to the localized landscape. These types of estimates are not available with the distance benchmark approach commonly used. Taken together, I found that my projection approach represented a substantial improvement in early responses to wildlife disease outbreaks and helped to partially address a critical weakness of distance benchmarks – the underestimation of affected areas.

The expansion of management zones beyond those estimated by simple zones may be preferable for estimates of CWD extent as disease foci are commonly underestimated (Miller and Fischer 2016). My projection-based approach produced a larger estimated disease extent that was based in empirical relationships of CWD spread and growth. Thus, it allowed for an expansion in ways that align with an understanding of disease progression. Furthermore, my projected estimates based on CWD spread and growth in Wisconsin outperformed repeated realizations of a random clustering process thereby supporting an expectation of similar disease progression between the two locations. As a result, my projection was able to provide reliable risk gradients that were specific to the area of interest and were useful for targeted management interventions immediately upon the first detection of disease in a new location (Ogden et al. 2008). Rapid

disease interventions are particularly warranted for CWD as it now affects free-ranging deer in 26 U.S. states, Canada, Norway, Finland, and Sweden, (USGS 2019) and can cost state agencies millions of dollars annually (Carlson et al. 2018).

The availability of parameter estimates from Hefley et al. (2017) resulted in landscape-specific gradients in estimated probability of infection and a derived log-probability surface suitable for estimating the point of introduction. The estimated surface was diffuse, but the centroid proved reliable for the location of first occurrence across a range of positive detections (Fig. 2). The lack of sensitivity of my technique across a range of positive detections suggests broad applicability to many locations that vary in disease intensity. The characteristic clustering of CWD detections reduced spatial variability and allowed for a reasonable assumption of a single point of origin, an assumption that is not always possible (Russell et al. 2003, Russell et al. 2005). Lastly, widely available historical surveillance records (Miller and Fischer 2016) unique to my geographic region informed my estimate of time since introduction (Martin et al. 2006, Alban et al. 2008). However, based on surveillance limitations and the difficulty in detecting a single positive animal, it is important to note that my time since introduction estimate was an approximation. Despite this limitation, my projected results still outperformed distance benchmarks in ways that are critical to informing management efforts immediately upon disease detection in a new area.

I assumed, for the purposes of model projection, that similarity in landscape composition would result in similarities in disease dynamics between locations (Conn et al. 2015). White-tailed deer show consistency in space use patterns across similar landscapes in the Midwestern U.S. (Walter et al. 2009). Habitat fragmentation, and specifically proportion forest cover, influences dispersal rates and distance, and spatial distribution of deer. Both study areas in

Wisconsin and Michigan shared similarities in percent hardwood forest (38%) and human development (3% versus 6%, respectively). Finally, CWD presence has been associated with space use and movement patterns (Evans et al. 2014, Edmunds et al. 2016) supporting my use of projection within an ecoregion.

I accounted for localized differences in space-use patterns and disease dynamics by performing repeated runs across the range of fitted values from Wisconsin and evaluating the effect on the probability of infection and extent estimates. Spatially explicit probability of disease infection varied with disease extent (minimum extent: $3.93 \times 10^3$ km$^2$; maximum extent: $9.91 \times 10^3$ km$^2$), and ultimately in the construction of a proposed management zone. Most variation occurred in forested tracts and along river corridors. Mechanistically, the variation in disease spread estimates in forest and river corridors stems from variability in original model fit (Hefley et al. 2017) but is likely a result of complex interactions between CWD dynamics and space use patterns of white-tailed deer in northern forests and agricultural regions of the upper Midwestern U.S. (Etter et al. 2002, VerCauteren and Hygnstrom 2012). Model refinements and variability reductions will occur with additional years of data (Chatfield 1995), or focused data collection efforts in areas with the highest coefficient of variation (Ascough II 2008).

Numerous studies have estimated disease origins and reconstructed wildlife disease processes (Smith et al. 2002, Weldon et al. 2004, Pfeiffer et al. 2007, Hefley et al. 2017), but none have estimated apparent disease origin and disease affected areas using model projection. Hefley et al. (2017) used the same modeling framework applied here to estimate disease origins and relative rates of spread and growth in forested areas of Wisconsin using a single year of high-resolution monitoring data (14,648 sampling records; Hefley et al. 2017). While their approach is ideal for precise estimates of the origin using an entire record of data observations

(i.e., single year including presence/absence of disease), waiting for a complete accounting from a full year is often not possible. For example, CWD was first discovered in western Michigan during an early season youth hunt necessitating targeted surveillance before monitoring data were collected. My approach provided a viable alternative to distance benchmarks that relied on data that existed at the time of need. Indeed, these types of data limitations represent a common challenge in CWD management because of the immediate response outlined in many state CWD management plans.

## MANAGEMENT IMPLICATIONS

My approach addresses a fundamental need universal to wildlife disease managers – the need to estimate affected area early upon emergence, or detection of disease in a new area or host (Langwig et al. 2015, Russell et al. 2017). For diseases warranting active interventions, such as targeted removals, projection provides estimates of risk that allow for more precision management efforts to occur. The ability to identify locations at high risk may ultimately improve the efficiency and effectiveness of disease intervention, if effective methods for removal can be developed at larger scales. Distance benchmarks remain useful, such as in cases where information regarding disease process is lacking; however, using methods such as those developed here that incorporate specific information regarding the disease context at the location of discovery (i.e., landscape configuration, number of positive detections) has the potential to greatly improve disease management efforts across a diversity of wildlife diseases, such as bovine tuberculosis (Schmidt et al. 1997), rabies (Rosette et al. 2001), and avian influenza (Martell-Moran et al. 2011), that currently rely solely on distance benchmarks to define rapid responses to detection.

# CHAPTER 4: INCORPORATING COMPLEX ECOLOGICAL DYNAMICS INTO DISEASE MODELS TO BETTER PREDICT THE SPREAD AND PERSISTENCE OF CHRONIC WASTING DISEASE

## INTRODUCTION

The spread and persistence of wildlife disease can result from complex ecological interactions among a host, a pathogen, and the habitats in which they co-occur. Host behaviors, including movements and contact patterns, influence the spread of disease and the species affected (Altizer et al. 2011, Clements et al. 2011, Bahl et al. 2016, Caron et al. 2016); pathogens experience habitat-specific viability and persistence (Cook et al. 1990, Randolph et al. 2000); and host-pathogen dynamics are mediated by the landscape context in which they occur (Altizer et al. 2004, Altizer et al. 2006, Morgan et al. 2007). When these interactions align, wildlife disease can emerge and become established in areas both proximate to, and far removed from, previously known infection sites (Bar-David et al. 2006, Lawson et al. 2011, Frick et al. 2017). Established disease has been implicated in loss of biodiversity (Skerratt et al. 2007), host population declines (Daszak et al. 1999, Frick et al. 2010, Edmunds et al. 2016), loss of genetic diversity (O'Brien and Evermann 1988), and zoonotic threats to humans (Cunningham et al. 2017). In actively managed wildlife diseases, unanticipated emergence can challenge mitigation efforts (Carter et al. 2007), necessitating better understanding of mechanisms of spread and formally incorporating those mechanisms into predictive disease models.

One of those mechanisms, the movement ecology of hosts, has direct implications on how fast and how far diseases spread and can help partially explain complex spatial distributions of outbreaks (Cullingham et al. 2011, Daversa et al. 2017). For example, chronic wasting disease

(CWD), an infectious disease affecting cervids in at least 26 U.S. states, 3 Canadian provinces, South Korea, Norway, and Finland (Hopkins et al. 2019), is thought to spread by multiple movement phases of affected deer species (Cullingham et al. 2011). Deer perform home ranging behaviors within highly localized areas, but undertake longer distance transient movements such as dispersal, excursion, and migration (Hawkins and Klimstra 1970, Rosenberry et al. 1999, Long et al. 2005). Previous studies have asserted that home-ranging and long-distance movement phases likely contribute to the complex geographic distribution of disease-positive animals (Grear et al. 2006, Blanchong et al. 2008, Kelly et al. 2010, Cullingham et al. 2011, Lang and Blanchong 2012).

Further challenging an understanding of disease dynamics are the complicated interactions between pathogens and the environment that may contribute to spatial variation in transmission rates, invasion success, and persistence patterns (Breban et al. 2009, Frick et al. 2017). The pathogenic agent of CWD, a prion, has been shown to vary in its infectivity and bioavailability according to the pH and isoelectric point of the soil substrate on which it is shed (Johnson et al. 2007, Dorak et al. 2017). Prions can adsorb to negatively charged particles, such as montmorillonite clay, potentially reducing the bioavailability of the pathogen and its transmission potential (Johnson et al. 2007, Dorak et al. 2017). Taken together, the interaction between deer, the prion, and their shared environment suggests that CWD outbreaks may be better understood and predicted by incorporating more ecological complexity into predictive disease models.

Despite increasing recognition that wildlife diseases, like CWD, are spreading by multiple co-occurring mechanisms that include a long-distance pathway, it has been difficult to observe multiple spread mechanisms and incorporate them into disease models (Filipe and Maule

2004, Russell et al. 2005). Documenting long-distance spread is challenging (Macdonald and Voigt 1985) because this type of spread is rare and occurs far removed from locations where disease is known to exist, one or a few diseased animals may quickly be removed by scavengers or predators (McCallum and Dobson 1995), or diseased individuals are often asymptomatic and hard to visually identify (Levinson et al. 2013). Furthermore, there are few modeling frameworks available that incorporate multiple mechanisms of spread (Altizer et al. 2011). Examples of past efforts to consider multiple mechanisms of spread include the addition of long-tailed contact kernels (Filipe and Maule 2004), or constant rates of global infection to classical diffusion processes (Russell et al. 2005). Neither approach has allowed for the evaluation of unique relationships between habitat conditions and distinct mechanisms of spread that are likely critical to understanding the emergence of wildlife disease.

In this paper, I sought to improve our understanding of factors that promote or impede disease spread and persistence in systems with multiple host movement patterns and unique pathogen responses to environmental conditions. I accounted for limitations in imperfect disease detection that are inherent to wildlife disease surveys. I selected CWD as a model system and evaluated whether a model that included localized spread mechanisms, long-distance spread mechanisms, and prion persistence in the environment would improve model accuracy compared to a model that combined multiple spread and persistence mechanisms into a single linear relationship.

## METHODS

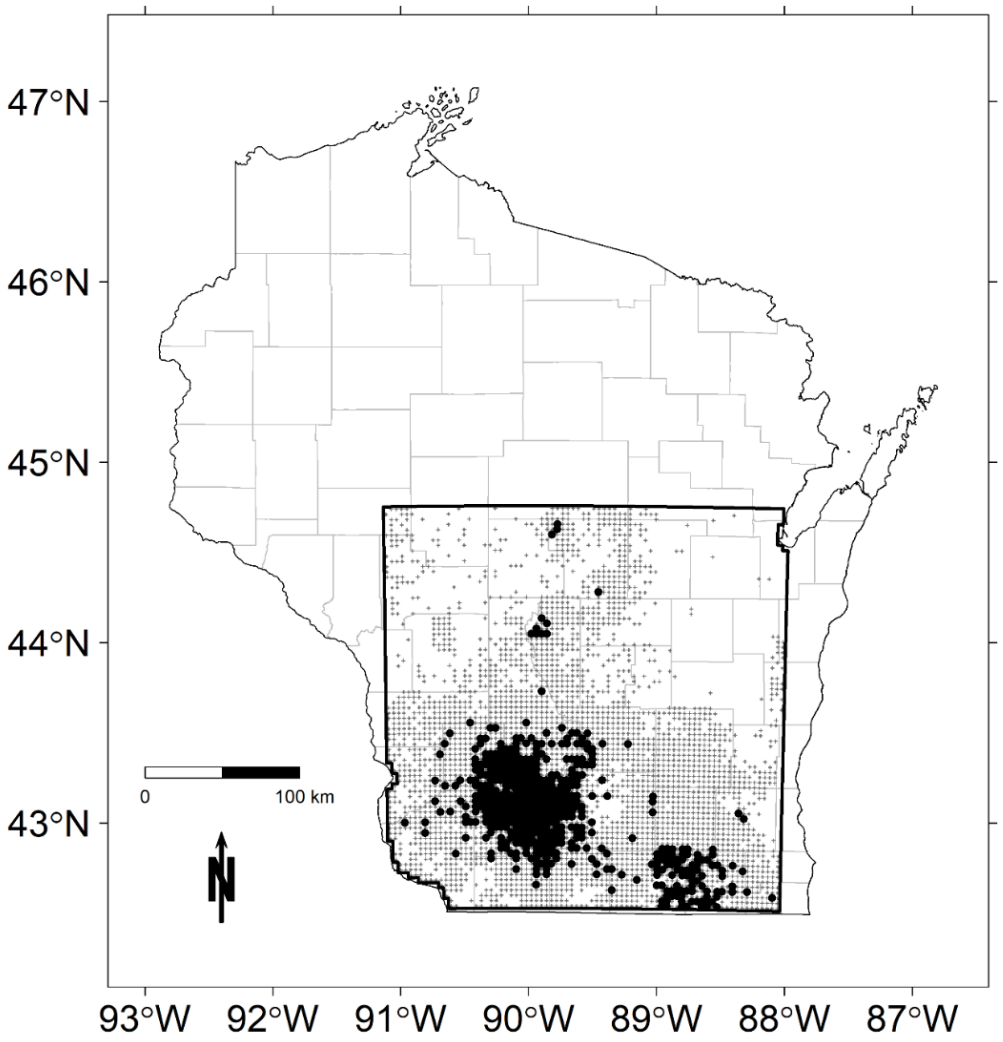
### *General Approach*

To develop a single, unifying statistical framework that considered disease detection and the ecology of white-tailed deer and CWD, I used dynamic occupancy modelling (DOM).

Dynamic occupancy models are a class of occupancy models that are often employed to predict species occurrence patterns, including colonization and extinction patterns. I chose DOMs because of several attributes of these models: 1) they can incorporate mixing functions that partition disease monitoring data into distinct ecological mechanisms (MacKenzie et al. 2003, Broms et al. 2016); 2) they can account for correlated error structures present in spatiotemporal data; and, 3) they can account for imperfect detection that is inherent to disease surveillance data and that may bias parameter estimation (Mosher et al. 2016).

To fit my DOM, I used CWD monitoring records from hunter-harvested white-tailed deer (*Odocoileus virginianus*) in Wisconsin, U.S. from 2002 – 2016 (Figure 4.1). Individual records included location (quarter-section; Public Land Survey System [PLSS]), method of collection, disease status, and sex and age of the sampled animal. I aggregated these data to a resolution of 10.4 $km^2$ (2 × 2 PLSS section) to ensure sufficient sampling across sampling units and to improve disease detection estimates. I evaluated covariate effects of landscape composition, presence of large rivers, and soil substrate data. Landscape data for each sampling unit (e.g., proportion forest, development, and agriculture) was acquired from the 2011 National Land Cover Database, presence of large rivers was defined as waterways of stream order ≥ 7 from Wisconsin Department of Natural Resources flowline data, and soil substrate was included as a weighted mean of proportion clay content at 5-cm depth at a resolution of 10 m. These data were acquired from the United States Department of Agriculture Natural Resource Conservation Service Soil Data Viewer interfaced with ArcMap version 10.6 (US Department of Agriculture Natural Resource Conservation Service 2009).

Figure 4.1 Chronic wasting disease (CWD) surveillance records in Wisconsin, U.S. from 2002 – 2016. Gray symbols indicate locations with no detected disease, whereas black symbols indicate locations where CWD has been detected. In total, there were 92,333 samples with 935 positives in the study area (black outline; total area: $6.12 \times 10^7$ km). Data source: Wisconsin Department of Natural Resources.



To evaluate whether a multi-mechanism DOM that incorporated disease persistence, localized spread, and long-distance spread improved model accuracy, I compared my model output to a model that only incorporated a single disease spread mechanism (i.e., logistic regression with a single linear state process equation). Both the multi- and single-mechanism DOM models were hierarchical and included: a common model parameterization to account for imperfect disease detection [*observation process*]; a common model parameterization to quantify spatial dependence in the first year of disease observation [*state process*]; and two unique model parameterizations (i.e., single and multi-mechanism parameterizations) that were used to predict and forecast CWD dynamics in subsequent years.

*Disease Detection [Observation Process]*

I estimated the probability of disease detection by subsetting the complete monitoring record to include only the first 2 days of deer firearm season in each year of the 15-year time periods (n = 50,783, positives = 678). I chose the first two days of firearm season for repeated observations to limit changes in disease state during a time when closure is assumed. I used each successive day to represent a separate observation at each sampling unit and observation period, $y_{i,j,k}$. True CWD occurrence, $z_{i,k}$, was estimated by a detection probability [observation process], $p_{i,j,k,}$ at each 10.4 km$^2$ sampling unit, $i$ $(i = 1,\ldots,5913)$, during years, $k$ $(k = 2002,\ldots,2015)$, and observation periods, $j$ $(j = 1,2)$ using,

$$logit(p_{i,j,k}) = \alpha_{det} + \beta Weight_{i,j,k} + \beta Prevalence_{k},$$

$$y_{i,j,k} \sim Bernoulli(z_{i,k} \mid p_{i,j,k}).$$

Weighted surveillance points, $Weight_{i,i,k}$, were quantified for each sampling unit, observation period, and year, using sex- and age-specific hazard values from Jennelle et al. (2018). The use of weighted surveillance points to represent sampling effort allowed us to consider the quality

and quantity of collected samples according to infection risk. In general, point values increased with age and are higher in males than in females (Jennelle et al. 2018). I included annual apparent prevalence, $Prevalence_k$, as a predictive covariate, calculated as the number of diseased animals divided by the number of animals tested in each respective year across the entire study area.

