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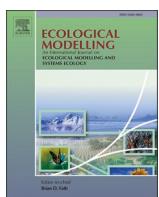
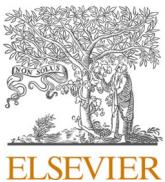


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An individual-based model for direct and indirect transmission of chronic wasting disease in free-ranging white-tailed deer

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ABSTRACT

Chronic wasting disease (CWD) is an infectious prion disease that infects members of the *Cervidae* family (i.e., deer) resulting in widespread ecological, economic, and recreational ramifications. We introduce a spatially explicit individual-based model (IBM) that integrates individual deer movement and behavior with population and disease dynamics to forecast CWD in populations of free-ranging white-tailed deer (*Odocoileus virginianus*). We use a Susceptible-Exposed-Infectious-Dead (S-E-I-D) epidemiological framework to explore spatiotemporal dynamics of CWD within an agriculturally dominated area in Michigan, USA. The IBM results closely mimicked documented short- and long-term dynamics of white-tailed deer populations and CWD in the Midwestern, USA. We applied pattern-oriented modeling using annual apparent CWD prevalence rates reported by Midwestern state wildlife agencies to validate the disease model. The introduction of a single infected deer to the modeled landscape (93 km²) led to an outbreak of CWD in 100 out of 350 model simulations (29 %); prevalence never exceeded 1.47 % for repetitions where the outbreak ended. For the 100 simulations where disease persisted, the deer population declined by 87 % by year 50 following initial introduction of CWD. Mean (±SD) prevalence after 5, 10, 25, and 50 years was 1.1 % (±1.0 %), 3.4 % (±3.3 %), 46.5 % (±18.8 %), and 51.8 % (±18.1 %), respectively, which highly correlated ($r = 0.99$) with annual CWD prevalence reported in Wisconsin white-tailed deer populations for years 1–21 post initial detection. Combined with a global sensitivity analysis, the IBM indicated that prevalence of CWD at year 20 was most sensitive to harvest rate of yearling and adult female deer and least sensitive to prion shedding rate, prion half-life, and deer group numbers, indicating that deer population parameters were more influential than disease parameters on CWD dynamics. Our IBM serves as a tool to explore and better understand indirect and direct transmission of CWD within free-ranging cervid populations. Users of this model can adjust parameter values to explore how interactions among individual deer and between deer and their environment affect CWD dynamics. This IBM also serves as a framework for applying and assessing spatially and temporally explicit management scenarios.

1. Introduction

Chronic wasting disease (CWD) is an emerging infectious disease spreading among cervid (i.e., species of the *Cervidae* family) populations across North America (Williams and Young, 1992; USGS, 2024). This disease has infected or currently infects cervids across 32 states in the United States, four provinces in Canada, Finland, Norway, Sweden, and South Korea (Sohn et al., 2002; Koutsoumanis et al., 2023; USGS, 2024). Eradicating CWD seems unlikely, as researchers have made little

advancement toward finding a vaccine or treatment (Colby and Prusiner, 2011; Xu et al., 2013; Goñi et al., 2015; Napper and Schatzl, 2023). Similarly, field and research testing of prevention strategies have been limited, are difficult to conduct, and, in many cases, not effective towards limited CWD introductions to new free-ranging cervid populations. Management strategies for controlling the disease once an outbreak occurs have generally been ineffective (Uehlinger et al., 2016; Fischer and Dunfee, 2022), although Miller et al. (2020) and Conner et al. (2021) found that maintained and increased hunting pressure can

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modulate apparent prevalence trends in mule deer populations in Colorado and other western U.S. and Canadian regions.

Mathematical modeling is a useful tool for studying infectious diseases and their management because methods such as field or clinical studies are often cost-prohibitive, put scientists and the public at risk of pathogen exposure, and potentially cause localized deer population declines where the disease persists or prevalence increases. While mathematical models are useful, understanding and predicting wildlife disease dynamics in free-ranging cervid populations is often challenging because disease systems are complex and not fully understood. This challenge is apparent for CWD. Researchers and wildlife agencies have monitored and studied the CWD disease system for four decades (Gross and Miller, 2001; Samuel and Storm, 2016; Uehlinger et al., 2016), yet few advancements in quantitative modeling have occurred until recently (Winter and Escobar, 2020; Rogers et al., 2022; Cook et al., 2023). Uncertainty associated with pathogen parameters (e.g., indirect and direct transmission rates, basic reproduction number (R_0), and others; Uehlinger et al., 2016) and high variation associated with the host and environment (Ketz et al., 2019) pose challenges to CWD modeling.

In a review conducted by Uehlinger et al. (2016), most (6 of 9) field-based studies that evaluated management strategies for CWD were based on mathematical modeling that predicted management effects on CWD dynamics. No single optimal management strategy emerged from modeling nor field studies assessed in the review, as findings varied considerably given study-specific contexts. Additionally, the studies acknowledged limitations to their work. For example, 5 of 6 modeling studies assessed by Uehlinger et al. (2016) were unsure of how to accurately parameterize CWD transmission mode as a model variable.

Models for CWD dynamics must readily incorporate individual heterogeneity in deer behavior and local deer, management, and landscape information. Deer behavior depends on habitat characteristics of occupied landscapes. For example, in the Midwest US, higher deer birth and death rates are observed annually compared to other US regions, resulting in a higher turnover rate for cervid populations inhabiting this region (Nixon et al., 1991; Hewitt 2011). Additionally, year-round food abundance and landscapes with fragmented habitats associated with agriculturally dominated areas affect home-range sizes, movement rates, and contact rates among deer (Hewitt, 2011). These movement and contact rates have an important role in possible pathogen transmission for individual animals (Wobeser, 2006; Manlove et al., 2022). Furthermore, differences in CWD and deer population outcomes due to variations in deer and disease management practices among local jurisdictions are expected, furthering the need to account for local conditions when modeling CWD in free-ranging cervid populations.

Individual-based models (IBMs) are useful when working with complex systems that contain high uncertainty and variation, such as the deer-CWD system (Bonabeau, 2002). In addition, IBMs are becoming increasingly applied for epidemiology because they incorporate population processes, including individual and group movements, social behaviors, and local interactions with the environment, all of which affect transmission of infectious pathogens (Ramsey and Efford, 2010; Ramsey et al., 2014; Merler et al., 2015). Researchers can incorporate real landscapes into IBMs, typically by coupling the IBM with geographic information systems software, which allows for exploration of disease transmission over space and the effects of landscape characteristics on the disease system (Perez and Dragicevic, 2009). An individual-based framework is more amenable to incorporating individual variation, complex social structure among hosts, and spatially explicit pathogen transmission, properties of CWD transmission that have often been left out of past models (Uehlinger et al., 2016; but see Kjaer and Schaub, 2022). Further, long-lasting yet unverified assumptions about the disease system, such as primary transmission pathways, can be tested through simulation (Kelly et al., 2013; Kjaer and Schaub, 2022). We introduce a stochastic, spatially explicit epidemiological IBM of CWD within a free-ranging white-tailed deer (*Odocoileus virginianus*) population in Michigan to explore and predict spatiotemporal dynamics of

CWD. Specifically, our IBM integrates deer population dynamics and individual deer movements and behaviors to produce the complex dynamics associated with free-ranging white-tailed deer populations and CWD. We then couple this IBM with a global sensitivity analysis to further improve our understanding of how each population and disease process affects CWD dynamics.

2. Methods

The IBM includes three main model components: a deer population module, a deer movement module, and an epidemiological module. We developed each module of our IBM in Python (v 3.7) and corresponding analyses in program R (v 3.5.2). The movement module was adapted from a deer movement model developed by Butts et al. (2022), which applied an exploratory data analysis approach to develop a Langevin model that describes movement patterns trained on GPS location data obtained from white-tailed deer inhabiting central New York (see Supplementary Text S1 for Python code). We use a standardized and familiar protocol, the Overview, Design concepts, and Details (ODD) protocol, to describe our IBM (Grimm et al., 2006, 2010, 2020). A complete, detailed model description, including the Details section of the ODD protocol, is included in Supplementary Text S2, but we provide a summary of our IBM here (Grimm et al., 2020). The ODD protocol for the movement model was published by Butts et al. (2022).

2.1. Model description – overview and details

2.1.1. Purpose and patterns

The overall purpose of our model is to simulate direct and indirect transmission of CWD following its introduction into a free-ranging deer population in an agro-forested landscape. We parameterized the IBM with values reported in the white-tailed deer and CWD literature and by wildlife agencies to assess disease dynamics through time and space. For CWD parameters that remain unknown in the literature, we apply a pattern-oriented modeling approach (Grimm et al., 1996, 2005) using apparent prevalence rates reported by U.S. state wildlife agencies annually and commonly observed patterns in these data. The three main criteria we used to guide our parameter estimation included: (1) annual CWD prevalence rates that follow those reported by state wildlife agencies; (2) male prevalence rate greater than female rate at any given time (Miller and Conner, 2005; DeVivo et al., 2017; Samuel and Storm, 2016); and (3) annual direct transmission events more numerous than indirect transmission events early in the disease epidemic (Ketz et al., 2019, Samuel, 2023).

2.1.2. Entities, state variables and scales

Entities in the model are free-ranging white-tailed deer that interact with each other and the landscape. Each deer has ten entity-level state variables that influence its behavior and characterize its physical and biological properties (Table 1). State variables age and sex define the demographic group for each deer (Table 1). We randomly assign a social group number to each deer at model initialization, with number of groups based on average group size reported from observational data collected within the study area (Courtney, 2023), which guides movements (Section 2.1.4.8) and probability of contacting other deer (Section 2.1.4.11). Deer may demonstrate three disease states in this model: susceptible, exposed, or infectious (Table 1). We consider every uninfected deer in the model as susceptible to CWD, as no immunity has been reported to date (Brandt et al., 2018; Napper and Schatzl, 2023). Between 3 and 6 months following initial infection of a deer, the deer changes disease state from exposed (i.e., infected but not yet infectious) to infectious (Henderson et al., 2015).

