Received: 24 January 2018 | Accepted: 18 June 2018

DOI: 10.1111/1365-2435.13183

Functional Ecology | BRITISH ECOLOGICAL SOCIETY

RESEARCH ARTICLE

Landscape structure and ecology influence the spread of a bat fungal disease

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Funding information
Biotieteiden ja Ympäristön Tutkimuksen Toimikunta, Grant/Award Number: 286405; H2020 Marie Skłodowska-Curie Actions, Grant/Award Number: 706196

Handling Editor: Amy Pedersen

Abstract

1. White-nose syndrome (WNS), affecting multiple North American bat species during the hibernation period, is a highly pathogenic disease caused by the psychrophilic fungus *Pseudogymnoascus destructans* (*Pd*). Because the fungal pathogen persists in the hibernation site environment independently of the hosts, previous theory on spatial disease dynamics cannot predict WNS epidemics. However, the ability to understand factors contributing to the spread of white-nose syndrome (WNS) in North America is crucial to the management of infected and susceptible bat populations as well as the conservation of threatened and endangered bat species.
2. Utilizing recent theory on environmental opportunistic pathogens, we modelled the effect of (a) landscape clustering, (b) environmental conditions in hibernacula and (c) microbial competition on the spread of WNS. We used available, already published data to construct and parameterize our model, which takes into account the spatial distribution of hibernation sites, temperature conditions in both the outside ambient and hibernation site environment, bat population dynamics, dispersal and infection by the pathogen, which also has its host-independent dynamics with the environment. We also consider the effect of outside-host competition between the pathogen and other micro-organisms on spatial disease dynamics.
3. Our model suggests that pathogen loads accumulate in poorly connected hibernacula at short host dispersal, which can help found the epidemic. In contrast, invasion of the landscape is most successful at long host dispersal distances, with homogenous hibernation site distribution and heterogeneous between-hibernation site temperatures. Also, increasing the mean temperature across hibernacula increases fungal growth rate, leading to higher disease prevalence and faster invasion rate. Increasing spatial heterogeneity in hibernaculum temperatures results in the formation of disease hotspots in warmer hibernacula, facilitating more effective spread of the disease in the landscape. Cold-adapted competing microbes can prevent invasion, and therefore, overwintering in cold hibernacula increases probability of host survival.
4. Sites that were suboptimal for overwintering prior to WNS may have importance in preventing local extirpations. Although the model is tailored for WNS, due to

pressing need for results that can assist in planning conservation measures, these novel results can be broadly applied to other environmentally transmitted diseases.

KEYWORDS
Chiroptera, dispersal, landscape structure, opportunistic pathogen, outside-host competition, White-nose syndrome, WNS

1 | INTRODUCTION

The introductions of novel wildlife pathogens have increased in the past decades with catastrophic effects on Earth's biodiversity (Daszak, Cunningham, & Hyatt, 2000). These introductions have led to population declines, species extinctions and shifts in community composition, with significant impacts on ecosystem processes and services (Frick et al., 2010; Holdo et al., 2009; Martin, 2001; Skerratt et al., 2007). Understanding and predicting pathogen dynamics can assist in planning conservation measures in locations where the pathogen already persists as well as in pathogen-free locations (Cunniffe, Cobb, Meentemeyer, Rizzo, & Gilligan, 2016). The spread of a novel disease across a landscape within a naïve host population depends on the extent of initial population decline, the host density dependence of the pathogen, host dispersal behaviour, competitive pressure affecting the pathogen, and the presence, heterogeneity and connectedness of environmental reservoirs in the landscape (Briggs, Knapp, & Vredenburg, 2010; De Castro & Bolker, 2005). As a result, emerging pathogens display a variety of spatial spread patterns due to differences in host ecology (Keeling et al., 2001; LaDeau, Marra, Kilpatrick, & Calder, 2008; Meentemeyer et al., 2011; Smith, Lucey, Waller, Childs, & Real, 2002).

White-nose syndrome (WNS) is a highly pathogenic disease caused by the psychrophilic fungus *Pseudogymnoascus destructans* (*Pd*). It infects multiple North American bat species during the hibernation period (Dzal, McGuire, Veselka, & Fenton, 2011; Frick et al., 2017). WNS was first observed in Schoharie County, New York, in 2006 and is currently spreading at a pace of 200–900 km per year (Blehert et al., 2009; Foley, Clifford, Castle, Cryan, & Ostfeld, 2011; Gargas, Trest, Christensen, Volk, & Blehert, 2009). So far, this non-endemic pathogen of Eurasian origin has spread to 32 states in the United States and seven provinces in Canada within a decade (Lorch et al., 2016; U.S. Fish & Wildlife Service, 2016). The spread, together with estimated mortalities exceeding 5.7 million bats in infected caves, has generated concern over the local extirpations or even extinctions of common bat species (Boyles & Brack, 2009; Frick et al., 2015, 2017; Thogmartin et al., 2013). Understanding the mechanisms facilitating the spread of WNS is crucial for management of infected and vulnerable bat populations, as well as the conservation of threatened and endangered bat species.

Because environmental transmission is necessarily a spatial process, its role in disease dynamics depends on the spatial structure of the host population (Kilpatrick, Briggs, & Daszak, 2010). The seasonally variable ecology and habitat preference of temperate bats can be expected to have a profound effect on the geographic advance of the pathogen. White-nose syndrome only occurs during overwintering at hibernation sites (from here on: hibernacula), usually caves or mines, where bats are susceptible while in torpor (Field et al., 2015; Lilley et al., 2017; Verant et al., 2014). The cold-adapted fungus, *Pd*, can only proliferate and infect bats in the low-temperature and high-relative-humidity conditions of the hibernacula (Verant, Boyles, Waldrep, Wibbelt, & Blehert, 2012), whereas outside the hibernation period the host are able to clear the infection in a matter of weeks (Fuller et al., 2012). Thus, the host populations can be considered as a metapopulation, occupying small patches of suitable habitat during the hibernation season (hibernacula), in a highly fragmented landscape. We can expect that host population survival is influenced by heterogeneity in both the quality and the distance between these habitat patches. One can expect spatial processes to influence how a pathogen spreads in such a metapopulation, where environmental pathogen reservoirs get established, and the resulting effects on host occupancy and population size (Leach, Webb, & Cross, 2016).

