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Disentangling the effects of exposure and susceptibility on transmission of the zoonotic parasite *Schistosoma mansoni*

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Summary

1. For all parasites, transmission is composed of two processes: host contact with parasites ('exposure') and risk of infection given such contact ('susceptibility'). Classic models, such as mass action (density-dependent) transmission, lump these processes together.

2. However, separating these processes could enhance predictions for disease dynamics, especially for free-living parasites. Here, we outline three transmission models that partition exposure and susceptibility.

3. Using data from a study of *Schistosoma mansoni* (trematode) infections in *Biomphalaria glabrata* snails, we competed these three models against four alternative models, including the mass action model (which lumps exposure and susceptibility).

4. The models that separately accounted for exposure and susceptibility best predicted prevalence across the density gradients of hosts and parasites, outperforming all other models based on Akaike information criterion. When embedded into a dynamic epidemiological model, the exposure-explicit models all predicted lower equilibrium densities of infected snails and human-infectious cercariae.

5. Thus, population-level epidemiological models that utilize the classic mass action transmission model might overestimate human risk of schistosomiasis. More generally, the presented approach for disentangling exposure and susceptibility can distinguish between behavioural and immunological resistance, identify mechanisms of 'disease dilution' and provide a more complete dissection of drivers of parasite transmission.

Key-words: epidemiology, exposure, *Schistosoma*, susceptibility, transmission

Introduction

For all parasites, transmission is fundamentally composed of two key processes: contact with hosts ('exposure') and the risk of infection given such a contact ('susceptibility'). However, classic transmission models, such as density and frequency dependence, lump these processes into a single transmission rate parameter, β (McCallum, Barlow & Hone 2001). Here, we argue that disentangling these two fundamental processes can better predict transmission for many parasites, especially those with free-living infective stages. Disentangling exposure and susceptibility matters because parasites that attack (i.e. invade or penetrate) hosts are removed from the environment, regardless of their subsequent infection success. In other words, once they invade a host, parasites either infect or die (King, Jokela & Lively 2011). Thus, the per capita transmission rate depends on both exposure and susceptibility. However, the depletion of free-living parasites from the environment hinges only on the exposure rate.

Disentangling exposure and susceptibility using theory and experiments can facilitate a much deeper understanding of host–parasite interactions. It can provide more predictive, mechanistic alternatives to classic transmission functions, which often fit data poorly (Dwyer, Elkinton & Buonaccorsi 1997; Fenton *et al.* 2002). It can also help partition the effects of environmental, ontogenetic and genetic variation on disease spread (Theron, Rognon & Pages 1998; Hall *et al.* 2007; Civitello *et al.* 2012) and identify mechanisms for 'dilution' or 'decoy' effects, in which certain species or individuals inhibit disease spread in focal hosts (Thieltges *et al.* 2008). For example, decoy hosts, with high exposure rates but low (or zero) susceptibility, should depress disease spread the most. Finally, separating exposure and susceptibility could

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reveal whether hosts evolve to avoid exposure to parasites or immunologically resist parasites after contact.

Here, we outline a framework to partition exposure and susceptibility for hosts confronted with free-living parasites. This approach can be applied to experiments that track infection intensity or prevalence across density gradients of hosts and parasites. Using data from a classic study of *Schistosoma mansoni* infections in *Biomphalaria glabrata* snails (Carter, Anderson & Wilson 1982), we competed three exposure-explicit transmission models against four alternatives, including the classic mass action model, that lump exposure and susceptibility. If depletion of miracidia via snail exposure influences transmission, then it could alter the ecological dynamics and human risk of exposure for *Schistosoma*. More broadly, disentangling exposure and susceptibility could enhance our understanding of the ecological and evolutionary drivers of transmission for many parasites.