We used a spatial extent of 93-km² at 30 m resolution. Each 30 × 30 m grid cell is assigned two values retrieved from underlying maps to guide deer movement: a habitat use value (i.e., can a deer occupy this grid cell?; Fig. 1) and a habitat suitability value (i.e., likelihood a deer

Table 1

State variables assigned to each white-tailed deer (entities) in the individual-based model (IBM) for estimating chronic wasting disease (CWD) dynamics.

Variable	Description
Age	Deer age in months
Sex	Deer sex
Group number	Group number of the deer
Location	X (i.e., UTM Easting of a deer) and Y (i.e., UTM Northing of a deer) position of a deer
Covariance matrix	Covariance matrix of UTM Easting and UTM Northing location data
Vital status	Identifies whether the deer is alive or dead during a time step
Disease status	Deer disease status indicating no exposure to CWD (i.e., susceptible), exposure to CWD (i.e., exposed and infected but not yet infectious; yes/no) or infected by CWD (i.e., infectious; infected and infectious; yes/no)
Time since infected	A counter tracking the number of days since a deer was initially infected with CWD
Birth interval	A counter tracking number of months since a deer last gave birth
Dispersal interval	A counter tracking number of months since a deer last dispersed

moves into this cell; Fig. 2; Section 2.1.4.8). A proportion of young deer are allowed to move into and away from the assessment area (Section 2.1.4.10; Table 2). Excluding this subset of dispersing deer, if the movement module generates a new location for a deer that is outside of

the study boundary, the model will generate another new location for that deer until one within the study boundary is identified. One time step in the model represents one day. Each month is 30 days (i.e., time steps) in the model and thus each year is 360-time steps.

2.1.3. Process overview and scheduling

The model includes three main processes: (1) free-ranging white-tailed deer population dynamics, (2) deer movement, and (3) disease transmission dynamics applying a Susceptible-Exposed-Infectious-Dead (S-E-I-D) epidemiological framework (Anderson and May, 1991) with an environmental prion component. Fig. 3 shows the order of events implemented at each time step.

2.1.4. Model processes

The processes listed in Fig. 3 are described below.

2.1.4.1. Aging. This process increments age in months of individual deer after 30 daily time steps (i.e., 1 month). If a deer reaches 144 months (i.e., 12 years) of age, the vital status state variable is switched to dead and the individual is removed from the simulation.

2.1.4.2. Birth. The number of fawns born each year is probabilistic for each female deer, independent of the number or proximity to male deer in the model. Births occur between simulated days 121 (May 1) and 150

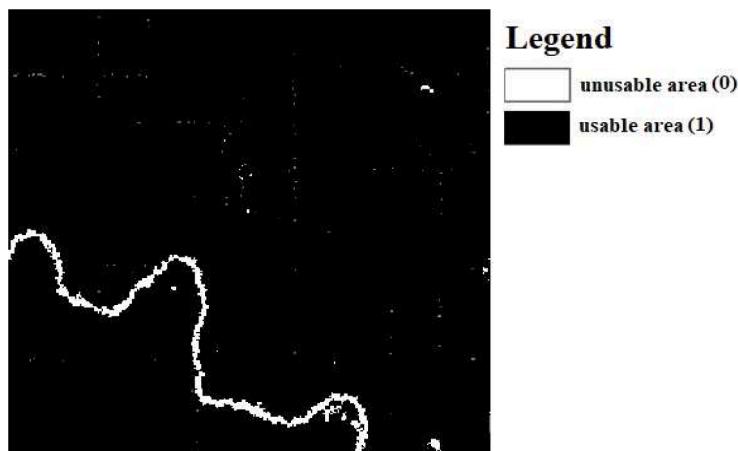


Fig. 1. Map of usable habitat for deer across the 93-km² modeled landscape. Cells with a value of 0 (i.e., white cells) indicate unusable areas, and cells with a value of 1 (i.e., black cells) indicate usable areas. Deer and group centers cannot be located within a cell that has a value of 0.

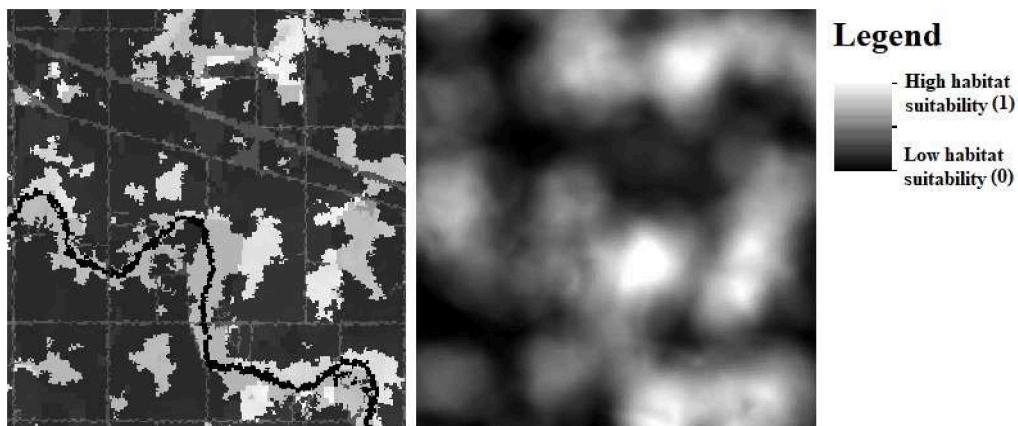


Fig. 2. Map of habitat suitability for deer across the 93-km² modeled landscape. The left panel shows the original resource selection map based on Quinn (2010). The right panel shows a smoothed version of the left panel map using moving window analysis, which was applied to account for neighboring cell suitability values and was ultimately used to guide deer and deer group placement throughout the model. For both maps, white indicates highly suitable areas for deer and black indicates low suitability areas.

Table 2

State variables assigned to model components in the individual-based model for CWD dynamics in free-ranging deer populations.

Model Component	Model Module	State Variable	Default Value(s)
Deer	Demographic	Maximum Age	12 yrs ^a
		Population proportion	12 % ^b
		Adult Males	
		Population proportion	33 % ^b
		Adult Females	
		Population proportion	9 % ^b
		Yearling Males	
		Population proportion	10 % ^b
		Yearling Females	
		Population proportion	36 % ^b
	Parturition	Fawns	
		Average group size	5 ^c
		Adult Birth Rate	1.8 fawns/doe (range = 0–3 fawns) ^{a,d}
		Yearling Birth Rate	1.25 fawns/doe (range = 0–3 fawns) ^a
		Fawn Birth Rate	0.4 fawns/doe (range = 0–1 fawn) ^a
Mortality	Mortality	Fetal Sex Ratio	0.5 ^{d,e,f}
		Adult Male Baseline	0.24 deer/yr ^g
		Non-harvest Rate	
		Adult Female Baseline	0.075 deer/yr ^g
		Non-harvest Rate	
		Yearling Male Baseline	0.28 deer/yr ^g
		Non-harvest Rate	
		Yearling Female	0.28 deer/yr ^g
		Baseline Non-harvest Rate	
		Fawn < 2 Months	0.34 deer/yr ^h
		Fawn 2–12 Months	0.08 deer/yr ^h
		Adult Male Harvest Rate	0.42 deer/yr (97.5 % CI = 0.28–0.56) ^g
		Adult Female Harvest Rate	0.16 deer/yr (97.5 % CI = 0.10–0.22) ^g
		Yearling Male Harvest Rate	0.36 deer/yr (97.5 % CI = 0.21–0.50) ^g
Deer	Movement	Yearling Female Harvest Rate	0.17 deer/yr (97.5 % CI = 0.07–0.28) ^g
		Fall Adult (2–2.5 yr)	0.09 deer/yr ^g
		Male Dispersal	
		Fall Yearling Male Dispersal	0.13 deer/yr ^g
		Spring Adult (2–2.5yr)	0.27 deer/yr ^g
		Male Dispersal	
		Spring Yearling Male Dispersal	0.38 deer/yr ^g
		Spring Yearling Male Immigration & Emigration	0.08 deer/yr ^g
		Direct Transmission	0.017 (range = 0.1–0.2) ^b
		Indirect Transmission	Prion Half-life 48 months ^{i,j}
Disease	General	CWD-associated Mortality	0.055 (range = 0.004–0.1) ^b
	Direct Transmission	Indirect Transmission	0.0003 (range = 0.0001–0.001) ^b

^a Michigan Department of Natural Resources (unpublished).

^b Model-derived or estimated value.

^c Courtney (2023).

^d Green et al. (2017).

^e Mori et al. (2022).

^f Verme (1983).

^g J. Trudeau (unpublished).

^h Rohm et al. (2007).

ⁱ Miller et al. (2004).

^j Tennant et al. (2020).

(June 30) each year. Adult female deer can birth 0 to 3 fawns each year, with a population-level mean of 1.8 fawns per adult female (Table 2; Green et al., 2017). Yearling females average 1.25 fawns with a range of 0 to 3 fawns each year (Table 2). In the Midwestern United States, fawns may also give birth (average=0.4). Each birthed fawn has a 50/50 chance of being born male or female (Verme, 1983; Mori et al., 2022).

2.1.4.3. Birth interval. Female deer in the model are assigned a state variable that tracks the time since last birth to prevent a female deer from giving birth twice within the same birthing period (May–June) each year.