The spread characteristics and persistence of WNS differentiate it from many other infectious diseases affecting metapopulations, such as measles in humans (Grenfell & Harwood, 1997). The ability of the pathogen to survive and propagate in hibernacula over the summer even in the absence of the host adds a parallel transmission pathway in addition to host-to-host contacts (Leach et al., 2016; Raudabaugh & Miller, 2013). This can have important consequences on disease dynamics, with models showing that increased environmental longevity generally facilitates increased pathogen persistence and spread relative to direct transmission alone (Almberg, Cross, Johnson, Heisey, & Richards, 2011; Breban, Drake, Stallknecht, & Rohani, 2009). However, pathogen success can also be affected by microbial competition in the hibernacula, where the outcome of competition depends on factors, such as psychrotolerance, ability to consume different substrates, and tolerance to fungicides/bactericides (Micalizzi, Mack, White, Avis, & Smith, 2017; Wilson, Held, Freiborg, Blanchette, & Salomon, 2017; Zhang et al., 2014; Zhang, Chaturvedi, & Chaturvedi, 2015). For instance, many nonpathogenic *Pseudogymnoascus* species appear to be better adapted to the saprotrophic, outside-host lifestyle, and *Pd* can only become more competitive towards these at low temperatures (Wilson et al., 2017).

The purpose of this study is to model the effect of (a) spatial clustering of hibernacula, (b) environmental conditions in hibernacula and (c) microbial competition on the spread of the WNS. The model considers the spatial distribution of hibernacula, temperature conditions in both the outside ambient and hibernaculum environment, bat population dynamics, dispersal and infection

by the pathogen, which also has its host-independent dynamics with the environment. We also consider the effect of outside-host competition between the pathogen and other micro-organisms on spatial disease dynamics. We use available, already published data to construct and parameterize our model, focusing on data produced on *Myotis lucifugus*, one of the most heavily affected species (Frick et al., 2010). Previous papers modelling the spread of WNS have used either a U.S.-county-based approach (Maher et al., 2012; O'Regan et al., 2015) or colony-level covariates (Wilder, Frick, Langwig, & Kunz, 2011) to model the spread of the disease across the continent. However, it is not our aim to accurately pinpoint certain areas in North America which are susceptible to the disease, but rather to predict combinations of factors which affect the spread of disease to assist in conservation planning. Thus, we are investigating the role of both landscape structure and host-independent ecology of the pathogen in disease spread at a more general level, potentially providing deeper insight to the epidemiology of WNS and other environmental pathogens.

2 | MATERIALS AND METHODS

Here, we describe a mean field (not individual-based) model of disease epidemiology of bats. Within a season, bats reproduce, disperse and potentially become infected, but the actual ordering of these events is not relevant (or at least not relevant in the context of the model, which is not event-based). Similarly, each hibernaculum, in a spatial network of habitat patches, should be considered to include both the hibernaculum and the surrounding habitat. Therefore, information on the exact location of the bats is not necessary, with the exception of the location during hibernation period, when all bats are in a hibernaculum. Therefore, the dispersal process can be considered as a change in the hibernating location for bats (or the density of bats in this case). These assumptions are simplifications, and the model does not attempt to capture all aspects of bat behaviour. That said, the model captures relevant aspects of the focal system, while trying to retain some level of generality. Where possible, we produced parameters for the model using estimations from publications presented in Table 1.

2.1 | Local dynamics

The population dynamics are modelled as differential equations, with the host population divided into susceptible (S), exposed (E) and infected (I) compartments (Figure 1), each containing active (summer) and hibernating period (winter) compartments (subscripts a and h, respectively). In addition, the model includes the environmental microbial community, which contains free-living *Pd* (F) and competing microbes (M). Please see Table 1 for key. The dynamics in the system are described as follows:

$$\frac{dS_a}{dt} = r(T_A)N_a\left(1-\frac{N_a}{K_h}\right) - \beta_e S_a f(F) + \delta_E E_a - \omega_{a\to h}(T_A)S_a + \omega_{h\to a}(T_A)S_h \quad (1.1)$$

$$\frac{dE_a}{dt} = \beta_e S_a f(F) - r(T_A)E_a\frac{N_a}{K_h} + \delta_I I_a - \delta_E E_a - \omega_{a\to h}(T_A)E_a + \omega_{h\to a}(T_A)E_h \quad (1.2)$$

$$\frac{dI_a}{dt} = -r(T_A)E_a\frac{N_a}{K_h} - \delta_I I_a - \omega_{a\to h}(T_A)I_a + \omega_{h\to a}(T_A)I_h \quad (1.3)$$

$$\frac{dS_h}{dt} = -\frac{\beta_d S_h I_h}{1+\rho S_h} - \mu_h(T_H)S_h + \omega_{a\to h}(T_A)S_a - \omega_{h\to a}(T_A)S_h \quad (1.4)$$

$$\frac{dE_h}{dt} = \frac{\beta_d S_h I_h}{1+\rho S_h} - \mu_h(T_H)E_h - \varphi E_h + \omega_{a\to h}(T_A)E_a - \omega_{h\to a}(T_A)E_h \quad (1.5)$$

$$\frac{dI_h}{dt} = -\mu_h(T_H)I_h + \varphi E_h - \alpha_f I_h + \omega_{a\to h}(T_A)I_a - \omega_{h\to a}(T_A)I_h \quad (1.6)$$

$$\frac{dF}{dt} = r_f(T_H)F\left(1-\frac{F+c_{fm}M}{K_f}\right) + \eta I_h \quad (1.7)$$

$$\frac{dM}{dt} = r_m(T_H)M\left(1-\frac{M+c_{mf}F}{K_m}\right) \quad (1.8)$$

Due to their insect diet, bats switch between an active period and a hibernation period depending on the availability of prey, which is dependent on the temperature of the ambient environment T_A (Speakman & Rowland, 1999). Active bats exhibit logistic growth, limited by the total active bat population $N_a = (S_a + E_a + I_a)$. Hibernating bats do not reproduce and are affected by hibernation mortality (rate $\mu_h(T_H)$) dependent on hibernaculum temperature (T_H) (Webb, Speakman, & Racey, 1996). Susceptible active bats become exposed through contact with environmental, free-living *Pd* fungus (Lorch et al., 2013) following a sigmoidal infectivity response (Anttila, Laakso, Kaitala, & Ruokolainen, 2015; Anttila et al., 2017):

$$f(F) = \frac{(F/ID_{50})^k}{1+(F/ID_{50})^k}, \quad (2)$$

Parameters ID_{50} and κ indicate the pathogen dose at which half of the hosts become infected and the steepness of the infectivity function, respectively (Langwig et al., 2015). The utilization of a sigmoidal infectivity response incorporates a dose-dependent probability of infection into the model (Anttila et al., 2017; Regoes, Ebert, & Bonhoeffer, 2002). This prevents infections from occurring when the pathogen density is low, but also leads to saturating infection rates at higher doses.

