Chapter 5: Healthy herds or predator spreaders? Insights from the plankton into how predators suppress and spread disease

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Lay summary

Sometimes predators suppress disease in their hosts, but other times they spread disease. Here, we explore the factors that drive these divergent outcomes, laying out a framework explaining different mechanisms by which predators can influence disease in their prey. We review evidence for these different mechanisms from a variety of predator-prey/host-parasite systems, but focus particularly on the prey/host species that has been the focus of our work for the past 15 years: the ecologically important lake crustacean, *Daphnia*. In this system, bluegill sunfish serve as a "healthy herds" predator, reducing disease in our focal host, *Daphnia dentifera*. Phantom midge larvae, on the other hand, are "predator spreaders", fueling disease outbreaks in *Daphnia*. A key question that continues to motivate our research is: what determines whether predators promote or prevent disease?

Abstract

Predators are often thought to decrease the size of disease outbreaks, particularly through selective predation on infected hosts and/or predation on free-living infectious stages of parasites. But we also see cases in nature where higher predator densities are associated with more disease, not less. How and why do predators sometimes fuel disease outbreaks but other times thwart them? Answering this question could help explain spatial and temporal variation in disease, and could also explain why attempts to control disease by manipulating predators sometimes fail. Here, we lay out eight mechanisms by which predators can suppress or spread disease in prey populations. We explore each of these mechanisms generally and also review evidence from the study system that has been the focus of much of our research. This system focuses on the crustacean *Daphnia dentifera*, a dominant herbivore in lake food webs in the Midwestern United States. *D. dentifera* is prey to bluegill sunfish and phantom midge larvae, as well as host to a virulent fungal pathogen. We review evidence for bluegill sunfish as "healthy herds" predators that reduce disease, and for midge larvae as "predator spreaders" that fuel disease outbreaks. We find that both predators can impact disease via multiple mechanisms. Bluegill feed selectively on infected hosts, and also depress disease in *Daphnia* by reducing the density of midge larvae which spread disease. Bluegill also increase the abundance of *Ceriodaphnia* which reduce disease. Midge larvae increase disease in their hosts, in part by releasing spores into the water column where they can be consumed by additional hosts. We call for further research aimed at uncovering the relative importance of the different mechanisms, as well as into how global change might alter the impacts of these predators on disease. Such studies should allow us to better predict how and when predators should suppress or spread disease.

5.1 Introduction

Predators may strongly shape disease in wildlife populations (Packer *et al.*, 2003; Ostfeld & Holt, 2004). Typically, most theory envisions that predators suppress disease, especially in cases where predators prey selectively on infected hosts (Packer *et al.*, 2003; Hall, Duffy & Cáceres, 2005). This has led to the prominent idea that predators "keep the herds healthy" – an idea that is so prominent that it has made its way into cartoons and candy bar wrappers. However, empirically, we know that predation is not always associated with reduced disease. Indeed, sometimes we see exactly the opposite pattern: a strong *positive* relationship between predation and disease. One of the most striking patterns in the host-parasite system that our work focuses on is that host populations in lakes that have more invertebrate predators are more likely to have outbreaks of a virulent fungus (Figure 1) (Figure 1; Cáceres, Knight & Hall, 2009; Strauss *et al.*, 2016). A key question that emerges, then, is what determines whether predators promote or prevent disease?

Rates of parasitism in a single host can vary substantially across space and over time; understanding when predators would be predicted to control disease and when they would be predicted to fuel it might help explain this spatiotemporal variation. One well-studied example of spatiotemporal variation in parasitism comes from red grouse and the parasitic nematode, *Trichostrongylus tenuis* (Hudson, 1986; Hudson, Dobson & Newborn, 1992) (see also Chapter 1, this volume). Between 1979 and 1983, the number of worms per bird varied between 1000 (in 1982) and 9000 (in 1983) (Hudson, 1986). Looking across space, some estates had <1000 worms per bird on average, while others had an average of >10 000 worms per bird (Hudson, Dobson & Newborn, 1992). As will be discussed more below, some of this variation is likely explained by variation in predation pressure. Another example is provided by Lyme disease, which is a vector-

