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Sickness-induced lethargy can increase host contact rates and pathogen spread in water-limited landscapes

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Abstract

1. Severe infections in vertebrates commonly elicit sickness behaviour that includes anorexia and lethargy. Intuitively, sickness-induced lethargy (SIL) should reduce contact among hosts. Therefore, for directly transmitted pathogens, sickness behaviour should reduce pathogen spread. However, there are indications that the relationship between SIL and host contact rates can be reversed under specific social conditions.
2. Here, we used an agent-based model to investigate the possibility that the nonsocial environment can also impact the relationship between SIL and host contact rates.
3. Our results demonstrate that in water-limited landscapes, SIL can increase host contact rates and associated pathogen spread. Based on our results, we hypothesize that a sickness-induced increase in contact rates should be particularly likely and most pronounced in animals that are highly water dependent such as African buffaloes living in savanna environments.
4. In the context of virulence evolution, our findings contradict the expectation that the direct transmission of pathogens generally favours the evolution of reduced pathogen virulence compared to vector- and water-borne transmission. Instead, our findings suggest that the opposite effect is possible in water-limited landscapes: compared to vector- and water-borne transmission, direct transmission can favour the evolution of increased virulence.
5. Our findings could be relevant in contexts other than direct transmission in water-limited landscapes. For example, in addition to aggregating around limited water sources, sick individuals might aggregate at, or around, limited food sources, which could facilitate the spread of pathogens with different transmission modes. Therefore, sickness-induced behavioural changes could critically affect the transmission of many pathogens in different environmental contexts.

KEYWORDS
evolution of virulence, host contact rates, host–pathogen interactions, sickness behaviour, water-limited landscapes

1 | INTRODUCTION

Research has shown that host behaviour can influence the risk of being infected by pathogens, and vice versa, that infection can also influence the behaviour of the hosts. For example, several studies have addressed how variation in contact patterns affects the dynamics of pathogen transmission and the evolution of pathogen virulence (Bansal, Grenfell, & Meyers, 2007; Boots & Mealor, 2007; Boots & Sasaki, 1999; Eames & Keeling, 2002; Eubank, Guclu, Kumar, & Marathe, 2004; Kamo & Boots, 2004; Kao, Danon, Green, & Kiss, 2006; Lion & Gandon, 2015, 2016; Meyers, Pourbohloul, Newman, Skowronski, & Brunham, 2005; Nunn, Thrall, & Kappeler, 2014; Nunn, Thrall, Stewart, & Harcourt, 2008; Read & Keeling, 2003; Salathé et al., 2010; Wild, Gardner, & West, 2009). The reverse effect, that is, from pathogens to host behaviour, has been studied primarily by behaviourists interested in whether and how behavioural changes following infections are adaptive from the perspectives of the host (Adelman & Martin, 2009; Hart, 1988, 2011; Lopes, 2014; Lopes, Adelman, Wingfield, & Bentley, 2012) or the pathogen (Lefevre et al., 2009; Libersat, Delago, & Gal, 2009; Poulin, 1994; Poulin & Maure, 2015), and whether and how pathogens affect the evolution of social behaviours (Griffin & Nunn, 2012; Kappeler, Cremer, & Nunn, 2015; Nunn, Jordán, McCabe, Verdolin, & Fewell, 2015; Patterson & Ruckstuhl, 2013). Although several studies emphasized the importance of reciprocal effects, that is, from host behaviour to pathogens and from pathogens to host behaviour (e.g., Ewald, 1980; Nesse, Williams, & Mysterud, 1995), interactions between pathogens and behaviour have often been studied in isolation (Ezenwa et al., 2016).

Considering reciprocal effects between host behaviour and pathogens simultaneously can have far-reaching consequences. One notable example is the hypothesis proposed by Paul Ewald, that in general vector- and water-borne pathogens should be expected to be more virulent than directly transmitted pathogens (Ewald, 1983, 1991, 1994). This evolution towards relatively lower virulence in directly transmitted pathogens should be caused by a feedback loop between pathogens and host behaviour: (a) infection with a pathogen results in reduced host contacts and (b) reduced contact due to infection reduces the spread of directly transmitted pathogens. If, in addition, increasing virulence elicits more intense reduction in contact rates, then increased virulence would be costly to pathogens in the sense that it leads to an infection-induced reduction in pathogen spread. These additional costs are expected to occur for directly transmitted pathogens but not for vector- or water-borne pathogens that do not rely on contact among hosts. Therefore, compared to vector- or water-borne pathogens, one would generally expect the evolution of lower levels of virulence in directly transmitted pathogens. This example illustrates the potential importance of reciprocal effects between host behaviour and pathogens for the spread and evolution of pathogens. In addition, it highlights that such reciprocal effects can emerge when infections lead to reduced contact.

A reduction in contact of infected hosts can be mediated by two main mechanisms. The first mechanism is the avoidance of infected individuals: as for example reported in Caribbean spiny lobsters (*Panulirus argus*) and mandrills (*Mandrillus sphinx*) (Behringer, Butler, & Shields, 2006; Poirotte et al., 2017). The second mechanism is sickness-induced lethargy (SIL). It is well established that in a wide range of vertebrates, infections can lead to lethargy, which is associated with anorexia, reduced drinking, reduced movement and reduced social interactions (for reviews on this topic, see Adelman & Martin, 2009; Hart, 1988; Hart, 2011; Lopes, Block, & König, 2016). Nevertheless, despite these observations, it is not fully established that infections generally lead to reduced contacts.