The model assumes bats can become exposed to the pathogen either by environmental transmission while active (rate $\beta_e f(P)$) or by direct transmission during hibernation (rate $\beta_d/(1+\rho S_h)$, the first terms in equations (1.4) and (1.5)). In turn, exposed bats become infected during hibernation (via germination of fungal spores) at rate φ. While environmental transmission follows a density-dependent, sigmoidal response, direct transmission describes a frequency-dependent, saturating response (Frick et al., 2015; Langwig et al., 2012, 2015; Lorch et al., 2011; Reynolds, Ingersoll, & Barton, 2015).

We assume that infected, or exposed, bats may not contribute to reproduction due to the length of healing processes (Fuller et al., 2012), but still suffer density-dependent mortality. We include an additional disease mortality factor during hibernation (rate α_f). Infected

TABLE 1 The parameter values and ranges used. Parameter values for the models have been estimated using the referenced publications. Parameter values with no starting point reference available were estimated by model fitting

Symbol	Parameter name	Unit	Values	Reference
r_{max}	Bat population growth rate	1/day	0.0052	Fenton and Barclay (1980); Reynolds et al. (2015)
K_h	Bat population carrying capacity	1000 bats = $unit_b$	10	Meyer, Stevens, and Blackwood (2016)
σ_r	Bat population growth half-saturation	$unit_b$	10	Estimated by model fitting
k_r	Bat population growth steepness	–	6	Estimated by model fitting
K_f	Fungal carrying capacity	10^6 spores = $unit_f$	100	Reynolds et al. (2015)
K_m	Competitor carrying capacity	10^6 spores = $unit_m$	100	Wilson et al. (2017)
β_e	Environmental transmission	$1/unit_f$ 1/day	0.05	Reynolds et al. (2015)
ID_{50}	50% infective dose	–	140	Langwig et al. (2015)
κ	Infectivity steepness	–	5	Estimated by model fitting
δ_I	Recovery (infected to exposed)	1/day	0.15; 0.075	Ballmann et al. (2017); Carpenter et al. (2016); Fuller et al. (2012)
δ_E	Recovery (exposed to susceptible)	1/day	0.0; 0.075	Carpenter et al. (2016); Fuller et al. (2012)
β_d	Direct transmission	$1/unit_b$ 1/day	0.001	Frick et al. (2015); Langwig et al. (2012, 2015); Lorch et al. (2011)
ρ	Direct transmission saturation	$1/unit_b$	0.2	Frick et al. (2015); Langwig et al. (2012, 2015); Lorch et al. (2011)
c_μ	Hibernation mortality coef.	–	0.01	Webb et al. (1996)
c_3	Hibernation mortality coef.	–	–1.0e-4	Webb et al. (1996)
c_2	Hibernation mortality coef.	–	8.3e–3	Webb et al. (1996)
c_1	Hibernation mortality coef.	–	–8.3e–2	Webb et al. (1996)
c_0	Hibernation mortality coef.	–	0.35	Webb et al. (1996)
$\sigma_{a\rightarrow h}$	Torpor rate half-saturation	$unit_b$	8.0	Thomas, Dorais, and Bergeron (1990)
$k_{a\rightarrow h}$	Torpor rate steepness	–	10	Thomas et al. (1990)
$\sigma_{h\rightarrow a}$	Arousal rate half-saturation	$unit_b$	14.0	Thomas et al. (1990)
$k_{h\rightarrow a}$	Arousal rate steepness	–	20	Thomas et al. (1990)
φ	Development of symptoms	1/day	0.01	Langwig et al. (2015); Lorch et al. (2011); Warnecke et al. (2012)
α_f	Disease mortality	1/day	0.04	Frick et al. (2010, 2017); Lilley et al. (2017); Warnecke et al. (2012)
η	Fungal shed rate	$1/unit_b$ 1/day	0.65	Reynolds et al. (2015)
$b_{1,f}$; $b_{1,m}$	Fungal/competitor growth coef.	–	1.25	Wilson et al. (2017); Zhang et al. (2014)
$b_{2,f}$; $b_{2,m}$	Fungal/competitor growth coef.	–	0.0377	Wilson et al. (2017); Zhang et al. (2014)
$b_{3,f}$	Fungal growth coef. (min)	°C	7.0	Zhang et al. (2014)
$b_{3,m}$	Competitor growth coef. (min)	°C	7.0; 6.0–8.0	Zhang et al. (2014)
$b_{4,f}$; $b_{4,m}$	Fungal/competitor growth coef.	–	0.25	Zhang et al. (2014)
$b_{5,f}$	Fungal growth coef. (max)	°C	15.0	Zhang et al. (2014)
$b_{5,f}$	Competitor growth coef. (max)	°C	15.0; 14.0–16.0	Zhang et al. (2014)
c_{fm}	Competition strength, pathogen to community	–	0.0; 0.5	Anttila et al. (2013)
c_{mf}	Competition strength, community to pathogen	–	0.0; 0.0–1.0	Anttila et al. (2013)
c_d	Decay of spatial temperature correlation	1/(10 kilometres)	0.1	Estimated by model fitting

(Continues)

TABLE 1 (Continued)

Symbol	Parameter name	Unit	Values	Reference
c_t	Temporal temperature correlation coefficient	–	0.65	Ruokolainen, Lindén, Kaitala, and Fowler (2009); Vasseur and Yodzis (2004)
γ	Migration decay	1/(10 kilometres)	1.25; 0.5–2.0	Norquay et al. (2013)
λ	Landscape clustering coef.	–	10^2; 10^1–10^3	Estimated by model fitting
μ_T	Mean hibernaculum temp.	°C	7.5; 7.0–8.0	Brack (2007); Humphries et al. (2005)
$\sigma_{\mu T}$	Variability in hibernaculum t.	°C	0.2; 0.0–0.4	Brack (2007); Humphries et al. (2005)

bats clear the infection during the active season, even to the point where no *Pd* is detectable on the bat (Ballmann, Torkelson, Bohuski, Russell, & Blehert, 2017; Carpenter, Willcox, Bernard, & H Stiver, 2016). We tested both recovery to exposed state only (I_a to E_a, rate δ_I) and further recovery to susceptible state (E_a to S_a, rate δ_E) with halved rates. The resulting dynamics were qualitatively similar, and the latter recovery pattern is presented in Supporting Information Figure S1. The free-living *Pd* fungus and competing microbes grow in the cave depending on the hibernaculum temperature T_H and compete with each other (Micalizzi et al., 2017; Wilson et al., 2017; Zhang et al., 2014). The *Pd* fungus is shed to the hibernaculum environment by the exposed bats (rate η), where it can survive in the absence of the host (Hoyt et al., 2014; Reynolds et al., 2015).