Materials and methods

We reanalysed data from a classic study of *Schistosoma* transmission to snails (Carter, Anderson & Wilson 1982) to statistically compete seven transmission models. The authors exposed *B. glabarata* snails to *S. mansoni* miracidia for 3 h at 25 °C in 1 L water. They factorially crossed the density of hosts (five levels: 1, 3, 5, 7 and 9 hosts L^{-1}) and parasites (five levels: 1, 3, 5, 10 and 20 miracidia L^{-1}) and visually diagnosed snails. Treatments with lower host density were replicated more. However, we could only obtain treatment-level total counts of infected and uninfected hosts (their Table 1). Thus, here, we conservatively consider each treatment as one replicate.

MODEL CONSTRUCTION

We considered seven transmission models that tracked changes in the densities of susceptible hosts, S, infected hosts, I, and free-living parasites, P, with differential equations. Because the data that we analysed stem from a short-term infection experiment, we fit models that ignore processes that occur at longer time-scales, for example, birth and deaths of hosts and parasites. We started with a general template in which transmission dynamics are determined by two per capita rates: the transmission rate, T, and the depletion rate of free-living parasites, D (eqns 1a–c):

$$dS/dt = -T \times S \times P \quad 1a$$

Table 1. (A) Construction, (B) parameterization and (C) competition of transmission models fit to the infection data

(A). Model construction: competing models for disease transmission

Model	Transmission rate, T[1]	Equation	Depletion rate, D[1]	Equation
Mass action	β	2a	$-\beta$	2b
Exposure-susceptibility	$\varepsilon\sigma$	3a	$-\varepsilon$	3b
Asymptotic exposure	$\varepsilon\sigma/(1 + \varepsilon h(S + I))$	4a	$-\varepsilon/(1 + \varepsilon h(S + I))$	4b
Disproportionate exposure	$\varepsilon\sigma$	5a	$-\varepsilon(S + \alpha I)/(S + I)$	5b
Power law – hosts	βS^a	6a	$-\beta(S + I)^a$	6b
Power law – parasites	βP^b	7a	$-\beta P^b$	7b
Power law – hosts and parasites	$\beta S^a P^b$	8a	$-\beta(S + I)^a P^b$	8b

(B). Model parameterization: maximum likelihood parameter estimates for each model

Model	ε (L host^{-1} day^{-1})	σ (host parasite^{-1})	β (L day^{-1})	h (day host^{-1})	α (–)	a (–)	b (–)
Mass action	–	–	1·128	–	–	–	–
Exposure-susceptibility	17·21	0·415	–	–	–	–	–
Asymptotic exposure	32·16	0·462	–	0·002	–	–	–
Disproportionate exposure	50·88	0·602	–	–	2·52	–	–
Power law – hosts	–	–	1·248	–	–	−0·342	–
Power law – parasites	–	–	1·92	–	–	–	−0·311
Power law – hosts and parasites	–	–	2·808	–	–	−0·451	−0·375

(C). Model competition: model selection statistics

Model	Prevalence, $p(t)$	Parameters	AICc	ΔAICc	Akaike weight
Disproportionate exposure	Numerical simulation	3	114·6	0	0·980
Exposure-susceptibility	$1 - \exp(\sigma P_0/S_0 (\exp(-\varepsilon S_0 t) - 1))$	2	122·9	8·3	0·015
Asymptotic exposure	$1 - \exp(\sigma P_0/S_0 (\exp(-\varepsilon S_0 t/(1 + \varepsilon h S_0)) - 1))$	3	125·4	10·8	0·004
Power law – hosts and parasites	Numerical simulation	3	129·4	14·8	$6{\cdot}0 \times 10^{-4}$
Power law – hosts	Numerical simulation	2	192·1	77·5	$1{\cdot}5 \times 10^{-17}$
Power law – parasites	Numerical simulation	2	223·6	109·0	$2{\cdot}1 \times 10^{-24}$
Mass action	$1 - \exp(P_0/S_0 (\exp(-\beta S_0 t) - 1))$	1	236·9	122·3	$2{\cdot}7 \times 10^{-27}$

[1]Per capita rates.

$$dI/dt = T \times S \times P \quad 1b$$

$$dP/dt = -D \times (S + I) \times P \quad 1c$$

we then specified functions for these rates, T and D, for each model (eqns 2–8; Table 1A).