There are several indications that social behaviours and the social environment can modulate the effects of infection on contact rates. For instance, social factors can modulate sickness behaviour (Adelman & Martin, 2009; Lopes, 2014; Lopes et al., 2012). Furthermore, contact rates can also depend on the reactions of other uninfected individuals. This possibility has been already emphasized by Paul Ewald who argued that directly transmitted pathogens can evolve increased virulence in some contexts in which infections increase contact. Such situations might occur in hospitals if lethargic infected people come in contact with many uninfected attendants (Ewald, 1994). A similar effect has been documented in an experimental study on house finches (*Carpodacus mexicanus*). The authors of this study suggested that uninfected individuals may specifically seek proximity with infected individuals, presumably because uninfected individuals benefit from the reduced competitive ability of infected individuals (Bouwman & Hawley, 2010). This example highlights the possibility that social behaviours and the social environment can reverse the relationship between SIL and host contact rates.

Here, we investigate the possibility that not only the social environment but also properties of the nonsocial environment might impact the relationship between SIL and host contact rates. To this end, we focus on a common property of the nonsocial environment of wild animals: movement constraints that are imposed by the distribution of limited resources. Specifically, we focus on constraints due to limited availability of drinking water in dry landscapes. One major reason for this focus is the expectation that limited water availability forces animals to share the same water source(s) and thus facilitates water-borne transmission of pathogens. Therefore, based on Ewald's hypothesis we would expect that, under these conditions, pathogens that can be transmitted directly and via water evolve towards increased virulence. This expectation rests on the assumption that infections lead to reduced contact (see above). However, this expectation might be wrong because limited availability of drinking water does not only affect water-borne transmission; it also influences movement patterns and thus contact rates among hosts. To explore the potential implications of such constraints for the relationship between SIL and contact rates, we use an agent-based model in which we implemented basic assumptions about movement from which contact rates and the related spread of pathogens emerge. To investigate the role of SIL on the spread of directly

transmitted pathogens in water-limited environments, we contrasted situations in which the pathogens do not elicit sickness behaviour to situations in which they elicit varying degrees of sickness intensity.

2 | MATERIALS AND METHODS

2.1 | Model description

The model description is based on the overview, design concepts and details (ODD) protocol for describing individual- and agent-based models (Grimm et al., 2006, 2010). Table 1 contains an overview of all model parameters.

2.1.1 | Overview

Purpose

We aimed to investigate how movement due to limited water availability can influence the effect of SIL on (a) contact rates of infected individuals and (b) the related spread of directly transmitted pathogens. Movement constraints were assumed to arise from the need of individuals to forage and drink on a regular basis in landscapes with limited availability of drinking water. We also assume that infection-induced lethargy can change the movement behaviour of the host by (a) increasing resting and/or (b) decreasing the visitation of water sources for drinking. Of specific interest is the question of whether and under which conditions infection-induced changes in these behaviours can increase host contact rates and pathogen spread.

TABLE 1 Overview of model parameters

Parameter	Description	Value in the baseline analysis
Environmental parameters		
g	Food growth rate	0.01
Forager specific parameters		
N	Number of individuals	1,000
l_s	Baseline step length	1
a	Maximum turning angle	30
u_{F^*}	Baseline foraging utility	1
u_{R^*}	Baseline resting utility	0.1
u_{D^*}	Baseline drinking utility	1, 100
t_D	Number of time steps after drinking during which drinking is suppressed	50
Pathogen-related parameters		
s	Intensity of sickness-induced lethargy	1, 2, 4, 8, 16, 32, 64, 128, 256, 512, 1,024
d	Contact distance	1
p_c	Infection probability at contact	0.0001, 0.0005, 0.001
p_r	Infection probability from reservoir	0.00001
e	Incubation time	50
l_i	Infection length	1,000

State variables and scales

The model contains three entities: food patches, water patches and foragers. Both types of patches are situated in a 101 × 101 grid that forms a two-dimensional torus. Each cell in this grid is either a water patch or a food patch. In our baseline analysis, we assumed a single water source in the centre of the simulation space (Figure 1). Food patches can either contain food or be empty. The model contains a fixed number N of foragers that are characterized by the following state variables: (a) location (x and y coordinate) in continuous space; (b) spatial orientation; (c) infection status and (d) number of time steps since the last water uptake; and (e) utilities for resting, foraging and drinking, which determine the probability that the forager engages in these behaviours.

Process overview and scheduling

The model proceeds in discrete time steps in which three main processes occur. The first main process captures environmental dynamics of re-growing food in a subset of the depleted food patches. The second main process captures the behaviours of foragers, which include resting, foraging, drinking and associated movement. The third main process captures the pathogen dynamics based on an SEIS model that includes pathogen transmission, incubation and clearance. The SEIS model assumes that

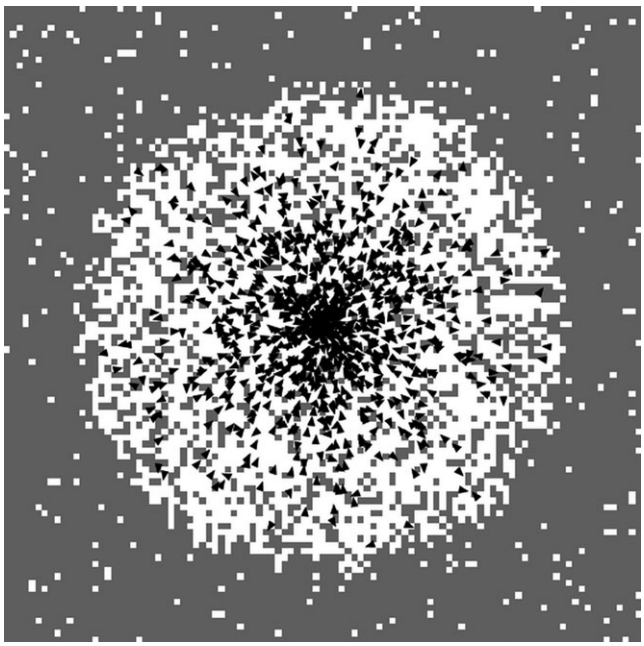

FIGURE 1 Snapshots of a simulation of host movement in a landscape with a point water source at the centre. Foragers are marked black. Food patches are coloured white if empty and grey if they contain food. The single water patch is not visible due to the high concentration of foragers around water

susceptible individuals (S) can become exposed (E), after which they become infectious (I) and finally again become susceptible (S). After a fixed incubation time, all exposed individuals become infectious and all infectious individuals will clear the pathogen after a fixed time period.