83 borne disease that has emerged as a problematic infection of humans; Lyme cases in humans
84 vary greatly spatially as well as temporally (Li *et al.*, 2014). Just within the state of Virginia in
85 the United States, counts of human Lyme cases ranged from 66-1233 between 1998 & 2011 (Li
86 *et al.*, 2014). There was also substantial variation across space, with much higher rates in some
87 counties. Perhaps most interestingly, while there was a general trend over time towards more
88 counties with Lyme and more Lyme within counties, some counties that had high rates of Lyme
89 in one year had very low rates in a subsequent year (Li *et al.*, 2014). Most of the research on
90 ecological drivers of variation in Lyme disease risk to humans has focused on variation in host
91 community composition (Ostfeld & Keesing, 2000; Salkeld, Padgett & Jones, 2013; Wood &
92 Lafferty, 2013; Turney, Gonzalez & Millien, 2014). However, as discussed below, predators can
93 also explain some of the spatiotemporal variation (Levi *et al.*, 2012).
94 Understanding the different mechanisms by which predators can influence disease is also
95 important because it can inform disease control measures. One recent paper argued that
96 "managing assemblages of predators represents an underused tool for the management of human
97 and wildlife diseases" (Rohr *et al.*, 2015), and another recent paper raised the potential of
98 reducing Lyme disease risk in humans via predator manipulation (Levi *et al.*, 2012). Perhaps
99 most notably, the United Kingdom continues to cull badgers – where culling is a particularly
100 efficient form of predation by humans – in an effort to reduce disease in livestock from bovine
101 tuberculosis (Department for Environment Food and Rural Affairs, 2016) (see also Chapter 22,
102 this volume). The assumption of culling campaigns is that higher predation will drive "healthy
103 herds". However, past culling campaigns have actually *increased* bovine tuberculosis (Donnelly
104 *et al.*, 2003). Unless we develop a more comprehensive understanding of when and how
105 predators influence disease, management strategies that propose to reintroduce or augment

106 predator populations could backfire (Choisy & Rohani, 2006).

107 In this chapter, we review eight different mechanisms by which predators can influence
108 disease in their prey populations. We give general examples of each mechanism, but also focus
109 in particular on the *Daphnia*-parasite system that has been the focus of our research over the past
110 15 years (Box 1).

111

112 **5.2 What are the mechanisms via which predators can suppress or promote disease?**

113 We lay out eight different mechanisms by which predators can influence disease in their prey
114 populations (Table 1), describing the theory underlying the mechanism, providing empirical
115 examples from diverse study systems, and then providing evidence from our focal *Daphnia*-
116 parasite system (Box 1; Figure 2).

117

118 1. Predator-driven reduction in host density:

119 Theoretically, if predators reduce the density of their prey (i.e., the host) populations, this should
120 reduce disease in systems with density-dependent transmission (Packer *et al.*, 2003; Keeling &
121 Rohani, 2008). However, empirical evidence of predators reducing host density and that, in turn,
122 reducing disease has been mixed. Some correlative studies show a negative relationship between
123 predators and disease, as predicted by the general theory; for example, lobsters reduced densities
124 of sea urchins, reducing the likelihood that a population experienced an outbreak of a bacterial
125 disease (Lafferty, 2004). Experimental studies have also revealed a negative relationship
126 between predators and disease mediated by prey/host density: for example, in an aphid-parasitoid
127 system, treatments that contained a predator had reductions in both host density and parasitism
128 (Snyder & Ives, 2001). However, in other cases, empirical studies have shown that density

129 reduction is ineffective at controlling disease or even counterproductive. Widespread non-
130 selective culling of hosts has not been effective at reducing rabies in dogs and wildlife (Morters
131 *et al.*, 2013). Culling of badgers in small areas where there have been bovine tuberculosis
132 outbreaks (reactive culling) not only failed to reduce disease, but actually increased tuberculosis
133 incidence in cattle, perhaps due to increased long distance movements (Donnelly *et al.*, 2003)
134 (see also Chapter 22, this volume). Thus, while predators sometimes reduce disease via prey/host
135 density reduction, this pattern is not universal.