2.1.4.4. Hunter harvest mortality. Deer are exposed to a daily probability of being harvested between October 1 and January 30 each year corresponding to most deer hunting seasons for Midwestern states. We applied estimated sex- and age class-specific harvest rates obtained from a field study conducted on mid-Michigan white-tailed deer (Table 2).

2.1.4.5. Baseline mortality. Deer experience a daily probability of mortality year-around that accounts for deer-vehicle collisions, predation, and other mortality events.

2.1.4.6. Fawn mortality. Fawns are exposed to a fawn-specific mortality function each day during their first year of life (Table 2). Fawns < 2 months of age have a higher daily probability of mortality than fawns aged 2–12 months (daily rates of 0.0057 and 0.00027, respectively; Rohm et al., 2007).

2.1.4.7. Chronic wasting disease mortality. Deer infected with CWD for more than 10 months are subjected to a daily probability of dying from the disease (Table 2; Samuel and Storm, 2016). This function also sets infected deer to dead after they have been infected with CWD for 5 years, as 5 years appears to be the maximum amount of time reported that a cervid has survived following initial infection of CWD (Williams, 2005; Argue et al., 2007).

2.1.4.8. Movement. We incorporated a data-driven deer movement model developed by Butts et al. (2022) using GPS location data from white-tailed deer in central New York (Quinn et al., 2013), which provides foundational rules for how deer move across the modeled landscape. Members of the same group move independently but their movements are biased towards the center of their group. We call this movement ‘within-basin movement,’ as each group center acts as a basin within which the movement of group members occurs.

In addition to within-basin movement, the model produces basin hopping movements, indicating the shift of entire social groups to a new area. We refer to this group movement as ‘basin hops’ (Butts et al., 2022; Quinn, 2010). Thus, group location is dynamic through time. Habitat suitability value of cells influences where deer groups relocate within the study area when they execute a basin hop.

2.1.4.9. Seasonal dispersal. We added a component to the foundational movement model produced by Butts et al. (2022), which allows male yearlings and young adults (age 2–2.5 years) to disperse to new social groups during the spring and fall (Table 2; Trudeau, unpublished data; Nixon et al., 1991). During the months of June and October of each year, each male yearling and young adult has a daily probability of changing social groups equal to the percentage of Michigan deer reported to seasonally disperse an average distance that is less than the spatial extent of the modeled study area (e.g., < 15.5 km for this example) each season (Table 2). The remaining dispersing deer (i.e., deer that disperse beyond the length of the study area) will emigrate from the population (see Section 2.1.4.10). If a deer is chosen by the model to disperse within the study area, a new group will be randomly selected for it to join.

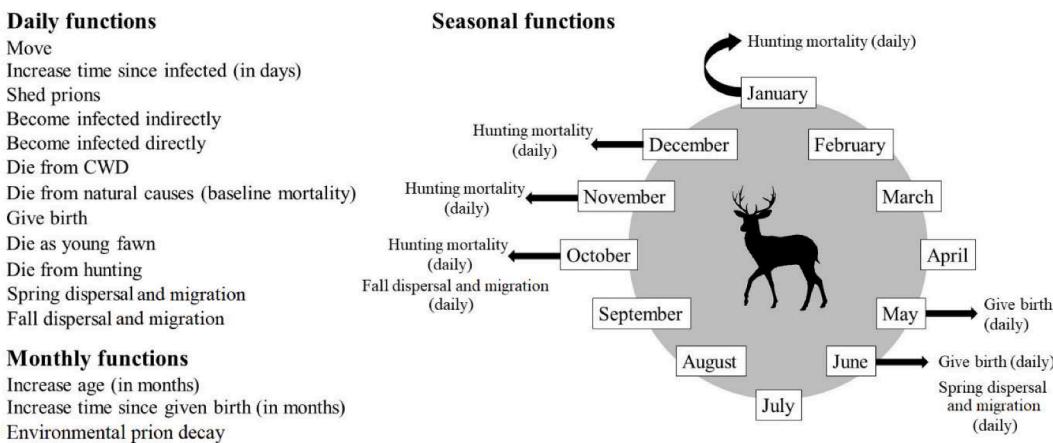


Fig. 3. Scheduling daily and monthly deer population state variables for simulating chronic wasting disease (CWD) dynamics in a white-tailed deer population using an individual-based model.

2.1.4.10. Emigration and Immigration. We mimic an open population by allowing male yearlings and young adults to move in and out of the study landscape during the months of June and October when young deer are most likely to leave their social groups and search for new ones (Trudeau, unpublished data; Nixon et al., 1991). Deer chosen at random to emigrate are removed from the population. During this same period, yearlings and young adults are added to the population at the same rate to simulate immigration into the study area.

2.1.4.11. Direct disease transmission. If two deer are positioned within 25 m of one another during a given time step (i.e., one day), and one is infectious while the other is neither infectious nor exposed, there is a probability that direct disease transmission occurs. The model does not incorporate the seasonal dissolution and reformation of social groups each year nor seasonally dependent contact rates between deer within and among social groups (Schauber et al., 2007; Silbernagel et al., 2011; Williams et al., 2014). To account for seasonal differences in social behavior and contact rates among deer observed in field studies, we multiply the constant direct transmission rate by a monthly coefficient to account for varying probability of contact given proximity based on the time of year and sex and group membership of the two deer (Courtney, 2023; Table 3). To force male prevalence greater than female prevalence each year, we applied a correction factor of 6 (estimated via pattern-oriented modeling) that is multiplied by the contact and direct transmission rates during the months of September through January.

2.1.4.12. Prion deposition. Deer infected with CWD for longer than 90 days become infectious during a randomly determined time step that falls between day 90 and 180 post-infection (Henderson et al., 2015). Once infectious, a deer will shed prions into grid cells it occupies during each time step. In addition, death of an infectious deer results in deposition of prions into the grid cell where it died. The number of prions deposited from a carcass or live deer at each time step is a function of amount of time the deer has been infected (Henderson et al., 2015).

For each deer in a given grid cell during a given time step t , we estimate the number of prions deposited into that cell as:

$$p_L = \frac{t_{DPI}}{30} + 1,$$

and

$$p_D = 50 \left[\frac{t_{DPI}}{30} + 1 \right]$$

where p_L is the daily number of prions shed by a live deer, p_D is the number of prions shed by a dead deer during the time step its death occurred, and t_{DPI} is the total number of days that the deer has been infected with CWD (i.e., days post initial infection). We divide t_{DPI} by 30 to allow the number of prions shed by deer to increase monthly instead of daily. We assume that deer shed 50 times the number of prions into the environment during one time step at death than when alive.

2.1.4.13. Indirect disease transmission. If a susceptible deer moves into a contaminated grid cell where infectious deer deposited prions during a previous time step, there is a probability that the susceptible deer becomes infected with CWD. We apply a negative exponential relationship to represent the probability of indirect transmission during a given time step given the density of prions in each cell:

$$p_{IT}(\alpha, n, dt, v) = 1 - e^{-\alpha N/V},$$

where α represents the user-defined rate at which prions affect deer, N represents the number of prions in the cell, and V represents the area of the cell. Rates of indirect disease transmission for CWD remain unknown so we ran the model using a wide range of parameter values and applied pattern-oriented modeling with reported annual prevalence rates to determine a range of suitable values (Table 2).

2.1.4.14. Prion decay. We allow prions that have been deposited into

Table 3

Monthly coefficients used to adjust the constant monthly rate for direct transmission of chronic wasting disease (0.017) to account for changes in the probability of two deer contacting each other by season and sex. Coefficients are estimated from empirical deer observations in the southern portion of the Lower Peninsula of Michigan, USA (Courtney, 2023), where lower coefficients correspond to lower likelihoods of direct contact. Females are further categorized as group and non-group members to account for potential differences in contact rates.

	Jan	Feb	Mar	April	May	June	July	Aug	Sept	Oct	Nov	Dec
Male-male	0.034	0.034	0.034	0.034	0.051	0.051	0.051	0.119	0.119	0.017	0.017	0.017
Male-female, female-male	0.034	0.034	0.034	0.017	0.017	0.017	0.034	0.034	0.034	0.085	0.034	0.034
Female-female												
Group members	0.119	0.119	0.119	0.068	0.034	0.017	0.017	0.068	0.068	0.068	0.068	0.068
Non-group members	0.051	0.051	0.051	0.017	0.017	0.017	0.017	0.017	0.017	0.017	0.017	0.017

the environment to decay over time with a half-life of 4 years (i.e., 48 months), which produces a monthly decay rate (r) of 0.0144 using the following equation:

$$r = -\frac{\ln\left(\frac{1}{2}\right)}{t},$$

where t represents prion half-life in months. To implement this decay function in the model, we multiply the prion concentration of each cell by $(1-r)$ after each month.

2.1.5. Initialization

We initialized the model with 1250 deer in a 93 km² study area in Clinton County, Michigan, USA (~13.5 deer/km²) and a sex-age structure of 15 % adult males, 45 % adult females, 7 % yearling males, 8 % yearling females, and 25 % fawns, taken from a sex-age-kill (SAK) model developed by Michigan Department of Natural Resources (MDNR, unpublished) for the mid-Michigan region.

Habitat usability and suitability for the modeled landscape are depicted in two spatial layers (Figs. 1, 2). These habitat variables guide placement of deer and deer group centers simulated in the model. We started the model with composition values for the deer population estimated by the MDNR SAK model for each sex and age class. We then assessed how those values changed after each year as an emergent property of the model. Once the composition remained relatively constant (< ±1 %) for each sex and age class across years (i.e., 4 years), we considered population composition stabilized and used those values as initial composition values of the modeled deer population for all analyses (Table 2). For each variable in the model, default values were based on field studies conducted within the study area or literature for free-ranging white-tailed deer populations in Michigan or other agriculture-forested regions (Table 2). We initialize an outbreak of CWD by introducing an infectious CWD-infected yearling male deer into the simulated population at model initialization (i.e., time step 0).

