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Comparing the Indirect Effects between Exploiters in Predator-Prey and Host-Pathogen Systems

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abstract: In multipredator and multipathogen systems, exploiters interact indirectly via shared victim species. Interspecific prey competition and the degree of predator specialization are known to influence whether predators have competitive (i.e., $(-,-)$) or noncompetitive (i.e., $(-,+)$ or $(+,+)$) indirect interactions. Much less is known about the population-level indirect interactions between pathogens that infect the same populations of host species. In this study, we use two-predator-two-prey and two-host-two-pathogen models to compare the indirect effects between predators with the indirect effects between pathogens. We focus on how the indirect interactions between pathogens are affected by the competitive abilities of susceptible and infected hosts, whether the pathogens are specialists or generalists, and the transmission pathway (direct vs. environmental transmission). In many cases, indirect effects between pathogens and predators follow similar patterns, for example, more positive indirect effects with increased interspecific competition between victim species. However, the indirect effects between pathogens can qualitatively differ, for example, more negative indirect effects with increased interspecific host competition. These contrasting patterns show that an important mechanistic difference between predatory and parasitic interactions (specifically, whether interactions are immediately lethal) can have important population-level effects on the indirect interactions between exploiters.

Keywords: consumer-resource interactions, indirect effects, predator-prey, host-pathogen, host-parasite, interspecific competition.

Introduction

Many predator-prey and host-pathogen systems are made up of multiple exploiter species who attack the same victim species (Cohen et al. 1990; Cleaveland et al. 2001; Pedersen et al. 2005; Rigaud et al. 2010). In these systems, the exploiter species interact indirectly through their effects on the shared victim species. Because exploitation of an individual victim by an exploiter of one species depletes the pool of victims available to an exploiter from another species, it seems intuitive that the two species of exploiters have competitive (i.e., $(-,-)$) indirect interactions at the population level. However, there are numerous empirical examples where indirect competition is not the outcome. For example, crayfish and bass both prey on small darters, but bass facilitate crayfish predation on darters because of behavioral shifts (Rahel and Stein 1988). Similarly, two aphid predators have much higher predation rates on aphids when they co-occur (Losey and Denno 1998). Moreover, classic theoretical work on multipredator-multiprey systems shows that noncompetitive (i.e., $(-,+)$ or $(+,+)$) indirect interactions between predators can arise when the shared prey species interspecifically compete for resources (Levine 1976; Vandermeer 1980, 2004; Abrams and Nakajima 2007; Abrams and Cortez 2015). Empirically, we also know that pathogens that coinfect an individual host do not necessarily compete. For example, some helminths that coinfect rabbit guts show mutualistic interactions (Lello et al. 2004), and nematode infections facilitate tuberculosis in African buffalo (Ezenwa et al. 2010). However, when compared with multipredator systems, there has been much less theoretical work on multipathogen-multihost systems and the population-level indirect effects between pathogens that share the same populations of host species. In this study, we explore the population-level indirect effects between pathogen species that share the same populations of host species (but do not coinfect the same individual host) and compare them with the indirect effects between predator species that share the same prey species.

The indirect interactions between consumers that use the same resources are one commonly studied type of indirect effect (Menge 1995; Abrams et al. 1996). Theory for two-predator-two-prey systems predicts that the signs and magnitudes of the indirect effects between predators

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depend on the specificity of the predators and the levels of intraspecific and interspecific prey competition (Levine 1976; Vandermeer 1980, 2004; Abrams and Nakajima 2007; Abrams and Cortez 2015). Specifically, positive indirect effects between predators are promoted by increased predator specialization and strong or asymmetric interspecific prey competition. Negative indirect effects are promoted when predators are generalists and interspecific prey competition is low. (But note that these predictions depend on the metric used to measure the indirect effects [Abrams and Nakajima 2007; Abrams and Cortez 2015].). Positive indirect effects between consumers have been observed in empirical systems with asymmetric competition between prey species (Dodson 1970; Davidson et al. 1984; Brown et al. 1986).

While the indirect effects between predators have received much attention, we know much less about the indirect effects between pathogens that infect the same set of host species. Understanding the indirect interactions between pathogens and the factors that influence them is important for disease control efforts. If two pathogens have negative indirect interactions, then control measures that decrease the number of infections of one pathogen may cause an increase in the number of infections of the other pathogen. On the other hand, if two pathogens have positive indirect interactions, then reductions in the number of infections of one pathogen may also decrease the number of infections of the other pathogen. While important, our understanding of the indirect interactions between pathogens is limited because there are only a limited number of empirical and theoretical studies on multihost-multipathogen systems (Rigaud et al. 2010; Johnson et al. 2013; Lively et al. 2014; Buhnerkempe et al. 2015; Johnson et al. 2015). Moreover, current theory is limited because the existing models assume no competition between host species (Holt and Dobson 2006), assume each pathogen can infect only one host species (Chilvers and Brittain 1972), or are multistrain, multihost models that focus on pathogen evolution (Regoes et al. 2000; Gandon 2004; Zhang et al. 2007). Consequently, it is unclear what indirect interactions arise between pathogens that infect the same populations of host species.

It is reasonable to think that predators and pathogens have similar population-level indirect interactions because predation and parasitism are both exploitative interactions. However, predatory and parasitic interactions differ in that parasitic interactions are not immediately lethal, and there are many reasons why this difference could cause predators and pathogens to have different population-level indirect effects. First, infected hosts can continue to compete with susceptible hosts for resources, whereas captured prey are immediately removed. This creates additional indirect pathways through which pathogen populations can interact. In addition, competition between susceptible and infected hosts (*S*-*I* competition) and competition between infected hosts (*I*-*I* competition) may be weaker or stronger than competition between susceptible hosts (*S*-*S* competition). For example, snails (*Batillaria cumingi*) infected with the trematode *Cercaria batillariae* move to a different part of the intertidal zone (Miura et al. 2006), suggesting that *S*-*I* competition is less than *S*-*S* or *I*-*I* competition. In contrast, individual growth rates of uninfected snails of a second species (*Cerithidea californica*) were independent of the prevalence of the trematode *Euhaplorchis californiensis* (Lafferty 1993), suggesting that *S*-*S* and *S*-*I* competition are equal. Finally, infections of the trematode *Diplostomum phoxini* cause gigantism in the snail *Lymnaea peregra* (Ballabeni 1995), and if larger individuals have higher feeding rates, then *S*-*I* and *I*-*I* competition will be greater than *S*-*S* competition. In general, increased competitive ability of infected hosts can occur if infected hosts have increased appetite or resource acquisition rates (Ponton et al. 2011; Shikano and Cory 2016; Bernardo and Singer 2017).

The second reason is that while the indirect interactions between predators involve just the indirect effects between the two predator populations, the indirect interactions between the pathogens involve all the pairwise indirect effects between the infected classes in each host species. For example, consider a host-pathogen community with two host species ($i = 1, 2$) and two directly transmitted pathogen species ($j = 1, 2$), where I_{ij} denotes the density of hosts in population *i* infected by population *j*. The indirect interactions between pathogen 1 and pathogen 2 involve all indirect effects of hosts infected by pathogen 1 (I_{11}, I_{21}) on all hosts infected by pathogen 2 (I_{12}, I_{22}), and vice versa. The indirect effects between different pairs of infected host classes do not necessarily have the same signs or magnitudes, and they may be affected differently by factors like the degree of pathogen specialization and competition between hosts.

The third reason delayed mortality may lead to different population-level indirect effects is that hosts can be coinfected by multiple pathogen species. This allows for pathogens to indirectly interact via pathogen-induced mortality of the host (because death of an infected host often means the infecting pathogens die as well), depletion of within-host resources, and the immune system (e.g., immunosuppression of a host by one parasite species can benefit another parasite species; Cressler et al. 2014; Griffiths et al. 2014; Johnson et al. 2015). As an initial step toward understanding the population-level indirect effects between pathogens and to simplify the comparison between predator-prey and host-pathogen systems, we assume that pathogens cannot coinfect hosts. This allows us to focus on the indirect effects that arise because of the depletion of available

hosts but at the cost of removing the indirect effects that arise between coinfecting pathogens; we return to this point in "Discussion."

In this study, we use two-prey-two-predator and two-host-two-pathogen models to explore and compare the indirect effects between exploiters that utilize the same victim species. Specifically, we compare the indirect effects between predators and the indirect effects between horizontally transmitted pathogens with either direct or environmental (e.g., spore-based) transmission. Our analysis focuses on how the signs and magnitude of the indirect effects are influenced by the interaction type (predation vs. parasitism), the levels of interspecific and intraspecific competition between victim species, the degrees of specialization of the exploiters (specialists vs. generalists), and the pathogen transmission mechanism (density-dependent vs. frequency-dependent direct transmission vs. environmental transmission).