136 Theory points us to specific scenarios where we would predict to see predator-driven
137 reductions in host density drive increased disease in hosts (that is, predators promoting disease).
138 First, if parasites actively seek and attack hosts, reducing host density might increase disease.
139 Empirical support for this mechanism comes from an experiment that manipulated predator
140 density and monitored the densities of their tadpole prey and the abundance of parasites that
141 attacked the tadpoles (Rohr *et al.*, 2015). In high predator diversity treatments, higher predator
142 density was associated with lower tadpole host density and higher abundances of parasite
143 metacercariae per tadpole; however, in low predator diversity treatments, higher predator density
144 was associated with fewer metacercariae per tadpole (Rohr *et al.*, 2015). Second, even in cases
145 where parasites do not actively seek and attack hosts, increased host density can sometimes
146 decrease encounter rates. In our *Daphnia*-parasite system, high host densities depress host
147 feeding rate, reducing spore uptake; in these cases, there can be a unimodal relationship between
148 host density and disease risk, with disease highest at intermediate densities (Civitello *et al.*,
149 2013). Third, if hosts invest more in defense at high densities – a phenomenon known as density
150 dependent prophylaxis (DDP) (Wilson & Cotter, 2009) – decreased host density might increase
151 disease. While we do not know of empirical examples where predator-driven changes in host

density and DDP combined to alter disease levels, DDP on its own has empirical support from a variety of invertebrate systems (reviewed in Wilson & Cotter, 2009).

Predators can only reduce disease via reductions in prey/host density if there is a clear relationship between host density and disease. Evidence for such a relationship in our *Daphnia*-parasite system is equivocal. Looking across populations, there is no significant relationship between density of our focal host, *Daphnia dentifera*, and prevalence of the fungal parasite *Metschnikowia* in lakes in Southwestern Michigan (Cáceres *et al.*, 2006; Hall *et al.*, 2010) or Indiana (Penczykowski *et al.*, 2014; Strauss *et al.*, 2016). Looking within populations, a study of fine-scale dynamics of fungal epidemics in five Michigan lakes revealed that the density of infected individuals at a given time was actually slightly *negatively* related to the density of susceptible individuals at the time of infection (Duffy *et al.*, 2009); it is not possible to say at this time what underlies this pattern, though it is consistent with density-dependent prophylaxis. Moreover, in our *Daphnia*-parasite system, the relationship between host density and disease can depend on the metric used: Indiana lakes did not show a significant relationship between overall host density and infection prevalence, but did show a significant positive relationship between overall host density and the density of infected hosts (Strauss *et al.*, 2016). Finally, as discussed in the previous paragraph, we sometimes see a unimodal relationship between host density and infection prevalence. This occurs as a result of impacts of host density on feeding rate, since hosts ingest spores while feeding (Civitello *et al.*, 2013). Overall, it seems unlikely that predators reduce disease in our *Daphnia* system simply due to reductions in host density.

2. Selective culling: If predators prey selectively on infected hosts (perhaps because they are easier to detect or catch), they should be particularly effective at reducing disease in their host

populations (Packer *et al.*, 2003; Hall, Duffy & Cáceres, 2005). In most cases, we predict a reduction in disease when predators prey selectively on infected hosts. However, in certain specific scenarios, it is possible for selective predation to increase disease in prey populations (Holt & Roy, 2007).

There is some empirical support for a "healthy herds" effect of selective predation. Red grouse that are infected with a cecal nematode are more easily detected by dogs that have been trained to locate birds by scent; if predators also locate grouse by scent, this argues that predators should prey selectively on infected grouse (Hudson, Dobson & Newborn, 1992) (see also Chapter 1, this volume). Moreover, estates that had higher predator control (and, therefore, lower predation rates) had birds that were more heavily infected, suggesting that predators reduce infection burdens in their host populations (Hudson, Dobson & Newborn, 1992). In the introduction of this chapter, we noted that some estates averaged <1,000 worms per bird, while others had >10,000 on average; this variation correlated with the number of (human) keepers on the estate, with estates with the most keepers having the highest disease burdens (Hudson, Dobson & Newborn, 1992). Keepers control predators of grouse, so estates with more keepers should have fewer predators. Thus, this pattern is consistent with healthy herds predation reducing disease burden in grouse.