Initialization

All simulations were initialized with all food patches containing food and with N foragers. For each forager, we set the time steps since drinking to 0, the coordinates to a random location (based on a bivariate uniform distribution over the whole simulation area) and the spatial orientation to a random angle (based on a uniform distribution over all possible orientations).

2.1.2 | Submodels

Environmental dynamics

The environmental dynamics consisted of a single process of food regrowth. In each time step, a proportion g of all empty food patches is replenished. These patches are selected at random among empty ones.

Behavioural dynamics

The behavioural dynamics are determined by a stochastic process determining whether an individual is resting, foraging or drinking. At each time step t, we assign a utility $u_{t,i,j}$ for each behaviour j that an individual i could perform (i.e., resting, foraging or drinking). Specifically, we assume the probability for an individual i to perform behaviour j in time step t to be given by:

$$p_j = \frac{u_{t,i,j}}{\sum_{\text{all } k} u_{t,i,k}}. \quad (1)$$

While we assumed that foraging utilities remain constant for all time steps and individuals, drinking and resting utilities are assumed to vary over time and among individuals depending on the need to drink and/or on the infection status of the forager. Therefore, the foraging utility $u_{t,i,F}$ is always set to u_{F^*}. Resting utilities are assumed to increase for infectious individuals. For noninfectious individuals, the resting utility is set to the baseline resting utility u_{R^*}. For infectious individuals, the resting utility is set to su_{R^*}, where s quantifies the SIL intensity.

The baseline drinking utility u_{D^*} captures the degree of water dependency of the host, with higher values generating a higher priority of drinking and thus reflecting more water-dependent host. We assume two different scenarios for how the drinking utility changes over time. In the first scenario, drinking utility depends only on the number of time steps $n_{t,i}$ that passed as an individual i had drunk irrespective of their infection status. For $n_{t,i}$ smaller than the threshold t_D, we assume that drinking is suppressed and set $u_{t,i,D}$ to 0, and for values larger or equal to t_D, we set $u_{t,i,D}$ to u_{D^*}. Thus, drinking behaviour could only occur after t_D time steps since the last water uptake. In the second scenario, we assume that sickness behaviour reduces the drinking utility of infectious individuals. Therefore, in this second scenario we set $u_{t,i,D}$ to $u_{D^*}s$ for $n_{t,i} \geq t_D$. Here, s quantifies the proportional decrease in drinking utility triggered by sickness.

If a forager i rests, then it was assumed to do nothing. If a forager i decides to forage, it first checks whether it is already on a food patch that contains food. If this is the case, it consumes all the food on that patch leaving the patch empty. If a forager is on an empty food patch, then it starts moving in search for food following a correlated random walk. Specifically, based on its previous spatial orientation $o_{i,t-1}$ a new orientation $o_{i,t}$ is drawn from a uniform distribution in the interval $[o_{i,\,t-1} - a,\, o_{i,t-1} + a]$ and the forager moves forward with step length l_s. In both drinking scenarios, when a forager i decides to drink, it either drinks if it is on the water patch or otherwise adjusts its spatial orientation $o_{i,t}$ to face the water patch and then moves forward with step length l_s.

Pathogen dynamics

As described above, the pathogen dynamics are described based on an SEIS model (Keeling & Rohani, 2008). Pathogens can be transmitted either from an external reservoir or from infectious individuals to susceptible individuals. In either case, a susceptible individual first becomes exposed for e time steps. Thereafter, the individual becomes infectious for l_i time steps, after which the pathogen is cleared and the forager again becomes susceptible. It is only during this infectious state, not during the exposed phase, that we assume that SIL is occurring and affecting the utility of drinking and resting as described above. Pathogen transmission from the reservoir occurs for each susceptible individual in each time step with a constant probability p_r. Pathogen transmission from infectious individuals can only occur between individuals who are "in contact," that is that are within a distance equal or less than d spatial units (where one unit equals the length of an edge of a grid cell). Each infectious individual that is within contact distance transmits pathogens to a susceptible individual with probability p_c.

2.1.3 | Model analysis

The model analysis consisted of three main parts. In the first part, we investigated how sickness behaviour affects contact rates when sickness only affects resting or when it affects both resting and drinking. To assess the effect of sickness on the contact rate between hosts, we did not allow pathogens to spread. In the second part of the analysis, we assessed how different intensities of SIL affect the prevalence of pathogens. To do so, we allowed the pathogens to spread.

In the third part, which we describe in the electronic supplementary materials, we performed additional analyses to assess the robustness of our findings. The main motivation for performing these additional analyses relates to difficulties to parameterize our model based on available data in the literature. We performed a local sensitivity analysis of the main model parameters: the food growth rate g, the number of individuals N, the maximum turning angle a, the baseline resting utility u_{R^*}, the number of time steps after drinking

when drinking utility t_D is activated, the contact distance d, and the infection length l_i.