*Disease Occupancy [State Process]*

**First Year Disease Occupancy, Year 2002**

Observation year 2002 was modeled the same for both parameterizations by using a restricted spatial regression model (RSR; Johnson et al. 2013). Upon first detection of CWD in year 2002, there was already a large focus of disease present in the sampling area. Thus, the probability of disease occurrence in year 2002, $\psi_{(i,k=2002)}$, was modeled as a function of sampling unit covariates, and a spatial random effect that accounted for dependency in non-random spatial observations (Broms et al. 2016):

$$logit(\psi_{(i,k=2002)}) = \alpha + Ke,$$

$$e \sim Normal(0, \sigma^2 (K'QK)^{(-1)}),$$

where, K was a Moran operator matrix and Q was a precision matrix resulting from an intrinsic conditional autoregressive (ICAR) model (Johnson et al. 2013). The Moran operator matrix captured the positive spatial dependence that resulted from clustering, while the ICAR matrix modeled first-order positive spatial dependence in residuals with values of -1 for neighboring sampling units, and 0 for non-neighbors. To improve computational efficiency, I included only the first 250 eigenvectors of ICAR matrix based on Broms et al. (2016). Thus, the combination of *Ke* is an autocovariate that considered occupancy status of neighboring sampling units to

provide a spatial estimate of the existing clustered distribution of positives in the first year of observation (Broms et al. 2016).

**Multi-mechanism Disease Occupancy, Years 2003 – 2015**

For the multi-mechanism DOM, the probability of disease occurrence, $\psi_{i,k+1}$ , was estimated using a mixing function that explicitly incorporated 3 ecologically distinct CWD occurrence mechanisms: disease persistence, localized spread, and long-distance spread. The parameterization was:

$$\psi_{i,k+1} = z_{i,k}\,\varphi_{i,k} + (1 - z_{i,k})I_{Ni,k}\,\gamma_{i,k} + (1 - z_{i,k})(1 - I_{Ni,k})\delta_{i,k},$$

$$logit(\varphi_{i,k}) = \alpha_{\varphi,0} + \beta_{\varphi}\,X_{(i,k)},$$

$$logit(\gamma_{i,k}) = \alpha_{\gamma,0} + \beta_{\gamma}\,X_{(i,k)},$$

$$logit(\delta_{i,k}) = \alpha_{\delta,0} + \beta_{\delta}\,X_{(i,k)},$$

$$z_{i,k+1} \sim Bernoulli(\psi_{i,k+1}),$$

where $z_{i,k}$, was the true occupancy state of the preceding sampling year, $\varphi_{i,k}$ was probability of disease persistence, $\gamma_{i,k}$ was probability of localized disease spread mediated by the indicator variable $I_{Ni,k}$ (if $I_N = 1$, then disease was detected in an adjacent cell, and $\gamma$ is estimated), and $\delta_{i,k}$ was the probability of long-distance spread ($I_N = 0$). The effects of landscape covariates and distance from any prior positives regardless of year detected were tested for long-distance spread; whereas, the impact of landscape covariates and number of infected adjacent cells were evaluated for localized spread. The number of adjacent CWD positive neighbors ranged from 0 – 8 according to a queen's configuration. Lastly, I evaluated the proportion of clay for potential effect on the persistence of CWD once present in a sampling unit. All landscape covariates and

distance measures, except for the categorical variable for the number of neighbors, were standardized to a mean of 0 and standard deviation of 1.

**Single-mechanism Disease Occupancy, Years 2003 – 2015**

For the single mechanism DOM, the probability of disease occurrence, $\psi_{i,k+1}$ , was parameterized using a logistic regression equation without a mixing function:

$$logit(\psi_{i,k+1}) = \alpha_{\psi,0} + \beta_{\psi} X_{(i,k)},$$

$$z_{i,k+1} \sim Bernoulli(\psi_{i,k+1}),$$

where $X_{(i,k)}$, was the same set of covariates used in the multi-mechanism DOM parameterization, and where $z_{i,k}$, was the true occupancy state of the preceding sampling year.

*Covariate Selection*

I selected predictive relationships by first running a global multi-mechanism model including all covariates evaluated and then removing those whose 95% Bayesian Credible Interval (CRI) overlapped zero. Each candidate model was fit using 40,000 iterations, a thin rate of 15, and 20,000-iteration burn-in. Successful convergence occurred when Rhat values were < 1.1. All statistical analyses were performed using programs jagsUI version: 1.5.0 and R version: 3.6.1 (Plummer 2003, R Core Team 2019).

*Model Performance Evaluation*

To assess whether the multi-mechanism model was more accurate than a single spread mechanism model, I used the posterior mean of the probability of disease occurrence and out-of-sample data to compare the 2 candidate models using Bernoulli deviance (i.e., $\sum_{i=1}^{I}(y_i \log(\psi_i) + (1 - y_i) \log(1 - \psi_i))$, where, $y_i$ , is the observed disease occurrence and $\psi_i$, is the estimated occurrence probability at sites, *i*, across all years (Hefley et al. 2017). For my application, the model with a lower Bernoulli deviance score was deemed more accurate as it symbolized a

greater level of agreement between probability of occurrence estimates and the true occupancy state of a sampling unit. I used all monitoring records (n = 41,550, positives = 257) that fell outside of my observation period defined by the first 2 days of firearm season to evaluate model performance. Prediction accuracy considered out-of-sample data collected on any day outside of the observation period during years 2002 – 2015. Forecasting accuracy was assessed using the complete record of data, regardless of whether it occurred during the first two days of firearm season, from year 2016. I summarized accuracy assessments using 3 primary measures: the overall Bernoulli deviance scores for both forecasting and prediction using both detection and non-detection sites, Bernoulli deviance scores for each mechanism of disease spread and persistence (i.e., localized spread, long-distance spread, and persistence) at sampling units where disease was detected, and Bernoulli deviance scores by mechanism at sampling units where disease was not detected.

## RESULTS

### *Disease Detection and First Year of Disease Occurrence*

For the multi-mechanism DOM (Fig. C.1), I found that the overall probability of detection for disease occurrence ranged from 0.11 (95% CRI: 0.08 – 0.17) in 2002 to 0.37 (95% CRI: 0.30 – 0.47) in 2015. The detection probability had an intercept of -1.53 (95% CRI: -1.72 – -1.34) and was positively correlated with weighted surveillance points (Posterior mean: 0.21, 95% CRI: 0.17 – 0.25; Fig. 4.2A and Fig. C.2) and apparent disease prevalence (Posterior mean: 0.50, 95% CRI: 0.37 – 0.64; Fig. 4.2B and Fig. C.2). For the single mechanism DOM, the overall probability of detection for disease occurrence was similar, ranging from 0.12 (95% CRI: 0.08 – 0.18) in 2002 to 0.39 (95% CRI: 0.32 – 0.49) in 2015 with similar intercept (-1.50, 95% CRI: -1.69 – -1.31), positive correlations with apparent prevalence (0.51, 95% CRI: 0.37 – 0.64), and

weighted surveillance points (0.21; 95% CRI: 0.18 – 0.25). For the occurrence probabilities in the first year of observation (2002) I modeled both the multi-mechanism and single mechanism DOMs as an intercept-only RSR equation.

Figure 4.2 Panels A – F Effects plots for the multi-mechanism model parameterization. Panels A and B are detection covariate relationships. Panel C is the relationship between disease persistence and proportion clay content of soil. Panel D is the relationship between localized disease spread and the number of CWD-affected neighbors. Panels E – F are the relationships between long-distance spread, proportion agriculture, and distance from prior positives.

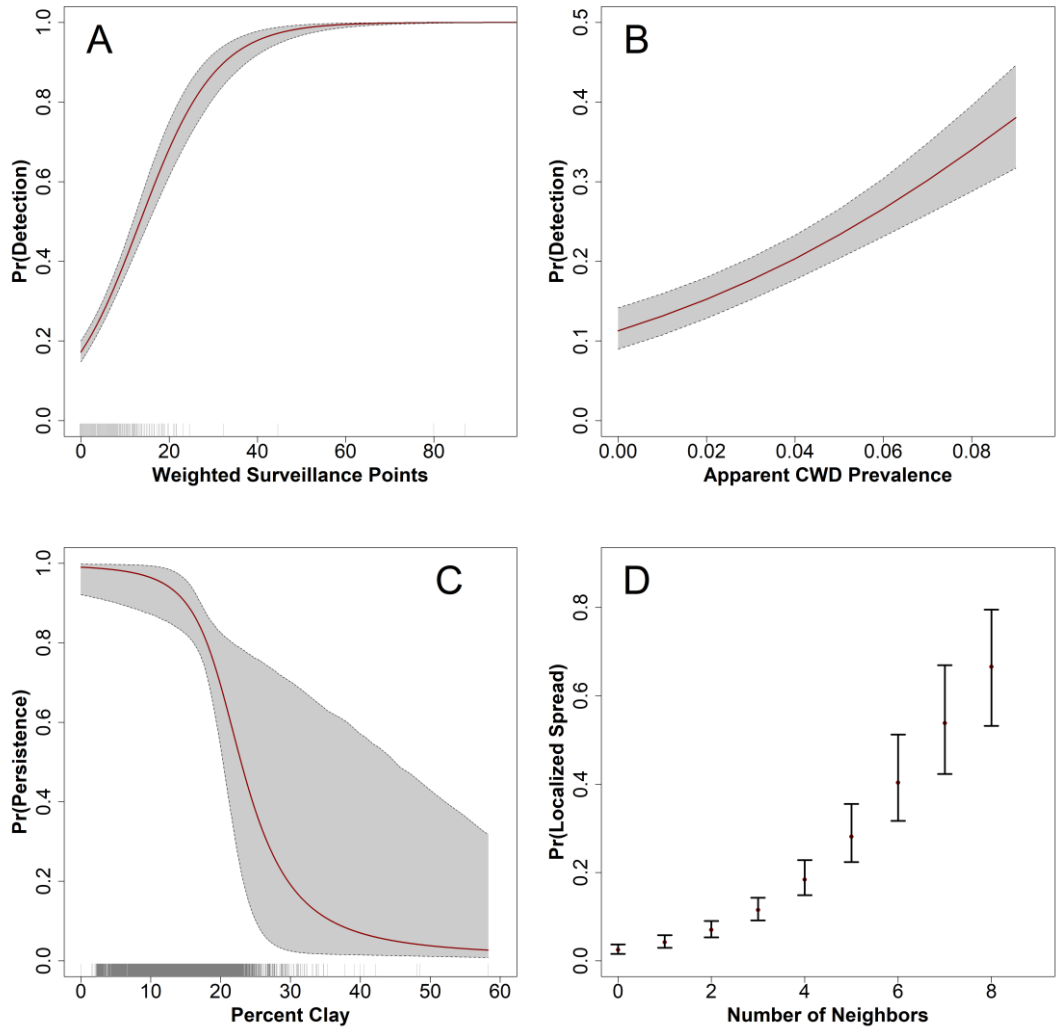
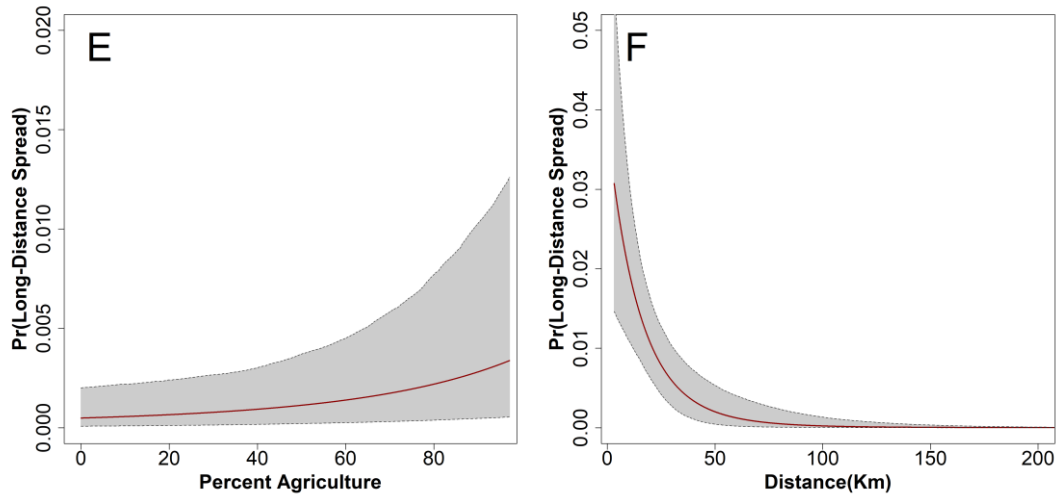


Figure 4.2 (cont'd)




*Multi-mechanism DOM*

In years 2003 to 2015, the multi-mechanism DOM estimated large differences in the probabilities for each of the 3 CWD occurrence mechanisms, supporting their separate inclusion in my modeling framework. I found that the mean annual probability of CWD persistence was 0.84 (95% CRI: 0.33 – 0.99), probability of localized spread was 0.04 (95% CRI: 0.02 – 0.23), and probability of long-distance spread was 0.008 (95% CRI: $1\times10^{-7}$ – 0.04). Furthermore, each mechanism was best explained by its own set of unique covariate relationships. My selection criteria resulted in the elimination of proportion human development (95% CRI: -3.2 – 0.36), agriculture (95% CRI: -0.02 – 0.94), and deciduous forest cover (95% CRI: -0.07 – 0.46) as drivers of localized spread, and proportion human development (95% CRI: -4.31 – 0.93) and distance to large rivers (95% CRI: -0.36 – 0.73) for long-distance spread. I removed the proportion of deciduous forest cover from the long-distance spread regression because it was correlated with proportion of agriculture (Pearson's coefficient: -0.59) and had a weaker predictive relationship (mean posterior estimate for forest: 0.84 [95% CRI: 0.05 – 1.87]; mean posterior estimate for agriculture: 1.22 [95% CRI: 0.14 – 2.59]). I retained covariates for the

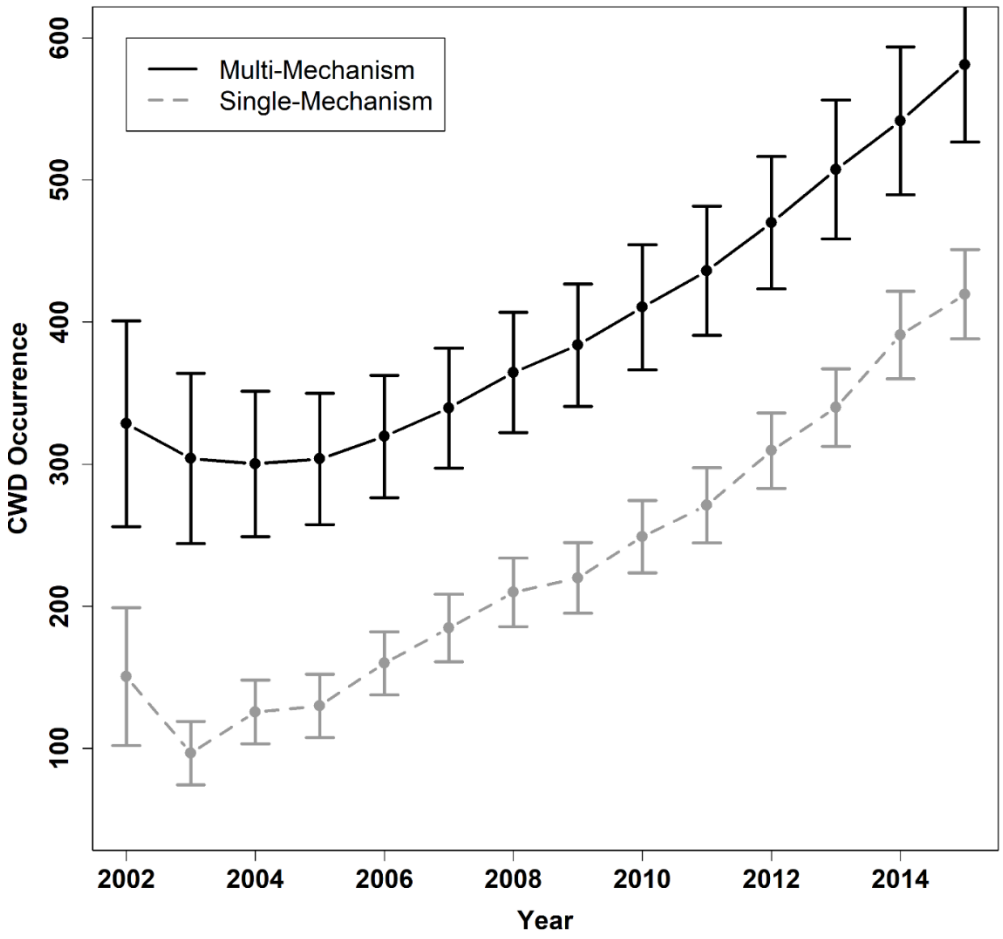
number of affected adjacent sampling units for localized spread, proportion deciduous forest and distance to prior positives for long-distance spread, and proportion clay content for persistence of disease in a location of previous detection.