Two-Predator-Two-Prey Systems

We begin by analyzing the indirect effects between predators in two-predator-two-prey systems. In the model, two predator species (P_1, P_2) consume two prey species (N_1, N_2) that compete for resources (fig. 1*A*). We assume that the predators cannot directly interact and that they indirectly interact only through their consumption of the shared prey. To simplify the presentation, we focus on a Lotka-Volterra type model similar to the one studied in Abrams and Cortez (2015). However, as shown in appendix S1.2 (apps. S1, S2 are available online), our results extend to models with other functional forms (e.g., predator type 2 functional responses). The model is

$$\frac{dN_i}{dt} = \underbrace{N_i(r_i - \alpha_{i1}N_1 - \alpha_{i2}N_2)}_{\text{growth and competition}} \underbrace{-b_{1i}P_1N_i - b_{2i}P_2N_i}_{\text{predation}} \text{ for } i = 1,2,$$

$$\frac{dP_j}{dt} = P_j(\underbrace{c_{j1}b_{j1}N_1 + c_{j2}b_{j2}N_2}_{\text{predation and conversion}} \underbrace{-m_j - q_jP_j}_{\text{mortality}}) \text{ for } j = 1,2, \tag{1}$$

where r_i is the maximum exponential growth rate of prey i, which accounts for births and deaths unrelated to predation; α_{ij} are the intraspecific and interspecific competition coefficients for the prey; b_{ji} is the attack rate of predator j on prey i; c_{ji} is the corresponding predator-to-prey conversion efficiency; m_j is the per capita mortality rate of predator j; and q_jP_j is a nonlinear mortality rate due to intraspecific predator interactions (e.g., lethal territorial conflicts between predators).

The Jacobian of model (1) evaluated at the stable coexistence equilibrium $\rho^* = (N_1^*, N_2^*, P_1^*, P_2^*)$ is

$$J = \begin{pmatrix} -\alpha_{11}N_1^* & -\alpha_{12}N_1^* & -b_{11}N_1^* & -b_{21}N_1^* \\ -\alpha_{21}N_2^* & -\alpha_{22}N_2^* & -b_{12}N_2^* & -b_{22}N_2^* \\ c_{11}b_{11}P_1^* & c_{12}b_{12}P_1^* & -q_1P_1^* & 0 \\ c_{21}b_{21}P_2^* & c_{22}b_{22}P_2^* & 0 & -q_2P_2^* \end{pmatrix}. \tag{2}$$

Written more generally, the sign structure of the Jacobian is

$$\begin{array}{cc} \text{prey competition} & \text{predation} \\ \begin{pmatrix} \boxed{\begin{matrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{matrix}} & \boxed{\begin{matrix} J_{13} & J_{14} \\ J_{23} & J_{24} \end{matrix}} \\ \boxed{\begin{matrix} J_{31} & J_{32} \\ J_{41} & J_{42} \end{matrix}} & \boxed{\begin{matrix} J_{33} & J_{34} \\ J_{43} & J_{44} \end{matrix}} \end{pmatrix} & \text{“=”} \begin{pmatrix} \boxed{\begin{matrix} - & - \\ - & - \end{matrix}} & \boxed{\begin{matrix} - & - \\ - & - \end{matrix}} \\ \boxed{\begin{matrix} + & + \\ + & + \end{matrix}} & \boxed{\begin{matrix} - & 0 \\ 0 & - \end{matrix}} \end{pmatrix}. \\ \text{consumption} & \text{mortality} \end{array} \tag{3}$$

Each entry of the Jacobian defines how an increase in the density of one species affects the growth rate (at equilibrium) of the other species (illustrated in fig. 1*A*). Entries J_{11} and J_{22} and entries J_{12} and J_{21} (top left box) are negative because of intraspecific and interspecific prey competition, respectively. The entries in the top right and bottom left boxes are negative and positive, respectively, because of the predatory interactions between the species. Entries J_{33} and J_{44} are negative because of intraspecific predator interactions. Entries J_{34} and J_{43} are zero because we assume there are no direct interspecific interactions between predators.

Computing Indirect Effects Using Responses to Small Increases in Mortality

Throughout, we focus on the indirect effects of predator 1 on predator 2. While the indirect effect of predator 2 on predator 1 may have a different sign or magnitude, our general predictions about how prey competition influences the sign and magnitude of that indirect effect is the same. This is because there is a natural symmetry in the sign structures of the species interactions; for example, all predator-prey pairs have (+,−) interactions, and the prey have (−,−) interactions. Thus, any predictions about the indirect effect of predator 2 on predator 1 are identical to the predictions about the indirect effect of predator 1 on predator 2 after replacing all instances of predator 1 with predator 2, and vice versa.

Following Levine (1976) and Vandermeer (1980), the indirect effect of predator 1 on predator 2 is measured by how the equilibrium density of predator 2 (P_2^*) changes after a small increase in the mortality rate of predator 1 (m_1). Mathematically, the indirect effect is defined by the derivative $-\partial P_2^*/\partial m_1$, which is computed using the Jacobian-based theory in Yodzis (1988); see appendix S1.1 for details. The indirect effect is negative ($-\partial P_2^*/\partial m_1 < 0$) when increased mortality of predator 1 causes an increase in the equilibrium density of predator 2. The indirect effect is

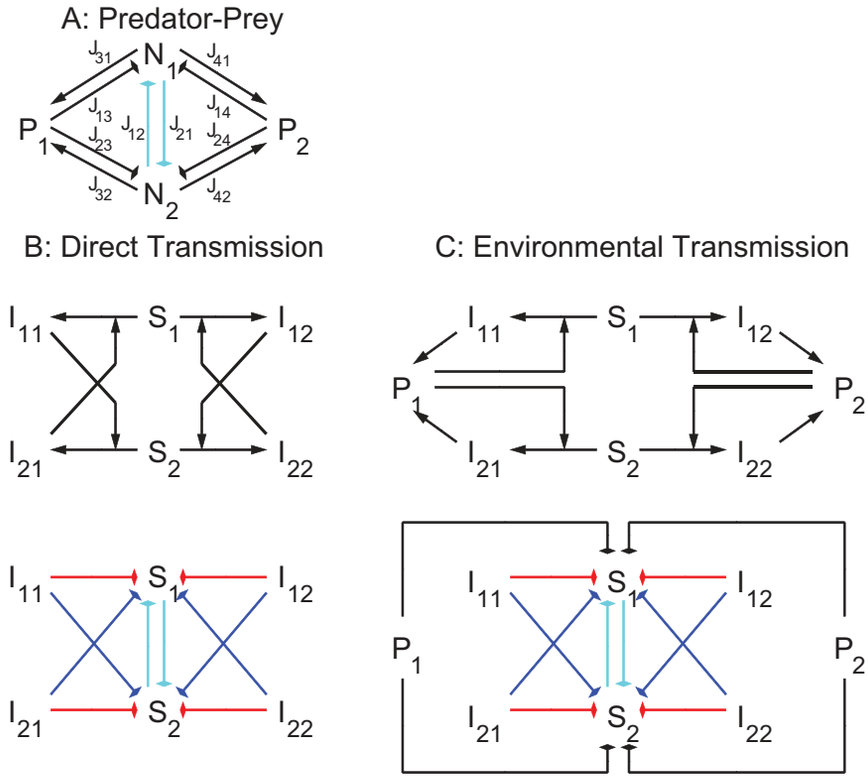

Figure 1: Direct interactions between species in the exploiter-victim models considered in this study. Pointed and flat arrows denote positive and negative direct effects, respectively. *A*, Predator-prey system with two predators (P_1, P_2) and two prey (N_1, N_2). Black pointed and flat arrows denote the predatory interactions. Cyan arrows denote interspecific prey competition. The labels J_{ij} denote corresponding entries in the Jacobian (eq. [3]). *B*, Direct transmission two-host-two-pathogen system where hosts in population i are either susceptible (S_i) or infected with pathogen j (I_{ij}). Black pointed arrows denote transmission. Red and blue flat arrows denote intraspecific and interspecific competition, respectively, between infected and susceptible individuals and the negative effects of transmission on susceptible hosts. Cyan flat arrows denote interspecific competition between susceptible hosts. *C*, Environmental transmission two-host-two-pathogen system where P_i is the density of infectious propagules of pathogen i and hosts in population i are either susceptible (S_i) or infected (I_{ij}) with pathogen j. Black flat arrows denote infection and release of infectious propagules. Red and blue flat arrows denote intraspecific and interspecific competition, respectively, between infected and susceptible individuals. Cyan flat arrows denote interspecific competition between susceptible hosts. Black flat arrows denote negative effects of transmission on susceptible hosts.

positive ($-\partial P_2^*/\partial m_1 > 0$) when increased mortality of predator 1 causes a decrease in the equilibrium density of predator 2. We use this particular metric because it is the most commonly used metric in the literature (e.g., Bender et al. 1984; Yodzis 1988; Novak et al. 2011), but previous studies have used other metrics (Abrams 1987, 2001; Abrams and Nakajima 2007; Abrams and Cortez 2015). Because our method focuses on equilibrium densities, we consider only indirect effects that arise at stable coexistence equilibria.