2.2. Model parameterization and calibration

We parameterized and verified our model at the individual and emergent collective levels to determine the realism and applicability of this model (Dion et al., 2011). We monitored the number of deer that reached their maximum lifespan (i.e., 12 years) and the number of deer that reached maximum disease duration (i.e., five years) after each simulation. The literature reports that few deer should reach these maximum life and disease spans in Midwestern regions of the USA (Table 2).

To understand disease dynamics, we calculated prevalence as the number of infectious and exposed deer divided by the total population size during a given time step. We also calculated sex-specific prevalence of CWD. We recorded the total number of direct and indirect transmission events that occurred after each time step and the number of CWD-related mortality events. As a proxy for geographic spread of CWD, we calculated the proportion of cells with shed prions (i.e., where infected deer inhabited the study area). We verified the disease model at the emergent collective level by calculating prevalence of CWD after each year and compared the model predictions to annual apparent prevalence rates reported by wildlife agencies within the Midwestern USA. We developed a range of possible estimates for each disease variable by excluding values that led to population extirpation, CWD prevalence greater than observed by wildlife agencies, or consistent disease extirpation in the model. We then chose the best estimate within each range based on reported annual prevalence from field studies.

Based on verification of disease dynamics produced by the model, we calibrated estimates for the unknown parameters in the model: direct and indirect transmission rate and disease mortality rate (Table 2). We refer to these estimates as default values and used these values in the

baseline scenarios. We also identified a range of possible values around the default value for each parameter (Table 2). Once we obtained best estimates for the unknown disease parameters, we calculated Spearman correlation coefficients to quantify the degree of association between observed and model-predicted annual rates of CWD prevalence.

2.3. Data analysis

We identified the number of repetitions needed for model convergence by evaluating stability of average CWD prevalence at year 50 as the model output. We produced 500 model repetitions and calculated the average value of the output iteratively across repetitions, starting with two and ending at the 500th repetition. Successful stabilization of model output was achieved once changes in prevalence of CWD at year 50 were less than 0.001 after adding subsequent model repetitions.

We quantified uncertainty and sensitivity of variables in the model via a global sensitivity analysis. We employed a mixed-method technique recommended for computationally expensive IBMs with many (10+) variables and interactions among those variables (Campolongo et al., 2011; Pianosi et al., 2016; Ligmann-Zielinska et al., 2020). To save on computation time, we assessed model sensitivity for 15 of 18 parameters, excluding adult male seasonal dispersal and migration and fawn (0–2 month) mortality (Table 4). Adult male seasonal dispersal and migration rates were lower than yearling male seasonal rates, so we assumed the model would be similarly sensitive, if not less so, to the adult movements. We excluded fawn (0–2 month) mortality because there are few realistic management options to affect 0–2-month-old fawn mortality to reduce CWD prevalence. The model output we used to conduct the sensitivity analysis was prevalence of CWD at model year 20.

We used an elementary effects method (i.e., Morris method) as a screening method to initially identify order of variable influence on estimates of CWD prevalence at year 20, identify variables involved in input interactions, and identify which variables were non-influential inputs and could be omitted from further sensitivity analyses (Morris, 1991, 2006). Second, we conducted a global variance-based decomposition, which decomposes the output variance and assigns partial variances to the inputs and their interactions, on the inputs found influential by the Morris method (Saltelli et al., 2008; Ligmann-Zielinska and Sun,

Table 4

Triangular distributions of variable estimates specified for each of 15 model variables assessed by the Morris screening method within the global sensitivity analysis (Kotz and van Dorp, 2004). Initial variable values were drawn at random from the listed range of values. We report daily rates in this table except for deer group number and prion half-life, which is in months.

	Minimum value	Maximum value	Most likely value
Deer group number	50	630	251
Direct transmission rate	0.0001	0.002	0.00052
Indirect transmission rate	0.0001	0.002	0.00065
Prion shedding rate	0.001	20	1
Prion half-life (months)	3	120	48
Disease mortality rate	0.00005	0.002	0.00015
Harvest mortality rate			
Adult male	0.0002	0.007	0.0031
Adult female	0.0002	0.007	0.0013
Yearling male	0.0002	0.007	0.003
Yearling female	0.0002	0.007	0.00144
Fawn mortality (2–12 months)	0.0002	0.003	0.0012
Immigration & emigration rate (male yearlings)			
Spring	0	0.03	0.00267
Fall	0	0.03	0.00267
Dispersal rate (male yearlings)			
Spring	0	0.03	0.01267
Fall	0	0.03	0.00433

2010; Zhang et al., 2019). We employed Sobol' quasi-random sampling, also referred to as radial sampling, to reduce computational cost by producing more evenly distributed samples and to ensure that the entire model input space was assessed (Sobol', 1993; Saltelli et al., 2008). A full description of the global sensitivity analysis is provided in Supplementary Text S3.

3. Results

Our IBM reproduced short- and long-term population dynamics characteristic of Midwestern white-tailed deer, as represented by seasonal population fluctuations within each year and stationarity of the population across years (Fig. 4). Confidence intervals around the average total population size increased through time in response to compounding stochasticity associated with birth and death events each year (Fig. 4). In addition, our model reproduced long-term CWD dynamics observed in field observations reported from endemic areas of Wisconsin (Wisconsin Department of Natural Resources, 2023; Fig. 5). Visual displays for three time periods illustrate deer locations and density of prion deposition (Fig. 6). Our assessment of model convergence identified stabilization of model output after 322 repetitions (Fig. 7). Therefore, we report results that are averaged across 350 model repetitions to account for stochasticity in the model. The proportion of deer in each sex and age class in the simulated deer population took three years to stabilize when CWD was not introduced in the model. The population stabilized at 33 % adult females, 12 % adult males, 10 % yearling females, 9 % yearling males, 18 % female fawns, and 18 % male fawns.

Out of 350 model repetitions, CWD persisted (i.e., prevalence >0.1 % at year 50) in 100 (28.6 %) model simulations after the introduction of one infected deer. For the model runs where CWD persisted, total population size decreased 0.5 % by year 10, 7.7 % by year 25, and 87.1 % by year 50 following initial introduction of CWD in the population (Fig. 8). In 102 of the 350 model repetitions (29.1 %), the outbreak of CWD ended at least once (i.e., 0 infected deer by the end of a year) after persisting for at least the first year. In those 102 model repetitions, there were 118 individual events where the outbreak ended, indicating that the outbreak ended and restarted multiple times during some model runs. The percentage of outbreaks that ended but led to reintroduction of CWD via indirect transmission through environmental prions was 23 %. CWD was reintroduced and faded out up to three times within an individual model run. Year 5 was the mean year when outbreaks were most likely to end (mean=5.0, median=3.0, SD=4.2, range=1–23 years). For outbreaks that ended after persisting for at least one year, highest prevalence of CWD reached was 1.47 %. Reintroduction events via indirect transmission ranged between 1 and 17 years following the last year of the previous outbreak of CWD.

After 50 years following introduction of the disease and for the 29 %

of cases where CWD persisted in the landscape (93 km²), final deer population size averaged 170 (a population decline of 86 %). Mean prevalence of CWD was 0.4 %, 3.4 %, 27.7 %, 58.9 %, 60.7 %, and 51.8 % after the first, tenth, twentieth, thirtieth, fortieth and fiftieth years, respectively (Fig. 9). The difference between prevalence for males and females increased during the first 30 years followed by a decrease around year 35 post-initial infection, with 5.3 % and 2.3 % after year 10, 37.0 % and 22.4 % after year 20, 69.5 % and 52.9 % after year 30, 69.5 % and 55.5 % after year 40, and 59.1 % and 47.3 % after year 50, respectively (Fig. 9). The Spearman correlation coefficient assessing the degree of association between observed prevalence values reported annually by the Wisconsin Department of Natural Resources (2023) and our model-predicted prevalence values was 0.9, 0.988, 0.985, and 0.994 when assessing the first 5, 10, 15, and 21 years, respectively, following initial introduction of CWD (Fig. 5). Apparent prevalence rates are reported for only 21 years in most counties in Wisconsin, so we could not compare reported rates to the model-derived rates beyond 21 years. Although wildlife agency reports of sex-specific prevalence differ in their extent spatially and temporally, (Illinois Department of Natural Resources, 2023; Government of Alberta, 2023), and Saskatchewan (Saskatchewan, 2023) report 40 %, 54 %, 67 % higher prevalence rates, respectively, in male white-tailed deer than females.

3.1. Model parameterization and calibration

Numbers of exposed and infectious deer, prevalence, the proportion of the study area affected by prions, and the numbers of direct and indirect transmission events were calculated only for model runs where CWD persisted in the population (29 % of total runs). We found that direct transmission of CWD was higher than indirect transmission as time progressed (but direct transmission estimates were highly uncertain; Fig. 10). Our model predicted an average (lower 2.5 % and upper 97.5 % quantiles) of 3027 (102, 5395) direct transmission events and 538 (18, 773) indirect transmission events after 50 years (Table 5). The average (2.5 %, 97.5 % quantiles) number of deer that reached their maximum lifespan after running the model 350 times was 134 (128, 181). The average number of infected deer that reached five years post-initial infection (i.e., maximum disease timeline) was 470 (2, 590), which was 15.5 % of the total number of deer that became infected with CWD throughout the 50-year simulation. The model estimated an average (2.5 %, 97.5 % quantiles) of 245 (2, 335) CWD-related mortalities, and 120 (1, 183) infected deer emigrated away from the study area (Table 5). The mean proportion of grid cells making up the study area that contained shed prions at 50 years post-initial infection was 0.57 (0.02, 0.66; Table 5).