The sub-model for disease persistence had a positive intercept (2.41; 95% CRI: 1.55 – 3.46) and a negative correlation with proportion clay content in the soil (-1.74; 95% CRI: -3.25 – -0.33; Fig. 4.2C and Fig. C.2). For localized CWD occurrence, I estimated an intercept of -3.70 (95% CRI: -4.22 – -3.21), and a positive correlation with the number of affected adjacent sampling units (0.55; 95% CRI: 0.43 – 0.68; Fig. 4.2D and Fig. C.2). Finally, long-distance spread had a large negative intercept (-7.11; 95% CRI: -8.99 – -5.54), a positive correlation with agriculture (0.54; 95% CRI: -0.07 – 1.17; Fig. 4.2F and Fig. C.2) , and a negative correlation with distance to prior positives (-2.98; 95% CRI: -4.95 – -1.33; Fig. 4.2G and Fig. C.2).

*Single mechanism DOM*

In years 2003 to 2015, the single mechanism DOM estimated a negative intercept (-4.02; 95% CRI: -4.95 – -3.27) and a positive correlation with number of affected neighbors (0.63; CRI: 0.55 – 0.71) and agriculture (0.09; 95% CRI: -0.18 – 0.38), and negatively correlated with soil clay content (-0.26; 95% CRI: -0.60 – -0.09) and distance to prior positives (-0.96; 95% CRI: -1.83 – -0.22). Thus, I found general agreement in the direction of covariate estimates (i.e., positive or negative correlation) with some variation in the magnitude of effect size. The major discrepancies between covariate effects were in estimates associated the distance from prior positives. Lastly, the multi-mechanism DOM consistently estimated that CWD occurred at more sampling units across a larger area (Fig. 4.3).

Figure 4.3 Number of sampling units predicted to be occupied by CWD using the single and multi-mechanism DOMs from 2002 – 2015. The single mechanism model consistently estimated a lower number of occupied sites when compared against the multi-mechanism parameterization.




*Model Performance Evaluation*

I found that the single mechanism model was better at overall prediction across all sampling units in the study area (Bernoulli Deviance: 6588.96 versus 7082.10, respectively; Table 4.1) but, this finding was driven by the lower probability of occurrence estimated at sampling units where CWD was not detected (Table 4.1; Fig. 4.4B). When I evaluated the ability of my models to predict the locations where CWD did occur, I found that the multi-mechanism model was more accurate (Table 4.1; Fig. 4.4A).

I found no improvement in model accuracy for the multi-mechanism model at locations of CWD persistence (1641.02, 1561.36, respectively); however, there were marked accuracy improvements for localized spread (370.96, 462.46, respectively; Fig. 4.4D), and long-distance spread predictions (139.99, 179.98, respectively; Fig. 4C). In particular, I found that the multi-mechanism model accurately predicted an elevated probability of occurrence at 25% of sampling units where long-distance spread occurred (Fig. 4.4C). In contrast, the single mechanism model showed no apparent predictive capacity at any of these sampling units (Fig. 4.4C, Fig. 4.5C and Fig. 4.5D). Lastly, the multi-mechanism model was better at forecasting future patterns of disease occurrence across the entire out-of-sample dataset including locations of CWD detection (Table 4.1, Fig. 4.5E and Fig. 4.5F).

Table 4.1 Results of Bernoulli deviance accuracy assessments for the mixing and nonmixing model that were fit using a subset of the surveillance record in Wisconsin from 2002 – 2015. Prediction accuracy was estimated using 45% of the total CWD surveillance dataset that fell outside of the first two days of firearm season during years 2002 – 2015. Forecasting accuracy was estimated using the complete surveillance record from 2016. Lower scores indicate a model with a superior accuracy (in italics).

| Model Structure | All Data | Detection Sites | Non-Detection Sites | Persistence | Localized Spread | Long-Distance Spread |
|---|---|---|---|---|---|---|
| | | | Prediction | | | |
| Multi-Mechanism DOM | 7082.10 | 2007.71 | 5074.39 | 1641.02 | *370.96* | *139.99* |
| Single-Mechanism DOM | *6588.96* | *1983.57* | *4605.39* | *1561.36* | 462.46 | 179.98 |
| | | | Forecasting | | | |
| Multi-Mechanism DOM | *769.81* | *156.93* | 612.87 | *156.93* | - | - |
| Single-Mechanism DOM | 860.10 | 565.83 | *294.27* | 565.83 | - | - |

Figure 4.4 Panels A – D Accumulation curves for disease observations against the estimated probability of disease for both the mixing and nonmixing model parameterizations. Panel A includes all out-of-sample prediction data (i.e., detection and non-detection sampling units, years 2002-2015). Panel B includes all predictions from sampling units where CWD was not detected. Panel C includes all predictions at sampling units where long-distance spread was detected. The gray panel indicates the marked improvement of the mixing model to predict locations where long-distance spread of CWD occurs. Panel D includes all predictions at sampling units where localized spread was detected. Dotted line indicates an idealized model with perfect accuracy for comparison.

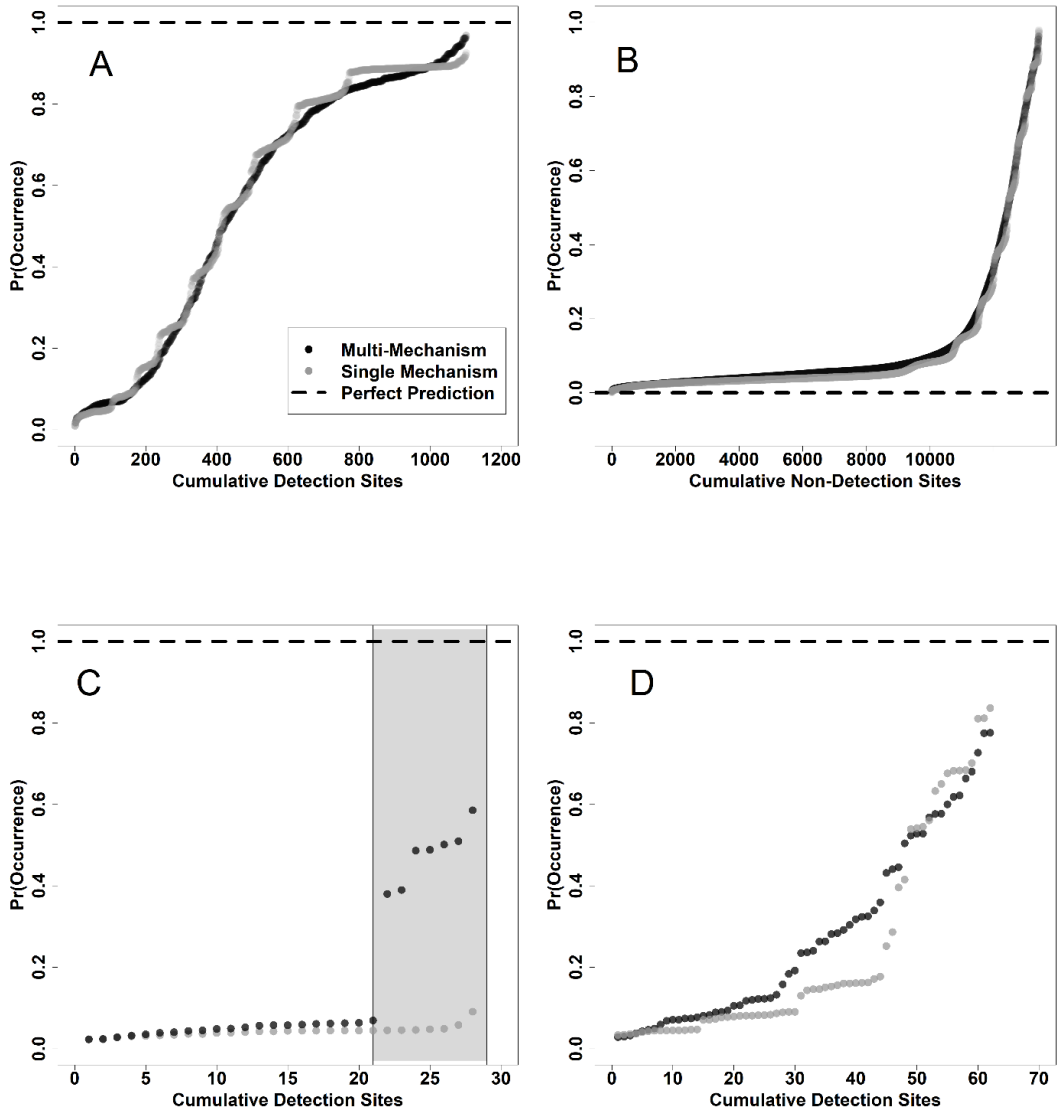


Figure 4.5 Panels A – F Panel A is the predicted probability of disease occurrence in surveillance year 2015 for the multi-mechanism model. Panel B is the predicted probability of disease occurrence in surveillance year 2015 for the single mechanism model. Panels C and D are the data observations from surveillance years 2002 – 2015 used to predict the multi-mechanism (Panel C) and single mechanism (Panel D) probability surfaces. Panels E and F are the locations of CWD detection in surveillance year 2016. The forecast for the single mechanism (Panel F) model underestimates the locations of CWD detection compared to the multi-mechanism model (Panel E).

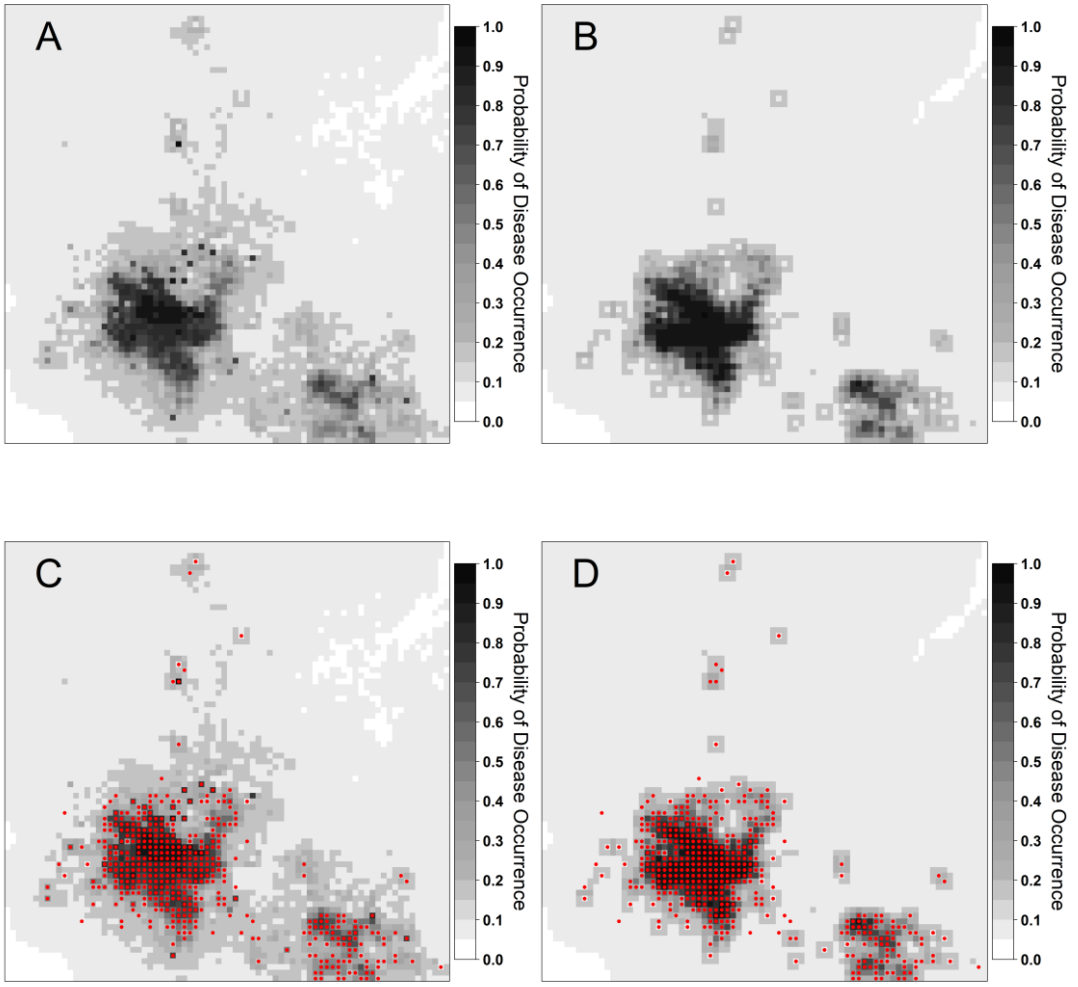
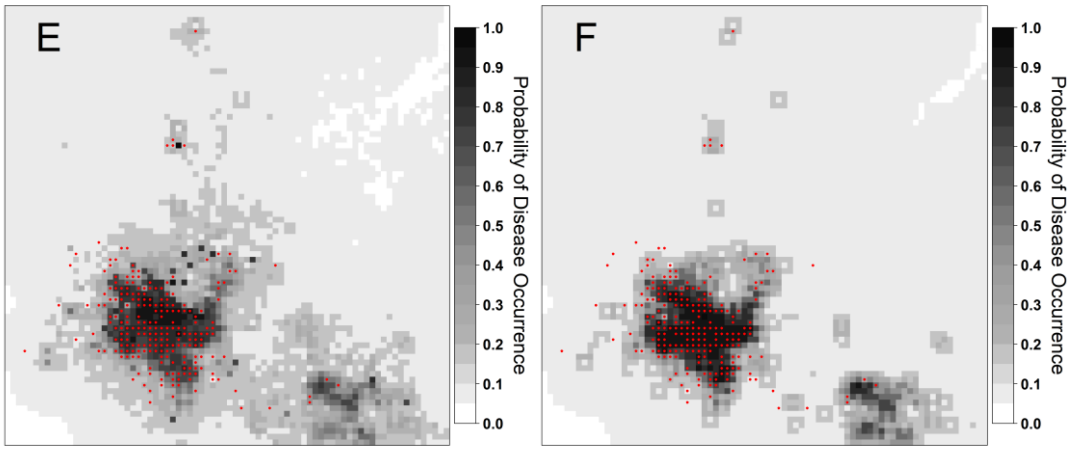


Figure 4.5 (cont'd)




**DISCUSSION**

I developed a unifying statistical model that more accurately described the occurrence of CWD by accounting for imperfect detection and by incorporating more of the complicated disease ecology of host and pathogen. I showed that disease occurrence was best estimated by partitioning disease observation data into multiple co-occurring mechanisms hypothesized to drive the localized spread, long-distance spread, and persistence of CWD. Of interest was the ability of my multi-mechanism DOM to improve model forecasts and to predict long-distance spread of disease. I evaluated the effect of weighted surveillance effort and apparent prevalence on disease detection and found that my approach was able to estimate disease occurrence using only a subset of the available monitoring data. The relationships between disease detection, effort, and apparent prevalence are valuable to informing the efficient use of resources to conduct ongoing disease monitoring efforts across both space and time. Thus, my multi-mechanism framework with detection estimates offers advantages over single-mechanism models that will improve our understanding of the interactions that drive wildlife disease occurrence patterns.

The emergence of wildlife diseases, such as CWD, can occur in locations far removed from prior positives, challenging an ability to detect and predict new cases. My multi-mechanism DOM quantitatively isolated long-distance disease spread and predicted an elevated probability of occurrence at 25% of the locations where long-distance spread was detected. The relationship between the probability of long-distance spread and distance from prior positives suggested that transient movements of white-tailed deer may be a contributing factor (Lang and Blanchong 2012). The probabilistic distance decay function generally matched reported distances of deer dispersal in agro-forested landscapes of the upper Midwest providing supporting evidence that dispersals may be partially responsible for the spread of CWD (Fig. 4.5F). Fifty-nine percent of probabilities of long-distance spread from this study fell within the mean dispersal distances of white-tailed deer (19km) reported in Nixon et al. (1994), and 85% fell within the maximum distance (38 km).

I found positive relationships between the probability of long-distance spread and the proportion of agriculture, a factor known to affect space use patterns of white-tailed deer (Etter et al. 2002, VerCauteren and Hygnstrom 2012). These findings agreed with Nobert et al. (2016) which documented a positive association between CWD risk for individual deer and an increasing proportion of agriculture. One hypothesized mechanism for this positive association is the increase in deer density that occurs in suitable habitats that are interspersed between areas of high agriculture (Compton et al. 1988). Increased density leads to increased rates of direct contact amongst individuals (Kjaer et al. 2008, Silbernagel et al. 2011) and a potential for increased environmental contamination (Saunders et al. 2012). As a result, I hypothesize that tracts of interspersed forest in agriculturally dominated areas within the known dispersal range of white-tailed deer may be at an elevated risk of CWD emergence.

My framework considered the relative contribution of environmental pathogen persistence to disease occurrence, a dynamic that is not well understood and infrequently considered in disease models (Lange et al. 2016). Using my multi-mechanism DOM, I found that CWD persistence was negatively correlated with proportion clay content in the soil, a relationship previously identified in northern Illinois (Dorak et al. 2017), but has been challenged in other studies on prion dynamics (Johnson et al. 2007). However, the consistency in findings from this study in Wisconsin and Dorak et al. (2017) in northern Illinois suggests that the proportion of clay in soils may help explain broad patterns in the persistence of CWD. While a detailed discussion on the interactions between soil substrate and CWD prion are beyond the scope of this paper, further examination is warranted. I suggest that modeling frameworks, like mine, may be particularly useful because they can jointly consider disease spread and persistence dynamics and thereby control for spatial confounding that can occur when locations of elevated deer space use and clay content in soils coincide.