In addition, to further assess the robustness of our findings we aimed to capture a broad array of different pathogens by investigating two additional models of pathogen transmission: an SEIR and an SEI model. Both models share key features with the SEIS model. These include the described transition from susceptible to exposed and the transition from exposed to infectious individuals. In contrast to the SEIS model, in the SEIR model, it is assumed that hosts acquire immunity to the pathogen after clearance, which prevents subsequent infections. Therefore, it is assumed that infectious individuals do not become susceptible again and instead transition into a recovered state (R) and then always remain in this state. In the SEI model, it is assumed that pathogens are never cleared, and thus, infectious individuals never change their infection status.

Effects of SIL on contact rates

To assess the effect of SIL on contact rates, we compared scenarios without SIL to scenarios with a range of different SIL intensities. For this purpose, we varied the intensity of SIL s between a minimum of 1, which represents the absence of SIL, and a maximum of 1,024 (to efficiently capture the effects of this parameter, we chose to investigate exponentially distributed values, see Table 1 for details).

In addition, we compared different scenarios in which we varied (a) the degree of water dependency of the host and (b) whether sickness suppresses drinking altogether. To investigate the effect of the variation in water dependency, we investigated two values of the baseline drinking utility u_{D^*}: 1, which corresponds to weakly water-dependent hosts, and 100, which corresponds to highly water-dependent hosts. To investigate the effect of SIL on drinking, we first ran simulations for different degrees of water dependency in which the drinking utility was not affected by infection state. We then repeated all simulations considering the effect of the infection state on the drinking utility (for details see section "Behavioural dynamics" in the model description).

For this specific analysis, we assumed that at any point in time, only a single individual could be infectious (i.e., we assumed $p_c = p_r = 0$). This allowed us to investigate the effect of SIL in a single social environment in which all other individuals showed no sickness behaviour. This approach also ensured that the observed variation in the contact rates of infectious individuals was not influenced by the pathogen dynamics at the population level. In our analysis, we investigated the two aforementioned scenarios: sickness either affects only resting or affects both resting and drinking.

In our simulations, we repeatedly selected a single focal individual to become infectious while varying the intensity of SIL according to the values provided in Table 1. For each of these conditions, we ran a single simulation for 101,000 time steps. The first 1,000 time steps were treated as a burn-in phase during which we did not record contact rates. During the next 100,000 time steps, the identity of the infectious individual changed over time. Specifically, every l_i time steps a new individual was randomly chosen to be infectious, and the infection status of previously infectious individual was reset to be susceptible. For each of the 100,000 time steps, we recorded the number of other foragers that came within contact distance d of the focal individual. To investigate how sickness behaviour affects the spatial distribution of foragers, we recorded for each time step the distance from the focal individual to the water patch.

Pathogen transmission dynamics

To investigate how different intensities of SIL affect pathogen transmission dynamics, we extended the aforementioned baseline scenarios to simulate pathogen transmission. We ran simulations with an infection length l_i of 1,000 time steps and an infection probability for the reservoir p_r of 0.00001. During these simulations, we systematically varied the infection probability at contact p_c (see Table 1). Each simulation was run for 1,001,000 time steps. Again, the first 1,000 time steps were treated as a burn-in phase, and we recorded the mean prevalence of infectious individuals across the following 1,000,000 time steps.

3 | RESULTS

3.1 | SIL only increases resting

In scenarios in which SIL only translates into an increase in resting utility, we observed that the presence of SIL (i.e., SIL intensity $s > 1$) can strongly increase contact rates among hosts (Figure 2a,b). Therefore, the presence of SIL can strongly increase the prevalence of infections (Figure 2c,d). The specific relationship between the SIL and contact rates changes depending on the baseline drinking utility. In the scenario with low drinking utility ($u_{D^*} = 1$), the highest contact rates and mean prevalence were reached for intermediate sickness intensities (Figure 2a,c). In contrast, in the scenario with high drinking utility ($u_{D^*} = 100$), the highest contact rates and mean prevalence were reached for the highest sickness intensities investigated (Figure 2b,d).

The increase in contact rates caused by SIL and the differences in contact rates related to the baseline drinking utility can both be explained by how SIL affects the time budget and space use of individuals. From our model assumptions, SIL increases the time individuals spend resting, which automatically decreases the time spent foraging and drinking (Figure 2e,f). Because infectious individuals spend less time foraging, they also spend less time moving away from water after drinking. This reduction in movement away from water occurs because in our model only movement performed during foraging drives individuals away from the water source. Therefore, infectious individuals remain closer to the water source (Figure 3). Because contact rates are generally higher in areas closer to water (because of crowding of individuals around a point water source) (Figure 1, Supporting Information Figure S1), a shift in space use towards areas close to water leads to an increase in contact rates.

However, shifts in space use can only occur if individuals are moving. If SIL is so intense that infectious individuals do not move, then their space use would not change over the course of an infection. This effect explains why the contact rates are lower