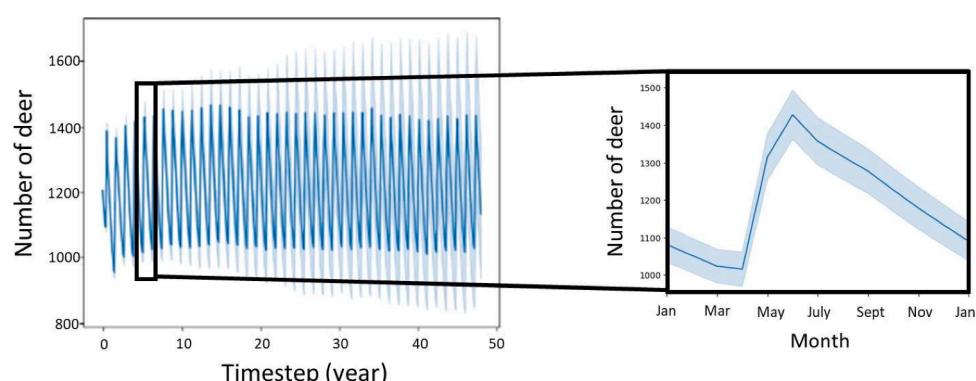


Fig. 4. Average (with 95 % confidence intervals) total population size (deer/93km²) for 50 years predicted by the individual-based model for a Michigan white-tailed deer population unaffected by chronic wasting disease estimates from 350 model runs.

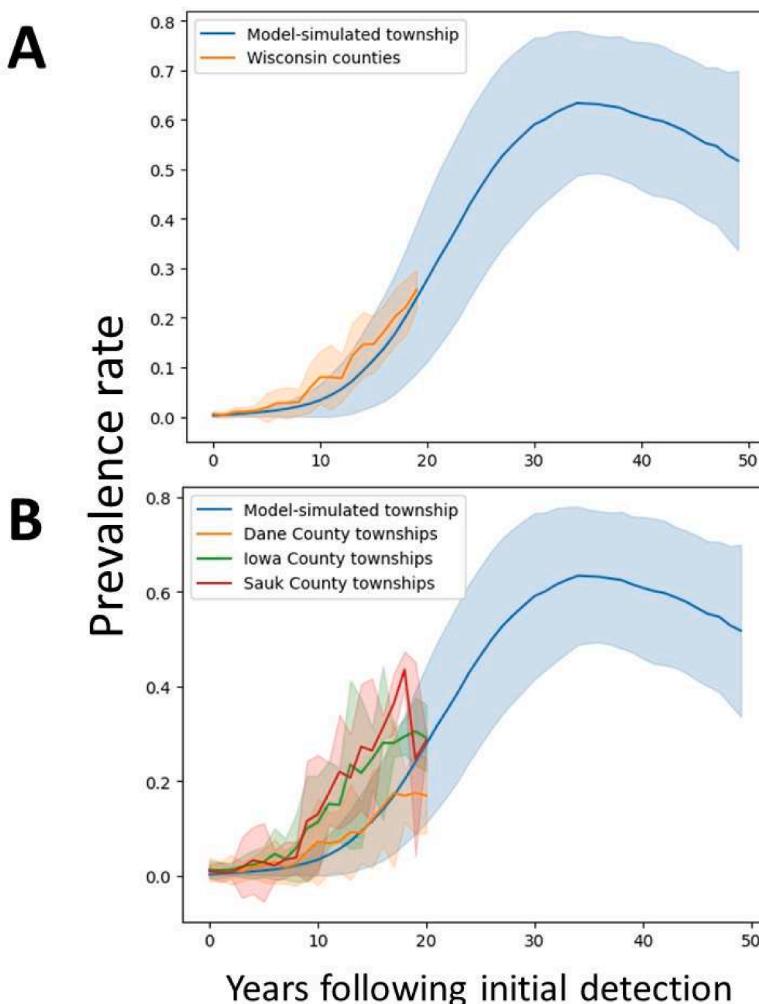


Fig. 5. Annual prevalence of chronic wasting disease (CWD) in a Michigan white-tailed deer population simulated by the individual-based model and average apparent prevalence calculated for CWD-affected counties in Wisconsin. We calculate an average annual rate at the county level for each year following initial detection for Columbia, Dane, Green, Iowa, Lafayette, Richland, and Sauk counties ($r = 0.994$; Fig. 5A). We calculate average annual rates at the township level for Dane, Iowa, and Sauk counties ($r = 0.923$ – 0.990 ; Fig. 5B). We calculated mean prevalence and 95 % confidence intervals for the 100 simulated model repetitions that resulted in an outbreak of disease. The shaded areas indicate 95 % confidence intervals for each dataset.

3.2. Global sensitivity analysis results

The Morris screening method identified three variables that did not influence prevalence of CWD after 20 years based on their mean total effect values and, thus, were excluded from further sensitivity analyses: group number, prion half-life, and prion shedding rate (Table 6). To reduce computation time, we also excluded spring dispersal rate, which ranked fourth lowest (Table 6). CWD mortality rate had the largest total and interaction effect values on CWD prevalence at year 20 (Table 6). Indirect and direct transmission rates ranked second and third, respectively, for total and interaction effects (Table 6).

Due to computational limitations, we could not complete enough model runs to account for all model variation and, thus, to achieve model convergence necessary to calculate first-order S_i indices for each factor. Therefore, we only present the amount of model variance contributed by each variable but not the extent of interactive effects driving the variance (Table 7). Adult female harvest was the largest contributor to variation in CWD prevalence for all model years assessed (i.e., years 5, 10, 15, and 20; Fig. 11). Yearling female harvest rate accounted for the second most variation observed in CWD prevalence at years 10, 15, and 20. Fall immigration and emigration rate was second most influential on CWD prevalence in model year 5 (Fig. 11). Yearling and adult male harvest rates were least influential on CWD prevalence

for model years 5, 10, 15, and 20.

4. Discussion

We developed an IBM for predicting CWD dynamics in free-ranging deer based on deer and disease model components and assess the effects of each of those components through a rigorous sensitivity analysis. The deer component includes modules that represent population-level processes of demographics, parturition, mortality, and movement. The disease component includes modules for disease-related mortality, and direct and indirect transmission. Complexities of the deer-CWD system make modeling challenging (Uehlinger et al., 2016), but development of IBMs and high-performance computing has advanced our ability to portray these systems. The IBM described herein mimicked CWD disease dynamics in deer to year 21 (temporal extent of available validation data).

Individual-based frameworks have been used to model chronic wasting disease in the past (Belsare et al., 2020; Kjaer and Schaub, 2022), and we provide comparisons to those models in the following paragraphs. However, we expand on modeling of CWD dynamics by coupling our IBM with a two-step global sensitivity analysis to further explore the effects of each system process on disease dynamics. The sensitivity analysis indicated that some deer population processes, such

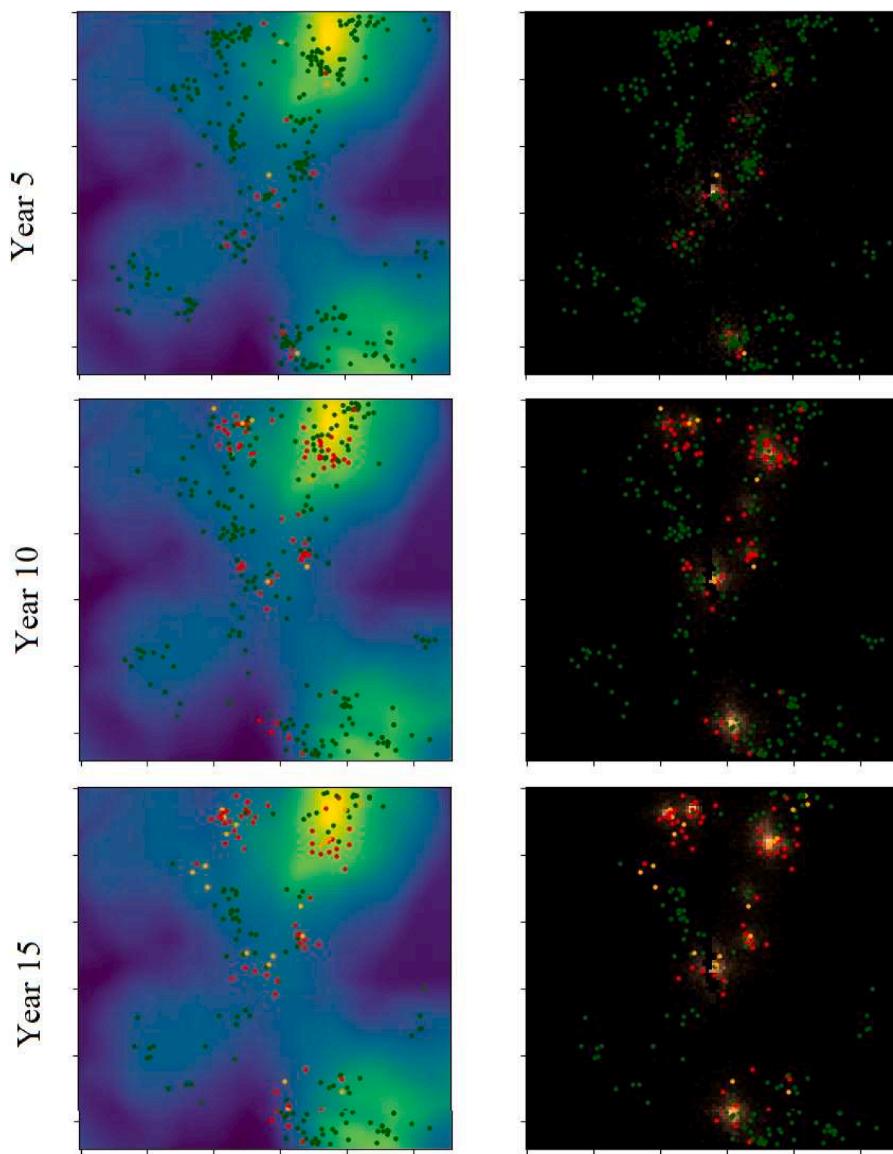


Fig. 6. Location of modeled deer after the fifth, twenty-fifth, and fiftieth model year on the habitat selection (left panel) and environmental prion map (right panel). Deer are indicated by points on each map. Green points indicate deer unaffected by but susceptible to chronic wasting disease (CWD). Newly infected deer that are not yet infectious are indicated by orange points and infected and infectious deer are colored red. Infectious deer shed prions into the landscape, indicated by the change in colors of cells on the prion map. Cells change from black to dark brown to light brown in cells where prions are shed.