While many studies properly account for the bias that imperfect detection introduces into state process estimates (Mosher et al. 2019), detection probability is often treated as a nuisance parameter (Furnas and McGrann 2018). I considered detection probability and relationships with sampling effort and apparent prevalence as informative to future management activities. In particular, the relationship between disease detection and weighted surveillance effort can be useful to inform sample optimization across both space and time. The repeated sampling design that required data from only the first two days of firearm season can lead to substantial reductions in the effort required to produce spatially accurate representation of disease occurrence risk. Thus, my approach is useful to guide future sampling allocations to locations

conditional on empirical disease condition estimates, the magnitude of prior sampling efforts, and can be used to target the most productive sampling periods.

My study highlights an apparent discrepancy between the proper modelling framework as determined by overall Bernoulli Deviance scores, and one that produces results that best align with a model's capacity to promote system understanding. Using Bernoulli Deviance scores, I found that the single mechanism model was most accurate for all sampling unit conditions (i.e., detection and non-detection locations), but that the multi-mechanism model was more accurate for predicting and forecasting locations where CWD spread actually occurred. For wildlife diseases that are heavily managed and typically underestimated in extent (Walsh 2012, Miller and Fischer 2016), the prioritization of modeled results that best predict the locations of occurrence will lead to substantial improvements in mitigation efforts. Furthermore, the partitioning of mechanisms represents an improvement in our ability to disentangle the complicated dynamics that exist when pathogens and hosts interact in a shared environment. In my application, the improved understanding of individual dynamics may be particularly important for long-distance spread of disease because of the potential for disease establishment in locations distant from prior positives.

More generally, my findings support empirical and theoretical studies that found that simple diffusion models are inadequate to predict wildlife disease spread (Hastings et al. 2005, Blanchong et al. 2008). Many diseases, especially those that affect migratory species, spread in complex ways and present major challenges to detection and management. For example, saiga antelope (*Saiga tatarica*) transmit trichostrongyloid nematodes to livestock during seasonal migrations of up to 1200 km across Central Asia (Bekenov et al. 1998, Morgan et al. 2007, Altizer et al. 2011), elk transmit brucellosis at communal feedlots during seasonal migrations

(Cross et al. 2010, Schumaker et al. 2012), and *Charadriiform* birds appear to move avian influenza virus along their seasonal migration corridor between South America and Canada (Krauss et al. 2010). Furthermore, many pathogens, including viruses, bacteria, parasites, and prions, can survive or remain infectious when disassociated from hosts depending on the suitability of the ambient environment (Lange et al. 2016). My model provides an approach to quantitatively isolate, and subsequently integrate, relationships that affect hosts and pathogens, ultimately improving our understanding of these complex disease systems.

# CHAPTER 5: CONCLUSIONS, MANAGEMENT IMPLICATIONS, AND FUTURE DIRECTIONS

In chapter 1, I argued for the importance of developing decision-making tools that can guide CWD surveillance and monitoring design across an entire disease emergence spectrum. (Fig. 1.1). I sought to design studies that were linked to three decision-making Checkpoints and guided by distinct research questions as follows: Checkpoint 1 – What is the comprehensive pre-introduction risk of CWD based on a suite of locally relevant hazards?; Checkpoint 2 – Can an existing modeling framework be used to improve rapid estimates of disease extent when compared against current methods that rely on distance-based thresholds?; Checkpoint 3 – Can our understanding of the multiple drivers of disease spread and persistence be improved if more of the ecological complexity inherent to CWD and host behaviors are explicitly considered? and, relatedly, can the disease testing burden be reduced by implementing a statistical framework that requires less data than has been collected in many locations? In the following sections I discuss the answers to these questions and review the broader implications of my dissertation research to disease management endeavors.

Chapter 2 developed an analytical approach to estimate the comprehensive pre-introduction risk of CWD that relied on expert-elicitation and existing datasets. Expert-elicitation provided a defensible and low-cost approach to perform a risk-based CWD assessment despite partial observability and structural uncertainties that have challenged our understanding of the relationships between known, or presumed hazards, and CWD introduction risk (Williams et al. 1996). For my application to Michigan, I found spatial agreement between high-risk areas estimated by experts and the known locations of CWD occurrence from monitoring years 2015 to 2018. Further, the spatial agreement held even when hazards that were dependent on the

knowledge of CWD occurrence were excluded, adding further support for the accuracy of this approach prior to any knowledge of localized CWD occurrence patterns. As a result, chapter 2 provided a low-cost, rapid and accurate approach for performing comprehensive CWD risk assessments. Further, because my approach is largely customizable to different systems and available datasets, it has the potential to be a proactive decision-making tool that is useful across a diversity of wildlife disease systems.

In chapter 3, I sought to guide the immediate response to a new disease detection by combining knowledge gained studying endemic disease elsewhere with the localized conditions surrounding disease detections in a new location. Specifically, I evaluated whether management zones created using existing modeled results were more effective at incorporating future disease detections when compared against the current approach of using distance-based extent estimates. For my analytical approach, I relied on a combination of data sources including locations of current-year positive animals, historical surveillance records and projected model results from a disease endemic location within the same ecoregion. I found that disease extent estimates that were based on these model projections were larger compared to distance benchmarks ($9.91 \times 10^3$ $km^2$ versus $3.46 \times 10^3$ $km^2$, respectively), but were better at encompassing future disease detections. Furthermore, my projections provided an opportunity to improve the precision of rapid response efforts by producing spatially-explicit estimates of disease occurrence risk that were otherwise unavailable. Thus, my approach in chapter 3 addressed a fundamental need universal to wildlife disease managers – the need to accurately estimate affected areas early upon emergence, or detection of a disease in a new area (Langwig et al. 2015, Russell et al. 2017).

In chapter 4, I sought to incorporate more of the ecological complexity of white-tailed deer and CWD prions to improve the accuracy of spatial disease occurrence models. In addition,

I wanted to estimate factors that affected the efficient detection of disease so that monitoring efforts could use these findings to optimize future disease sampling across both space and time. I found that disease occurrence was best estimated by partitioning observation data into multiple co-occurring ecological mechanisms hypothesized to drive the localized spread, long-distance spread, and persistence of CWD. I found that each mechanism occurred with a different probability (0.04, 0.008, 0.84, respectively), and was best estimated by its own unique set of predictive covariates.

The probability of localized spread was best estimated using a categorical variable that accounted for the number of adjacent disease-affected sampling units. This finding indicated that on a localized scale, CWD dynamics may be best explained by diffusive spread that is independent of the surrounding landscape composition. For long-distance spread, I found that the probability of CWD occurrence was best estimated by a positive relationship with proportion agriculture, as well as a distance-decay relationship that matched the distances of documented dispersals across similar agro-forested landscapes. These findings indicated that tracts of interspersed forest in agriculturally dominated areas within the known dispersal range of CWD positive white-tailed deer may be at an elevated risk of CWD emergence. One of the particularly interesting findings was the ability of my multi-mechanism model to predict long-distance spread in ways that more simplistic models could not. Predictive capacity for these types of spread events may enable future disease management efforts to be targeted in locations that are far removed from current disease cases and, thus, potentially prevent new locations of disease establishment that can increase the rate of CWD spread.

For CWD persistence, I documented a negative relationship between soil clay content and the repeated annual detection of disease in the same sampling unit. This relationship

matched another study by Dorak et al. (2017) from Illinois and as a result provided broad geographic support for the role that clay soils may have in promoting repeated CWD occurrence. Taken together, the separate and combined effects of these distinct spread and persistence mechanisms may result in improved understanding of CWD dynamics that aids in the design of future management efforts.

Further contributing to CWD management in chapter 4 was the documented relationships between weighted surveillance effort, apparent prevalence and disease detection. These quantitative relationships are useful to inform ongoing disease sampling efforts and can help provide opportunities for spatial targeting of resources to the appropriate areas. Lastly, the multi-mechanism model was more accurate for forecasting disease occurrence patterns, and thus provides clear advantages over prior models that incorporate only a single quantitative mechanism of spread.

*Management Implications and Future Directions*

Chronic wasting disease prevention and management has been called the most "fiscally appropriate and forward thinking" strategy that managing agencies can adopt (Gillin and Mawdsley 2018). Since the discovery of CWD, research has been conducted that has examined the pathology (Williams and Young 1980), epidemiology (Miller and Wild 2004), individual risk of infection (Heisey et al. 2014), and impacts to population health (Edmunds et al. 2016) resulting from the disease. These findings have elucidated critical information on how the disease is transmitted and spread but have provided limited information that is directly relevant to the many time-sensitive management decisions that are considerate of the localized disease stage. I developed a series of decision-making tools that apply to each step of the CWD emergence spectrum and that allow managers to: appropriately identify locations at high risk of

disease exposure; mount and sustain strategic and long-term management efforts that maximize the likelihood of successful outcomes; and, finally, build public and stakeholder trust by implementing decision-making protocols that are objective and scientifically valid.

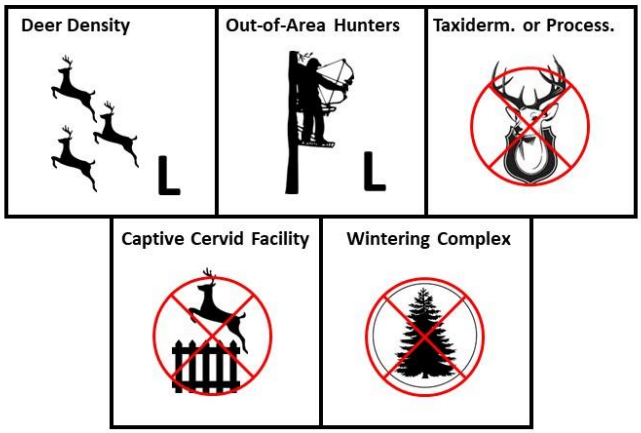
Whether or not managers choose to allocate limited existing resources to surveillance and monitoring efforts is ultimately a question of their collective risk tolerance. However, once a decision is made to proactively or reactively manage CWD, this dissertation provides valuable methodology to inform decision-making based on localized disease conditions. Furthermore, moving past the immediate decision on resource allocations, my analyses can guide targeted and effective interventions to areas at highest risk. Ultimately, without targeted and effective management interventions, CWD will continue to spread unabated and negatively impact cervid species, their ecosystems, and human stakeholders.

# APPENDICES

## APPENDIX A: SUPPLEMENTAL RESULTS FOR CHAPTER 2

Figure A.1 Complete questionnaire that was used for the expert-elicitation exercise. The questionnaire included 18 unique scenarios, a question that elicited direct hazard rankings, and a question that provided an opportunity for experts to justify their responses.

1. Imagine a township that has the following conditions:
    1. Low deer density
    2. Low number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

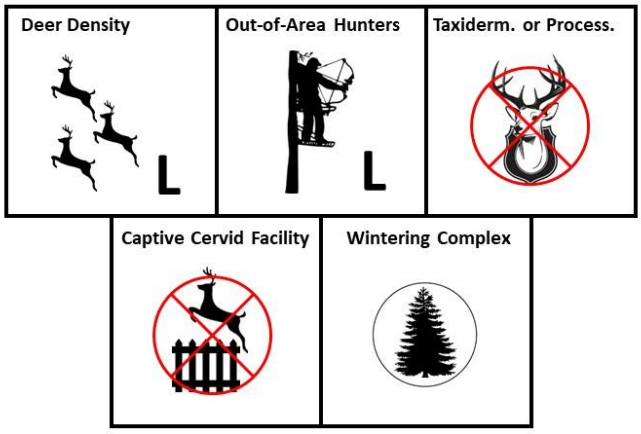
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

2. Imagine a township that has the following conditions:
    1. Low deer density
    2. Low number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. Has Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

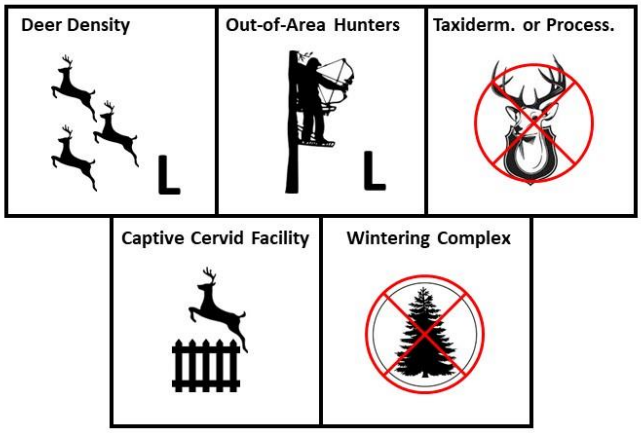
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

3. Imagine a township that has the following conditions:
    1. Low deer density
    2. Low number of out-of-area hunters
    3. No taxidermists and/or processors
    4. Has captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

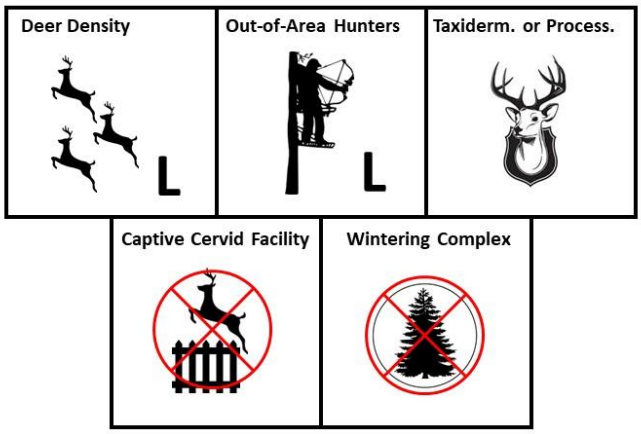
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

4. Imagine a township that has the following conditions:
    1. Low deer density
    2. Low number of out-of-area hunters
    3. Has taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

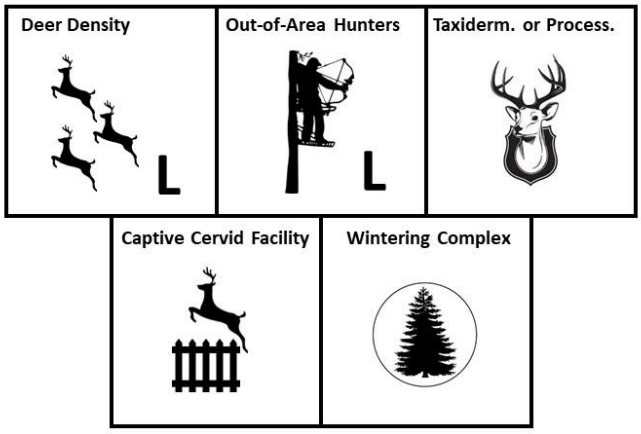
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

5. Imagine a township that has the following conditions:
    1. Low deer density
    2. Low number of out-of-area hunters
    3. Has taxidermists and/or processors
    4. Has captive cervid facilities
    5. Has Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

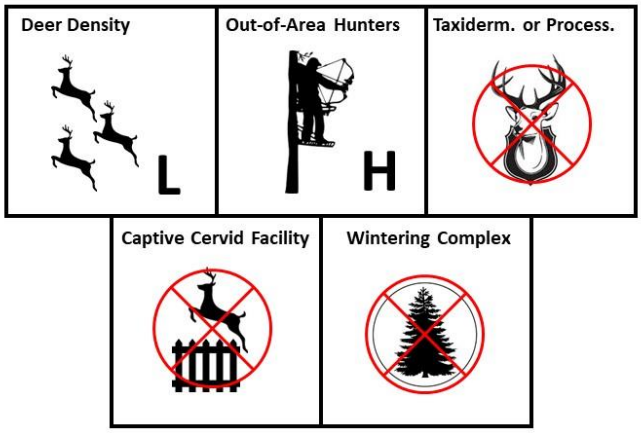
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

6. Imagine a township that has the following conditions:
    1. Low deer density
    2. High number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

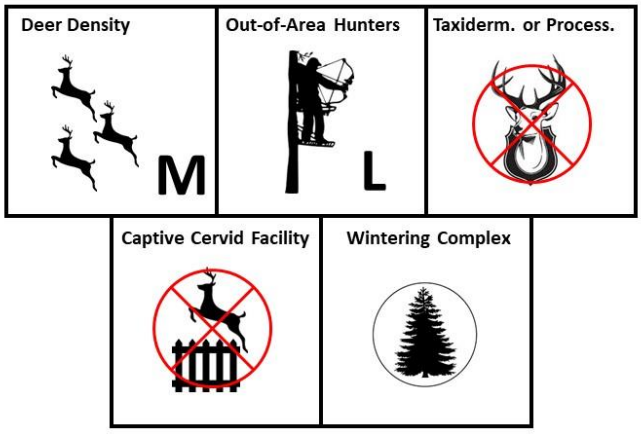
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

8. Imagine a township that has the following conditions:
   1. Medium deer density
   2. Low number of out-of-area hunters
   3. No taxidermists and/or processors
   4. No captive cervid facilities
   5. Has Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

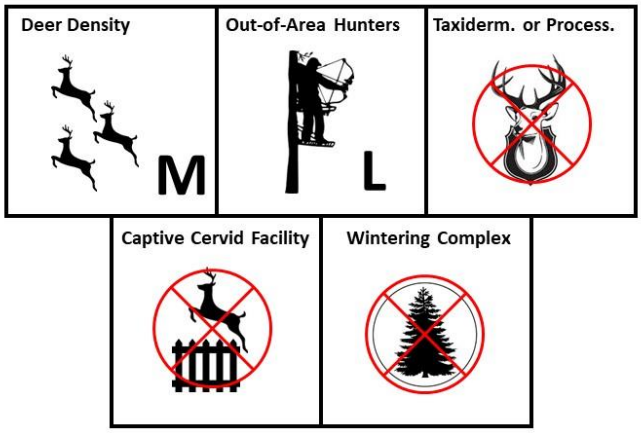
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

7. Imagine a township that has the following conditions:
   1. Medium deer density
   2. Low number of out-of-area hunters
   3. No taxidermists and/or processors
   4. No captive cervid facilities
   5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