The advantage of our Jacobian-based approach is that we can write the indirect effects between the predators as sums and products of Jacobian entries representing intraspecific prey competition (J_{11}, J_{22}), interspecific prey competition (J_{12}, J_{21}), intraspecific predator competition (J_{33}, J_{44}), and predatory interactions (J_{i3}, J_{i4} for $i = 1, 2$ and J_{1j}, J_{2j} for $j = 3, 4$). This allows us to isolate how all the direct effects in the system contribute to the signs and magnitudes of the indirect effects between the predators. We walk through this analysis in detail for our predator-prey model. The analysis is similar for the host-pathogen models, but details are presented only in the appendixes because the equations for the indirect effects in the host-pathogen models are massive.

Computing the Indirect Effects between Predators

The indirect effect of predator 1 on predator 2 is

$$-\frac{\partial P_2^*}{\partial m_1} = \frac{1}{|J|}\left(\overbrace{J_{13}J_{21}J_{42} + J_{41}J_{12}J_{23}}^{\text{specialists}}}_{\text{interspecific prey competition, }+} \quad \underbrace{-J_{42}J_{11}J_{23} - J_{41}J_{13}J_{22}}_{\text{intraspecific prey competition, }-}\right), \tag{4}$$

where $|J| > 0$ is the determinant of the Jacobian (eq. [2]). Each term in equation (4) represents a chain of direct effects that produces an indirect pathway from P_1 to P_2. For example, the term $J_{13}J_{21}J_{42}$ involves the direct effect of predator 1 on prey 1 (J_{13}; black flat arrow in top left of fig. 1*A*), the direct effect of prey 1 on prey 2 (J_{21}; upward pointing gray arrow), and the direct effect of prey 2 on predator 2 (J_{42}; bottom right black flat arrow). Each term is labeled on the basis of whether that indirect pathway causes positive (+) or negative (−) indirect effects between the predators.

The term under the overbrace in equation (4) defines the indirect effect when both predators are specialists, where without loss of generality this means predator 1 consumes only prey 1 and predator 2 consumes only prey 2. The other terms represent the additional indirect pathways that arise when one or both predators are generalists. By writing the indirect effect in this way, we can determine how the indirect effects between predators are influenced by whether both predators are specialists ($J_{41} = J_{14} = 0$ and $J_{32} = J_{23} = 0$), only one predator is a specialist ($J_{41} = J_{14} = 0$ and J_{32} and J_{23} are both nonzero, or vice versa), or both predators are generalists (J_{41}, J_{14}, J_{23}, and J_{32} are all nonzero).

Indirect Effects between Predators

Effects of Interspecific Prey Competition on Specialist Predators. If both predators are specialists, then the predators have positive indirect effects on each other. The mechanism is the following. Increased mortality of predator 1 causes a decrease in its density, which results in higher density of prey 1 ($-J_{13} > 0$). This causes a decrease in the density of prey 2 because of interspecific competition between prey ($J_{21} < 0$), which reduces food availability for predator 2 and causes a decrease in its density ($-J_{42} < 0$). Overall, increased mortality of predator 1 causes a decrease in the density of predator 2, implying that predator 1 has a positive indirect effect on predator 2.

Effects of Interspecific Prey Competition on Generalist Predators. If one or both predators are generalists, then predators have negative indirect effects in the absence of interspecific prey competition and higher interspecific prey competition promotes positive indirect effects. The underlying mechanism is that increases in predator 1 mortality indirectly cause shifts in the prey densities. When interspecific prey competition is weak, the shifts in prey density increase the food availability or quality for predator 2. This causes the density of predator 2 to increase, implying a negative indirect effect. When interspecific prey competition is strong, the shifts in prey density decrease the food availability or quality for predator 2. This causes the density of predator 2 to decrease, implying a positive indirect effect of predator 1 on predator 2.

Summary. Table 1 summarizes how interspecific prey competition influences the signs of the indirect effects between the predators. Specialist predators always have positive indirect effects. Generalist predators have negative and positive indirect effects when interspecific prey competition is weak or strong, respectively, relative to intraspecific prey competition. These conclusions were first reported in Levine (1976) and Vandermeer (1980), and our work slightly generalizes their results.

Directly Transmitted Pathogens

We now explore the indirect effects between pathogens that share the same populations of host species, starting with horizontally and directly transmitted pathogens (i.e., pathogen transmitted via contact between susceptible and infected hosts). In all our host-pathogen models, we assume that there is no recovery from infection (i.e., infections are lethal) and an individual host cannot be coinfected by both pathogens. These assumptions make the host-pathogen models similar in structure to the predator-prey model, which allows us to focus on the indirect effects between pathogens caused by the depletion of the shared victim populations. However, the assumptions come at the cost of removing the direct and indirect interactions that involve recovered hosts and that occur between pathogens coinfecting the same individual host.

In the model, S_i and I_{ij} denote the densities of susceptible hosts and hosts infected by pathogen j ($j = 1, 2$) in population i ($i = 1, 2$). To simplify the presentation in the main text, we assume that infected hosts cannot reproduce and the transmission rates are governed by mass action kinetics. Our two-host-two-pathogen model with density-dependent direct transmission is

$$\begin{aligned}\frac{dS_i}{dt} &= \overbrace{S_i[r_i - \alpha_{i1}(S_1 + e_{11}I_{11} + e_{12}I_{12}) - \alpha_{i2}(S_2 + e_{21}I_{21} + e_{22}I_{22})]}^{\text{growth and competition}} \\ &\quad \underbrace{-(\beta_{i,11}I_{11} + \beta_{i,12}I_{12} + \beta_{i,21}I_{21} + \beta_{i,22}I_{22})S_i}_{\text{transmission}} \quad \text{for } i = 1, 2, \\ \frac{dI_{ij}}{dt} &= \underbrace{\beta_{i,1j}S_iI_{1j} + \beta_{i,2j}S_iI_{2j}}_{\text{transmission}} \quad \underbrace{-m_{ij}I_{ij}}_{\text{mortality}} \quad \text{for } i, j = 1, 2,\end{aligned} \tag{5}$$

where r_i is the maximum exponential growth rate of host i, which accounts for births and deaths unrelated to infection; α_{ij} are the intraspecific and interspecific competition coefficients for the host species; $\beta_{i,kj}$ is the transmission coefficient for hosts S_i and I_{kj}; and m_{ij} is the mortality for host i infected by pathogen j. The parameters e_{ij} account for how host reproduction and natural mortality are affected by resource competition between susceptible and infected hosts. Infected hosts are weaker, equal, or stronger competitors than susceptible hosts when $e_{ij} < 1$,

Table 1: Influence of different types of victim competition on indirect effects between exploiters

System	Type of competition			
	Interspecific prey	Intraspecific prey		
Predator-prey:				
Specialist	+	0		
Generalist	+	−		
	Interspecific *S*-*S*	Intraspecific *S*-*S*	Interspecific *S*-*I*	Intraspecific *S*-*I*
Host-pathogen:				
Direct transmission:				
Density dependent:				
Specialist	+	−	−	+
Generalist	+	−	+[a]	−[a]
Frequency dependent:[b]				
Specialist	±	±	±	±
Generalist	±	±	±	±
Environmental transmission:				
Infected host class indirect effects:				
No propagule loss during transmission:				
Specialist	+	−	−	+
Generalist	±	±	±	±
Propagule loss during transmission:[b]				
Specialist	−	+	±	−
Generalist	±	±	±	±
Infectious propagule indirect effects:				
No propagule loss during transmission:				
Specialist	+	−	±	+
Generalist	+	−	±	±
Propagule loss during transmission:[b]				
Specialist	−	+	±	−
Generalist	−	+	±	±

Note: Plus signs and minus signs indicate that the type of competition promotes positive and negative indirect effects, respectively. Plus-or-minus signs (±) indicate that the type of competition can promote positive or negative indirect effects depending on the model parameterization, and 0 indicates no effect. *S*-*S* indicates competition between susceptible hosts; *S*-*I* indicates competition between susceptible and infected hosts.