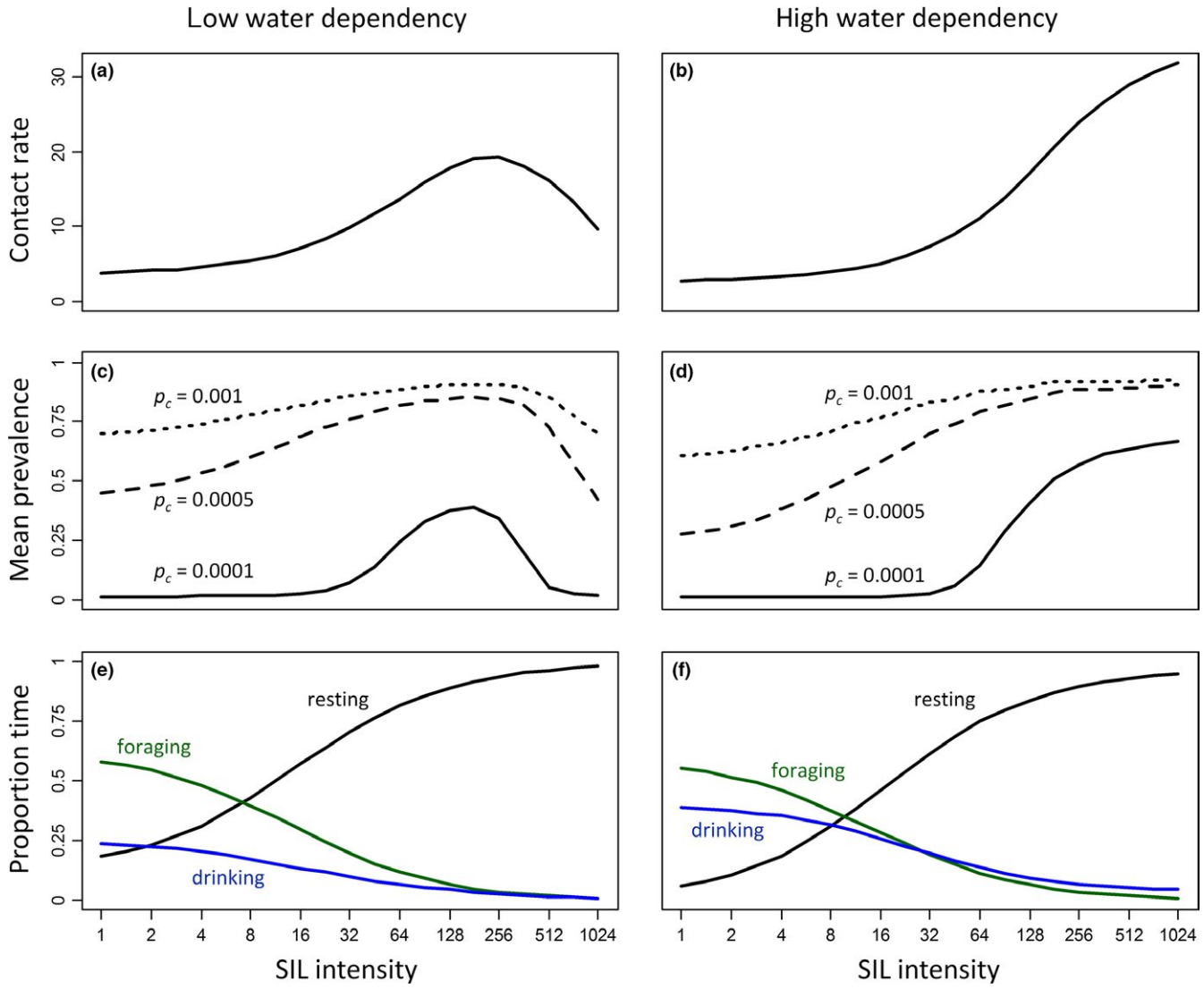

FIGURE 2 Effects of sickness-induced lethargy (SIL) on contact rates and pathogen transmission for scenarios in which sickness increases only resting utility and does not affect drinking utility. Note that a SIL intensity of 1 represents the absence of SIL (i.e., these individuals behave like noninfectious individuals). Left column (a, c, e): scenario with a baseline drinking utility of 1, that is low water dependency. Right column (b, d, f): scenario with a baseline drinking utility of 100, that is high water dependency. First row (a, b): effects on contact rates in the baseline analysis without pathogen transmission. Second row (c, d): effects on the prevalence of infected individuals in the analysis that includes pathogen transmission. Each prevalence value corresponds to the mean prevalence across 1,000,000 time steps of a single simulation run. Solid line: infection probability at contact p_c = 0.0001; dashed line p_c = 0.0005; dotted line p_c = 0.001. Third row (e, f): effects on time budget in the baseline analysis without pathogen transmission. Green line: foraging; blue line: drinking, including moving towards the water source; black line: resting

for the highest sickness intensities than for the intermediate sickness intensities in the scenario with a low baseline drinking utility (Figure 2a): at very high sickness intensities, individuals almost stop foraging and drinking (Figure 2e), which limits the shift in space use (compare black and grey bars in Figure 3a). In contrast, a higher baseline drinking utility ensures that even for very high sickness intensity, individuals continue to move towards the water (Figure 2f). In combination with a much-suppressed foraging behaviour, the high dependence on water ensures a very strong shift towards areas close to this resource (Figure 3b). This effect explains why we measured the highest contact rates in the simulations that combined a high baseline value of drinking utility and the highest intensity of SIL (Figure 2b).

3.2 | SIL increases resting and decreases drinking

When SIL impacts both the resting and drinking utilities, our analyses also show that the presence of SIL can increase contact rates among hosts (Figure 4a,b) and mean prevalence (Figure 4c,d). This time, however, we found that the maximal increase in contact rates was much lower. The maximal increase in contact rates occurred at lower intensities of sickness intensity. In addition, this scenario