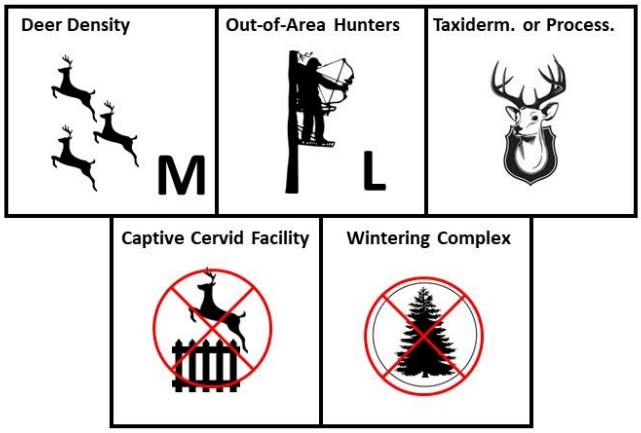
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

9. Imagine a township that has the following conditions:
   1. Medium deer density
   2. Low number of out-of-area hunters
   3. Has taxidermists and/or processors
   4. No captive cervid facilities
   5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

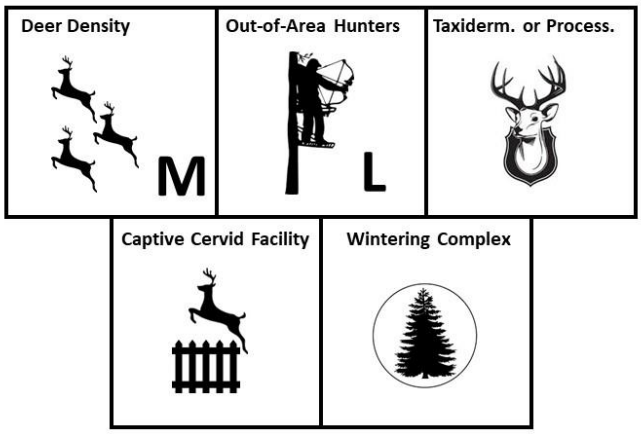
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

10. Imagine a township that has the following conditions:
    1. Medium deer density
    2. Low number of out-of-area hunters
    3. Has taxidermists and/or processors
    4. Has captive cervid facilities
    5. Has Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

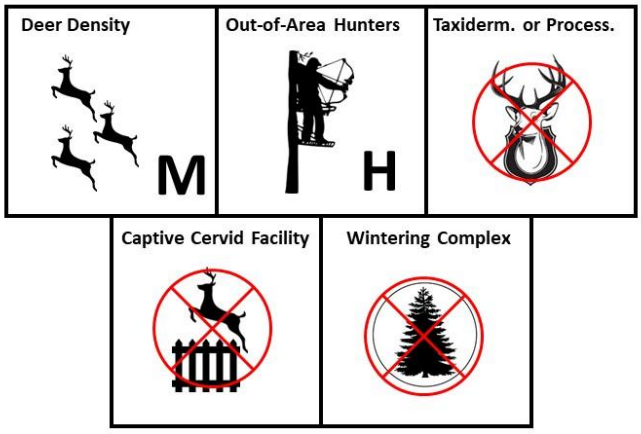
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

11. Imagine a township that has the following conditions:
    1. Medium deer density
    2. High number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

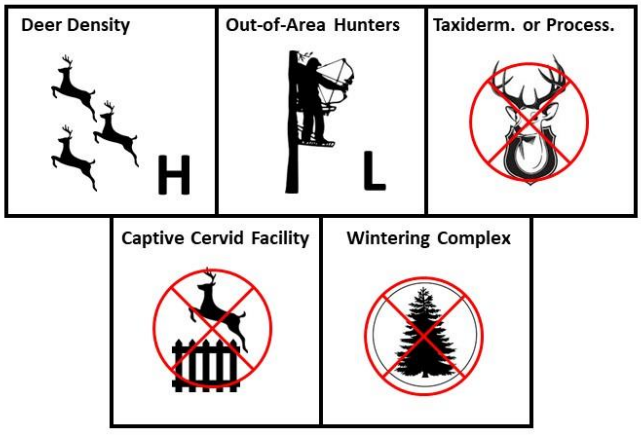
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

12. Imagine a township that has the following conditions:
    1. High deer density
    2. Low number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

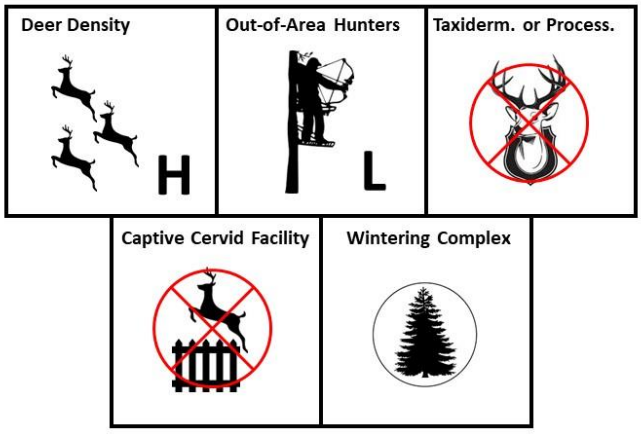
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

13. Imagine a township that has the following conditions:
    1. High deer density
    2. Low number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. Yes Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

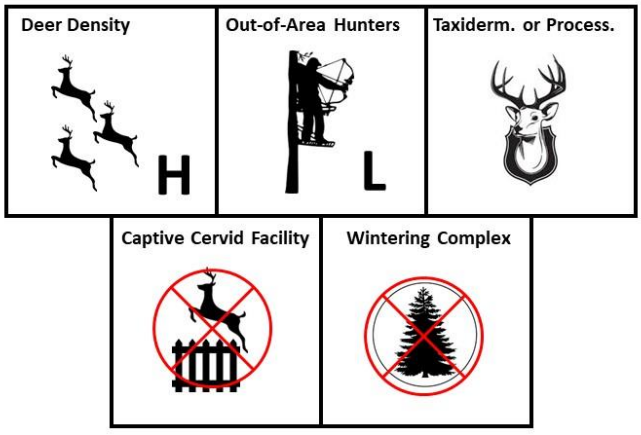
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

14. Imagine a township that has the following conditions:
    1. High deer density
    2. Low number of out-of-area hunters
    3. Has taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

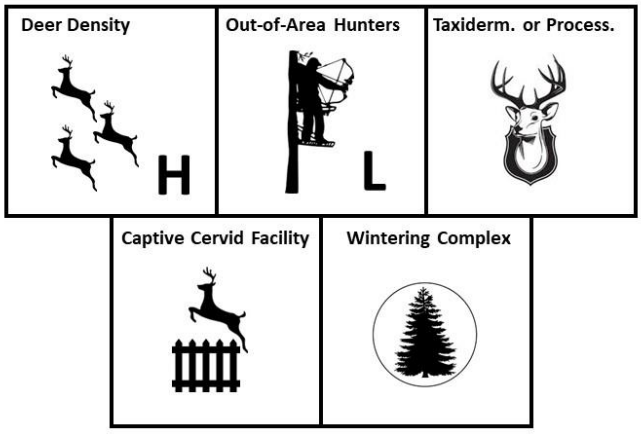
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

15. Imagine a township that has the following conditions:
    1. High deer density
    2. Low number of out-of-area hunters
    3. Has taxidermists and/or processors
    4. Has captive cervid facilities
    5. Has Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

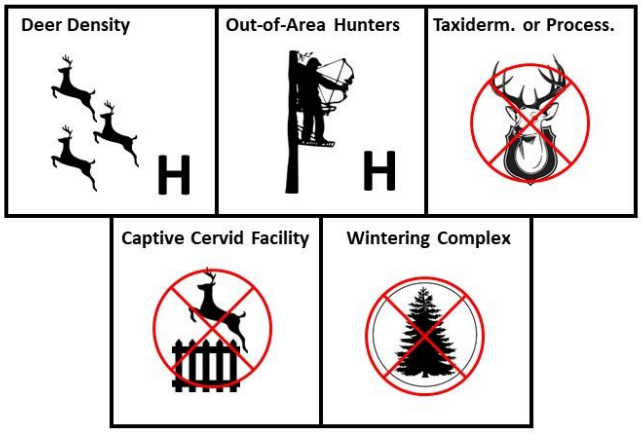
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

16. Imagine a township that has the following conditions:
    1. High deer density
    2. High number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

Highest probability of CWD occurrence_____

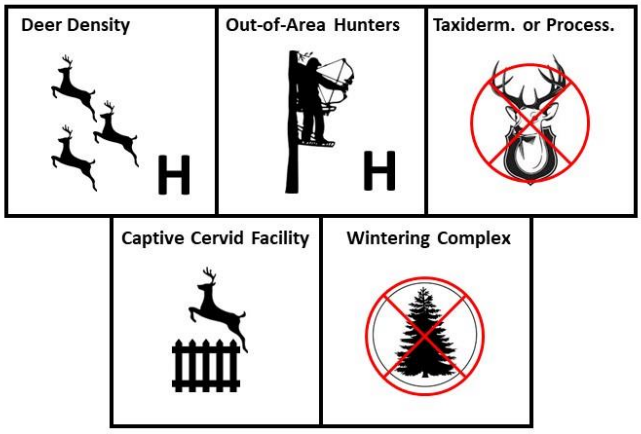
Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)

17. Imagine a township that has the following conditions:
    1. High deer density
    2. High number of out-of-area hunters
    3. No taxidermists and/or processors
    4. Has captive cervid facilities
    5. No Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

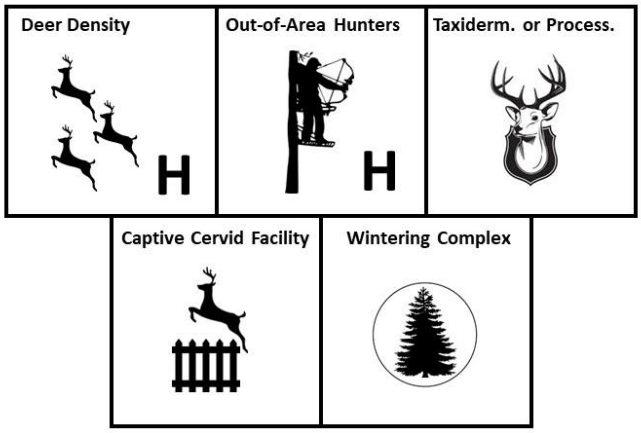
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

18. Imagine a township that has the following conditions:
    1. High deer density
    2. High number of out-of-area hunters
    3. Has taxidermists and/or processors
    4. Has captive cervid facilities
    5. Has Deer wintering complexes




**Based on your knowledge of CWD risk, what is the annual probability that CWD occurs in this township?**

Scale: 0 – 1 [CWD Never Occurs – CWD Always Occurs]

Lowest probability of CWD occurrence_____

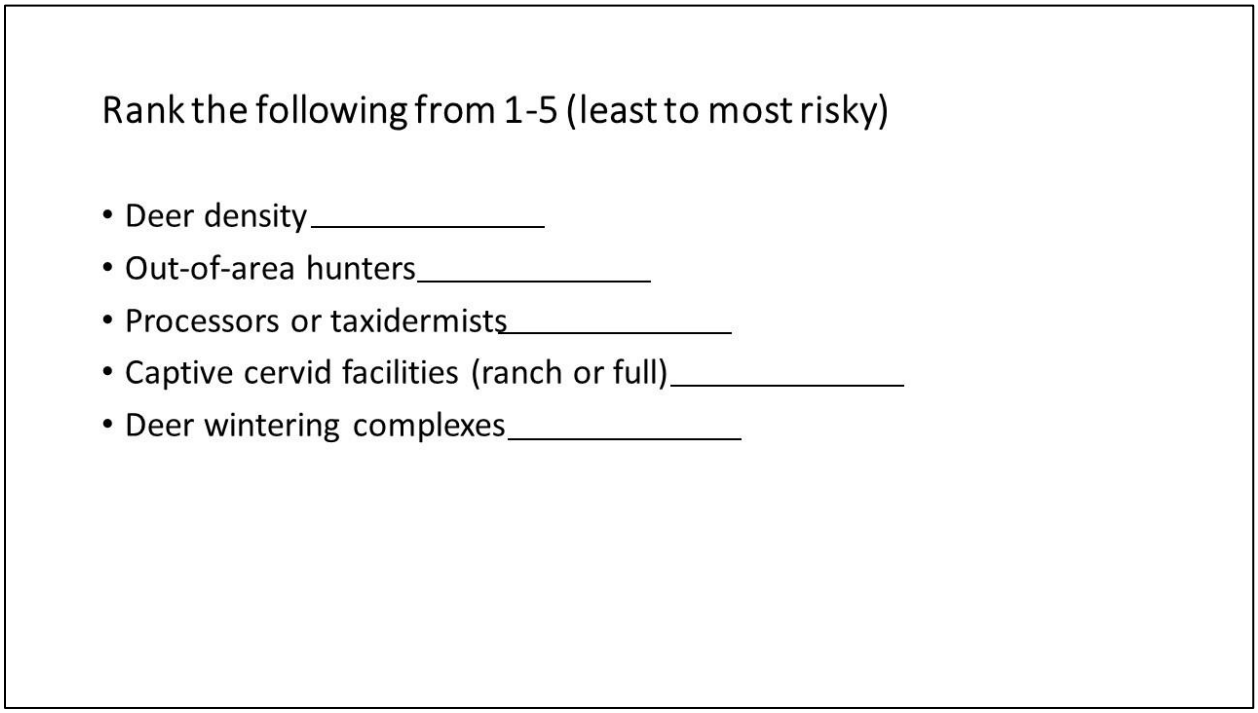
Highest probability of CWD occurrence_____

Most likely probability of CWD occurrence_____

Your confidence (50-100%) that the true probability of CWD occurrence falls within the range you provided _____%

For example, if you are completely *unsure* that the "true" value would be between the lowest and highest numbers that you provided, you would enter 50%.

Figure A.1 (cont'd)



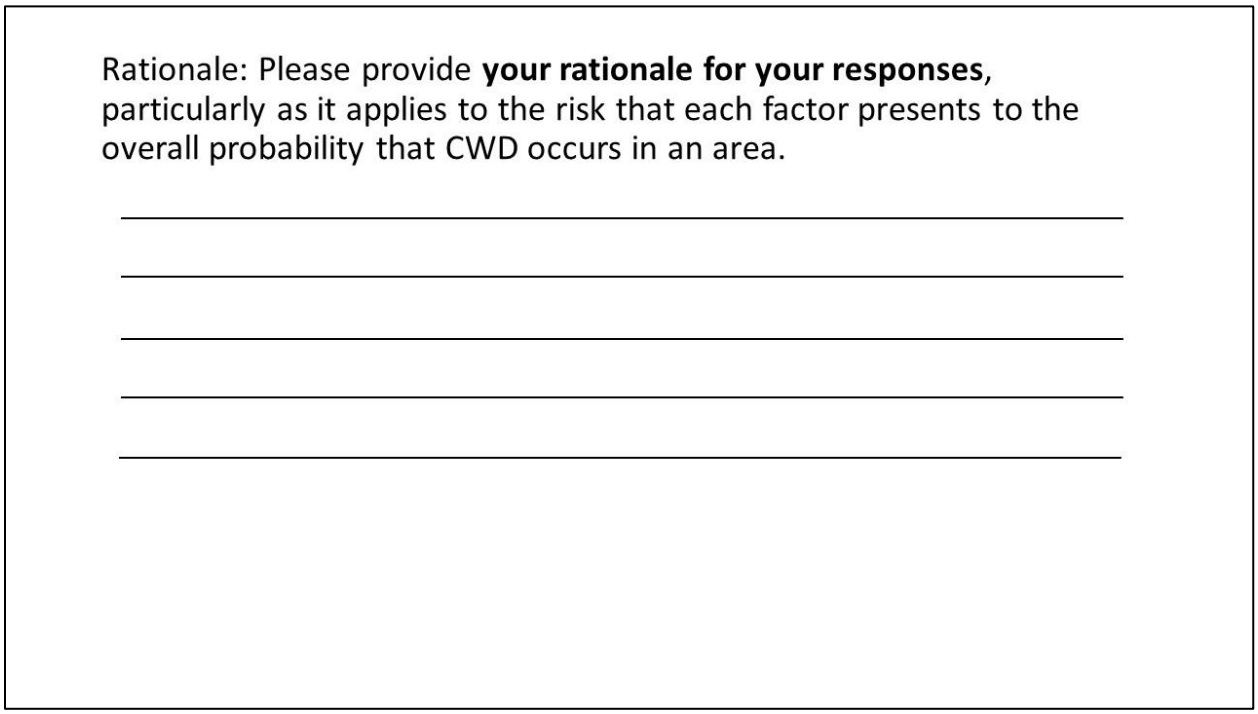



Figure A.2 The fitted results of each scenario that were presented to our experts as part of the modified Delphi process. Each plot depicts a unique scenario that corresponds to the numbered scenarios in question A.1. The individual responses are beta distributions with a unique mean estimate and associated error. The error bars represent 95% confidence intervals.