as female harvest rates and fawn mortality rate, had a larger impact on CWD prevalence than disease processes. The model also indicated that prion half-life, prion shedding rate, and deer group membership (a variable representing the social structure of deer sub-groups) had minimal influence on CWD prevalence at year 20. Sensitivity analysis indicated that adult and yearling female harvest rates explained the greatest amount of variation in CWD prevalence between years 8 and 20. Collectively, model results indicate that females are a demographic group that has a large effect on CWD dynamics in Michigan and this effect increases with age (i.e., adult females affect CWD prevalence most and fawn females affect prevalence least).

An important part of model development includes verification and validation (Augusiak et al., 2014). The IBM reproduced individual-level deer processes and macro-level population and disease dynamics typically observed in Midwestern white-tailed deer populations for 20 years. Our IBM found that a small proportion of the simulated deer remained alive for 12 years, consistent with observed longevity for Midwestern deer (Michigan Department of Natural Resources, unpublished).

Furthermore, we demonstrated that total number of modeled deer in the absence of CWD fluctuated annually and remained relatively stable over the 50-year model horizon. This pattern corresponds to population dynamics commonly observed in white-tailed deer populations inhabiting mixed agricultural and forested regions, particularly within the U.S. (Rosenberry et al., 2011). Thus, the deer demographic component of the IBM functioned as expected. We validated individual-level CWD processes by comparing the number of modeled deer that died from CWD-associated mortality and reached their maximum disease timeline (i.e., five years post initial infection) to published literature or independently collected field data from Wisconsin. Deer apparently do not live ≥ 5 years after CWD initial infection (Williams, 2005).

We hypothesized that direct CWD transmission events primarily drive CWD dynamics as the disease emerges in a population, whereas indirect transmission events remain low and are less influential until the disease becomes endemic in later years (>50 years). Modeled disease dynamics reflected these patterns. The proportion of modeled grid cells containing shed prions increased through time along with annual CWD

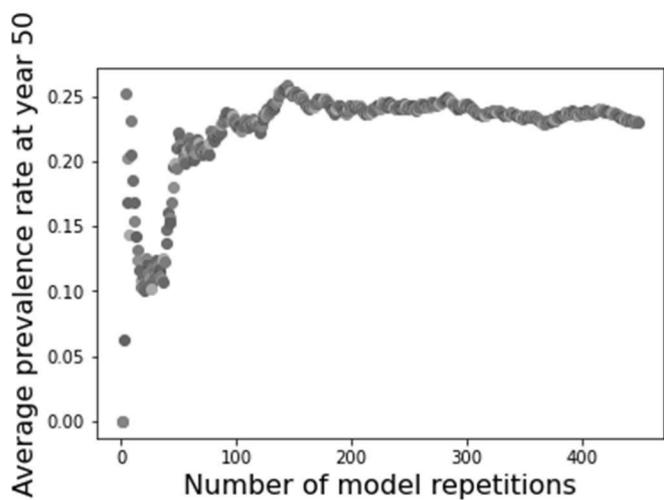


Fig. 7. Average prevalence of chronic wasting disease (CWD) after year 50 in the individual-based model calculated iteratively across 500 model repetitions to assess convergence (i.e., stability) of model output. Model output stabilizes (i.e., average model output does not change by >0.001 with subsequent repetitions) at 322 model repetitions.

prevalence (Spearman correlation coefficient = 0.863 for the first 50 years). Thus, it appears that indirect transmission grows proportionally with direct transmission over time.

We reported CWD prevalence values after each time step and compared those values to annual prevalence rates reported by the Wisconsin Department of Natural Resources. Our model CWD prevalence values were highly correlated (i.e., $r = 0.994$) with prevalence rates reported at the township level and averaged over six counties in Wisconsin for 21 years. The correlation between modeled and observed CWD prevalence was higher for the 21-year period compared to shorter duration (5–15 years). The lower correlation for earlier years suggests that our model is slightly better at predicting long-term CWD dynamics rather than dynamics occurring soon after initial infection. However,

this part of the model validation is complicated by potential variations in field data collection over time. In the years following initial detection of CWD in Wisconsin, surveillance and sampling efforts focused in the immediate area where CWD was first detected, which was labeled the CWD eradication zone (Heberlein, 2004). As CWD spread into new townships and counties, we suspect that apparent prevalence values were generated from smaller sample sizes until sampling capacity increased.

Annual CWD prevalence growth rate was 1.1 % for infected Wisconsin deer populations when apparent CWD prevalence was 5–15 % (Heisey et al., 2010). In our model, prevalence values between 5 and 15 % were observed for model years 12–16, with a mean annual CWD growth rate of 1.9 %. In the western U.S., annual growth rates of 1.15 % (Almberg et al., 2011) and 1.2–1.25 % have been estimated (Miller and Conner, 2005). Trends in reported prevalence in Colorado indicate slow increases until an inflection point is reached at a rate of approximately 5 %. Once reached, exponential acceleration in prevalence occurs (Miller et al., 2000; Colorado Parks and Wildlife, 2018). In an area endemic with CWD in Wyoming and which took a hands-off approach to CWD management, the state agency reported an increase in prevalence from 11 % to 36 % in ten years (Almberg et al., 2011). It took our model eight years (model year 15 to year 22) for prevalence of CWD to grow from 11 % to 35 %.

Many states within the U.S. report apparent prevalence of CWD in male cervids as 2- to 3-times greater than prevalence in females within a population (Miller and Conner, 2005; DeVivo et al., 2017; Samuel and Storm, 2016; but see Edmunds et al. 2016). By accounting for differences in monthly contact rates within and between different sexes of deer in the modeled population and applying a correction factor to males for indirect and direct CWD transmission, our goal was to reproduce these sex-specific trends in prevalence of CWD. We were able to produce higher prevalence among males consistently in our model, although the difference between male and female rates shrunk through time. Most wildlife agencies do not report male versus female apparent prevalence within a population. For the agencies that do, rates are often aggregated at larger spatial scales. Illinois Department of Natural Resources (IDNR) reports a ~75 % higher statewide prevalence for males during a 20-year period (2003–2023; IDNR 2023). For the 2022–2023 hunting season,

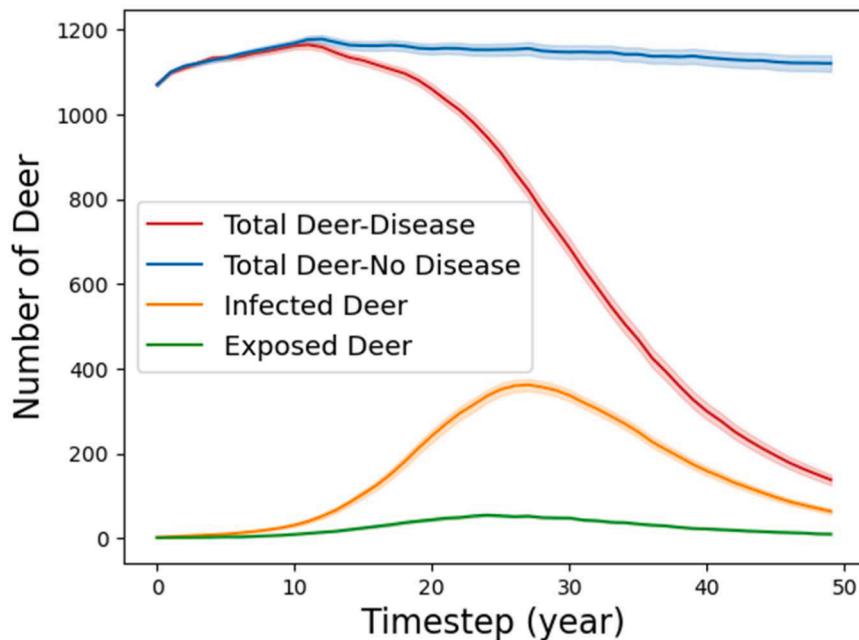


Fig. 8. Annual mean values (and 95 % confidence intervals) for total deer with chronic wasting disease (CWD) present in the population ('Total Deer – Disease'), total deer in an unaffected population ('Total Deer – No Disease'), total infected deer, and total exposed deer simulated and averaged over the 100 simulations where CWD persisted in the modeled population in the individual-based model. The shaded areas indicate 95 % confidence intervals around the annual mean values.