Outside the hibernacula, the ambient temperature varies with both a periodic and a stochastic component. The periodic component was generated as a sinusoidal wave 4°C x (2π(t/365)), which was added to a stochastic component generated as autoregressive, both spatially and temporally correlated variation with a standard deviation of 4°C (here, *t* indicates time). The autoregressive portion was generated as Gaussian noise with spatial correlation decreasing exponentially with distance $cor(T) = e^{-c_d d}$, where c_d denotes the decay of spatial correlation. One random number was generated for each day in each location. After this, the temporal correlation was applied as $T_t = c_t T_{t-1} + (1\text{-}c_t)Y_t$, where c_t is a temporal correlation coefficient, Y_t denotes the spatially correlated temperature value and T_t denotes the final spatially and temporally correlated temperature value. In the simulations, mean ambient temperature was set to 10°C (mean annual temperature in Albany, NY, WNS-point zero, www.usclimatedata.com). The ambient temperature (T_A) affects the bat arousal and torpor rates:

$$\omega_{h\to a}(T_A) = \omega_{max}\frac{(T_A/\sigma_{h\to a})^{k_{h\to a}}}{1+(T_A/\sigma_{h\to a})^{k_{h\to a}}} \quad (3.1)$$

$$\omega_{a\to h}(T_A) = \omega_{max}\left(1-\frac{(T_A/\sigma_{a\to h})^{k_{a\to h}}}{1+(T_A/\sigma_{a\to h})^{k_{a\to h}}}\right) \quad (3.2)$$

In the simulations, activation and hibernation functions were set such that 50% activation occurs at 14°C and 50% hibernation at 8°C (G. Turner, PAGC, personal communication).

Ambient temperature also affects the bat population growth rate (r_{max}):

$$r(T_A) = r_{max}\frac{(T_A\sigma_r^{-1})^{k_r}}{1+(T_A\sigma_r^{-1})^{k_r}} \quad (4)$$

The purpose of this temperature-dependent growth is mainly to prevent reproduction at lower ambient temperatures, that is, outside the breeding season. A sigmoidal function is used for smooth transition. Hibernaculum temperature (T_H) is set on an arbitrary average of 7.5°C with *SD* = 0.5°C variation around the annual mean (Brack, 2007; Humphries, Speakman, & Thomas, 2005). Hibernaculum temperatures followed the local ambient temperatures (with different

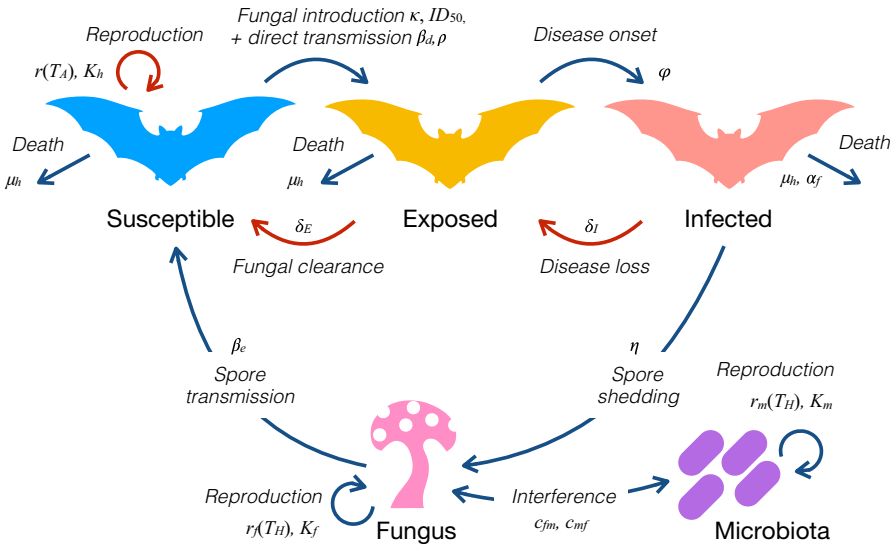

FIGURE 1 A schematic illustration of the local dynamics in the model. Susceptible bats (blue) can become exposed (yellow) to fungal spores in the hibernaculum. Germination of the spores in exposed bats turns them infected (red), which in turn sheds fungal spots to the environment. Infected bats can clear an infection during summer and either return to the exposed class or recover completely. All bats can also die naturally during hibernation, whereas the infected bats suffer extra mortality from the disease. Processes occurring during summer are coloured dark red, while those taking place during hibernation are coloured dark blue

means and variations), becoming colder during winter and warmer during summer. Hibernaculum temperature has an effect on hibernation mortality:

$$\mu_h(T_H) = c_\mu(c_3 T_H^3 + c_2 T_H^2 + c_1 T_H + c_o) \quad (5)$$

The during-hibernation mortality is set such that an arbitrary optimal temperature (lowest mortality) for hibernation, based on the literature (Brack, 2007; Hayman, Pulliam, Marshall, Cryan, & Webb, 2016; Humphries, Thomas, & Speakman, 2002; Langwig et al., 2017), is (around) 5°C, with mortality increasing towards both higher and lower temperatures.

The presence of certain microbial species in the environment can control the growth of *Pd* (Micalizzi et al., 2017; Wilson et al., 2017; Zhang et al., 2014, 2015). To account for potential antagonistic/competitive interactions in the hibernaculum, without specific assumptions about the actual mechanisms, we assume density-dependent competition between *Pd* (equation 1.7) and the overall microbial community (equation 1.8) (e.g., Anttila, Ruokolainen, Kaitala, & Laakso, 2013). The effects of competition on disease spread were tested in separate simulations, where the interaction strength of the microbial community against the pathogen (c_{mf}) was varied between 0.0 to 1.0 and that of the pathogen towards the microbial community (c_{fm}) was set to 0.5 (parameters not based on published results). In other simulation experiments, these were set to 0.0. The intrinsic growth rates of both the pathogen (*F*) and the microbial community (*M*) depend on temperature ($r_f(T)$, $r_m(T)$). To account for differential temperature adaptation, we assume that *F* and *M* can have different temperature optima. By varying the relative location of these optima along temperature variation, we can change the favourability of the environment for each "population." Hibernaculum temperature affects microbial growth rates as follows:

$$r_f(T_H), r_m(T_H) = \begin{cases} b_1[b_2(T_H - b_3)]^2[1 - e^{b_4}(T_H - b_5)], & 7 < T_H > 15 \\ 0, & \text{otherwise} \end{cases} \quad (6)$$

where T_H denotes hibernaculum temperature and the parameters $b_1,\ldots,b_5$ define the shape of the growth response. With the parameterization presented in Table 1, optimal growth is reached at approximately 12°C and decreases asymmetrically towards 7°C (minimum) and 15°C (maximum).