There is strong evidence for selective culling in fish-*Daphnia*-parasite systems, with visual fish predators feeding highly selectively on *Daphnia* infected with a diverse suite of pathogens, including the yeast *Metschnikowia*, the bacterium *Spirobacillus cienkowskii*, the chytrid *Polycaryum laeve*, and an undescribed oomycete that fills the body cavity with hyphae (Figure 3; Duffy *et al.*, 2005; Johnson *et al.*, 2006; Duffy & Hall, 2008). Corixids have also been found to prey selectively on *Daphnia magna* infected with the bacterium *Pasteuria ramosa*

198 (Goren & Ben-Ami, 2015).

199 Does this selective culling by fish reduce disease in *Daphnia*? Modeling, time-series data,
200 and across lake comparisons all suggest yes (Duffy *et al.*, 2005; Hall, Duffy & Cáceres, 2005;
201 Johnson *et al.*, 2006; Duffy & Hall, 2008; Duffy *et al.*, 2012; Rapti & Cáceres, 2016). For
202 example, lakes with smaller bodied individuals (indicating high fish predation) have less disease
203 (Duffy *et al.*, 2012), and, within lakes, disease outbreaks occur in autumn as lakes cool and fish
204 predation rates decrease (Duffy *et al.*, 2005). However, one experimental test did not find an
205 effect of fish predation on disease, perhaps due to very high transmission rates in the
206 experimental mesocosms (Duffy, 2007).

207

208 3. Shifts in host demography or class structure: If predators prey selectively on particular host
209 stages (or ages), and if those stages (ages) are differentially susceptible to parasites, this can lead
210 to predator-driven shifts in host demography altering disease in prey/host populations. If
211 predators shift demography towards ages or stages that are less susceptible to disease (or that
212 harbor lower disease burdens), that should reduce disease; however, if the shift is towards ages
213 or stages that are more susceptible or harbor higher disease burdens, then predators will promote
214 disease. A special case of a shift in host class structure can occur in systems with acquired
215 immunity. If there are costs associated with having been infected in the past or with being
216 immune, increased predation can drive increased disease under certain conditions (Holt & Roy,
217 2007). While we are not aware of a direct example of predators reducing disease via shifts in
218 host demography, predators that prey primarily on larval insects should reduce parasitism in
219 cases where the parasitoids attack developing larvae (e.g., Kistler, 1985). An empirical example
220 of a predator-driven shift in host demography driving an increase in disease comes from a system

where large snails are more likely to be infected by a trematode parasite, but also less vulnerable to predation by birds (Byers *et al.*, 2015). As a result, habitats with high predation pressure also have high disease (Byers *et al.*, 2015).

In our system, fish shift *Daphnia* populations towards smaller body sizes, both due to feeding preferentially on larger *Daphnia* (Brooks & Dodson, 1965) and by inducing plastic changes in body size (e.g., Hesse *et al.*, 2012). Smaller bodied animals are less susceptible to the fungal parasite (Hall *et al.*, 2007), so we would predict fish should shift the population towards a size structure that is more disease resistant. Conversely, midge larvae prey heavily on small-bodied *Daphnia* (Spitze, 1985; Elser *et al.*, 1987). In addition to finding experimentally that midge larvae prey more on juveniles than adults, our field surveys have revealed that lakes with more midge larvae have lower proportion juveniles at the start of the epidemic season (S.R. Hall, unpublished data). These findings support a role of predators in shifting host demography towards more vulnerable stages. In addition, if predators drive trophic cascades (as discussed below in mechanism #8), the increase in resources should speed development of the remaining juveniles into adults (de Roos & Persson, 2013). Together, in our system, it seems likely that visual predators (fish) shift the host population towards smaller, more resistant animals and that gape-limited predators such as midge larvae shift the host population towards larger, more susceptible individuals. However, we have not yet tested this experimentally.

4. Shifts in competitor community composition: Species often differ in their competence as hosts, with low competence hosts potentially "diluting" disease for high competence hosts (Keesing *et al.*, 2010). Host species that are highly competent hosts might also be more vulnerable to predation; for example, hosts with a "weedier" life history that invests little in