First, we considered the mass action transmission model (eqns 2a,b). This model assumes a constant per capita exposure rate between susceptible hosts and parasites, and exposure and susceptibility to infection are lumped into the transmission coefficient, β (McCallum, Barlow & Hone 2001). Further, each transmission event depletes a parasite from the environment, and infected individuals remove parasites from the environment during secondary transmission events. Thus, depletion of parasites through transmission depends on total host density, $N = S + I$.

Next, we considered three models that explicitly separate exposure and susceptibility. The *exposure-susceptibility* model assumes a constant per capita exposure rate, ε (eqns 3a,b). It also assumes a constant susceptibility, σ, or probability of infection given exposure to a parasite ($0 \leq \sigma \leq 1$). This per capita exposure rate, ε, represents the volume of the environment that is depleted of parasites per host per unit of time. This per capita rate does not depend on density. However, the total exposure rate (units: parasites per volume per unit of time) increases with density, because it is the product of the per capita exposure rate and the densities of hosts and parasites. Hence, this model explicitly models transmission as the product of two components: exposure rate, ε, and susceptibility, σ (i.e. $T = \varepsilon \times \sigma$; Table 1). In this model, both host classes ($S + I = N$) deplete parasites from the environment during exposure (i.e. not only after successful transmission). Thus, parasite removal depends on the exposure rate, ε, not on the transmission rate, β. If $\sigma = 1$, then this model reduces to the *mass action* model.

Secondly, we considered an *asymptotic exposure* transmission model (eqns 4a,b). The *mass action* and *exposure-susceptibility* models assume that parasites instantly invade hosts after a contact. However, parasites might spend some 'handling time', probing hosts and even reverting back to searching. This results in an asymptotic exposure rate that is analogous to a Type II functional response for predator foraging (Holling 1959; McCallum, Barlow & Hone 2001). This model reduces to the *exposure-susceptibility* model if the parasite's handling time, h, equals zero.

Thirdly, we considered a *disproportionate exposure* model (eqns 5a,b). Parasites might disproportionately attack susceptible hosts (e.g. to avoid competing with other parasites) or infected hosts [e.g. to 'hitchhike' on compromised hosts (Leung & Poulin 2007)]. Therefore, we returned to the *exposure-susceptibility* model and relaxed the assumption that parasites contact infected and uninfected hosts at the same rate. In this model, an additional parameter, α, represents the relative exposure rate for infected hosts. If $\alpha = 0$, then parasites completely avoid infected hosts. However, if $\alpha > 1$, then parasites disproportionately attack infected hosts. This model reduces to the *exposure-susceptibility* model if $\alpha = 1$.

Finally, we also considered three power law functions that are often used to model nonlinear transmission dynamics (Fenton *et al*. 2002). These phenomenological functions allow the per capita transmission rate to increase ($a > 0$, $b > 0$) or decrease ($a < 0$, $b < 0$) with the density of hosts and parasites, respectively. These models reduce to the density-dependent model when $a = b = 0$. In the *power law – hosts* model, we allowed the per capita transmission rate to depend on host density (i.e. $b = 0$; eqns 6a, b). In the *power law – parasites* model, we allowed it to depend on parasite density (i.e. $a = 0$; eqns 7a,b). Lastly, in the *power law – hosts and parasites* model, it could depend on both densities (eqns 8a,b).