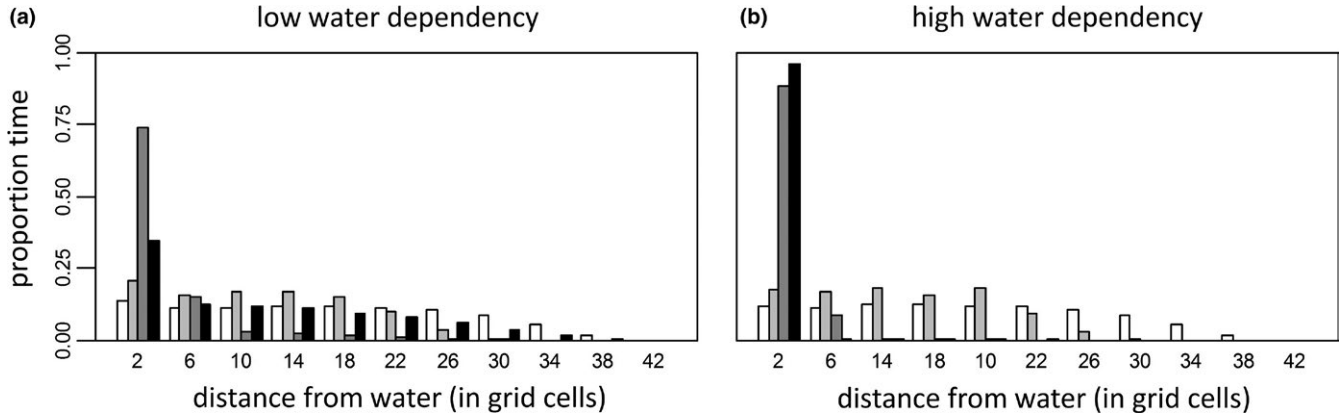

FIGURE 3 Space use of infectious individuals in scenarios in which sickness increases only resting utility and does not affect drinking utility. (a) Scenario with a baseline drinking utility of 1, that is low water dependency. (b) Scenario with a baseline drinking utility of 100, that is high water dependency. White bars: absence of sickness-induced lethargy (SIL), that is SIL intensity set to 1 (i.e., these individuals behave like noninfectious individuals); light grey bars: SIL intensity set to 8; dark grey bars: SIL intensity set to 128; black bars: SIL intensity set to 1,024

shows that high sickness intensities can sometimes result in a slight decrease in contact rates and a related decrease in mean prevalence.

The scenarios in which sickness lethargy affects drinking and those in which it does not thus produce different results. The differences are explained by how SIL in drinking affects the time budget and space use of individuals. According to equation 1, a reduction in the drinking utility effectively increases the probability of resting and the probability of foraging (compare Figures 2e,f and 4e,f). Even though these effects are relatively small, increased resting and foraging both reduce drinking and thus reduce the space use shift of infectious individuals towards water (compare Figures 3 and 5). In the extreme case of an almost complete suppression of drinking but maintenance of low levels of foraging, space use can shift away from the water (Figure 5a), which results in a decrease in contact rates (Figure 4a) and an associated decrease in mean prevalence (Figure 4c).

3.3 | Sensitivity analysis

The results of the sensitivity analysis show that the relationships between SIL and contact rates found in the baseline analysis (Figures 2 and 4) are robust to variation in the food growth rate g (Supporting Information Figure S2), the number of individuals N (Supporting Information Figures S3 and S4), the maximum turning angle a (Supporting Information Figure S5), the baseline resting utility u_{R^*} (Supporting Information Figure S6), the number of time steps after drinking when drinking utility t_D is activated (Supporting Information Figure S7), the contact distance d (Supporting Information Figure S8) and the infection length l_i (Supporting Information Figure S9). While the variation of some parameters affected the overall contact rates, the general patterns remained the same. In addition, results of simulations with SEIR and SEI models confirmed that pathogen transmission dynamics in all three models (SEIS, SEIR and SEI) show similar patterns in relation to SIL (Supporting Information Figures S10 and S11).

4 | DISCUSSION

Lethargy is a general reaction of a host to infection and can reduce interindividual contact. Therefore, SIL might be a critical driver in the evolution of pathogen virulence (Day, 2001; Ewald, 1994). Our simulation model shows that the relationship between the occurrence of lethargy and contact rates is more complex than often assumed. Two main factors that can complicate this relationship have previously been identified. First, the social context and reactions of uninfected individuals can change SIL and can even result in an increase in the contact rates for infectious individuals (Bouwman & Hawley, 2010; Lopes, 2014; Lopes et al., 2012). Second, it has been observed that sickness-related changes in mobility patterns can have complex effects on space use patterns in humans and therefore impact contact rates in complicated ways (Perkins et al., 2016).

Our analysis, which focuses on space use patterns in a wildlife context, emphasizes the potential importance of constraints on host mobility. Specifically, we found that lethargy can increase host contact rates and associated pathogen spread. This outcome emerges as the result of the realistic consideration that environmental conditions such as water limitation can constrain host movement patterns. Water can increase the contact rate and the spread of infection if infectious animals spend more time in the high-density areas where this patchy resource is located. For this to happen, it is only necessary to assume that infectious animals must rest more. This finding emphasizes that not only the social environment (Bouwman & Hawley, 2010), but also properties of the nonsocial environment can shape the relationship between infection-induced lethargy and host-host contact rates.

Whether and to what extent infections lead to increased contact rates in our model depends on the degree of the host's water dependence. This kind of water dependency is regulated in two ways in our model: (a) by the value of the baseline drinking utility and (b) by whether sickness behaviour decreases drinking utility. Higher values of drinking utility increase the priority of returning to water