Relative humidity was intentionally left out of the model for reasons mentioned in the discussion. The sensitivity of the model to the specific parameterization (Table 1) used in the simulation experiments was studied in a deterministic version of the model. Results of the sensitivity analysis are presented in Supplementary Information (Table S1). The sensitivity analysis highlights the importance of, for example, parametrizing the growth of *Pd* ($b_{1,f}$) correctly, as it appears to be very sensitive to changes in the model.

2.2 | Spatial dynamics

To study the role of spatial clustering, we simulated landscapes consisting of a network of 100 hibernacula, generated as a Poisson cluster point process using the stpp package in R (Gabriel, Diggle, & stan function by Barry Rowlingson, 2014). To generate a variety of spatial scenarios, the clustering intensities λ were varied between 10^1 (extremely clustered) and 10^3 (evenly spaced). Here, the term migration is used to describe small-scale bat movement from summer breeding grounds to hibernation sites, as well as visits to numerous hibernation sites during the swarming season. The little brown bat shows high degrees of philopatry, and long-distance migration is uncommon (Norquay, Martinez-Nuñez, Dubois, Monson, & Willis, 2013). We assume that bat migration within the network follows a simple radial exponentially decaying probability per unit time. This yields the migration probability density function $f(x) = \gamma^2 e^{-\gamma x} x$, where x is the spatial dimension, resulting in expected migration distance of $2/\gamma$ (twice the expected distance in one dimension). Although not based on any existing literature, we assumed it was biologically relevant that the probability of migration from each hibernaculum was cut off to a minimum probability of 0.005 to prevent excessive dispersal distances on a single step, normalized to unity between the destination hibernacula within reach. Because of a maximum dispersal distance, the hibernacula form a network, where only nearby nodes are reachable from a given node on a single migration event. The effects of node placement in the network were studied with two different metrics for each node, betweenness and hub score, explaining the expected time until infection reaches the node. The population dynamics were simulated for each hibernaculum in a network of 100 hibernacula for a period of 20 years.

2.3 | Output

We calculated several metrics from the simulated data to compare disease invasion under different scenarios and parameter combinations. *Invasion rate* was defined as the expected time to disease establishment in a patch, scaled by the simulation time span: *invasion rate* = $\Sigma(t_I)n^{-1}/t_{MAX}$, where t_I and t_{MAX} refer to the time of infection (the time point when a patch becomes infected) and total simulation time span, respectively, and n indicates the number of patches. An example of model code is available in the Data Accessibility section.

3 | RESULTS

Given the characteristic temperature tolerances of the host and the pathogen, hibernacula temperatures across the landscape have an expected effect on disease invasion patterns. Increasing the mean hibernaculum temperature [$\mu(T_H)$] from values close to the temperature optima of the host increases environmental growth of the pathogen (equation 6), which leads to steeply increasing pathogen invasion rate and disease prevalence (Figure 2a). Similarly, increasing spatial heterogeneity in hibernaculum temperature [$\sigma(T_H)$] also increases the rate of disease spread and prevalence (Figure 2c). Increasing variability in local

conditions creates more localities that favour fungal reproduction and thus act as disease hubs.

Landscape structure also has a significant influence on the expected rate of disease spread. Pathogen invasion rate and disease prevalence are lowest in strongly clustered landscapes, where the clusters are located far away from each other (Figure 2b,d). While increasingly compact and homogeneous landscapes are associated with high disease prevalence, the pattern in pathogen invasion rate is even more pronounced with a very clear threshold (Figure 2b,d). Invasion rate is maximized at low landscape clustering and long host dispersal scales (Figure 2b). It should be noted that the intermediate dispersal scale parameter (γ = 1.25) corresponds to an expected dispersal distance of 80 km, which is within the range observed for *M. lucifugus* (Davis & Hitchcock, 1965; Fenton, 1969; Humphrey & Cope, 1976). Similar to the close association between invasion rate and disease prevalence observed under varying temperatures (Figure 2a), disease prevalence and invasion rate monotonically increase with reduced landscape clustering and increasing dispersal scale (Figure 2b).

Landscape properties can possibly predict disease spread and prevalence well at the landscape level, but can the fate of a local