MODEL PARAMETERIZATION AND COMPETITION

We fit the models to the infection data using the mle2 function in the bbmle package in R (Bolker 2013). For each model, we found the parameter values that best predicted infection prevalence across the treatments. Each model provides a deterministic description of transmission. However, the experiment involved small numbers of individuals. Therefore, we treated infection as a stochastic process. Following this standard methodology for transmission experiments (Rachowicz & Briggs 2007), the likelihood function for the number of infected individuals at the end of the experiment follows the binomial distribution with two parameters: $p(t)$, the probability of infection predicted by the model and the initial number of susceptible hosts. To predict prevalence, we integrated the *mass action*, *exposure-susceptibility* and *asymptotic exposure* models given the initial conditions of the experiment and rearranged the result to obtain analytical expressions for infection prevalence as a function of time, $p(t) = I(t)/S(0)$ (Table 1C). We obtained predictions for the other models via numerical simulation with the lsoda function in the deSolve package in R (Soetaert, Petzoldt & Setzer 2010). After fitting the models, we compared them using the Akaike information criterion corrected for small sample size (AICc; Bolker 2008).

IMPLICATIONS FOR *S. mansoni* EPIDEMICS

The statistical analysis challenged the seven transmission functions to predict prevalence when the initial number of parasites was fixed and finite. However, in natural host–parasite systems, parasites are continually introduced into the environment by infected hosts. Therefore, we examined the implications of these alternative transmission functions under more realistic conditions by embedding them in a fully dynamic epidemiological model for parasites with free-living stages, such as *Schistosoma spp*. We examined how four of the transmission models, *mass action*, *exposure-susceptibility*, *asymptotic exposure* and *disproportionate exposure*, influence predictions of disease spread and human risk. We did not examine the power law models because they fitted the transmission data poorly and do not offer specific transmission mechanisms. We embedded these transmission functions in a model that focuses on the aquatic life stages of the parasite (miracidia, snail hosts and cercariae) to highlight the effects of the different functions for transmission to snail hosts. The model tracks changes in the density of susceptible host snails (S), infected host snails (I), free-living miracidia (M) and free-living cercariae (C) through time using differential equations based on previous models for schistosomiasis (Anderson & May 1979):

$$dS/dt = b(S + \rho I)(1 - c(S + I)) - d_h S - T \times SM \quad 9a$$

$$dI/dt = T \times SM - (d_h + v)I \quad 9b$$

$$dM/dt = i_m - D \times (S + I)M - d_m M \quad 9c$$

$$dC/dt = \gamma I - d_c C \quad 9d$$

Susceptible hosts increase through density-dependent births (with maximum rate b and competitive intensity c). Infected hosts suffer from reduced fecundity ($0 \leq \rho < 1$). Susceptible hosts die at background death rate d_h and become infected at the per capita transmission rate (T), through contact with infectious miracidia (eqn 9a). Infected hosts die at an elevated death rate, $d_h + v$, due to parasite virulence (eqn 9b). Free-living miracidia are introduced into the aquatic environment at a constant rate i_m, but they are depleted during the infection process (at the per capita rate D) and die at the background death rate d_m (eqn 9c; see Table 2 for parameter values). We incorporated the three transmission models individually by inserting the per capita transmission, T, and depletion, D, rates defined for each model (see Table 1). We numerically simulated the models across a range of values of the miracidial introduction rate, i_m, with the lsoda function in R (Soetaert, Petzoldt & Setzer 2010). We determined three indices of disease spread/human risk of exposure: (i) equilibrial infection prevalence among intermediate (snail) hosts, (ii) the equilibrial density of infected intermediate hosts and (iii) the equilibrial density of (human-infectious) cercariae.