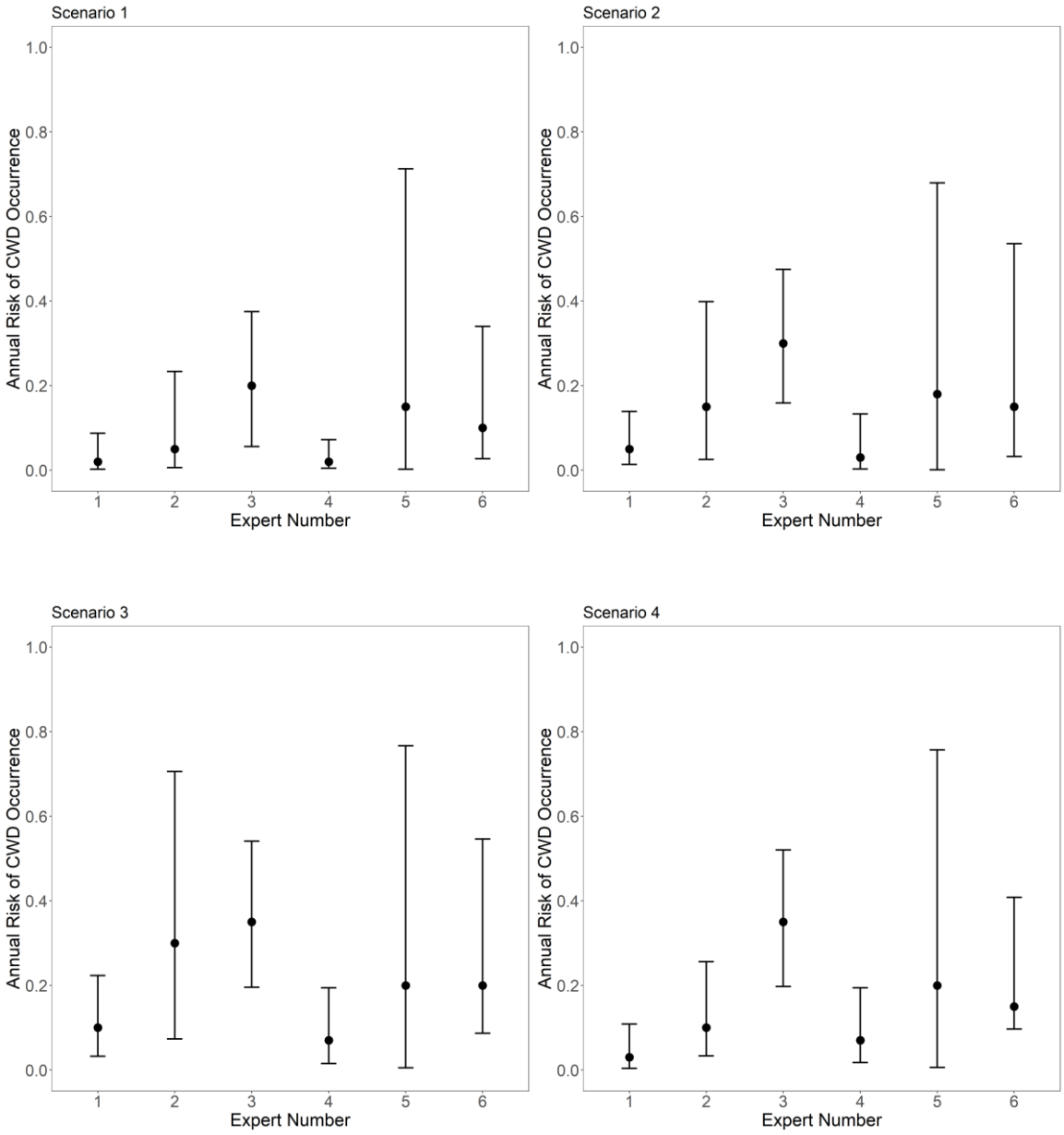


Figure A.2 (cont'd)

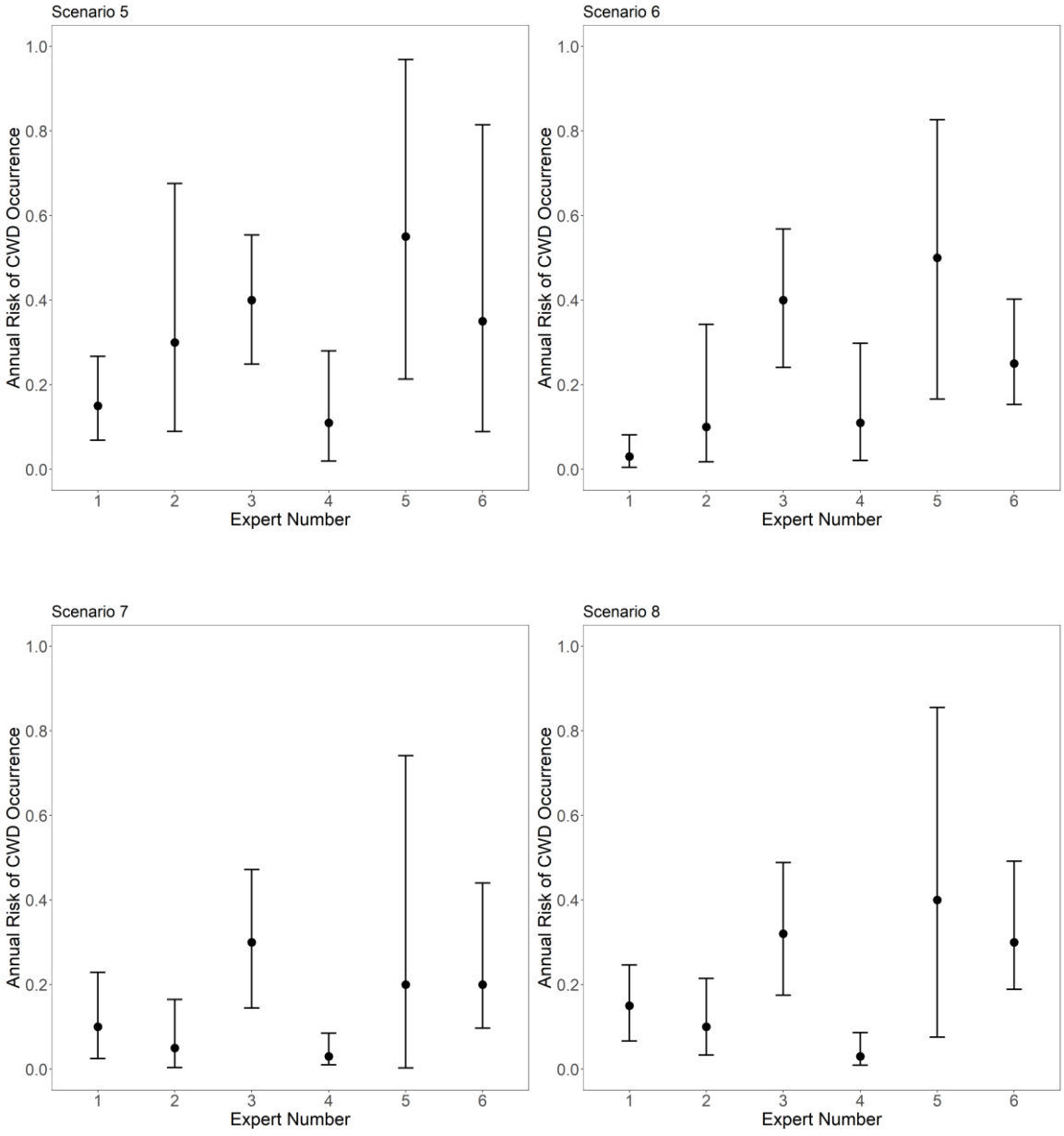


Figure A.2 (cont'd)

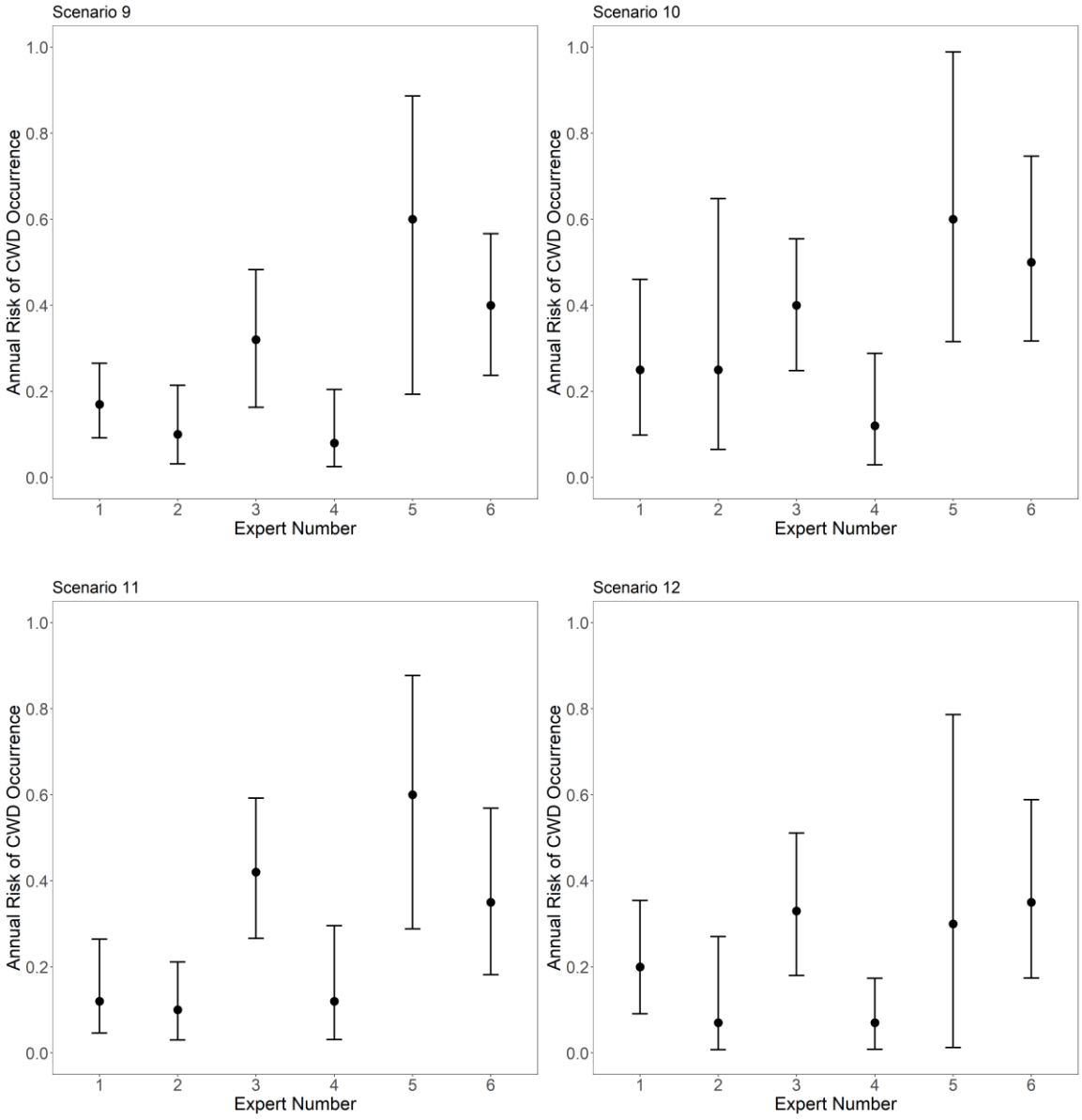


Figure A.2 (cont'd)

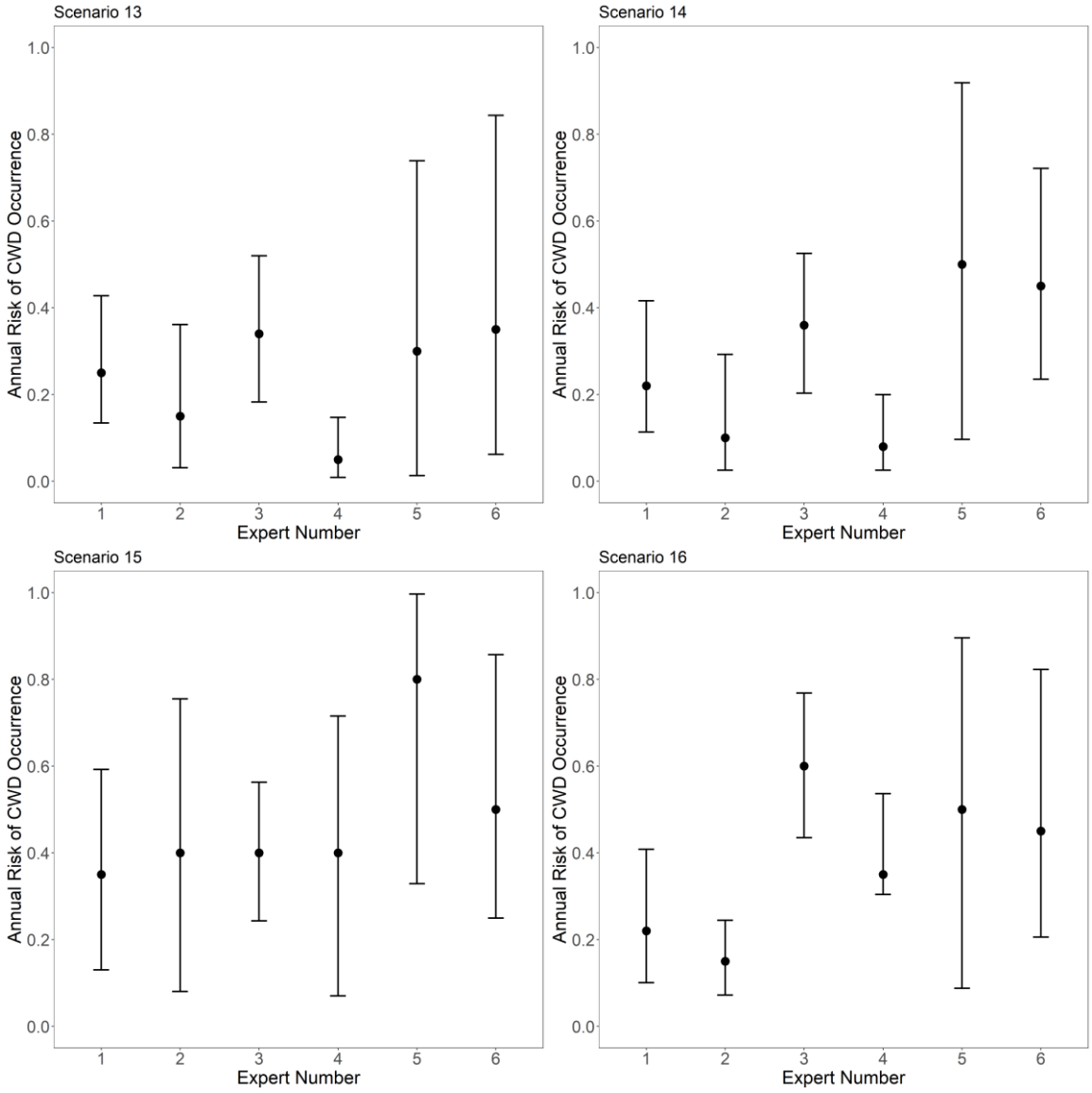


Figure A.2 (cont'd)

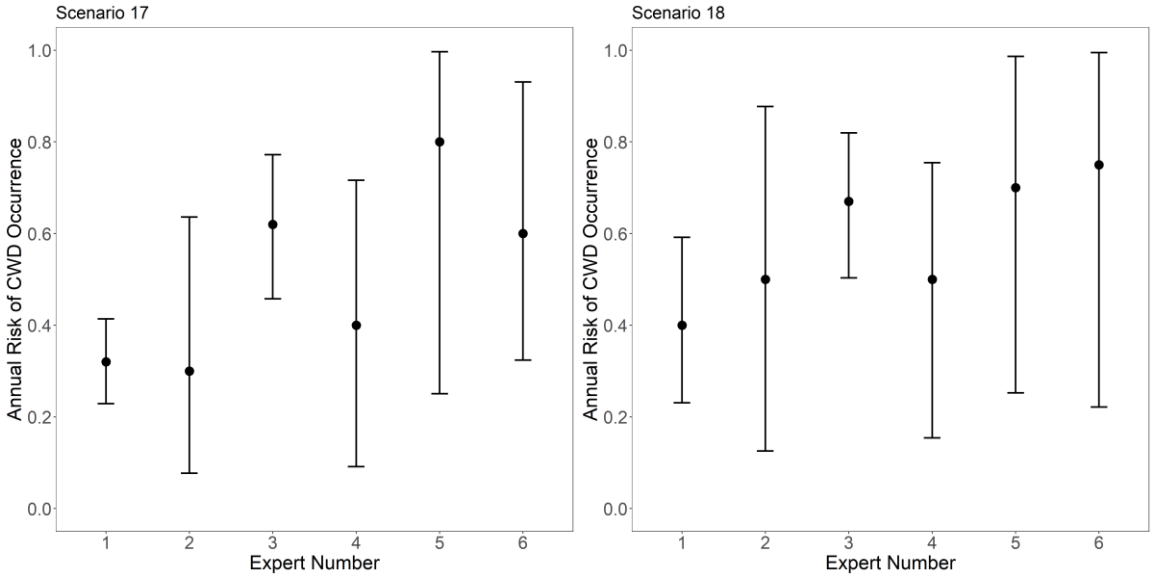
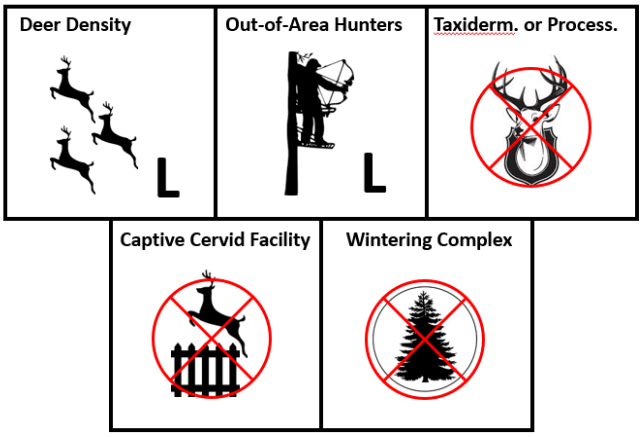


Figure A.3 Example of a scenario with expert-elicited data that was used for the modified Delphi process. The experts were asked to evaluate their [anonymized] responses relative to the group and determine whether any changes needed to be made. Only 1 expert chose to change their estimate on a single scenario.