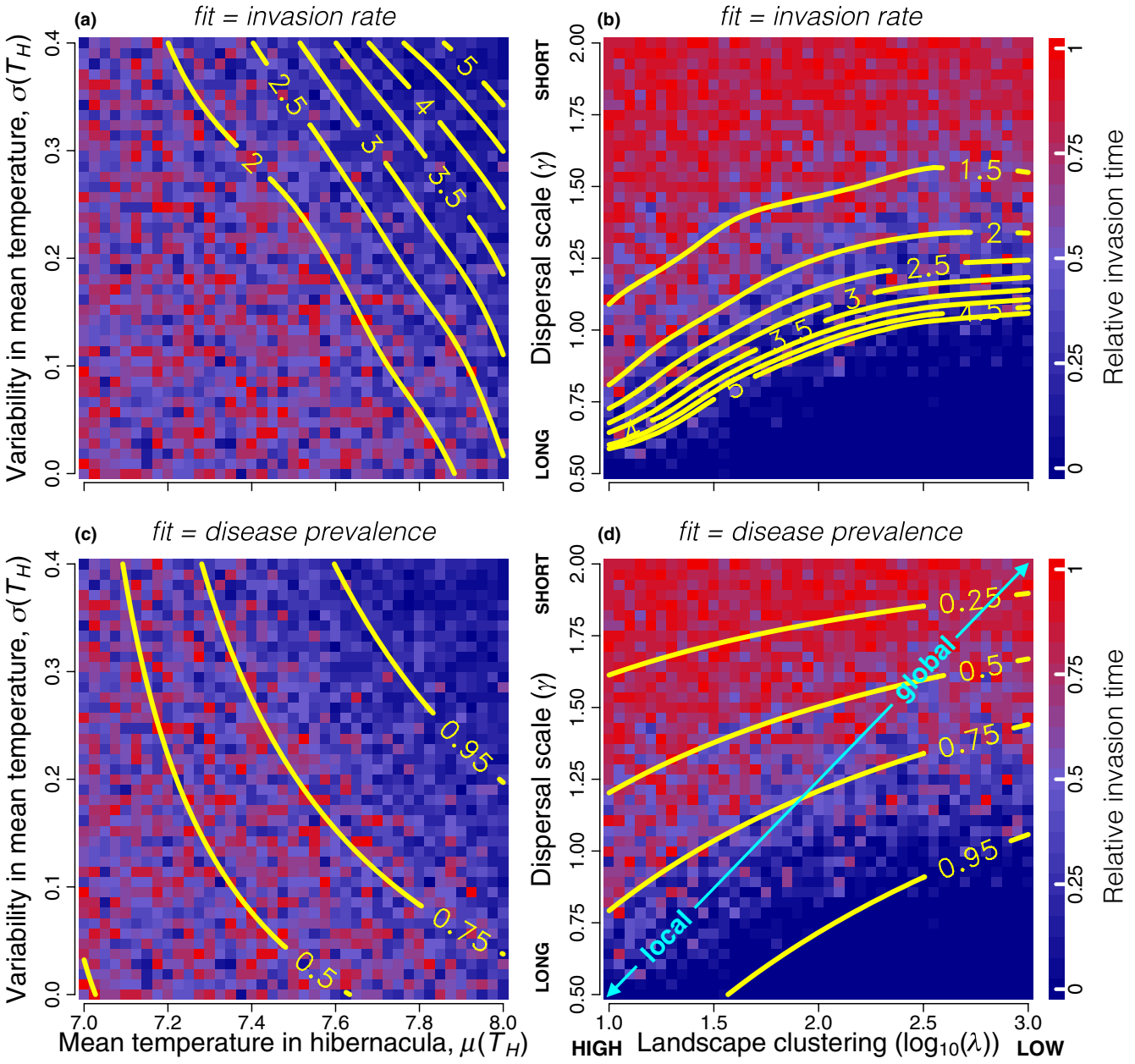

FIGURE 2 The expected relative infection time (RIT) of any hibernaculum (colour scale) is affected by the clustering of hibernacula in the landscape (controlled by parameter λ) and the variability of the mean hibernacula temperature, $\sigma(T_H)$. The colour scale indicates the mean relative amount of time (t_{max} = 1040 weeks, 20 years) hibernacula remain disease-free. In (a, b), the contour lines (yellow) indicate fitted invasion rate (1/RIT, GAM model), and in (c, d), they indicate fitted infection risk (proportion of infected hibernacula, logistic regression) across the landscape at each parameter combination (at t_{max}). The baseline mean temperature (at $\sigma(T_H)$ = 0) is here 7.5°C

hibernaculum be predicted based on its spatial positioning in the network? Using the data from Figure 2b, we tested whether distance from the source, node betweenness (those with higher betweenness are more accessible from any given node in the network) and node hub score (equivalent to eigenvector centrality, which measures the influence of a node in the network) explain how long it takes for a hibernaculum to become infected (analysing only those that eventually became infected), while controlling for the values for spatial clustering and dispersal scale. Distance from the source patch affects the likelihood of becoming infected, but while statistically significant (given the large sample size, $n = 152603$), the expected time to infection is only slightly increased by increasing distance ($p < 0.0001$, $b = 0.088$, scaled deviance = 41243). Increasing node betweenness (sqrt-transformed) also had a weak positive effect on invasion time ($p < 0.0001$, $b = 0.024$, scaled deviance = 668), whereas hub score was weakly negatively associated with invasion time ($p = 0.0012$, $b = -0.058$, scaled deviance = 11).

We also examined the effect of outside-host competition on pathogen invasion. When the pathogen and a competitor have a similar thermal tolerance ($\Delta T_{opt} = 0$), increasing competitive pressure reduces the risk of pathogen infection and decreases pathogen invasion rate, such that a relatively strong competitor can almost prevent invasion altogether (Figure 3a,b). This effect depends strongly and asymmetrically on the difference between species temperature optima. If the competitor is more cold-adapted than the pathogen ($\Delta T_{opt} < 0$), infection becomes more difficult even at lower competition pressure (Figure 3a; see also Supporting Information Figure S1 for a broader range of parameter combinations). In contrast, a more warm-adapted competitor ($\Delta T_{opt} > 0$) is less successful in preventing pathogen infection (Figure 3a). However, when concentrating on cases where the pathogen is able to invade the system, increasing difference in thermal optima increases the mean time of infection, because the pathogen is able to infect more hibernacula within the simulation time span (Figure 3c).

4 | DISCUSSION

Although the effect of landscape structure has been studied in other wildlife diseases (Heard et al., 2015; Real & Biek, 2007; Remais, Akullian, Ding, & Seto, 2010), it has received less attention with WNS as the focal disease (for examples, see Maher et al., 2012; O'Regan et al., 2015). Our modelling results show how habitat suitability and landscape structure could influence the invasion rate and prevalence of *Pseudogymnoascus destructans*, the causative agent of WNS. The initiation of an epidemic requires less connected hibernacula and short dispersal distances for an increase in pathogen load. However, high invasion rate and disease prevalence arise in homogeneous landscapes and under long scales of host dispersal, which, however, appear to be above the mean dispersal distance of *M. lucifugus* (Davis & Hitchcock, 1965; Fenton, 1969; Humphrey & Cope, 1976). Both disease prevalence and invasion rate are lower in spatially clustered landscapes. Because both the host and the pathogen are sensitive to temperature conditions in a hibernaculum, varying the mean temperature across hibernacula affects disease invasion. Higher mean temperature increases fungal growth rate (Verant et al., 2012), leading to higher disease prevalence and faster invasion rate. The same applies to increasing spatial heterogeneity in hibernaculum