Results

TRANSMISSION MODEL COMPETITION

In the experiment, prevalence increased with the density of *Schistosoma* miracidia, but decreased with host density (Fig. 1). The *mass action* model underestimated prevalence at low host density but overestimated it at high density (Fig. 1a). Thus, it fits the data poorly (ΔAICc = 122·3, $w = 2{\cdot}7 \times 10^{-27}$, Table 1C). The power law transmission functions all predicted prevalence better than the *mass action* model (Table 1C). Among them, the *power law – hosts and parasites* model fits best (ΔAICc = 14·8, $w = 6{\cdot}0 \times 10^{-4}$, Fig. 1b, Table 1C). The *exposure-susceptibility* model predicted prevalence substantially better than the *mass action* or *power law* models (ΔAICc = 8·3, $w = 0{\cdot}015$, Fig. 1c, Table 1C). However, the *asymptotic exposure* model did not improve the fit of the *exposure-susceptibility* model (ΔAICc = 10·8, $w = 0{\cdot}004$, not shown, Table 1C). Overall, the *disproportionate exposure* model performed far better than all of the other models (ΔAICc = 0, $w = 0{\cdot}980$, Fig. 1d, Table 1C).

IMPLICATIONS FOR *S. mansoni* EPIDEMICS

Once embedded in the dynamic epidemiological model, the four transmission models exhibited similar dynamics. In fact, as parameterized with the laboratory data, the *asymptotic exposure* model made identical predictions to the *exposure-susceptibility* model. Equilibrial values of snail infection prevalence, the density of infected snails and the density of cercariae all increased monotonically with the introduction rate of miracidia (Fig. 2). However, the *mass action* transmission model often overestimated these three quantities relative to the exposure-explicit models. Differences among these transmission models are

Table 2. State variables and parameters used in the epidemiological model (eqns 9a–d)

Term	Units	Definition	Value	Source
State variables				
S	host L^{-1}	Density of susceptible hosts	–	
I	host L^{-1}	Density of infected hosts	–	
M	miracidia L^{-1}	Density of free-living miracidia (first infective stage)	–	
C	cercariae L^{-1}	Density of free-living cercariae (second infective stage)	–	
Parameters in common				
b	day^{-1}	Maximum birth rate of hosts	0·06	Williams (1970)
ρ	–	Relative fecundity of infected hosts	0·75	Mangal, Paterson & Fenton (2010)
c	L $host^{-1}$	Strength of density dependence on host birth rate	0·025	Mangal, Paterson & Fenton (2010)
d_h	day^{-1}	Background death rate of hosts	0·003	Foster (1964)
v	day^{-1}	Parasite virulence on survival	0·007	Foster (1964)
γ	cerc $host^{-1}$ day^{-1}	Per capita production rate of cercariae by infected hosts	100	Plausible value, Cooper *et al.* (1992)[1]
d_m	day^{-1}	Loss rate of free-living miracidia	2·5	Anderson *et al.* (1982)
d_c	day^{-1}	Loss rate of free-living cercariae	2	Whitfield *et al.* (2003)
i_m	mir L^{-1} day^{-1}	Miracidia introduction rate	Varied	
Parameters governing transmission				
β	L mir^{-1} day^{-1}	Transmission coefficient	Presented in Table 1	This study[2]
ε	L $host^{-1}$ day^{-1}	Exposure rate		
σ	Host mir^{-1}	Per-parasite susceptibility		
α	–	Relative exposure rate of infected hosts		

[1]Daily production of cercariae over 10 weeks under high-density conditions (50 snails L^{-1}).
[2]Maximum likelihood parameter estimates from the appropriate model (mass action, exposure-susceptibility or disproportionate exposure) fit to the results of the infection experiment (Table 1).