[a] Terms of both signs are present, but most terms have the indicated sign.

[b] Symbols indicate signs of additional terms that arise under frequency-dependent direct transmission or when there is loss of infectious propagules during transmission due to uptake by susceptible hosts.

$e_{ij} = 1$, and $e_{ij} > 1$, respectively. In general, infected hosts are unlikely to be stronger competitors; however, it could occur when infection causes hosts to have increased appetite or resource acquisition rates (Ponton et al. 2011; Shikano and Cory 2016; Bernardo and Singer 2017).

We measure the indirect effect of pathogen 1 on pathogen 2 by assessing how a small increase in the mortality rate of class I_{11} (m_{11}) affects the equilibrium densities of hosts infected by pathogen 2 (I_{12}^* and I_{22}^*). In general, the indirect effect of pathogen 1 on pathogen 2 involves measuring (1) how an increase in m_{11} affects I_{12}^* and I_{22}^* and (2) how an increase in m_{21} affects I_{12}^* and I_{22}^*. However, similar to before, intraspecific and interspecific host competition influence all these responses in the same way because of the symmetry in the sign structures of the species interactions. Mathematically, we measure the indirect effect of pathogen 1 on pathogen 2 with the derivatives $-\partial I_{12}^*/\partial m_{11}$ and $-\partial I_{22}^*/\partial m_{11}$, which define how increased mortality of I_{11} affects the number of infections of pathogen 2 in conspecific hosts and heterospecific hosts, respectively. The mathematical formulas for the derivatives are given in equations (A12) and (A13) of appendix S1.3.1.

Indirect Effects between Pathogens with Density-Dependent Direct Transmission

We organize our results in terms of how the levels of competition between susceptible hosts (*S*-*S* competition) and competition between susceptible and infected hosts (*S*-*I* competition) affect the signs of the indirect effects between specialist and generalist pathogens. Many of our results generalize to other direct transmission models. The next subsection and appendix S1.3 address the generality of our results and differences that can arise in models with other transmission rates.

Effects of S-S Competition for Specialist Pathogens. First consider systems where both pathogens are specialists (i.e., pathogen 1 infects only host 1 and pathogen 2 infects only host 2). In such systems, interspecific *S*-*S* competition promotes positive indirect effects and intraspecific *S*-*S* competition promotes negative indirect effects. This is the same as what occurs in predator-prey systems. Indeed, in the absence of competition between susceptible and infected hosts (no *S*-*I* competition), the host-pathogen model (5) is identical in structure to the predator-prey model (1).

Effects of S-I Competition for Specialist Pathogens. In contrast to the above, interspecific *S*-*I* competition promotes negative indirect effects between specialist pathogens, and intraspecific *S*-*I* competition promotes positive indirect effects. Interspecific *S*-*I* competition promotes negative indirect effects because increased removal of I_{11} reduces interspecific competition with S_2, resulting in more hosts that pathogen 2 can infect. This means that interspecific *S*-*S* and *S*-*I* competition have opposing effects on the indirect effects between specialist pathogens. Overall, *S*-*I* competition decreases the magnitudes of the indirect effects between specialist pathogens.

Effects of S-S Competition on Generalist Pathogens. Now consider systems where one or both pathogens are generalists. Stronger interspecific *S*-*S* competition promotes positive indirect effects between generalist pathogens, whereas stronger intraspecific *S*-*S* competition promotes negative indirect effects. Similar to the predator-prey system, the underlying mechanism is that increased removal of I_{11} causes shifts in the abundances of susceptible hosts. When interspecific *S*-*S* competition is weak, the shifts increase host availability or quality for pathogen 2. This causes an increase in pathogen 2 infections, implying a negative indirect effect of pathogen 1 on pathogen 2. When interspecific *S*-*S* competition is strong, the shifts decrease host availability or quality for pathogen 2. This causes a decrease in pathogen 2 infections, implying a positive indirect effect of pathogen 1 on pathogen 2.

Effects of S-I Competition on Generalist Pathogens. Intraspecific and interspecific *S*-*I* competition can promote positive or negative indirect effects between generalist pathogens. However, in many cases, interspecific *S*-*I* competition promotes positive indirect effects between generalist pathogens, and intraspecific *S*-*I* competition promotes negative indirect effects; that is, *S*-*S* and *S*-*I* competition influence the indirect effects between generalist pathogens in the same way. Here, the phrase "in many cases" means that most of the terms in equations (A12) and (A13) of appendix S1.3.1 that involve interspecific *S*-*I* competition are positive and most of the terms that involve intraspecific *S*-*I* competition are negative. This suggests that intraspecific and interspecific *S*-*I* competition will often increase the magnitude of the indirect effects between generalist pathogens (e.g., make positive indirect effects more positive). However, in general, it is possible for *S*-*I* competition to decrease or increase the magnitude of the indirect effects between generalist pathogens.

Summary. Table 1 summarizes how interspecific and intraspecific *S*-*S* and *S*-*I* competition influence the signs of the indirect effects between the infected host classes. Interspecific *S*-*S* competition promotes positive indirect effects and intraspecific *S*-*S* competition promotes negative indirect effects for both specialist and generalist pathogens. For specialist pathogens, *S*-*S* and *S*-*I* competition have opposing effects; that is, interspecific *S*-*I* competition promotes negative indirect effects, and intraspecific *S*-*I* competition promotes positive indirect effects. For generalist pathogens, in most cases, *S*-*S* and *S*-*I* competition influence the indirect effects in the same way. However, in general, interspecific and intraspecific *S*-*I* competition can promote positive or negative indirect effects between generalist pathogens.

Indirect Effects between Pathogens with Nonlinear or Frequency-Dependent Direct Transmission Rates

In our density-direct transmission model (5), we assume that infected hosts cannot reproduce and the transmission rates are governed by mass action kinetics. As shown in appendix S1.3.1, our results are qualitatively unchanged if infected hosts can reproduce. In addition, all our results about *S*-*I* competition also apply to resource competition between infected hosts (*I*-*I* competition) in systems where infected hosts can reproduce. Our results are also unchanged for models with nonlinear infection rates where the transmission rate from I_{kj} to S_i depends only on the densities of I_{kj} and S_i, for example, the power-law transmission rate $\beta_{i,kj} S_i^p I_{kj}^q$ with exponents p and q (Liu et al. 1987; Hochberg 1991). The reason our results hold more generally is that our Jacobian-based method depends on only the signs of the Jacobian entries, which are unchanged when infected hosts can reproduce or for the nonlinear infection rates listed above.

However, if transmission is frequency dependent, then the sign structure of the Jacobian may differ, and this can alter predictions about the indirect effects between pathogens. In appendixes S1.3.2 and S1.3.3, we analyze direct transmission models with frequency-dependent transmission rates, for example, models with the transmission rates $\beta_{i,ij} S_i I_{jk}/N_i$ or $\beta_{i,ij} S_i I_{jk}/(N_1 + N_2)$, where $N_i = S_i + I_i$ is the total density of host i. There are two consequences of incorporating frequency-dependent transmission.

The first consequence is the creation of direct effects between the different infection classes. For example, if the transmission rate from I_{22} to S_2 is $\beta_{2,22}S_2I_{22}/(N_1 + N_2)$, then increases in the density of hosts infected with pathogen 1 (I_{11}, I_{21}) decrease the transmission rate through their effects on N_1 and N_2. This results in a direct effect of pathogen 1 on pathogen 2. In most cases, the direct effects are negative, but positive direct effects can arise between specialist pathogens when host coexistence is pathogen mediated. Overall, this means that in most cases, frequency-dependent transmission results in more negative total (direct plus indirect) effects between the pathogens as compared with density-dependent direct transmission.

The second consequence of incorporating frequency-dependent transmission rates is the creation of additional indirect pathways that result in all forms of *S*-*S* and *S*-*I* competition being able to promote positive or negative indirect effects between the pathogens (plus-or-minus signs in "Frequency dependent" rows in table 1). This makes it difficult to make general predictions about how host resource competition influences the indirect effects between the pathogens with frequency-dependent transmission.

Pathogens with Environmental Transmission

We now explore the indirect effects that occur between horizontally and environmentally transmitted pathogens. Here, new infections arise when susceptible hosts come in contact with infectious propagules in the environment that were released by infected individuals.