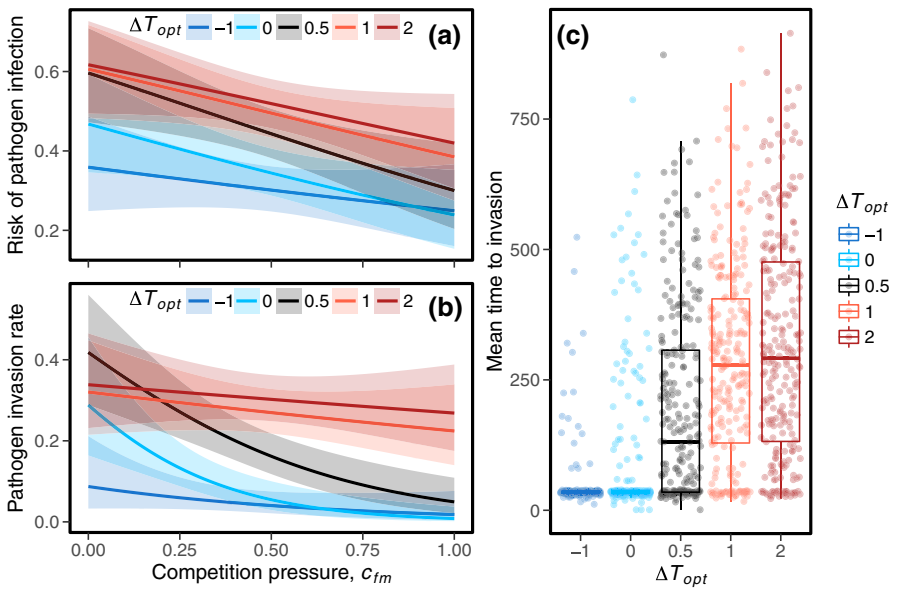

FIGURE 3 Competition in the outside-host environment (parameter c_{fm}) reduces (a) the risk of pathogen infection and (b) pathogen invasion rate at the level of hibernacula (the lines represent logistic regression fits, and shadings give the confidence bounds). The effectiveness of a competitor in preventing pathogen invasion depends on the difference in thermal optima between species (ΔT_{opt}). (c) Increasing difference in thermal optima, in favour of the pathogen ($\Delta T_{opt} > 0$), *increases* the expected time for infection, because the pathogen is able to infect more hibernacula within the simulation time span. The baseline mean temperature is here 7.5°C, as in Figure 2. As an example, the data were generated assuming $\sigma(T_H) = 0.2$, and $\lambda = 10^2$ (homogeneous landscape)

temperatures, which results in the formation of disease hotspots in warmer hibernacula, facilitating more effective spread of the disease in the landscape. Finally, we also demonstrate how outside-host competition between the pathogen and other micro-organisms can substantially inhibit pathogen invasion success, especially when the competitor(s) is better adapted to low temperatures.

The ecology of both the host and pathogen in our model system poses challenges for comparisons of our results with previous theoretical work on metapopulation models of obligate pathogens. This is because unlike the assumptions for patch-occupancy models (e.g., McCallum & Dobson, 2002) or explicit SIR models (e.g., Cross, Lloyd-Smith, Johnson, & Getz, 2005; Jesse, Ezanno, Davis, & Heesterbeek, 2008), local epidemics are unlikely to die out completely, due to the environmental reservoir of pathogens (but see Park, 2012). However, a reappearing prediction from such models is that pathogen persistence becomes more difficult if the host population is fragmented into smaller groups (Cross et al., 2005; Leach et al., 2016; Jesse, Mazzucco, Dieckmann, Heesterbeek, & Metz, 2011; E.B. Wilson & Worcester, 1945). Disease invasion rate is reduced due to lower disease transmission as well as increased number of dispersal events required for pandemic infection (Cross et al., 2005). Similarly, in our model, landscape clustering—effectively reducing global connectance—reduces pathogen invasion rate, but only at short dispersal distances (Figure 2b). The role of dispersal distance has been previously studied by Jesse and Heesterbeek (2011), who showed that pathogen persistence is most likely under intermediate dispersal scales. This arises because infections are severe, but only local at low movement distances, whereas infected hosts become "diluted" across space under long distances. This would lead to infections occurring globally but with epidemics remaining mild. Our model suggests a monotonic invasion rate across variable dispersal scale and landscape clustering, with higher invasion rates at a long dispersal distance especially in a highly homogeneous landscape. The sharp threshold, modulated by landscape clustering, after which invasion rate is increased by threefold, is most likely due to the sigmoidal response to pathogen density—likely to be a more realistic representation of disease transmission rate than the commonly assumed linear rate (Anttila et al., 2017). If immigration of exposed bats from neighbouring hibernacula is strong, that is, above the rate of recovery, mortality and emigration, it leads to an overproportionate increase in the amounts of pathogen produced, thus increasing the spread of the epidemic. This becomes even more pronounced with long dispersal distance facilitating rapid invasion of the landscape, and easy reachability of neighbouring, isolated hibernacula.

In a separate model, with smaller initial amounts of infected bats we see a dilution effect with increasing migration (Supporting Information Figure S3 Jesse & Heesterbeek, 2011), which also arises in our model due to an interaction between the sigmoidal infectivity response assumed here (equation 2)—and founder patch centrality, for example, responsible for the fractal pattern seen in the left-hand side of Figure 2a (Supporting Information Figure S2). If the focal and neighbouring hibernacula are suboptimal for outside-host reproduction, pathogen densities will remain below the infection threshold imposed by the infectivity function. In addition, if infected hosts do not migrate far from the founder hibernaculum (either because the landscape is clustered or because dispersal distance is short), pathogen load is more likely to accumulate even despite suboptimal outside-host conditions. A local outbreak can then fuel epidemics in the neighbouring hibernacula, enabling a spread of pathogen epidemics across the landscape.

The complex interaction between the conditions and positioning of the founder patch and overall landscape topology is likely to explain why we did not observe any clear patterns between the relative positioning of individual hibernacula and pathogen invasion rate. For example, increasing node betweenness was not associated with the time of invasion. Also, of those hibernacula that eventually became infected, expected time to infection only slightly increased with increasing distance from the source hibernaculum. Considering the dispersal capabilities of *M. lucifugus*, where individuals may not be dependent on the distance and quality of single hibernacula in the landscape, but are able to visit a number of sites regardless of their centrality (Burns, Frasier, & Broders, 2014), our results suggest that it may be difficult to predict the fate of individual hibernacula based on spatial patterns alone, beyond the point that those further away from the nearest epidemic are more likely to remain infection-free for longer. While measuring habitat connectivity empirically can be very challenging (Vuilleumier & Fontanillas, 2007), concentrating on potential dispersal hubs in the patch network might be a fruitful approach for better understanding disease spread (Saura, Bodin, & Fortin, 2014), especially if the locations of favourable disease hotspots are known.