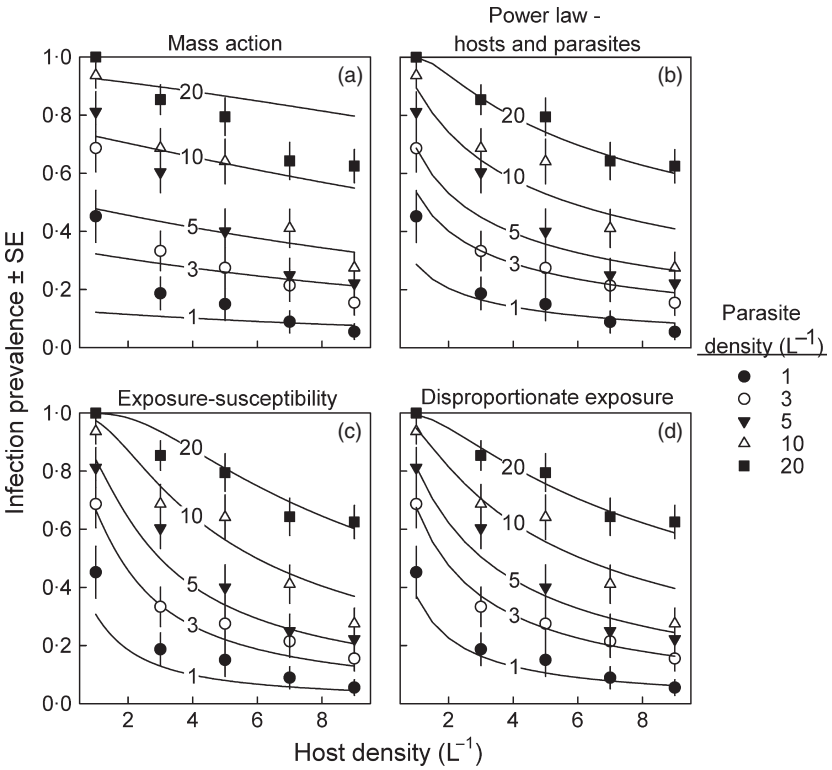

Fig. 1. Results of the model parameterization and competition. Best-fit predictions for four of the competing transmission models. Each prediction line is labelled with the corresponding parasite density and infection data are presented as treatment means (±SE). (a) The classic *mass action* model fits poorly. (b) The *power law – hosts and parasites* model fits somewhat better, but it cannot predict prevalence as well as the (c) *exposure – susceptibility* model. (d) The *disproportionate exposure* model predicted prevalence better than all of the other models. Indeed, all three exposure-explicit models readily explained the decrease in prevalence with host density.

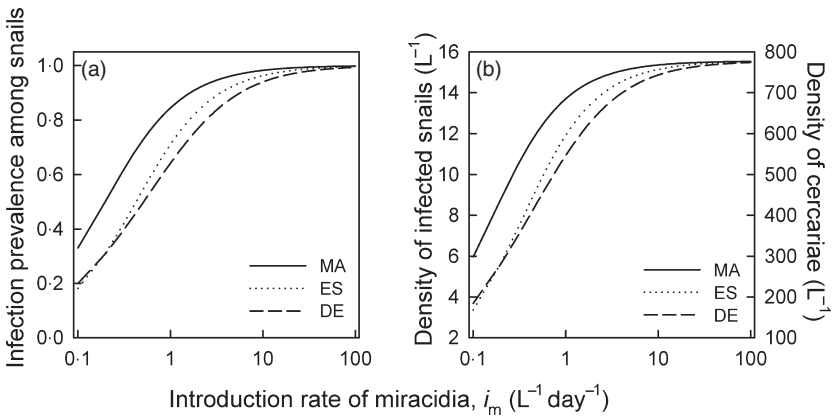

Fig. 2. Dynamics from the epidemiological model using the *mass action* (MA), *exposure-susceptibility* (ES) and *disproportionate exposure* (DE) transmission models. (a) Equilibrial infection prevalence among snail intermediate hosts. (b) Equilibrial density of infected snails (left *y*-axis) and human-infectious cercariae (right *y*-axis). The *mass action* transmission model often overestimated these quantities relative to the better performing exposure-explicit models. Under plausible miracidial introduction rates, $i_m \leq 1$ L^{-1} d^{-1}, the *mass action* model overestimated snail infection prevalence, the density of infected snails and cercarial density by 25–50% over the other models. Results for the *asymptotic exposure* model (not shown) are identical to those for the ES model.

largest with low miracidia introduction rates. At high miracidia introduction rates, all snails become infected regardless of the mechanisms underlying transmission.