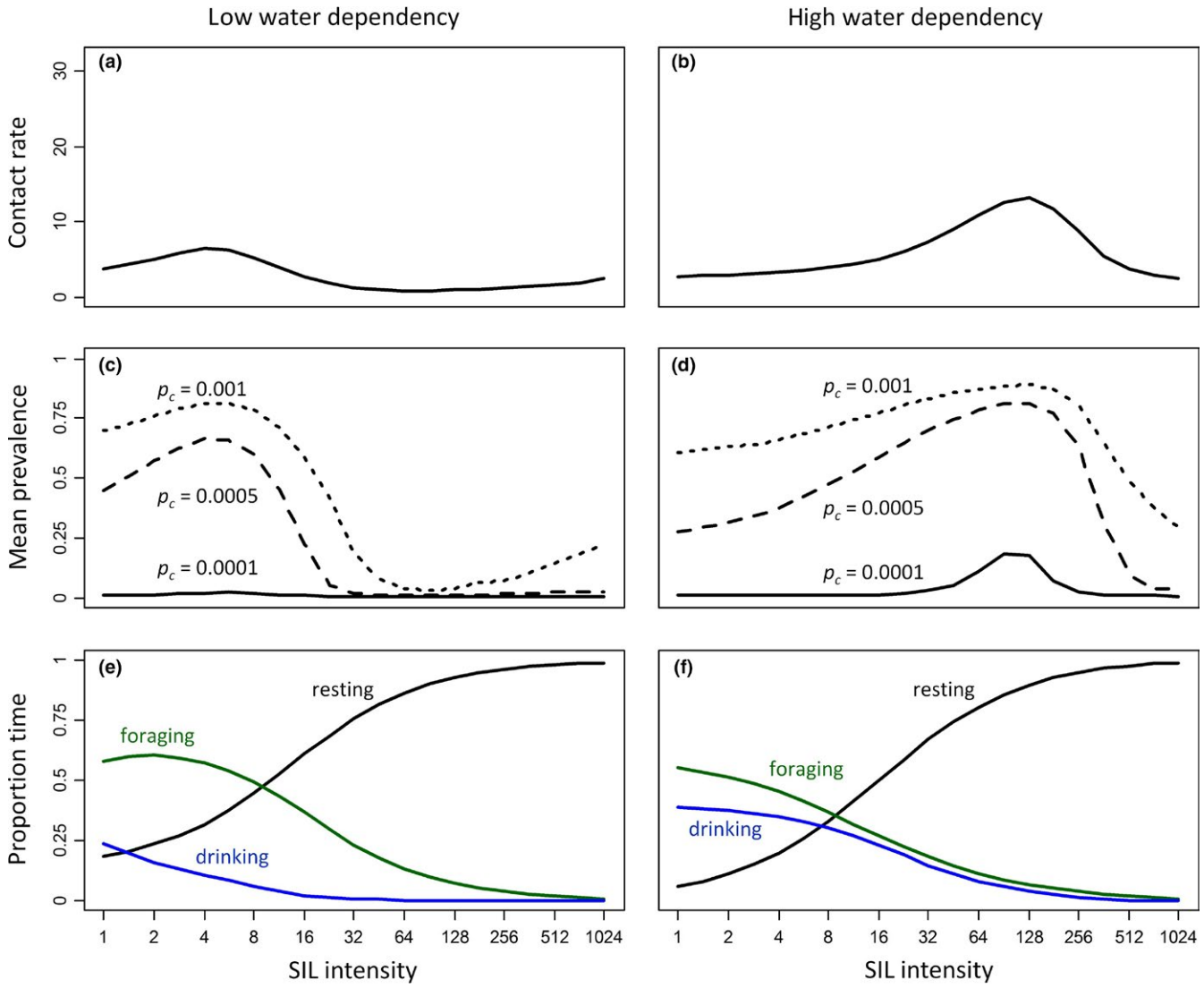

FIGURE 4 Effects of sickness-induced lethargy (SIL) on contact rates and pathogen transmission for scenarios in which sickness increases resting utility and decreases drinking utility. Note that a SIL intensity of 1 represents the absence of SIL (i.e., these individuals behave like noninfectious individuals). Left column (a, c, e): scenario with a baseline drinking utility of 1, that is low water dependency. Right column (b, d, f): scenario with a baseline drinking utility of 100, that is high water dependency. First row (a, b): effects on contact rates in the baseline analysis without pathogen transmission. Second row (c, d): effects on the prevalence of infected individuals in the analysis that includes pathogen transmission. Each prevalence value corresponds to the mean prevalence across 1,000,000 time steps of a single simulation run. Solid line: infection probability at contact p_c = 0.0001; dashed line p_c = 0.0005; dotted line p_c = 0.001. Third row (e, f): effects on time budget in the baseline analysis without pathogen transmission. Green line: foraging; blue line: drinking, including moving towards the water source; black line: resting

regularly. The highest degrees of water dependency therefore correspond to the scenarios in which the baseline drinking utility is higher and where sickness behaviour does not affect drinking utility. In these scenarios, we observed stronger increases in sickness-induced contact rates (Figures 2a,b and 4a,b). Based on these findings, we hypothesize that sickness-induced increases in contact rates should be more likely and most pronounced in animals that are highly water dependent.

For example, among large African herbivores inhabiting savanna ecosystems, browsers are generally less water dependent than grazers (Western, 1975). Whereas browsers such as common elands (*Taurotragus oryx*) can survive without drinking water, highly water-dependent grazers such as African buffaloes (*Syncerus caffer*) go to water at least once every day (Estes, 1991). We thus predict that sickness-induced increases in contact rates should be more likely and most pronounced in grazers than in browsers in savanna ecosystems. Empirical tests of this prediction are certainly challenging. A potentially fruitful avenue for dealing with these challenges could be the application of body temperature data loggers and movement tracking systems to simultaneously record changes in infection status and space use (e.g., Hetem et al., 2008).