1. Imagine a township that has the following conditions:
    1. Low deer density
    2. Low number of out-of-area hunters
    3. No taxidermists and/or processors
    4. No captive cervid facilities
    5. No Deer wintering complexes




| Expert Num. | Scenario | Low | High | Mid | Confidence |
|---|---|---|---|---|---|
| 1 | 1 | 0.01 | 0.05 | 0.02 | 0.5 |
| 2 | 1 | 0.02 | 0.15 | 0.05 | 0.75 |
| 3 | 1 | 0.1 | 0.3 | 0.2 | 0.75 |
| 4 | 1 | 0.01 | 0.05 | 0.02 | 0.75 |
| 6 | 1 | 0.05 | 0.25 | 0.1 | 0.75 |
| 5 | 1 | 0 | 0.5 | 0.15 | 0.85 |
| 7 | 1 | 0 | 1 | 0.5 | 1 |

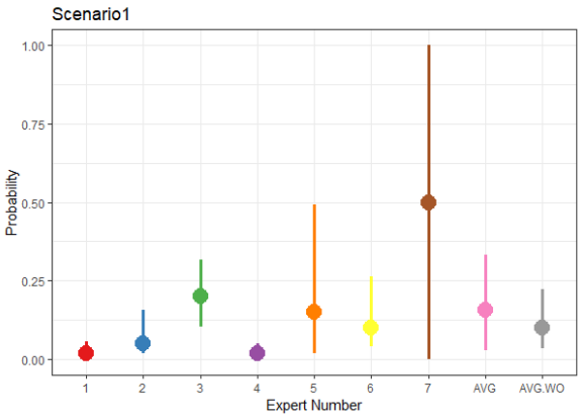
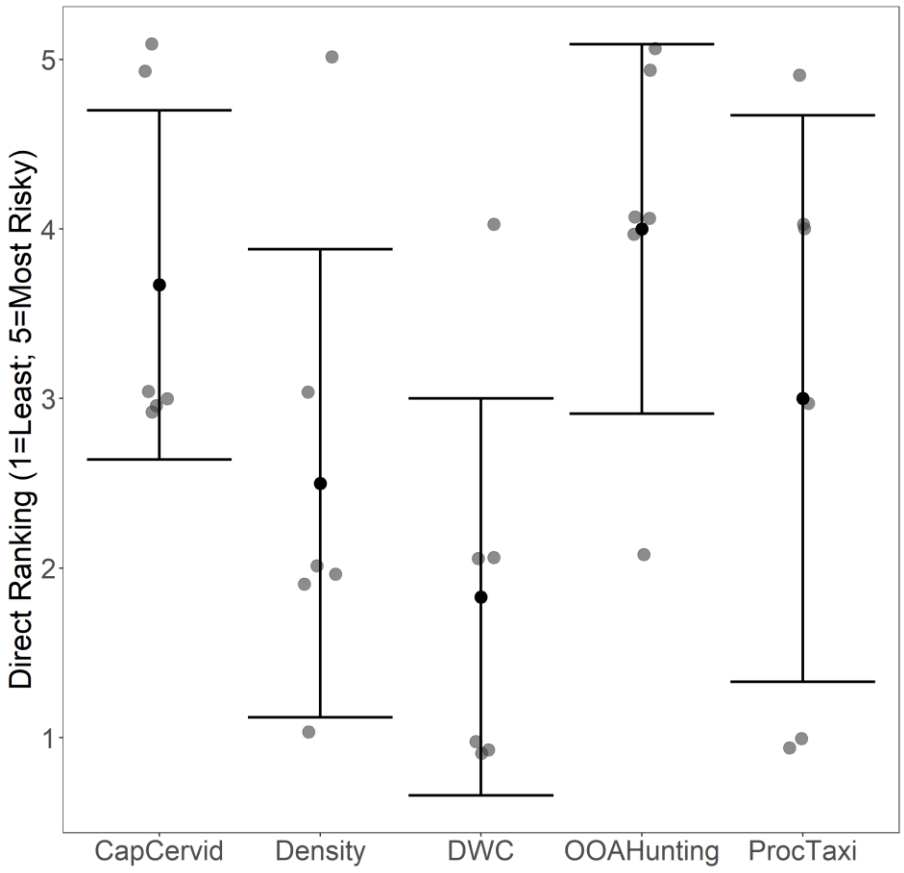


Figure A.4 Direct estimates of the relative risk for each hazard from each of the six experts (gray symbols). Overlaying the point estimates are boxplots that indicate group means and 95% confidence intervals. There was disparity between the relative ranking of individual experts for each of the five hazards. This resulted in a high degree of overlap for the boxplots of group means and 95% confidence intervals.



## APPENDIX B: SUPPLEMENTAL RESULTS FOR CHAPTER 3

Figure B.1 Comparison of the percent maximum probability of infection estimates at locations where CWD was detected by the time since CWD introduction. I observed little change in maximum probability estimates beyond 10 years of exposure (gray panel).

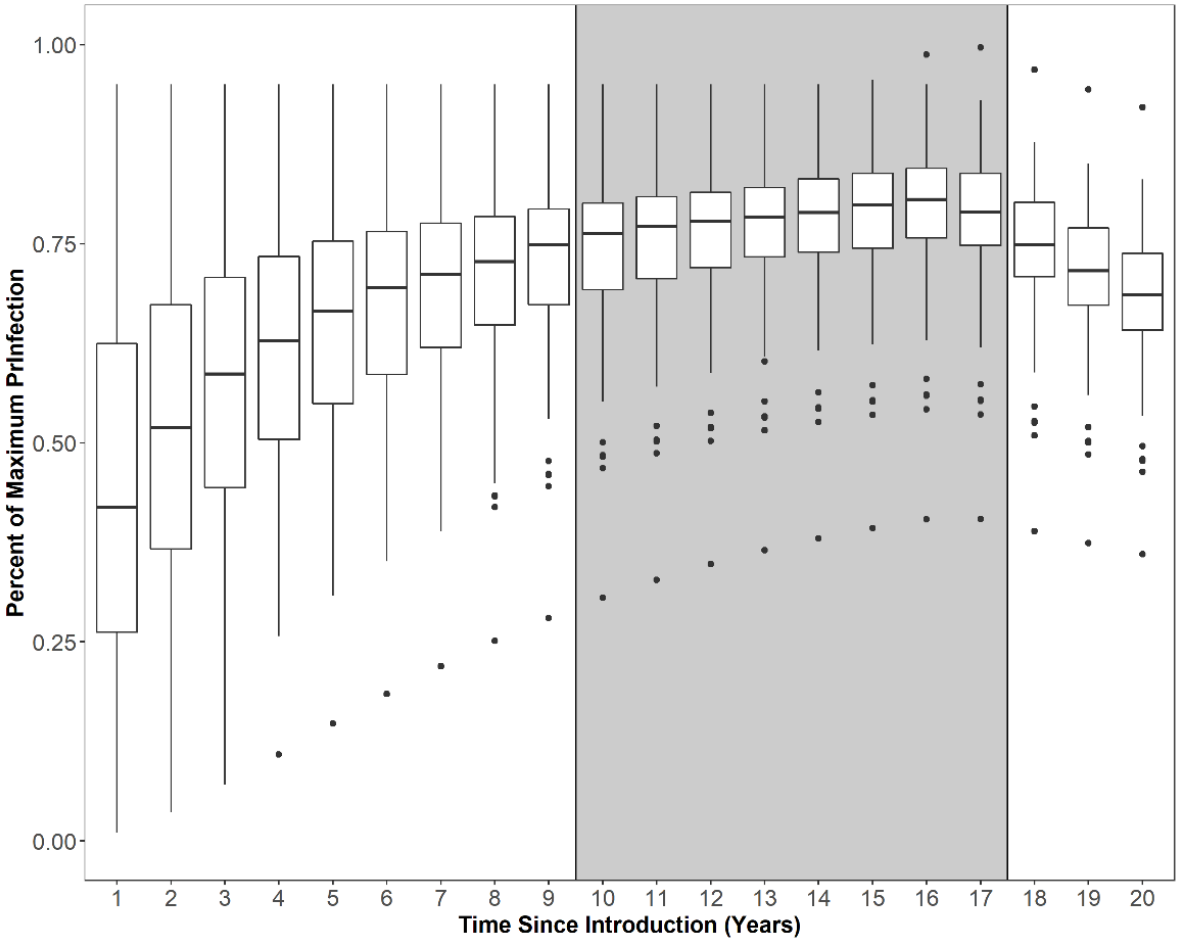
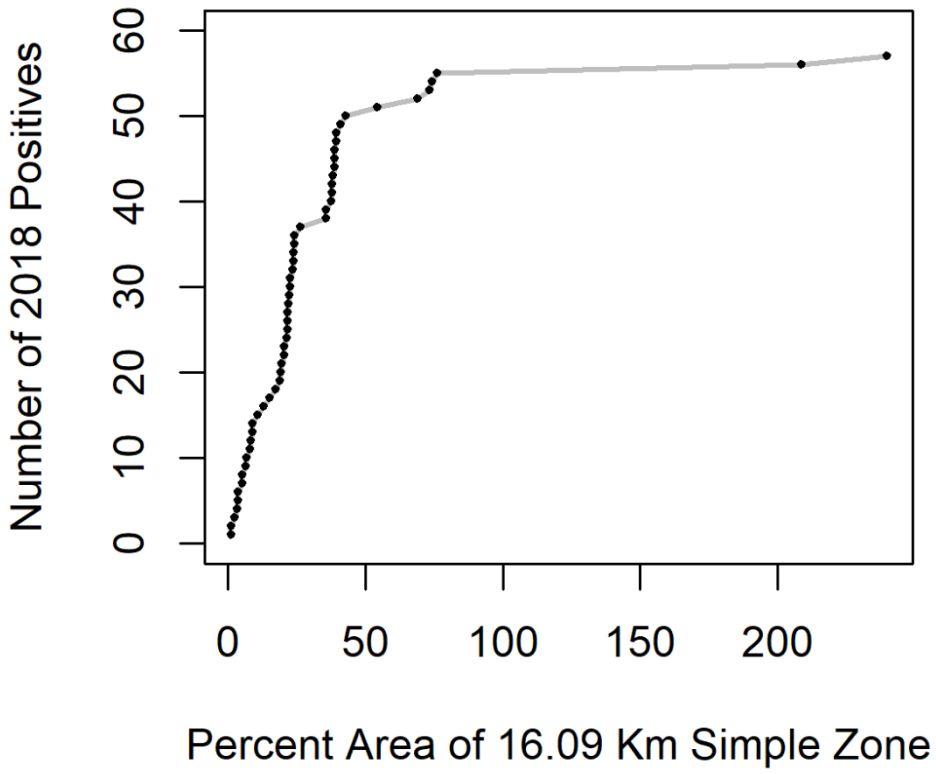


Figure B.2 Accumulation curve of the number of CWD positive detections encompassed within the extrapolated zone as a percent of a simple zone using a radius of 16.09 km. The majority of CWD detections were captured within an area that is smaller (<100%) than the area of the simple zone.




.

## APPENDIX C: SUPPLEMENTAL RESULTS FOR CHAPTER 4

Figure C.1 Site occupancy predictions for years 2002 – 2015 for the multi-mechanism DOM.

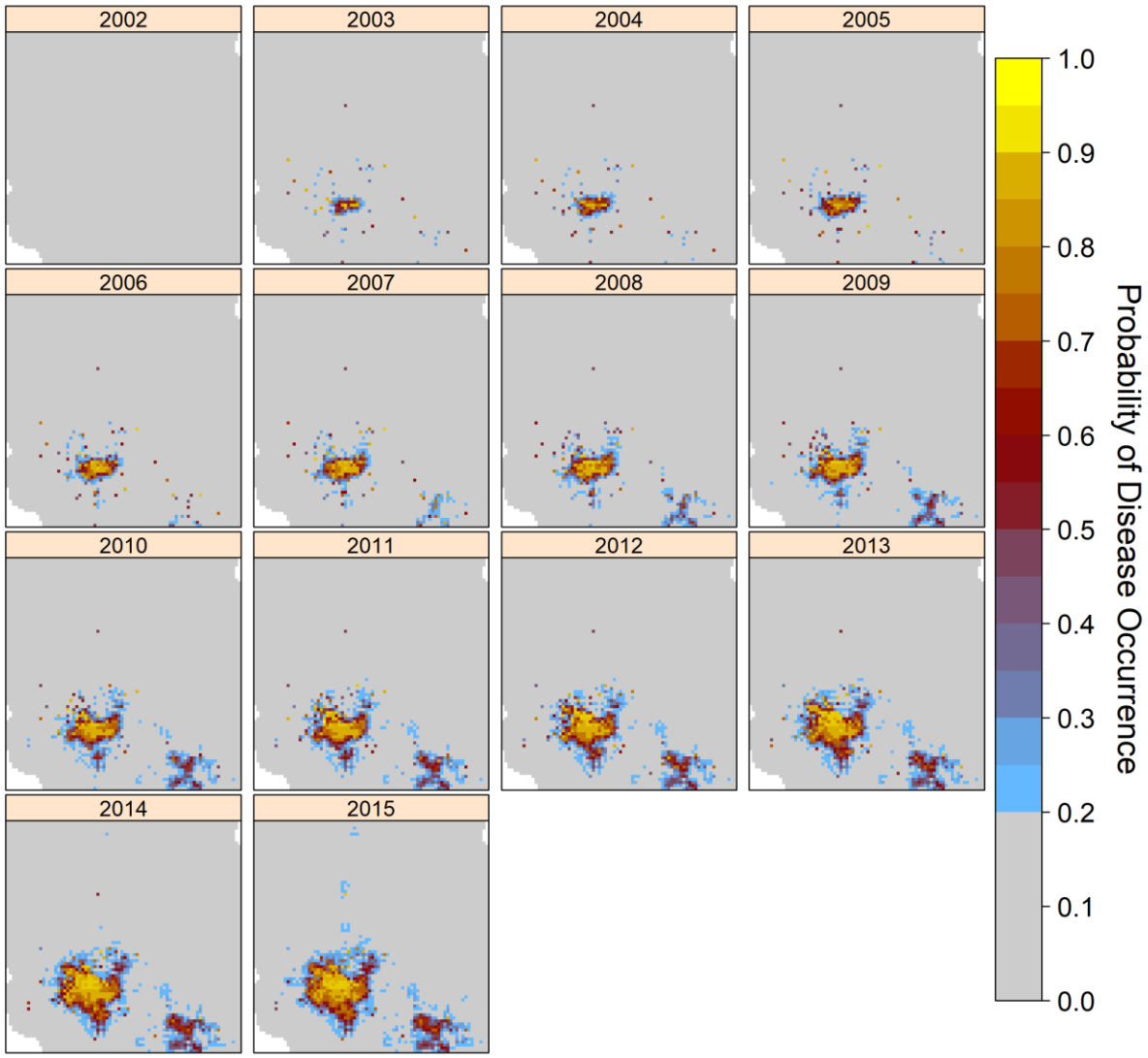
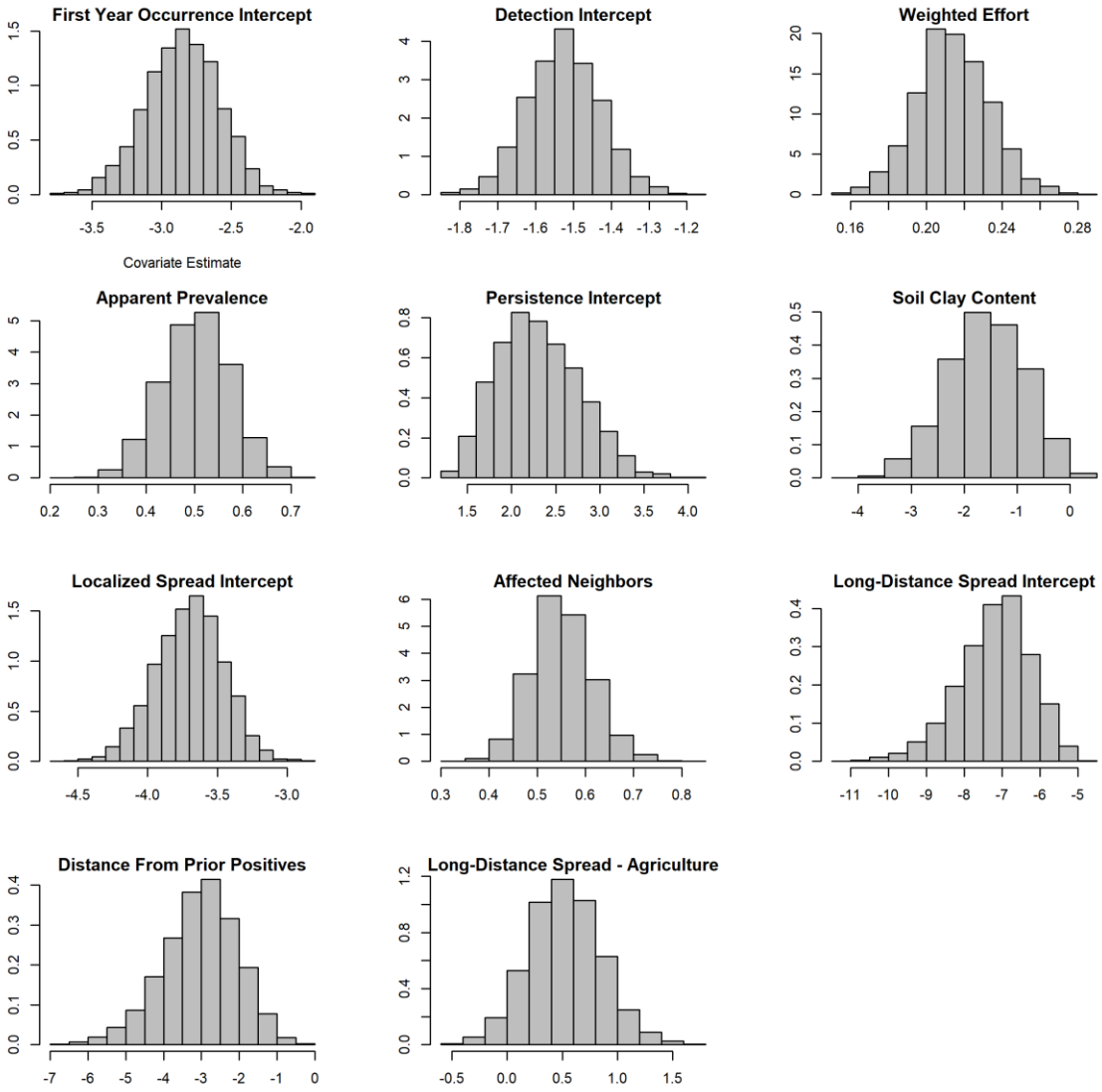


Figure C.2 Posterior distributions for model parameters of multi-mechanism DOM.