Discussion

Transmission fundamentally shapes disease dynamics (McCallum, Barlow & Hone 2001). Thus, disease ecologists must think critically about the key mechanisms that underlie parasite transmission. Here, we gained substantial predictive power by partitioning transmission into exposure and susceptibility. Specifically, the exposure-explicit models better predicted the nonlinear decrease in infection prevalence with host density. This improvement stemmed from the incorporation of basic epidemiological principles. In contrast, the power law models made worse predictions and cannot identify mechanisms driving these patterns.

The mechanistic, exposure-explicit models provided added insight into *Schistosoma* transmission. First, all three models suggested that penetrating miracidia have

only a moderate (*c.* 50%) probability of successfully infecting hosts. Therefore, on average, for every successful miracidial infection, approximately one more free-living parasite is removed from the environment. In contrast, the density-dependent transmission assumes that hosts are completely susceptible ($\sigma = 1$), which causes it to poorly predict prevalence. Thus, separating exposure and susceptibility should enhance predictions of disease spread, especially when host defences reduce the infection success of invading parasites. Comparing among the exposure-explicit models, we found little support for the *asymptotic exposure* model. That is, the infection patterns were consistent with an instantaneous 'handling time'. However, the *disproportionate exposure* model best fits the data. This model estimated that the exposure rate for infected hosts was 150% greater than for uninfected hosts. One possible explanation for this result is that *Schistosoma* miracidia prefer infected hosts. However, the more likely explanation for this result is that there were some underlying heterogeneities among hosts (e.g. host size or production of attractive chemical cues) that resulted in more miracidia invading particular hosts (Dwyer, Elkinton & Buonaccorsi 1997).

Once embedded into a general epidemiological model, the *exposure-susceptibility*, *asymptotic exposure* and *disproportionate exposure* models displayed similar qualitative behaviour to the *mass action* model. Snail infection prevalence, the density of infected snails and the density of human-infectious cercariae all increased with increasing rates of introduction of miracidia. Despite these similarities, the *mass action* model often overestimated disease spread and human risk of exposure to schistosomes. At extremely high rates of introduction of miracidia, all snail hosts become infected for all transmission models. However, snail infection rates in endemic areas are generally 1–25% (Anderson & May 1979; Moné *et al.* 2010), suggesting that lower rates of miracidial introduction (i.e. $i_m < 1\ L^{-1}\ d^{-1}$) may be most plausible. Under these conditions, the widely used *mass action* model for transmission to snails might overestimate human risk of disease by 25–50% because it underestimates the depletion of miracidia (Fig. 2b). Thus, depletion of miracidia via exposure could reduce disease spread in natural snail populations and human disease risk. Future studies should test for these patterns in natural populations.

Our model focused on the aquatic life stages of the parasite (miracidia and cercariae) to examine the consequences of the different transmission functions on snail infection dynamics and cercarial production. In this model, the density of cercariae represents human risk, but we did not explicitly model human infection dynamics. Future studies should incorporate other important aspects of schistosome epidemiology (e.g. exposure and susceptibility traits of humans, aggregation of worms in humans, human infection intensity–egg production relationships, and spatial, seasonal, and genetic variation) with the transmission mechanisms investigated here.