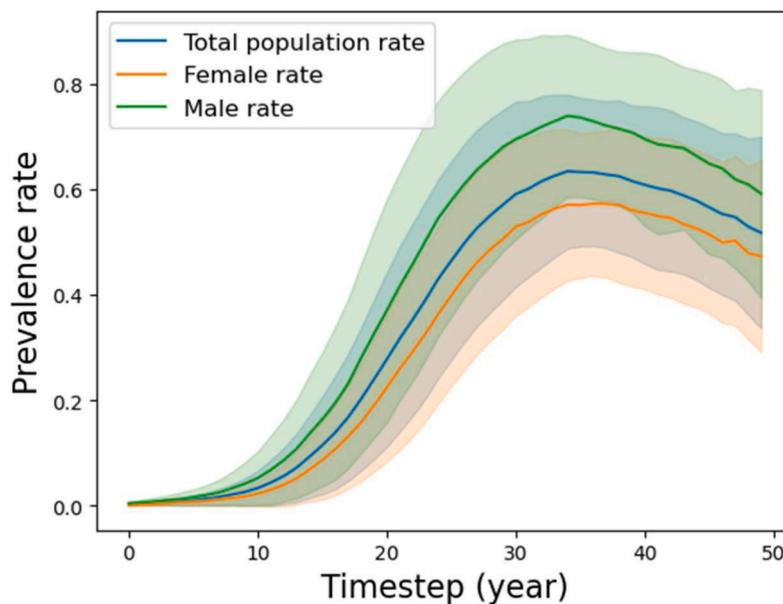


Fig. 9. Annual sex-specific prevalence of chronic wasting disease in the white-tailed deer population simulated in the individual-based model. The shaded areas indicate 95 % confidence intervals around the annual mean values.

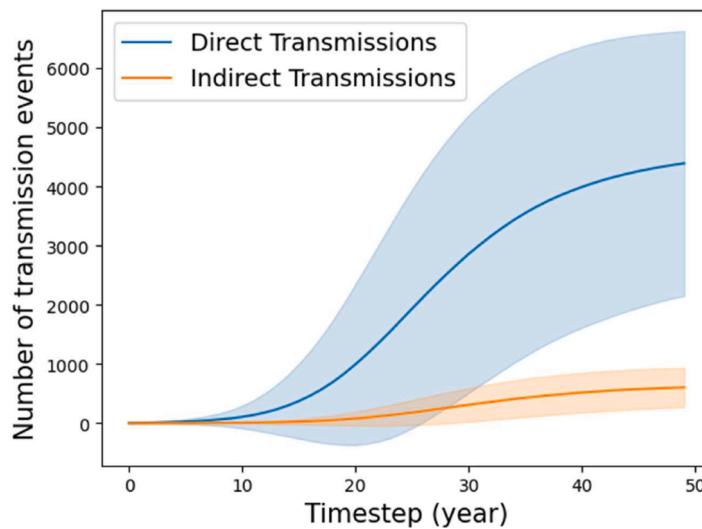


Fig. 10. Cumulative number of direct and indirect transmission events occurring in a population of free-ranging white-tailed deer infected with chronic wasting disease (CWD) in the individual-based model. The solid lines indicate the mean total number of events after each year across the 100 repetitions of the model where persistence of CWD occurred. The shaded areas indicate 95 % confidence intervals around the annual mean values.

the Government of Alberta reported 54 % higher prevalence statewide in male white-tailed deer than females ([Government of Alberta, 2023](#)). Similarly, in a subset of wildlife management zones chosen based on sufficient surveillance sampling (>5 males and >5 females), three-year pooled prevalence estimates measured a 67 % higher prevalence for male white-tailed deer ([Saskatchewan, 2023](#)).

It remains relatively unknown how differences in CWD prevalence among male and female white-tailed deer within a population change over time. [Illinois Department of Natural Resources, 2023](#) reports this difference for each hunting season, and it appears the statewide male apparent prevalence values have remained about 40 % greater than female prevalence for 20 years (2003–2023) with annual fluctuations but no long-term trends. We provide three hypotheses for observing a shrinking difference in male and female prevalence after year 35 in our model. Our first hypothesis is that our model calculates true prevalence whereas wildlife agencies calculate and report apparent rates that are

biased by sampling strategy and amount. It may be the case that deer populations are also experiencing this decreased difference in male and female prevalence through time, but agencies cannot detect it using current surveillance methods. Sampling strategies, such as the methods used by state wildlife agencies, can be explored in this model to test this hypothesis. Second, our model predicts differences in prevalence values for 50 years following the initial introduction of CWD into a deer population. Most wildlife agencies, such as those in the Midwest, have only detected the disease within the last 20–25 years. These agencies may start to observe a decline in sex-specific differences in prevalence later in the disease epidemic. Last, if male prevalence remains consistently higher than female prevalence through time, we expect that we underestimated the magnitude of male-male interactions or overestimated the magnitude of male-female interactions each year despite generating monthly contact coefficients that were based on observational field data within the study area. In recent years, researchers are finding that deer

Table 5

Chronic wasting disease (CWD) outcomes produced by the individual-based model after model year 50 summarized with means, standard deviations, medians, and upper (97.5%) and lower (2.5%) quantiles.

Model output	Mean	SD	Median	2.50%	97.50%
CWD prevalence (%)	52	19	53	20	81
Male CWD prevalence (%)	59	20	63	18	88
Female CWD prevalence (%)	47	18	47	16	79
Total deer	163	107	115	54	523
Total CWD-related deaths	245	103	269	2	335
Total deer that reached maximum disease lifespan	470	162	532	2	590
Proportion of cells with shed prions	0.57	0.13	0.60	0.02	0.66
Total direct transmission events	3,027	1,141	4,714	102	5,395
Total indirect transmission events	538	169	645	18	773
Total number of infected deer that emigrated out of study area	120	43	133	1	183

Table 6

Mean total effect (μ^*) and interaction effect (σ) measures calculated for each input variable in the individual based model used for predicting CWD prevalence at year 20 in deer assessed using the Morris screening method. Variables are ranked from highest to lowest μ^* value. Variables in bold were determined to be uninfluential input parameters based on their low μ^* value and removed from further model sensitivity analyses.

Parameter	μ^*	σ
CWD mortality	3871	10699
Indirect CWD transmission	2589	4977
Direct CWD transmission	2322	4224
Fawn (2-12 months) mortality	1856	3892
Adult female harvest	1519	2871
Yearling female harvest	1131	2579
Adult male harvest	699	1402
Yearling male harvest	655	1361
Fall immigration & emigration	469	1043
Spring immigration & emigration	337	725
Fall dispersal	240	569
Spring dispersal	182	330
Prion shedding rate	0.595	2.135
Prion half-life	0.054	0.151
Group number	0.007	0.014

Table 7

Total effect indices (i.e., normalized ST values) derived from the global sensitivity analysis of the individual based model for predicting chronic wasting disease (CWD) dynamics. The analysis uses a variance decomposition approach based on Sobol' sampling. Table values represent total amount of variance in predictions of CWD prevalence at model years 5, 10, 15, and 20, attributed to each model input factor. ST values are ordered from highest to lowest based on model year 20 values generated by the individual-based model.

Model factor	ST values			
	Year 5	Year 10	Year 15	Year 20
Adult female harvest	0.194	0.186	0.160	0.150
Yearling female harvest	0.102	0.128	0.115	0.123
Fawn (3-12 months) mortality	0.082	0.091	0.111	0.101
Fall immigration & emigration	0.126	0.098	0.095	0.093
Indirect CWD transmission	0.068	0.065	0.076	0.089
Direct CWD transmission	0.073	0.124	0.111	0.085
Adult male harvest	0.056	0.042	0.055	0.078
CWD mortality rate	0.082	0.082	0.073	0.076
Fall dispersal	0.107	0.084	0.087	0.072
Spring immigration & emigration	0.063	0.061	0.062	0.070
Yearling male harvest	0.048	0.040	0.056	0.065

signposts (e.g., scrapes, rubs, and licking branches) serve as reservoirs for prions in the environment and may play an important role in indirect transmission of CWD among male white-tailed deer during the rut, which may be a factor contributing to greater apparent prevalence reported and sustained over time for male deer (Egan et al., 2023; Hearst et al., 2023; Huang et al., 2024). It is possible to account for this chemical communication behavior among males during the rut and explore their effects on CWD dynamics by incorporating seasonal sex-specific indirect transmission rates into the model (Alexy et al., 2001). To force male prevalence at least 1.5 times greater than female prevalence, we included a correction factor, which was multiplied by direct transmission and contact rates when a susceptible male made contact with an infected individual, regardless of the sex of the infected deer, in September through January. We chose to add this correction factor during September through December because this period captures rut behavior and poor body condition by adult males, which are two possible reasons for higher prevalence reported for males (Hewitt, 2011). However, this correction factor was not sufficient to keep male prevalence at least 1.5 times greater than female prevalence across the 50-year model simulation.

A limitation to consider when comparing CWD prevalence generated by a model to rates reported by wildlife agencies is that we are comparing a true rate (i.e., modeled) to an apparent one (i.e., from agency field data collection). Agencies cannot compute true prevalence of a wildlife disease; they rely on apparent rates, which are estimated from a subsample of the affected population. This subsample is typically the number of deer that are harvested or collected via other disease sampling methods and tested for CWD each year. The total size of the subsample used to calculate apparent prevalence values and its precision changes each year in response to sampling intensity and bias (e.g., male dominated harvests). Factors affecting sampling intensity include hunter participation, such as the number of deer harvested that year, and harvest-associated regulations, such as mandatory testing of harvested deer.

When calculating and reporting apparent prevalence of CWD, we risk under or over reporting the extent of the disease in an area (i.e., directional bias), and the direction of this bias is scale dependent. Chronic wasting disease in free ranging cervid populations is spatially clustered and not uniformly distributed across an infected population, as is the case with most transmissible diseases (Joly et al., 2006; Osnas et al., 2009; Walsh, 2012; Hedman et al., 2020). If deer tested for CWD are not located within a clustered diseased area, which can be the case when relying on hunter-harvested and roadkill deer, the disease will be underreported. If a wildlife agency is successful in its ability to locate the origin or center of the outbreak and tests deer from that area more but reports it at a larger scale, such as at a county level, there is an opportunity to over report the disease. The former scenario is a common issue for agencies. Chronic wasting disease is rarely detected soon after its introduction to a population, therefore making it difficult to locate the center of the outbreak (Hefley et al., 2017; Cook, 2020). In addition, CWD is often managed and reported at the county scale or greater. If CWD is detected in a localized area within a county but sampling is not targeted and conducted arbitrarily across the entire county, the apparent prevalence value will be an underestimate of true prevalence.