In the model, P_j denotes the density of infectious propagules for pathogen j ($j = 1, 2$) and S_i and I_{ij} denote the densities of susceptible hosts and hosts infected by pathogen j in population i ($i = 1, 2$). To simplify the presentation, we assume that infected hosts cannot reproduce, depletion of infectious propagules during infection is negligible, and the transmission rates are governed by mass action kinetics; that is, $\gamma_{ij}S_iP_j$. As with the previous model, we also assume that there is no recovery from infection and that coinfection is not possible. The two-host-two-pathogen model with environmental transmission is

$$\begin{aligned}
\frac{dS_i}{dt} &= S_i \underbrace{[r_i - \alpha_{i1}(S_1 + e_{11}I_{11} + e_{12}I_{12}) - \alpha_{i2}(S_2 + e_{21}I_{21} + e_{22}I_{22})]}_{\text{growth and competition}} \\
&\quad \underbrace{-\gamma_{i1}S_iP_1 - \gamma_{i2}S_iP_2}_{\text{infection}}, \\
\frac{dI_{ij}}{dt} &= \underbrace{\gamma_{ij}S_iP_j}_{\text{infection}} \underbrace{-m_{ij}I_{ij}}_{\text{mortality}}, \qquad (6) \\
\frac{dP_j}{dt} &= \underbrace{\chi_{1j}I_{1j} + \chi_{2j}I_{2j}}_{\text{propagule release}} \underbrace{-\mu_jP_j}_{\text{degradation}},
\end{aligned}$$

where γ_{ij} is the per-propagule infection rate for host i and pathogen j, χ_{ij} is the propagule release rate for infected host I_{ij}, μ_j is the infectious propagule degradation rate for pathogen j, and all other parameters are defined as in the direct transmission model (5).

We measure the indirect effect of pathogen 1 on pathogen 2 in two ways. First, we determine how a small increase in the mortality rate of infected class I_{11} (m_{11}) affects the equilibrium densities of hosts infected by pathogen 2 (I_{12}^* and I_{22}^*). Mathematically, this is computed using the derivatives $-\partial I_{12}^*/\partial m_{11}$ and $-\partial I_{22}^*/\partial m_{11}$. Second, we determine how a small increase in the degradation of the infectious propagules for pathogen 1 (μ_1) affects the equilibrium density of infectious propagules for pathogen 2 (P_2^*). Mathematically, this is computed using the derivative $-\partial P_2^*/\partial \mu_1$. For both metrics, negative values imply negative indirect effects of pathogen 1 on pathogen 2, and positive values imply positive indirect effects.

These two metrics were chosen because they are similar to the metrics for the previous models. Comparing the results from the first metric ($-\partial I_{12}^*/\partial m_{11}$ and $-\partial I_{22}^*/\partial m_{11}$) with the results from the direct transmission model (5) allows us to determine how the indirect effects between infectious classes are influenced by the pathogen transmission mechanism. The second metric ($-\partial P_2^*/\partial \mu_1$) is analogous to the measure of the indirect effects between predators because infectious propagules in the environmental transmission model (6) play a role similar to the role played by predators in the predator-prey model (1). Specifically, infectious propagules can be thought of as questing predators (i.e., predators searching for prey), and the infectious classes can be thought of as predators that are handling their prey. Thus, comparing the second metric with the results from the predator-prey model (1) provides another way to compare the indirect effects between predators and pathogens.

While we focus on only the indirect effects between infectious classes and the indirect effects between the densities of infectious propagules, in general the indirect effects of pathogen 1 on pathogen 2 involve measuring how increases in m_{11}, m_{21}, and μ_1 each affect I_{12}^*, I_{22}^*, and P_2^*. These individual effects may differ in sign and magnitude, but because of the symmetry in the sign structures of the species interactions, intraspecific and interspecific host competition influence all the indirect effects in the same way. Additional details about the signs of the other indirect effects are given in appendix S1.4.1.

Indirect Effects between Pathogens with Environmental Transmission

Our results are organized as above. The next subsection and appendix S1.4 address the generality of our results and differences that can arise when there is nonnegligible

loss of infectious propagules during transmission or due to uptake by hosts.

Effects of S-S Competition on Specialist Pathogens. First, consider the case where the pathogens specialize on different host species. For both metrics, increased interspecific *S-S* competition promotes positive indirect effects and increased intraspecific *S-S* competition promotes negative indirect effects. The mechanism is that increased mortality of I_{11} causes an increase in susceptible hosts in population 1 (due to reduced transmission). This causes a decrease in the density of susceptible hosts in population 2 due to interspecific *S-S* competition. This in turn leads to fewer infections in population 2, which implies a positive indirect effect. Intraspecific *S-S* competition promotes negative indirect effects because the changes in host density described in the preceding sentences are smaller in magnitude or in the opposite direction when intraspecific *S-S* competition is strong.

Effects of S-I Competition on Specialist Pathogens. With only one exception, the effects of interspecific and intraspecific *S-I* competition are the opposite of *S-S* competition for both metrics. Specifically, increased interspecific *S-S* competition promotes negative indirect effects, and increased intraspecific *S-S* competition promotes positive indirect effects. The exception is a single term in $-\partial P_2^*/\partial \mu_1$ that results in increased interspecific *S-I* competition, causing a positive indirect effect between the spore densities; see appendix S1.4.1 for details.

The mechanism determining the signs of the effects of *S-I* competition is the following. Increased mortality of I_{11} reduces the density of infected hosts in population 1, which causes an increase in susceptible hosts in population 2 due to reduced interspecific *S-I* competition. This leads to more infections in population 2. The combined decrease in I_1 and increase in I_2 implies a negative indirect effect between the pathogens. Intraspecific *S-I* competition promotes positive indirect effects because the change in susceptible host density is smaller in magnitude or in the opposite direction when intraspecific *S-I* competition is strong.

Effects of S-S Competition on Generalist Pathogens. Depending on the parameterization of the model, interspecific and intraspecific *S-S* competition can promote more positive or more negative indirect effects between the infected host classes (first metric) of generalist pathogens.

The reason for the unclear pattern is that all hosts infected by pathogen 1 (I_{11}, I_{21}) release infectious propagules into a common pool of sources for new infections (P_1). Because of this, most of the indirect pathways from P_1 to P_2 intersect, which makes it difficult to tease apart how individual pathways affect the signs and magnitudes of the indirect effects between the host classes. This is analogous to analyzing contributions to traffic flow when many small roads merge together at a single point and then separate at a single point somewhere farther down. Because the contributions from each small road are mixed together during the merge, it becomes difficult to determine how traffic on any individual road before the merge contributes to traffic on another road after the separation. This mixing of the indirect pathways does not occur in the direct transmission model (5) because the infected classes I_{1j} and I_{2j} are distinct sources of new infections, which prevents the indirect pathways from merging.

For the indirect effects between the infectious propagules (second metric), interspecific *S-S* competition promotes positive indirect effects between the infectious propagule populations, and intraspecific *S-S* competition promotes negative indirect effects. The mechanism is that increased removal of infectious propagules cause shifts in the host densities. When interspecific *S-S* competition is weak, the shifts in host densities increase host availability or quality for pathogen 2. This causes the density of infectious propagules for pathogen 2 to increase, implying a negative indirect effect. When interspecific host competition is strong, the shifts in host densities decrease the host availability or quality for pathogen 2. This causes the density of infectious propagules for pathogen 2 to decrease, implying a positive indirect effect. Note that the merging of indirect pathways does not occur with the second metric because the infected classes are distinct sources of new infectious propagules.

Effects of S-I Competition on Generalist Pathogens. Depending on the parameterization of the model, all types of *S-I* competition can promote more positive or more negative indirect effects between infected host classes (first metric). As with *S-S* competition, this is because all hosts infected by pathogen 1 (I_{11}, I_{21}) release infectious propagules into a common pool of sources for new infections (P_1).

For the indirect effects between the infectious propagules (second metric), interspecific and intraspecific *S-I* competition can promote positive or negative indirect effects. However, for most of the terms in the equation defining $-\partial P_2^*/\partial m_1$, the terms involving interspecific *S-I* competition are positive, and the terms involving intraspecific *S-I* competition are negative. This means that in many cases, interspecific and intraspecific *S-I* competition will influence the indirect effects in the same way that interspecific and intraspecific *S-S* competition do.

Summary. Table 1 summarizes how interspecific and intraspecific prey competition influence the signs of the indirect

effects between the infected host classes and the indirect effects between the infectious propagules. For specialist pathogens, regardless of which metric is used, interspecific *S*-*S* competition promotes positive indirect effects, intraspecific *S*-*S* competition promotes negative indirect effects, and interspecific and intraspecific *S*-*I* competition promote the opposite. For generalist pathogens, between-host competition of any kind can promote positive or negative indirect effects between infected host classes, depending on the model parameterization. In contrast, interspecific *S*-*S* competition promotes positive indirect effects between the infectious propagules, intraspecific *S*-*S* competition promotes negative indirect effects between the infectious propagules, and in many cases *S*-*I* competition has the same effects.