## APPENDIX D: R CODE FOR ANALYSIS FOR CHAPTER 4

### R Code: Single Mechanism Dynamic Occupancy Model

```
 setwd("")

####Load Data####

 obsdata <- read.csv("Observations.csv")
 key <- read.csv("Key.csv") ##Provides geographic coordinates of cells
 xy <- c(key$X, key$Y)
 xy <- matrix(xy,  c(nsite, nobs))

####Spatial Autocorrelation####

 xy <- matrix(c(key$X, key$Y), c(nsite, nobs))
 occupancy.model <- model.matrix(~1,data=data.frame(rep(1, nsite)))
 spatial.model=list(model="rsr", moran.cut=250)
 Xz <-as.matrix(occupancy.model, site)
 Xz.vec <- as.vector(Xz)
 n.site=nrow(Xz)
 Q <- icar.Q(xy, threshold= 4551.922, rho = 1)
 A <- diag(diag(Q)) - Q
 P <- diag(n.site) - Xz %*% solve(crossprod(Xz), t(Xz))
 Op <- (nrow(A)/sum(A)) * (P %*% (A %*% P))
 e <- rARPACK::eigs(Op, as.integer(spatial.model$moran.cut))
 K <- e$vectors
 KtK <- diag(ncol(K))
 Q.alpha <- as.matrix(t(K) %*% Q %*% K)
 mu.a <- rep(0, nrow(Q.alpha))


 #####Create list to load into jags####

 Jags.data <- list(y=y, nsite=nrow(y), nyear = dim(y)[3], nrep = dim(y)[2],
           forest=forest, WhichNborsMat = WhichNborsMat, dist=distance, W2 = W2,
         K=K, Q.alpha= Q.alpha, mu.a=mu.a, agric=agric,  urban=urban, Xz.vec=Xz.vec,
         soil=soil, prev=Prev)


#####Specify model in JAGS language####

sink("NonMix.txt")

cat("

   model {
```

```
#Priors

alpha.occ.1 ~ dlogis(0, 1)#intercept for state model
for.occ ~ dlogis(0, 1)  #beta for forest (state model year 2-15)
ag.occ ~ dlogis(0, 1)  #beta for ag (state model year 2-15)
alpha.det ~ dlogis(0, 1)    #intercept for detection model
weight.det ~ dlogis(0, 1)    #beta for weighted probability
dist.emer ~ dlogis(0, 1)
neigh.occ ~ dlogis(0, 1)    #beta for infected neighbors
soil.pers ~ dlogis(0, 1)  #beta for persistence by soil
prev.det ~ dlogis(0, 1)    #beta for weighted probability


#####RSR Random spatial correlation####

sigma ~ dunif(0,100)
tau <- pow(sigma, -2)
alpha ~ dmnorm(mu.a, tau * Q.alpha)
RSR <- K %*% alpha


#####Likelihoods####

#####State submodel: psi1 (Year1) Define state conditional on parameter####

for (i in 1:nsite){

z[i,1] ~ dbern(psi[i,1])
logit(psi[i,1]) <- Xz.vec[i] %*% alpha.occ + RSR[i]


##### Observation model year 1####

for (j in 1:nrep){
muy[i,j,1] <- z[i,1] * p[i,j,1]
logit(p[i,j,1]) <- alpha.det + weight.det * W2[i,j,1] + prev.det * prev[i,j,1]
y[i,j,1] ~ dbern(muy[i,j,1])
} #j
} #i


#####Observation for subsequent years####
for (k in 1:(nyear-1)){
for (i in 1:nsite){
for (j in 1:nrep){
muy[i,j,(k+1)] <- z[i,(k+1)] * p[i,j,(k+1)]
logit(p[i,j,(k+1)]) <- alpha.det + weight.det * W2[i,j,(k+1)] + prev.det * prev[i,j,(k+1)]
y[i,j,(k+1)] ~ dbern(muy[i,j,(k+1)])
```

```
    }

    ####Neighborhood colonization, n.neigh= number of infected neighbors, i.nbors= indicator if neighbors are infected (binary:0,1)####

    n.neigh[i, k] <- sum(WhichNborsMat[i, ,k])
    i.nbors[i, k] <- ifelse(n.neigh[i, k] > 0, 1, 0)


    # State submodel: psi1 (All Years) Define state conditional on parameters

    logit(psi[i, (k+1)]) <- alpha.occ + neigh.occ * n.neigh[i,k] + for.occ *forest[i] + ag.occ * agric[i] + dist.emer * dist[i,k] + soil.pers * soil[i]

    z[i,(k+1)] ~ dbern(psi[i,(k+1)])

    } #i

    } #k

        } ##Close jags model

    ",fill = TRUE)

sink()

#####Bundle data####

jags.data <- list(y = y, nsite = dim(y)[1], nrep = dim(y)[2], nyear = dim(y)[3], forest = forest,

WhichNborsMat = WhichNborsMat, agric=agric, dist=dist, W2=W2, K=K, Q.alpha=Q.alpha, mu.a=mu.a, Xz.vec=Xz.vec, prev=prev, soil=soil)

#####Initial values####

zst <- apply(y, c(1, 3), max)   # Observed occurrence as inits for z
inits <- function(){ list(z = zst)}####


#####Parameters monitored####
params <- c("for.occ", "weight.det", "dist.emer", "alpha.occ", "alpha.det", "psi", "neigh.occ", "ag.occ", "soil.pers","p", "prev.det")


#####MCMC settings####
ni <- 40000
nt <- 15
nb <- 20000
nc <- 3


#####Load the correct library####
```

```
library("jagsUI")

#####Call JAGS####
out <- jags(jags.data, inits, params, "NonMix.txt", n.chains = nc, n.thin = nt,
          n.iter = ni, n.burnin = nb)
```

## R Code: Multi-mechanism Dynamic Occupancy Model

```
 setwd("")

####Load Data####

 obsdata <- read.csv("Observations.csv")
 key <- read.csv("Key.csv") ##Provides geographic coordinates of cells
 xy <- c(key$X, key$Y)
 xy <- matrix(xy,  c(nsite, nobs))

####Spatial Autocorrelation####

 xy <- matrix(c(key$X, key$Y), c(nsite, nobs))
 occupancy.model <- model.matrix(~1,data=data.frame(rep(1,5913)))
 spatial.model=list(model="rsr", moran.cut=250)
 Xz <-as.matrix(occupancy.model, site)
 Xz.vec <- as.vector(Xz)
 n.site=nrow(Xz)
 Q <- icar.Q(xy, threshold= 4551.922, rho = 1)
 A <- diag(diag(Q)) - Q
 P <- diag(n.site) - Xz %*% solve(crossprod(Xz), t(Xz))
 Op <- (nrow(A)/sum(A)) * (P %*% (A %*% P))
 e <- rARPACK::eigs(Op, as.integer(spatial.model$moran.cut))
 K <- e$vectors
 KtK <- diag(ncol(K))
 Q.alpha <- as.matrix(t(K) %*% Q %*% K)
 mu.a <- rep(0, nrow(Q.alpha))


 #####Create list to load into jags####

 Jags.data <- list(y=y, nsite=nrow(y), nyear = dim(y)[3], nrep = dim(y)[2],
           WhichNborsMat = WhichNborsMat, dist=distance, weight = weight,
         K=K, Q.alpha= Q.alpha, mu.a=mu.a, agric=agric,  Xz.vec=Xz.vec, soil=soil, prev=Prev)


#####Specify model in JAGS language####
```

```
sink("NonMix.txt")

cat("

   model {

   #Priors

   alpha.occ.1 ~ dlogis(0, 1)#intercept for state model
   for.occ ~ dlogis(0, 1)  #beta for forest (state model year 2-15)
   ag.occ ~ dlogis(0, 1)  #beta for ag (state model year 2-15)
   alpha.det ~ dlogis(0, 1)    #intercept for detection model
   weight.det ~ dlogis(0, 1)    #beta for weighted probability
   dist.emer ~ dlogis(0, 1)
   neigh.occ ~ dlogis(0, 1)    #beta for infected neighbors
   soil.pers ~ dlogis(0, 1)  #beta for persistence by soil
   prev.det ~ dlogis(0, 1)    #beta for weighted probability


   #####RSR Random spatial correlation####

   sigma ~ dunif(0,100)
   tau <- pow(sigma, -2)
   alpha ~ dmnorm(mu.a, tau * Q.alpha)
   RSR <- K %*% alpha


   #####Likelihoods####

   #####State submodel: psi1 (Year1) Define state conditional on parameter####

   for (i in 1:nsite){

   z[i,1] ~ dbern(psi[i,1])
   logit(psi[i,1]) <- Xz.vec[i] %*% alpha.occ + RSR[i]


   ##### Observation model year 1####

   for (j in 1:nrep){
   muy[i,j,1] <- z[i,1] * p[i,j,1]
   logit(p[i,j,1]) <- alpha.det + weight.det * weight[i,j,1] + prev.det * prev[i,j,1]
   y[i,j,1] ~ dbern(muy[i,j,1])
   } #j
   } #i


   #####Observation for subsequent years####
   for (k in 1:(nyear-1)){
```

```
   for (i in 1:nsite){
   for (j in 1:nrep){
   muy[i,j,(k+1)] <- z[i,(k+1)] * p[i,j,(k+1)]
   logit(p[i,j,(k+1)]) <- alpha.det + weight.det * weight[i,j,(k+1)] + prev.det * prev[i,j,(k+1)]
   y[i,j,(k+1)] ~ dbern(muy[i,j,(k+1)])
   }


   ####Neighborhood colonization, n.neigh= number of infected neighbors, i.nbors= indicator if
neighbors are infected (binary:0,1)####

   n.neigh[i, k] <- sum(WhichNborsMat[i, ,k])
   i.nbors[i, k] <- ifelse(n.neigh[i, k] > 0, 1, 0)


   #####State submodel: psi1 (All Years) Define state conditional on parameters####

   logit(psi[i, (k+1)]) <- alpha.occ + neigh.occ * n.neigh[i,k] + ag.occ * agric[i] + dist.emer *
dist[i,k] + soil.pers * soil[i]

   z[i,(k+1)] ~ dbern(psi[i,(k+1)])

   } #i

   } #k

        } ##Close jags model

   ",fill = TRUE)

sink()

#####Bundle data####

jags.data <- list(y = y, nsite = dim(y)[1], nrep = dim(y)[2], nyear = dim(y)[3],
WhichNborsMat = WhichNborsMat, agric=agric, dist=dist, W2=W2, K=K, Q.alpha=Q.alpha,
mu.a=mu.a, Xz.vec=Xz.vec, prev=prev, soil=soil)

#####Initial values####

zst <- apply(y, c(1, 3), max)   # Observed occurrence as inits for z
inits <- function(){ list(z = zst)}####

#####Parameters monitored####
params <- c("for.occ", "weight.det", "dist.emer", "alpha.occ", "alpha.det", "psi", "neigh.occ",
"ag.occ", "soil.pers","p", "prev.det")

#####MCMC settings####
ni <- 40000
```

```
nt <- 15
nb <- 20000
nc <- 3

#####Load the correct library####
library("jagsUI")

#####Call JAGS####
out <- jags(jags.data, inits, params, "NonMix.txt", n.chains = nc, n.thin = nt,
          n.iter = ni, n.burnin = nb)
```

**R Code: Multi-Mechanism Dynamic Occupancy Model**

```
# Specify model in JAGS language
sink("Mix.txt")
cat("
   model {

   #Priors
   alpha.det ~ dlogis(0, 1)    #intercept for detection model
   weight.det ~ dlogis(0, 1)    #beta for weighted probability
   prev.det ~ dlogis(0, 1)    #beta for apparent prevalence
   alpha.occ ~ dlogis(0, 1)    #intercept for state model year 1
   alpha.emer ~ dlogis(0, 1)   #intercept for emergent
   ag.emer ~ dlogis(0, 1)  #beta for emergence in forest
   dist.emer ~ dlogis(0, 1) #beta for emergence in forest
   alpha.est ~ dlogis(0, 1)    #intercept for established
   neigh.occ ~ dlogis(0, 1)    #beta for infected neighbors
   alpha.pers ~ dlogis(0, 1)    #intercept for persistence
   soil.pers ~ dlogis(0, 1)  #beta for persistence by soil

   #RSR Random spatial correlation
   sigma ~ dunif(0,100)
   tau <- pow(sigma, -2)
   alpha ~ dmnorm(mu.a, tau * Q.alpha)
   RSR <- K %*% alpha

   #Likelihoods
   # State submodel: psi1 (Year1) Define state conditional on parameters

   for (i in 1:nsite){
```

```
   z[i,1] ~ dbern(psi[i,1])
   logit(psi[i,1]) <- Xz.vec[i] %*% alpha.occ + RSR[i]

   # Observation model
   for (j in 1:nrep){
   muy[i,j,1] <- z[i,1] * p[i,j,1]
   logit(p[i,j,1]) <- alpha.det + weight.det * weight[i,j,1] + prev.det * prev[i,j,1]
   y[i,j,1] ~ dbern(muy[i,j,1])
   } #j
         } #i

   #observation for subsequent years

   for (k in 1:(nyear-1)){
   for (i in 1:nsite){
   for (j in 1:nrep){

   muy[i,j,(k+1)] <- z[i,(k+1)] * p[i,j,(k+1)]
   logit(p[i,j,(k+1)]) <- alpha.det + weight.det * weight[i,j,(k+1)] + prev.det * prev[i,j,(k+1)]
   y[i,j,(k+1)] ~ dbern(muy[i,j,(k+1)])

   }

   #Neighborhood colonization, n.neigh= number of infected neighbors, i.nbors= indicator if
neighbors are infected (binary:0,1).
   n.neigh[i, k] <- sum(WhichNborsMat[i, ,k]);
   i.nbors[i, k] <- ifelse(n.neigh[i, k] > 0, 1, 0)

   #Psi Mixture
psi[i, (k+1)] <- z[i,k] * phi[i,k] + (1-z[i,k]) * i.nbors[i,k] * gamma[i,k] + (1-z[i,k]) * (1-
i.nbors[i,k]) * delta[i,k]       #gamma established spread, delta emergent spread
   logit(gamma[i,k]) <- alpha.est + neigh.occ * n.neigh[i,k]  #established disease spread
   logit(delta[i,k]) <- alpha.emer + dist.emer * dist[i,k] + ag.emer * agric[i]  #emergent disease
spread
   logit(phi[i,k]) <- alpha.pers + soil.pers * soil[i]
   z[i,(k+1)] ~ dbern(psi[i,(k+1)])
   } #i
         } #k

   }

   ",fill = TRUE)
```

```
sink()


# Bundle data
jags.data <- list(y = y, nsite = dim(y)[1], nrep = dim(y)[2], nyear = dim(y)[3],
WhichNborsMat = WhichNborsMat, dist=dist, W2=W2, K=K, Q.alpha=Q.alpha, mu.a=mu.a,
agric=agric, Xz.vec=Xz.vec, prev=prev, soil=soil)

# Initial values
zst <- apply(y, c(1, 3), max)   # Observed occurrence as inits for z
inits <- function(){ list(z = zst)}

# Parameters monitored
params <- c( "alpha.occ", "weight.det", "dist.emer","alpha.det","neigh.occ",
  "alpha.est", "alpha.emer", "alpha.pers", "p","RSR", "prev.det", "soil.pers", "ag.emer")

# MCMC settings
ni <- 40000
nt <- 15
nb <- 20000
nc <- 3

#Load the correct library
library("jagsUI")

# Call JAGS
out <- jags(jags.data, inits, params, "Mix.txt", n.chains = nc, n.thin = nt,
          n.iter = ni, n.burnin = nb)
```

# LITERATURE CITED

# LITERATURE CITED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