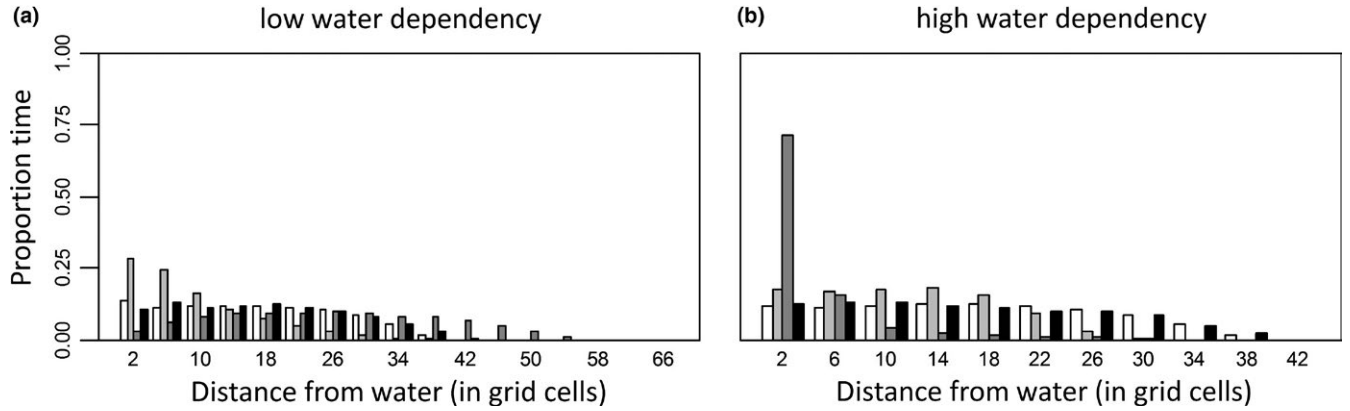

FIGURE 5 Space use of infectious individuals in scenarios in which sickness increases resting utility and decreases drinking utility. (a) Scenario with a baseline drinking utility of 1, that is low water dependency. (b) Scenario with a baseline drinking utility of 100, that is high water dependency. White bars: absence of sickness-induced lethargy (SIL), that is SIL intensity set to 1 (i.e., these individuals behave like noninfectious individuals); light grey bars: SIL intensity set to 8; dark grey bars: SIL intensity set to 128; black bars: SIL intensity set to 1,024

Our findings could be particularly important for understanding and predicting the spread and evolution of pathogens. For example, it is generally acknowledged that seasonal changes in host contact rates are a major determinant of seasonal variation in pathogen transmission (Altizer et al., 2006). An important driver of changes in contact rates could be seasonal changes in surface water availability in dry regions. For example, such an effect has been observed in African buffaloes in Zimbabwe (Miguel et al., 2013). African buffaloes are reservoirs for a number of economically important infectious diseases including foot and mouth disease (FMD) and bovine tuberculosis (BTB) (Alexandersen & Mowat, 2005; Renwick, White, & Bengis, 2007). Miguel et al. (2013) suggested that the concentration of buffaloes around water in the dry season increases contact with cattle, which might be a main source of FMD spillover from buffaloes to cattle. In addition to these general changes in ranging behaviour, the findings from our model suggest the possibility that pathogen transmission and spillover events could be strongly influenced by behavioural changes of infected animals.

Sickness behaviour of wildlife is generally poorly understood; this is true for African buffaloes. Nevertheless, there are some indications that diseases such as BTB elicit SIL in buffaloes, which might also affect ranging behaviour and contact rates. Specifically, it has been documented that BTB infection can be related to decreased body condition (Caron, Cross, & Du Toit, 2003) (but see Cross et al., 2009 for findings that suggest that effects on body condition might depend on environmental conditions). If these highly water-dependent animals show some form of SIL similar to what we assumed in our model, then the resulting aggregation near water sources could be an important influence on seasonal dynamics of disease transmission among buffaloes as well as spillovers to cattle.

In addition to influencing pathogen transmission dynamics, the influence of sickness on the distribution of animals around limited water sources could have far-reaching implications for the evolution of pathogen virulence. As described in the introduction, water-limited landscapes in which many animals share the same water source could facilitate an evolutionary transition from direct to water-borne transmission. Based on the assumption that SIL generally reduces contact (Ewald, 1983, 1991, 1994), we would have expected that such evolutionary transition generally results in the evolution of higher pathogen virulence. Our findings contradict this expectation. As already emphasized by Ewald (1994), if infections increase contacts among hosts, then direct transmission should generally increase virulence compared to vector- and water-borne transmission. Therefore, we would expect that evolutionary transitions from direct to water-borne transmission in water-limited landscapes might lead to a decrease in pathogen virulence. In sum, we propose that the effect of the transmission mode on the evolution of pathogen virulence can strongly depend on the ecology of the host.

At last, our findings could be relevant in contexts other than direct transmission in water-limited landscapes. For example, in addition to aggregating around limited water sources, sick individuals might aggregate at or around limited food sources, which could facilitate the spread of pathogens with different transmission modes. Such a scenario is consistent with observations on house finches that become infected with *Mycoplasma gallisepticum*, *a* pathogen that can be transmitted directly or environmentally, for example via fomites on bird feeders. Infected individuals were observed to spend more time at bird feeders (Hotchkiss, Davis, Cherry, & Altizer, 2005). In addition, time spend at feeders predicts both acquisition and transmission of this pathogen (Adelman, Moyers, Farine, & Hawley, 2015). Thus, sickness-induced behavioural changes might strongly influence the spread of this pathogen. This example emphasizes that sickness-induced behavioural changes could critically affect the transmission of many pathogens in different contexts, including anthropogenic resource provisioning. It is already well recognized that resource provisioning can change transmission dynamics by changing overall contact patterns among hosts (Becker, Streicker, & Altizer, 2015; Murray, Becker, Hall, & Hernandez, 2016). Further investigation into specific effects on the behaviour of infected individuals could be a fruitful avenue for future research.

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AUTHORS' CONTRIBUTIONS

We have no competing interests. M.F., S.K.–S., A.D.G. and A.C. conceived the study; M.F. implemented and analysed the model; M.F., S.K.–S., A.D.G. and A.C. wrote the manuscript. All authors gave final approval for publication.

DATA ACCESSIBILITY

This study does not use data.

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