Indirect Effects between Pathogens with Uptake of Infectious Propagules

In our environmental transmission model (6), we assume that infected hosts cannot reproduce, depletion of infectious propagules during infection is negligible, and the transmission rates are governed by mass action kinetics; that is, $\gamma_{ij}S_iP_j$. As shown in appendix S1.4.1, our results are qualitatively unchanged if hosts can reproduce. In addition, all our results about *S*-*I* competition also apply to resource competition between infected hosts (*I*-*I* competition) in systems where infected hosts can reproduce. Our results are also qualitatively unchanged for models with nonlinear infection rates that depend on only the densities of susceptible hosts and infectious propagules. This includes power-law transmission rates like $\gamma_{ij}S_iP_j^q$, where q is an exponent, and transmission rates like $\gamma_{ij}(P_j - c)^q/[(P_j - c)^q + H^q]$ that account for a minimal infectious dose (c) and half-saturation constant (H; Joh et al. 2009). As noted before, the reason our results hold more generally is that our Jacobian-based method depends on only the signs of the Jacobian entries, which are unchanged for the nonlinear infection rates listed above and when infected hosts can reproduce.

However, our results can qualitatively differ when infectious propagules are lost during infection or as a result of uptake by hosts, for example, loss of fungal spores due to ingestion by feeding susceptible and infected hosts (Searle et al. 2016). Here, we point out two ways in which uptake of infectious propagules affects the indirect effects between environmentally transmitted pathogens. Mathematical details are provided in appendixes S1.4.2 and S1.4.3.

First, uptake of infectious propagules during infection tends to decrease the magnitudes of the indirect effects between specialist pathogens, making those indirect effects closer to neutral. The reason is that loss of infectious propagules during infection creates additional indirect pathways where the signs of the pathways involving interspecific and intraspecific *S*-*S* and *S*-*I* competition are the opposite of the pathways that do not involve the loss of infectious propagules (compare signs of "No propagule loss during transmission" and "Propagule loss during transmission" for specialist pathogens in table 1). Consequently, these counteracting indirect pathways tend to make the indirect effects between the infected host classes and the indirect effects between infectious propagules of specialist pathogens closer to neutral.

Second, uptake of infectious propagules by infected hosts creates negative direct effects between the infected classes and spore propagule densities. For example, uptake of infectious propagules of pathogen 2 by hosts infected by pathogen 1 is a negative direct effect of pathogen 1 on pathogen 2. This means that uptake by infected hosts causes more negative total (direct plus indirect) effects between the pathogens. In addition, uptake by infected hosts creates additional indirect pathways that result in all forms of host competition being able to promote positive or negative indirect effects between the infected class and the indirect effects between infectious propagules densities (not shown in table 1). This makes it difficult to make general predictions about how host resource competition influences the indirect effects between the pathogens.

Comparing the Patterns of Indirect Effects between Predators and Pathogens

We now compare how the indirect effects between predators and the indirect effects between pathogens depend on the level of interspecific competition between their victim species. Instead of using the competition coefficients α_{12} and α_{21} from above, we parameterize competition between hosts (or prey) in terms of the geometric mean of the competition coefficients ($\alpha = (\alpha_{12}\alpha_{21})^{1/2}$) and their asymmetry ($(\alpha_{12}/\alpha_{21})^{1/2}$). For exploitative competition, α corresponds to the similarity in resource use of the hosts, with $\alpha = 0$ meaning no overlap and $\alpha = 1$ meaning complete overlap; $(\alpha_{12}/\alpha_{21})^{1/2}$ corresponds to the ratio of the mean resource uptake rate of host 2 to host 1. In the following, we show how the signs and magnitudes of the indirect effects can depend on the amount of interspecific host competition, measured in terms of the victim species' overlap in resource use (α). In our numerical examples, the indirect effect between predators is defined by $-\partial P_2^*/\partial m_1$; the indirect effect between infections propagules is defined by $-\partial P_2^*/\partial \mu_1$; and the indirect effects between the infected host classes are defined by $-\partial I_{12}^*/\partial m_{11} - \partial I_{22}^*/\partial m_{11}$, where the first derivative is always zero for specialist pathogens. In all cases, a positive value implies a positive indirect effect, and a negative value implies a negative indirect effect.

Specialist Exploiters

Specialist predators are predicted to have positive indirect effects for all levels of interspecific prey competition, with greater interspecific prey competition yielding indirect effects of larger magnitude (fig. 2*A*).

The indirect effects between the infected host classes of specialist pathogens often follow a similar pattern for both directly transmitted pathogens (fig. 2*B*) and environmentally transmitted pathogens (fig. 2*E*, 2*F*). Importantly, the levels of interspecific and intraspecific *S-I* competition can quantitatively alter the magnitudes of the indirect effects. First, if interspecific and intraspecific *S-I* competition decrease host densities, then the magnitudes of the indirect effects between the infected host classes will be smaller in magnitude (solid lines below dashed lines in fig. 2*B*, 2*E*). However, that does not imply that the indirect effects between the infectious propagules will be smaller in magnitude (solid blue and black lines above dashed line in fig. 2*F*). Second, recall that interspecific and intraspecific *S-I* competition promote negative and positive, respectively, indirect effects between specialist pathogens. Because of this, the indirect effects are larger when infected hosts are weaker interspecific competitors ($e_{12} < 1$ and $e_{21} < 1$; solid blue line above solid black line in fig. 2*B*, 2*E*, 2*F*) and smaller when infected hosts are stronger interspecific competitors ($e_{12} > 1$ and $e_{21} > 1$; solid red line below solid black line in fig. 2*B*, 2*E*, 2*F*).

Competition between infected and susceptible hosts (*S-I* competition) can also drive qualitatively different patterns in host-pathogen systems. First, the indirect effects between specialist pathogens can be negative. This can occur when infected hosts are stronger interspecific competitors than susceptible hosts (red lines in fig. 2*C*, 2*G*), transmission is frequency dependent (left side of fig. 2*D*), or infectious propagules are lost as a result of uptake by infected hosts (not shown). Second, the indirect effect can switch signs with increased interspecific competition when infected hosts are stronger interspecific competitors than susceptible hosts (red lines in