The Morris screening method for model sensitivity testing revealed that most of the variables associated with indirect transmission of CWD, but not indirect transmission rate itself, were not influential on prevalence of CWD after 20 years. This implies that direct transmission of CWD still has a greater influence on disease dynamics 20 years into the epidemic. As the disease enters an endemic state and as more deer become infected with CWD and advance into later stages of infection, more prions are shed into the environment and create additional opportunities for indirect disease transmission. At that time, shedding rate and half-life of prions may become more influential on disease dynamics. However, results from the global variance decomposition analysis complicate this finding. Indirect transmission rate had greater

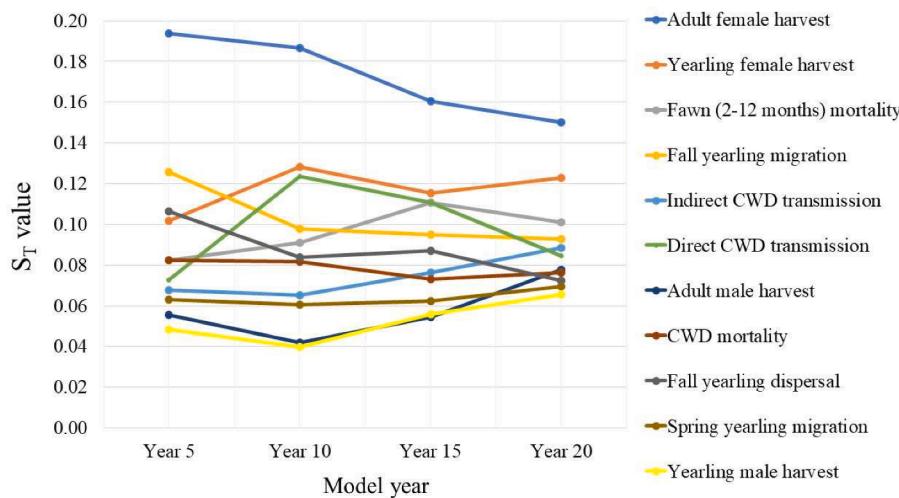


Fig. 11. Changes in total effect indices (i.e., normalized S_T values) derived from the global sensitivity analysis, which applied a variance decomposition approach using Sobol' sampling, indicating the total amount of variance in model output, chronic wasting disease (CWD) prevalence, attributed to each input factor across model years 5, 10, 15, and 20.

influence than direct transmission on prevalence at year 20, albeit the values were similar (0.089 and 0.085).

The sensitivity indices calculated for each model input by the Morris method and the variance decomposition analysis do not provide the same results. For example, the Morris method revealed prevalence of CWD at year 20 as most sensitive to CWD mortality rate whereas variance decomposition identified this variable as 8th most influential. The Morris method cannot adequately account for interactive effects among input variables. Therefore, although the Morris method is sufficient in identifying which input variables have minimal influence on model output, its results should not be used to rank variables according to their sensitivity indices. Alternatively, variance decomposition can decompose and quantify variable interactions and, thus, can be used to rank the influence of each input variable on model output.

Researchers and wildlife managers have estimated that, at some point, indirect transmission becomes more important than direct transmission on CWD dynamics in free-ranging cervid populations endemic with the disease. This estimate stems from the ideas that 1) CWD reduces population size and deer density over time, which reduces the number of contacts made and, thus, direct transmission events among deer, and 2) prions accumulate in the soil within affected areas over time, which increase the probability of local deer becoming infected indirectly through the environment (Edmunds et al., 2016; DeVivo et al., 2017). The sensitivity analysis we performed on the IBM supports this transition of influence between transmission modes and suggests that the transition occurs between 15 and 20 years post initial introduction of CWD.

The Morris screening method identified number of deer groups to be uninfluential on disease dynamics after 20 years. One hypothesis for this finding is that the number of deer (i.e., deer density) within the study area, which was held constant at initialization of our model, is more influential on disease dynamics than total number of groups of deer. Although studies report that deer in different social groups are less likely to interact when in proximity, this appears to hold true for females and juveniles only (Magle et al., 2013; Schauber et al., 2015; Grear et al., 2010). Furthermore, transmission of CWD may be driven by males in the deer population given their higher prevalence in most reported regions of the U.S. (Miller and Conner, 2005; DeVivo et al., 2017; Samuel and Storm, 2016). Males form looser social groups with other members of the same sex (Nixon et al., 1991), and interactions with other male and female deer prior to and during the rut (e.g., sparring, scraping, and breeding) are not known to be influenced by group membership.

Variance decomposition of model output identified that CWD

prevalence was most sensitive to harvest rates of adult and yearling females over time despite including a correction factor to ensure higher prevalence in males. Adult females made up the highest proportion of the population (i.e., 33 %), and were responsible for producing the most fawns each year, which is likely why the harvest rate of adult females is more influential on disease dynamics than harvest of other demographic groups. Yearling females age into adults and produced the second most fawns each year, which may explain the influence of their harvest on model output. These findings suggest that increased removal, whether through greater harvest rates or targeted culling, of female deer may be an effective management strategy for CWD. Past management efforts have focused on male-biased removal strategies given their higher apparent prevalence. However, Al-Arydah et al. (2012, 2016) also found that their CWD mathematical model was more sensitive to female than male harvest rate.

Increasing model sensitivity to the harvest rate of deer indicates that deer removal, regardless of method (i.e., hunter harvest or agency culling), as a management strategy for reducing CWD prevalence becomes more effective over time (i.e., the effect size increases with time). However, due to political and financial constraints, population reduction efforts as a method for controlling the growth and spread of CWD are often terminated within the first few years of their initiation (Heberlein, 2004; Holsman et al., 2010). Our results emphasize a need for continued population reduction throughout the disease epidemic and not just the first few years after disease detection.

Our CWD model is not the first to apply an IBM framework to assess CWD dynamics. Belsare et al. (2020) developed an IBM to assess CWD surveillance strategies with a focus on disease detection. This model has a lower spatial and temporal resolution and does not include indirect disease transmission. Although a local sensitivity analysis was performed, it assessed two model processes and the output of interest was CWD detection probability. Thus, we were not able to compare our results to results from the Belsare et al. (2020) model. Kjaer and Schauber (2022) produced an IBM that simulates direct and indirect transmission of CWD in white-tailed deer populations using similar temporal and spatial scales to our model. The authors focused on assessing the effects of landscape, deer removal, and transmission pathways on CWD dynamics but did report similar patterns of increasing prevalence and long-term population declines when CWD was present in modeled populations. Contrary to our findings, they found prevalence of CWD was highly sensitive to one parameter (prion half-life) by using a local sensitivity test. Despite assessing prion half-life over a wider range of values, which included the values (Kjaer and Schauber, 2022) assessed,

our model did not find prion half-life to be influential on long-term CWD dynamics using a global sensitivity analysis. Our goal was to provide researchers and wildlife managers with a model that serves as a tool to investigate and predict spatiotemporal dynamics of CWD in white-tailed deer populations and to assess factors affecting this disease system. This model simulates CWD in accordance with our current knowledge of CWD dynamics and Midwestern white-tailed deer behavior using available epidemiological and ecological field data. Moreover, we developed this tool using a framework that can easily be adapted to address other cervid species, geographic locations, and infectious disease systems. However, model complexity quickly grew during the development phase, which increased computation time of the model exponentially. Our next steps for this model include streamlining many of the population and disease functions to achieve our goal of providing a user-friendly tool for wildlife agencies and others to use without access to high-performance computing systems.

Wildlife managers and researchers may apply this model to assess disease management interventions, surveillance methods, or the effects of environmental conditions on direct and indirect transmission of CWD. In addition, wildlife agencies can incorporate this model into adaptive management plans for CWD to aid in decision-making by testing alternative management scenarios. Given the expenses and risks involved in the investigation of surveillance and management methods for CWD in free-ranging cervid populations, we suggest that wildlife agencies use this model to assess potential actions prior to decision making and implementing management in the field.

5. Conclusion

We developed an IBM to simulate CWD in free-ranging white-tailed deer populations given our best knowledge of the disease system to date. The ability of our model to reproduce short and long-term CWD dynamics observed in affected deer populations in the Midwest implies that our model represents the necessary details associated with white-tailed deer populations and CWD processes. Our model also demonstrates the importance of stochasticity that incorporates individual deer variation, as previous models have not been able to incorporate these details leading to difficulties when trying to reproduce observed CWD data (Uehlinger et al., 2016; Winter and Escobar, 2020). This IBM may serve as the foundation to conduct further analyses and address active research areas, such as additional parameter calibration and sensitivity tests or the assessment of management scenarios or genotypic variation on CWD processes.

CRediT authorship contribution statement

Noelle E Thompson: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **David J Butts:** Writing – review & editing, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Michael S Murillo:** Writing – review & editing, Visualization, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Daniel J O'Brien:** Writing – review & editing, Resources, Methodology, Investigation, Conceptualization. **Sonja A Christensen:** Writing – review & editing, Visualization, Resources, Project administration, Methodology, Investigation, Conceptualization. **William F Porter:** Supervision, Funding acquisition, Conceptualization. **Gary J Roloff:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

Data availability

I have shared my code at the 'Attach file' step and will publish it on GitHub.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ecolmodel.2024.110697](https://doi.org/10.1016/j.ecolmodel.2024.110697).

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