Ecologists and epidemiologists have rightly focused on transmission as a driving force in host–parasite interactions. Thinking critically about the mechanistic drivers of transmission itself can be equally illuminating. In this reanalysis, we inferred exposure rate and susceptibility for an intermediate host of a major human zoonotic parasite from patterns of transmission across density gradients of hosts and parasites. For many host–parasite systems, per capita exposure rates can be directly estimated (e.g. fungal parasites inadvertently consumed by *Daphnia* hosts, Civitello *et al.* 2013; viruses consumed by forest insects, Parker, Elderd & Dwyer 2010; and trematodes encountered by larval amphibians, Raffel *et al.* 2011). Similarly, many studies quantitatively control infectious doses (e.g. via direct injection or small environmental volumes to ensure exposure) to estimate host susceptibility (Raffel *et al.* 2011). Data on exposure or susceptibility can even be analysed simultaneously with infection data to better parameterize and discriminate among transmission models (e.g. Raffel *et al.* 2011; Civitello *et al.* 2013).

Regardless of how exposure rate and susceptibility are estimated, focusing on these key processes can reveal deeper insights into the ecology and evolution of disease. First, it can facilitate a more complete dissection of environmental, ontogenetic and genetic factors that drive variation in transmission (Rohr *et al.* 2008a,b). For example, larger/older hosts may release more chemical cues or be more attractive to parasites and disease vectors (Takken & Verhulst 2013). Larger or older hosts may also engage in more sexual or social contacts. Thus, exposure rate itself may depend on age or size. In other cases, larger/older hosts may be more resistant to infection than smaller/younger ones (Theron, Rognon & Pages 1998). Simultaneous effects of age/size on exposure rate and susceptibility could have large consequences on age-prevalence curves and disease dynamics in size-structured populations (Raffel *et al.* 2011). Second, it could better integrate parasites into food webs (Lafferty, Dobson & Kuris 2006). For example, many competitors and predators of focal hosts also contact parasites or prey upon free-living parasites or infected hosts. Resistant species with the greatest rates of exposure should strongly inhibit disease outbreaks in focal hosts (i.e. be the best 'decoy' or 'diluting' species (Thieltges *et al.* 2008). In addition, competitors and predators can alter host behaviour, physiology or morphology, which can modulate exposure or susceptibility (Raffel *et al.* 2010). Lastly, explicitly disentangling exposure and susceptibility can reveal key processes in host and parasite evolution. For example, it could reveal the relative importance of behavioural and immunological resistance for the evolution of host defence following disease outbreaks (Duffy *et al.* 2012).

Quantifying the effects of exposure-mediated parasite depletion in natural populations remains challenging, partly because free-living stages of many parasites are difficult to detect visually, with sentinel organisms, or using molecular tools (e.g. Worrell *et al.* 2011). However,

combining experiments and field surveys with models that disentangle exposure and susceptibility can facilitate new inferences for disease dynamics in natural populations. For example, parasite depletion via exposure and interference among hosts can explain a unimodal (hump shaped) relationship between host population density and the size of natural epidemics in a *Daphnia* – fungus system (Civitello *et al*. 2013). Additionally, depletion of free-living fungal spores through exposure to resistant *Daphnia* species strongly inhibits natural epidemics in the same disease system (Hall *et al*. 2009). In human disease systems, seasonality in contact (exposure) rates among children (caused by school schedules) can drive epidemiological dynamics (e.g. Rohani, Zhong & King 2010). Additionally, explicitly modelling the exposure of humans or livestock to soil-transmitted helminths can refine predictions for disease dynamics and chemotherapeutic control (Yakob *et al*. 2013). Thus, the use of more mechanistic yet still parsimonious transmission functions can enable deeper insights for disease spread in natural populations and communities.

Disease dynamics hinge on parasite transmission. Explicitly disentangling exposure and susceptibility can enhance predictions for disease spread and our understanding of the ecological and evolutionary drivers of transmission. For this snail–schistosome system, disentangling exposure and susceptibility was critical because host defences reduced the success rate of invading parasites. Behavioural, immunological and physical defences of hosts against invading parasites are ubiquitous features of disease systems (Parker *et al*. 2011). Thus, separately accounting for exposure and susceptibility could enhance predictions and yield deeper understanding of parasite transmission in many systems.

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