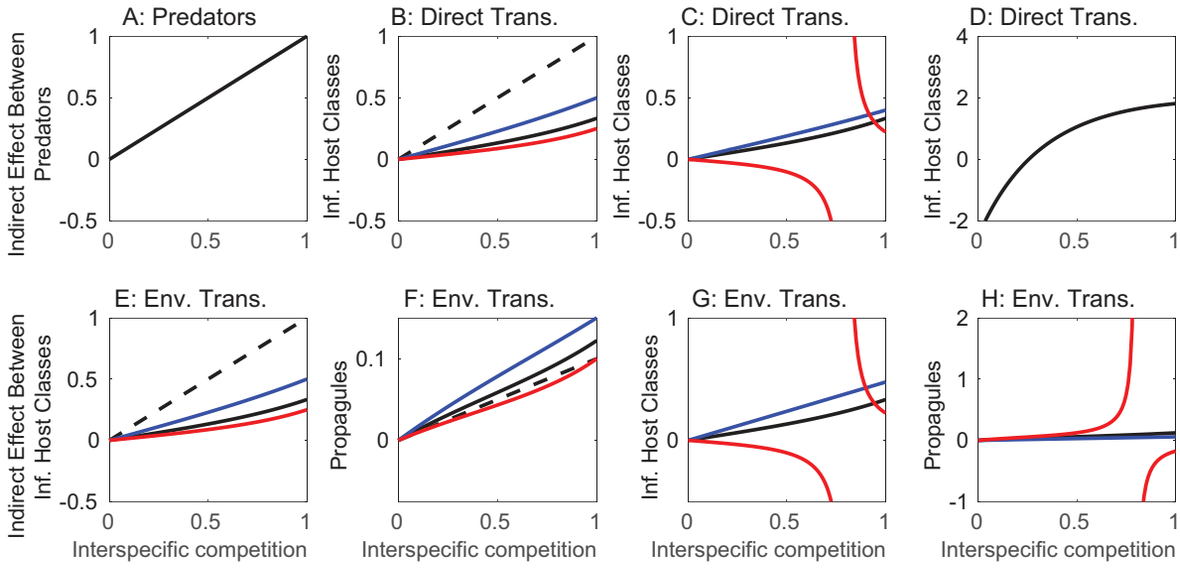

Figure 2: Examples of how the indirect effects between specialist pathogens or predators are influenced by competition between victim species. Each line shows the indirect effect of exploiter 1 on exploiter 2, defined by $-\partial P_2^*/\partial m_1$ for predators, $-\partial I_{22}^*/\partial m_{11}$ for infected host classes, and $-\partial P_2^*/\partial \mu_1$ for infectious propagules; positive values imply a positive indirect effect. *A*, Indirect effects between specialist predators. *B*, Indirect effects between specialist pathogens where infected hosts do not compete ($e_{ij} = 0$; dashed black line) or are weaker ($e_{ij} = 0.5$; blue line), equal ($e_{ij} = 1$; solid black line), or stronger ($e_{ij} = 1.5$; red line) intraspecific and interspecific competitors. *C*, Indirect effects between specialist pathogens where infected hosts are equal intraspecific competitors ($e_{11} = e_{22} = 1$) and weaker ($e_{12} = e_{21} = 0.5$; blue line), equal ($e_{12} = e_{21} = 1$; black line), or stronger ($e_{12} = e_{21} = 2.5$; red line) interspecific competitors. *D*, Example of negative total effects between specialist pathogens with frequency-dependent direct transmission in the absence of interspecific host competition. *E*, *F*, Indirect effects between infected host classes (*E*) and infectious propagules (*F*) where infected hosts do not compete ($e_{ij} = 0$; dashed black line) or are weaker ($e_{ij} = 0.5$; blue line), equal ($e_{ij} = 1$; solid black line), or stronger ($e_{ij} = 1.5$; red line) intraspecific and interspecific competitors. *G*, *H*, Indirect effects between infected host classes (*G*) and infectious propagules (*H*) where infected hosts are equal intraspecific competitors ($e_{11} = e_{22} = 1$) and weaker ($e_{12} = e_{21} = 0.5$; blue line), equal ($e_{12} = e_{21} = 1$; black line), or much stronger ($e_{12} = e_{21} = 2.5$; red line) interspecific competitors. See appendix S2 (available online) for model equations and parameters.

fig. 2*C*, 2*G*, 2*H*). This occurs because increased removal of infected hosts or infectious propagules causes an increase in the number of infected hosts or infectious propagules, respectively. This phenomenon is known as a hydra effect (Abrams 2009).

In total, increased interspecific prey competition always causes more positive indirect effects between specialist predators (fig. 2*A*). Similarly, increased interspecific host competition can cause more positive indirect effects between specialist pathogens with direct or environmental transmission (fig. 2*B*, 2*E*, 2*F*). However, increased interspecific host competition can also cause less positive or negative indirect effects between specialist pathogens when infected hosts are stronger interspecific competitors than susceptible hosts (red lines in fig. 2*C*, 2*G*), transmission is frequency dependent (fig. 2*D*), or infectious propagules are lost as a result of uptake by infected hosts.

Generalist Exploiters

For generalist predators, interspecific prey competition promotes positive indirect effects between predators, and intraspecific prey competition promotes negative indirect effects (Levine 1976; Vandermeer 1980). This results in a transition from negative to positive indirect effects between predators with increased interspecific prey competition (fig. 3*A*).

We predict that in many cases, increased interspecific host competition will produce the same pattern for generalist pathogens with density-dependent direct transmission (fig. 3*B*) or environmental transmission (fig. 3*E*, 3*F*). In addition, for both kinds of pathogens, intraspecific and interspecific *S-I* competition can make the indirect effects between the pathogens more positive or more negative. Figure 3*B*, 3*C*, 3*E*, and 3*F* show examples where for most levels of interspecific host competition, the indirect effects between pathogens in the absence of *S-I* competition are larger in magnitude than the indirect effects between pathogens in the presence of *S-I* competition (solid lines are closer to zero than dashed lines).

Two qualitatively different patterns can occur in host-pathogen systems with generalist pathogens. First, the indirect effects between the pathogens can be positive for all levels of interspecific host competition (fig. 3*G*, 3*H*). This differs from the above in that the indirect effects are positive in the absence of interspecific competition (left side of fig. 3*G*, 3*H*). Second, the indirect effects between the pathogens can decrease from positive to negative values with increased interspecific competition (fig. 3*D*). This differs from the above in that (1) the indirect effects are positive in the absence of interspecific host competition (left side of fig. 3*D*) and (2) the indirect effects become more negative as interspecific competition decreases (lines have a negative slope).

The underlying mechanism driving both patterns is asymmetric transmission. For directly transmitted pathogens, asymmetric transmission means that interspecific (i.e., between-species) transmission is greater than intraspecific (i.e., within-species) transmission for at least one of the pathogens. One way this can occur is when one or both pathogens must obligately switch between host species in order to complete their life cycles. For instance, species of *Schistosoma* (blood flukes) alternate between freshwater intermediate snail hosts and definitive vertebrate hosts (Basch 1991), and the trematode *Euhaplorchis californiensis* passes through (in order) snails, fish, and birds to complete its life cycles (Lafferty 1997).

For environmentally transmitted pathogens, asymmetric transmission means that hosts with high infection coefficients (γ_{ij}) have low propagule release rates (small γ_{ij}), and vice versa (e.g., γ_{11} is much larger than γ_{21} and χ_{11} is much smaller than χ_{21}). We note that asymmetric transmission alone is sufficient to get positive indirect effects between infectious host classes when interspecific host competition is low or absent (left side of fig. 3*G*). However, positive indirect effects between infectious propagules in the absence of interspecific host competition also requires that infectious propagules are lost as a result of uptake by susceptible and infected hosts. Said another way, if the loss of infectious propagules due to uptake by hosts is negligible, then the indirect effects between the infectious propagules is negative when interspecific host competition is negative or absent (dashed line is negative on the left side of fig. 3*H*). However, if the uptake rates of infectious propagules are sufficiently high, then positive indirect effects can arise between the infectious propagules in the absence of interspecific prey competition (solid line is positive on the left side of fig. 3*H*).

Discussion

In this study, we explored and compared the indirect effects between predators that share prey and the indirect effects between pathogens that share host species. While there are differences between predatory and parasitic interactions, their similarities suggest that the indirect effects between pairs of the two types of exploiters could be similar. Indeed, previous studies have used the similarities between the two types of exploitative interactions to gain an understanding about the dynamics of predator-prey and host-pathogen communities (Hall et al. 2008; Raffel et al. 2008; Lafferty et al. 2015). Our work has identified when the indirect effects between predators and between pathogens can differ quantitatively and qualitatively