Pathogens with free-living stages may confront lengthy exposure to environmental stress and competition before coming into contact with an uninfected host. Antagonistic interspecific interactions can therefore decrease the density of pathogens, reducing the probability of establishing an infection (Schmeller et al., 2014; but see Becker, Longo, Haddad, & Zamudio, 2017). Microbial competition can influence the environmental persistence of the *Pd*, which is of particular significance outside the hibernation period when hosts are absent (Hoyt et al., 2014). Local extirpation of bats is dependent on both bat-to-bat transfer and the environmental growth of the pathogen (Reynolds et al., 2015; M.B. Wilson et al., 2017). Here, increasing competitive pressure in the outside-host environment reduces the risk or completely prevents invasion, if the competitor is more cold-adapted. Furthermore, if the pathogen is able to invade the system, increasing difference in thermal optima between the competitor and the pathogen increases the mean time of infection. While this is somewhat counterintuitive at first glance, it can be understood as follows: When the competitor is more cold-adapted, the pathogen is only able to locally infect hibernacula that have favourable (relatively warm) temperature conditions. In contrast, when the pathogen is able to dominate in colder hibernacula, it can consequently infect more hibernacula. If the epidemic can advance further in the network, the expected time for infection also increases.

The recent westward spread of WNS in North America has been relatively gradual, inducing optimism that disease mitigation strategies

could be established in time to conserve potentially susceptible bats to WNS in western North America. Hibernation is a key to survival for many bats in temperate regions (Geiser, 2013). Without efficient hibernation, individuals of many species cannot survive winter when cold ambient temperatures lead to high energy costs and food is unavailable (Speakman & Rowland, 1999). Environmental conditions and basic pathogen traits alone appear to predict the infection risk well in WNS. The model predicts that although the spread of *Pd* is influenced by landscape properties, it will nevertheless infect all hibernacula given enough time. However, mean temperatures at hibernacula modulate infection risk, time to infection and the effect of microbial competition. Our results and the associated model sensitivity analysis also suggest hibernaculum temperature is the most important factor driving the environmental growth and viability of *Pd*, and subsequently, infection potential. The overlap in temperature optima between the pathogen and the host is narrow, and the infection probability decreases with decreasing temperature within the hibernacula. Our results suggest that bats have a higher probability of being able to overwinter with the pathogen in hibernacula that have a lower mean temperature. This is something that has already been observed in remnant, wild populations of *M. lucifugus* in WNS-positive regions (Hayman et al., 2016; Johnson, Scafini, Sewall, & Turner, 2016; Lilley et al., 2016). The spatial dilution of pathogens, caused by a suboptimal landscape, may also be responsible for the relatively slow initiation of WNS in the Pacific Northwest. So far only a few reports exist of infected bats from Washington State even though over 2 years have passed since the first bat tested *Pd*-positive in the area. This is in stark contrast to the wildfire-like initial spread of WNS in the Appalachian range on the East Coast of North America a decade ago.

We decided not to incorporate relative humidity (RH) into the models. Conidial fungi, such as *Pd*, have a higher probability of propagation (Hajek, Carruthers, & Soper, 1990), increased growth rate (Marroquin, Lavine, & Windstam, 2017) and increased probability of infecting the host at high RH (Hayman et al., 2016). An increase in RH also improves the survival of *M. lucifugus* during hibernation in the absence of *Pd* by reducing evaporative water loss (Hayman et al., 2016), which is why the species typically use hibernation sites with 90%–100% RH (but see Davis, 1970; Twente, 1955; Webb, 1995). Essentially, RH affects the hibernation success of *M. lucifugus* independently of the presence of *Pd* (Cryan, Meteyer, Boyles, & Blehert, 2010; Willis, Menzies, Boyles, & Wojciechowski, 2011). However, bearing this in mind, the model may not be applicable to other species, which prefer or are able to hibernate at lower RH, such as *Eptesicus fuscus* (Klüg-Baerwald & Brigham, 2017), or other species of bats often sharing hibernacula with *M. lucifugus*, which may express different infection potentials such as *Perimyotis subflavus* and *Myotis septentrionalis* (Hoyt et al., 2016). Also, less data are available on the spatial dynamics of these species, and their effect on the spread of WNS is unaccounted for in our model (Arnold, 2007; JB Johnson, Gates, & Ford, 2009; but see Kurta & Murray, 2002). Prior to the onset of WNS, *M. lucifugus* was by most estimates very much the dominant species in terms of individuals counted at hibernacula and can be expected to have significantly contributed to the spread (Langwig et al., 2012).

Our model suggests that prioritizing the preservation or restoration of high-quality habitat, which were optimal for *M. lucifugus* hibernation prior to WNS, may enhance the spread and impact of *Pd*. In areas where *Pd* has become established and endemic, these hibernacula with suitable resources/climate may become metapopulation-scale management traps: sites that are normally beneficial and attractive to bats, but become a net drain on the metapopulation owing to the impacts of disease (Leach et al., 2016). As these reservoirs are undetectable to the bats, these high-quality patches may continue to attract (and infect) susceptible immigrants. This is an example of an ecological trap that easily arises in spatial landscapes with "hidden" threats (e.g., Abrams, Ruokolainen, Shuter, & McCann, 2012; Leach et al., 2016). Similarly, we also expect that hibernacula with low temperature, regardless of landscape structure, will be less likely to develop pathogen reservoirs and may serve as refugia for susceptible bats, and thus, conservation strategies should be prioritized or at least biased towards these hibernacula.

ACKNOWLEDGEMENTS

We thank Mike Begon, Dave Daversa, Jenni Prokkola, Joseph S. Johnson and Riley F. Bernard for useful comments. We also acknowledge our funders H2020 Marie Skłodowska-Curie Actions (T.M.L., 706196) and Academy of Finland (J.A. and L.R., 286405).

AUTHOR CONTRIBUTIONS

T.M.L. and L.R. formulated the study question. T.M.L. supplied the reference data and wrote the first draft of the manuscript. J.A. and L.R. conducted parametrization and modelling. L.R. produced graphics. All authors contributed to writing the final version.

DATA ACCESSIBILITY

All data used have been obtained from cited, published articles. The model in its entirety is described in the supplementary information, and a simplified model is available at https://doi.org/10.5281/zenodo.1296303 (Lilley, Anttila & Ruokolainen, 2018).

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SUPPORTING INFORMATION

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How to cite this article: Lilley TM, Anttila J, Ruokolainen L. Landscape structure and ecology influence the spread of a bat fungal disease. *Funct Ecol*. 2018;32:2483–2496. https://doi.org/10.1111/1365-2435.13183