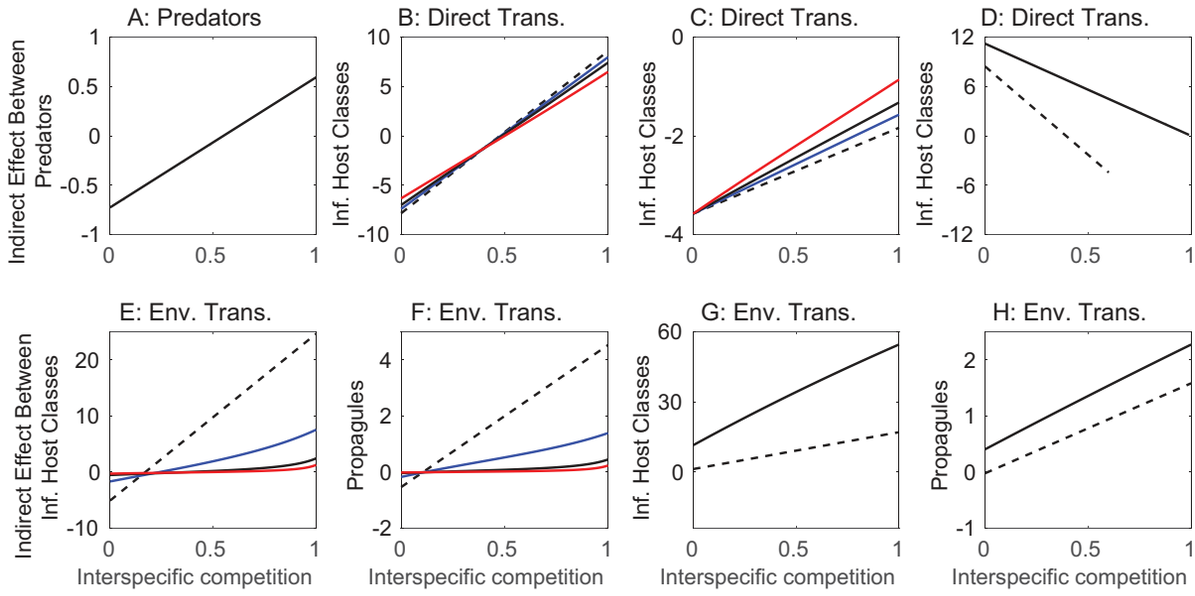

Figure 3: Examples of how the indirect effects between generalist pathogens or predators are influenced by competition between victim species. Each line shows the indirect effect of exploiter 1 on exploiter 2, defined by $-\partial P_2^*/\partial m_1$ for predators, $-\partial I_{22}^*/\partial m_{11} - \partial I_{12}^*/\partial m_{11}$ for infected host classes, and $-\partial P_2^*/\partial \mu_1$ for infectious propagules; positive values imply a positive indirect effect. *A*, Indirect effects between generalist predators. *B–D*, Indirect effects between generalist pathogens where infected hosts do not compete ($e_{ij} = 0$; dashed black line) or are weaker ($e_{ij} = 0.5$; blue line), equal ($e_{ij} = 1$; solid black line), or stronger ($e_{ij} = 2$; red line) intraspecific and interspecific competitors. *C*, Indirect effects between specialist pathogens where infected hosts are equal intraspecific competitors ($e_{11} = e_{22} = 1$) and weaker ($e_{12} = e_{21} = 0.5$; blue line), equal ($e_{12} = e_{21} = 1$; black line), or stronger ($e_{12} = e_{21} = 2$; red line) interspecific competitors. *D*, Examples of indirect effects between specialist pathogens that become more negative with increased interspecific host competition. *E*, *F*, Indirect effects between infected host classes (*E*) and infectious propagules (*F*) where infected hosts do not compete ($e_{ij} = 0$; dashed black line) or are weaker ($e_{ij} = 0.25$; blue line), equal ($e_{ij} = 1$; solid black line), or stronger ($e_{ij} = 2$; red line) intraspecific and interspecific competitors. *G*, *H*, Indirect effects between infected host classes (*G*) and infectious propagules (*H*) when loss of infectious propagules due to uptake by hosts is present (solid lines) or absent (dashed lines). See appendix S2 (available online) for model equations and parameters.

and that these differences can lead to different population-level patterns.

The underlying reason why the indirect effects between pathogens and the indirect effects between predators can differ in our models is that parasitic interactions are not immediately lethal. The delay in mortality results in multiple infected classes for each pathogen (one in each host population) and allows for consumption of resources by infected individuals. Both factors introduce additional pathways that can alter the signs and magnitudes of the indirect effects between pathogens. In particular, in predator-prey systems, specialist predators have positive indirect effects (fig. 2*A*), and the indirect effects between generalist predators transition from negative to more positive with increased interspecific prey competition (fig. 3*A*; Levine 1976; Vandermeer 1980, 2004; Abrams and Nakajima 2007; Abrams and Cortez 2015). These patterns can also arise in host-pathogen systems (fig. 2*B*, 2*E*, 2*F* and fig. 2*A*, 2*E*, 2*F*, respectively). However, other patterns are possible, including negative indirect effects between specialist pathogens (fig. 2*C*, 2*D*, 2*G*, 2*H*), positive indirect effects between generalist pathogens in the absence of interspecific host competition (fig. 3*D*, 3*G*, 3*H*), and indirect effects that become more negative with increased interspecific host competition (figs. 2*C*, 2*G*, 3*D*).

While we have not included them in our model, we also expect that the population-level indirect effects between pathogens will be affected by two other consequences of parasitic interactions not being immediately lethal: recovery from infection and coinfection by multiple pathogens. Both of these introduce additional indirect pathways through which pathogens indirectly interact. For recovery from infection, recovered hosts compete for resources, and a host that has recovered from an infection by pathogen 1 can become infected by pathogen 2. It is unclear how this will affect the indirect effects between pathogens because there is no direct analog of recovery in predator-prey systems. For coinfection, pathogens coinfecting the same individual host can interact indirectly via their molecular interactions with the host. Positive and negative within-host indirect effects can arise between coinfecting pathogens via upregulation or suppression of the immune system, depletion of within-host resources, and pathogen-induced

mortality (Cressler et al. 2014; Griffiths et al. 2014; Johnson et al. 2015). While some recent progress has been made (Lello et al. 2018; Clay et al. 2019; Park and Ezenwa 2020), it is still unclear how within-host indirect effects scale up to the population level. Altogether, this shows that while the indirect effects between predators follow relatively simple rules, the rules governing the indirect effects between pathogens will be more complex. This suggests that the indirect interactions between pathogens are likely to vary greatly across systems, opening up many opportunities to understand how different properties of host-pathogen communities influence the indirect interactions between pathogens. However, this also means that, in general, theory will be limited in its ability to make general predictions, and predictions will need to be made on a case-by-case basis.

Many previous studies have explored and discussed the costs and benefits of being a specialist versus generalist (e.g., see reviews in Futuyma and Moreno 1988; Leigh 1990; Finlay-Doney and Walter 2012). For both generalist predators and pathogens, the benefit of access to more potential victims comes at the cost of needing to overcome the different defense systems of each victim species. Conversely, specialists need to overcome only one defense system but at the cost of having fewer individuals to exploit. Our results show that the costs of being a specialist or generalist exploiter may be partially offset or exacerbated by the presence of another exploiter species. For example, the positive indirect effects between specialist predators always help offset the costs of specialization. In contrast, for generalist predators, the costs of being a generalist may be offset if interspecific competition is strong and exacerbated if interspecific competition between prey is weak. The implications of our results for specialist and generalist pathogens are similar, but whether costs are offset or exacerbated also depends on whether infected hosts are stronger or weaker competitors than susceptible hosts and the mechanism of transmission (e.g., density-dependent vs. frequency-dependent direct transmission or whether loss of infectious propagules during transmission is negligible).

While this suggests that the indirect effects between exploiters could provide an advantage to being a specialist or generalist, caution is advised because our results are based on only one metric for measuring the indirect effects (i.e., the change in equilibrium density of one exploiter in response to a small increase in mortality of the other exploiter, $\partial P_2^*/\partial m_1$). Previous studies on predator-prey systems (Abrams 1987, 2001; Abrams and Nakajima 2007; Abrams and Cortez 2015) have also used (1) the change in equilibrium density of one predator to a small decrease in the density of the other predator (i.e., dP_2^*/dP_1^*), (2) the change in equilibrium density of one predator in response to the removal of the other predator (i.e., a comparison of allopatric and sympatric densities), and (3) the phase relationships between oscillating predator populations. In general, these metrics are not guaranteed to agree. Indeed, Abrams and Cortez (2015) found for a two-predator-two-prey system that the equilibrium-based metrics agree when interspecific prey competition is low but often disagree when interspecific prey competition is high. In addition, at least two of the metrics necessarily disagree when increased mortality for one predator causes an increase in its density; that is, the predator exhibits a hydra effect (Abrams 2009). Pathogen hydra effects are possible in our host-pathogen models (they cause the discontinuities in fig. 2*C*, 2*G*, 2*H*). Also, while mortality manipulations of populations at equilibrium are conceptually and mathematically simple to work with, experiments involving the removal of some or all hosts infected by one pathogen more closely align with two of the other metrics. Thus, additional studies are needed to explore when the metrics differ and what that implies about the indirect effects between pathogens that infect the same host species.

Finally, a general conclusion from our work is that interspecific host competition is likely to have large effects on the dynamics and properties of host-pathogen systems. Previous studies on the coexistence of multiple hosts and multiple pathogens or pathogen strains have assumed that interspecific host competition is absent (Holt and Dobson 2006) or complete and symmetric ($\alpha_{12} = \alpha_{21} = 1$; Chilvers and Brittain 1972; Regoes et al. 2000; Gandon 2004; Zhang et al. 2007). Our results show that the level of interspecific host competition has a large impact on the signs and magnitudes of the indirect effects between pathogens. We have not focused on how asymmetric competition between host species influences the indirect effects between pathogens, but asymmetry is also likely important because asymmetric interspecific prey competition is predicted to promote positive indirect effects between predators (Abrams and Cortez 2015). In addition, previous studies on multihost-one-pathogen systems have shown that between-host competition has important effects on species coexistence (Bowers and Turner 1997; Greenman and Hudson 2000; Saenz and Hethcote 2006; Gyllenberg et al. 2012) and disease dynamics (Cáceres et al. 2014; Strauss et al. 2015; Searle et al. 2016). This strongly suggests that it is important for future theoretical work to include interspecific host competition in models in order to better understand the dynamics of multihost-multipathogen communities.

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Statement of Authorship

M.A.D. and M.H.C. designed the study. M.H.C. did the model analysis. M.H.C. wrote the first draft, and M.A.D. contributed to writing.

Data and Code Availability

No original data are presented in this paper. All code supporting the results are provided in the online supplemental material and the Dryad Digital Repository (https://doi.org/10.5061/dryad.pzgmsbchp; Cortez and Duffy 2020).

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