244 defenses against natural enemies might be more vulnerable to predation and disease. In these
245 cases, increased predation could decrease disease. Conversely, if there are tradeoffs in resistance
246 to different natural enemies (as discussed more below), predators may spread disease by
247 selecting for prey/host communities that are defended against predators but not parasites – that
248 is, predators may thwart a dilution effect by eating the diluters. Overall, predators can change
249 community composition in ways that strengthen or weaken the dilution effect.
250 One potential example of predators strengthening a dilution effect comes from the Lyme
251 disease system for which the dilution effect was originally proposed (Ostfeld & Keesing, 2000).
252 Lyme cases in humans are higher when red fox density is lower, perhaps as a result of foxes
253 preying on small mammals such as mice, which are highly competent hosts for the bacterium
254 that causes Lyme disease (Levi *et al.*, 2012).
255 In our *Daphnia*-parasite system, fish feed preferentially on larger *Daphnia* (Brooks &
256 Dodson, 1965) while midge larvae feed selectively on smaller bodied hosts (as discussed in
257 mechanism #3 above). Increased fish predation can drive shifts towards communities with higher
258 frequencies of *Ceriodaphnia*, while increased predation by midge larvae should result in fewer
259 *Ceriodaphnia*. Given that *Ceriodaphnia* are an important diluter host in our *Daphnia*-fungus
260 system (Strauss *et al.*, 2015; Strauss *et al.*, 2016), changes in community composition mediated
261 by predators alter disease in our focal host (Strauss *et al.*, 2016). (Note: by "diluter host", we
262 mean other potential hosts that generally reduce disease in our focal host.)
263
264 5. Shifts in predator community composition: Predators might also reduce disease in a focal host
265 by altering the density of other predators. Returning to the Lyme disease example: as discussed
266 above, more foxes drive lower abundance of small mammals such as mice, reducing disease risk

in humans (Levi *et al.*, 2012). Fox density, in turn, is driven by coyote density, with coyotes suppressing fox density; this leads to a positive relationship between the abundance of coyotes and disease in humans (Levi *et al.*, 2012).

Changing the density of other predators is a very important way in which fish influence disease in *Daphnia*. Bluegill sunfish prey upon midge larvae (González & Tessier, 1997); midge larvae spread disease, so this predation by fish on midge larvae can indirectly reduce disease in *Daphnia* (Strauss *et al.*, 2016). In our lake systems, in theory, increases in the densities of piscivorous fish could increase disease by reducing densities of healthy herds predators. Unfortunately, we do not have data on piscivorous fish in our study lakes, and so are unable to explore this hypothesis at present.

6. Trait-mediated indirect effects (TMIEs): Predators might have indirect effects on disease in hosts by impacting host traits relevant to infection (such as immune function, body size, behavior, and habitat use). In some cases, the TMIEs might increase disease, but in others they can reduce disease. A study on wood frog tadpoles found that exposure to predator chemical cues reduced the intensity of infections by the chytrid fungus *Batrachochytrium dendrobatidis* (Bd), possibly due to stress-induced immune system enhancement (Groner & Relyea, 2015). Conversely, beetles move belowground in response to aboveground predators, increasing their exposure to pathogenic nematodes and fungi (Ramirez & Snyder, 2009). Moreover, exposure to predators weakens the immune response of the beetles, rendering them even more susceptible to pathogens (Ramirez & Snyder, 2009). An influence of predators on immune function has been shown in a variety of systems. For example, a study on house sparrows found that exposure to a predator reduced their T-cell-mediated immune response and drove higher prevalence and

intensity of malaria infections (Navarro *et al.*, 2004). Because organisms have finite resources, investment in traits that protect against predators can mean that there will be fewer resources available to invest in defenses against parasites (including immune function). This means that there will often be tradeoffs that constrain an individual's ability to respond effectively to multiple natural enemies.

In our *Daphnia*-parasite system, we predicted TMIEs of fish predators would reduce disease, based on effects on host body size. While chemical cues from fish did indeed reduce host body size in an experimental study, they also increased the per spore susceptibility of hosts, canceling out the decreased susceptibility associated with smaller body size (Bertram *et al.*, 2013). In an earlier study, we found that exposure to chemical signals from midge larvae induced larger body size and higher susceptibility (Duffy *et al.*, 2011); however, the Bertram et al (2013) study did not find an effect of midge chemical cues on host body size or disease-related traits. Studies on other *Daphnia*-microparasite systems have found that TMIEs of fish did not influence *Daphnia*'s ability to induce life history changes in response to parasites (Lass & Bittner, 2002) and did not change parasite virulence but decreased parasite spore yield (Coors & De Meester, 2011). Combined with the results of the Bertram et al. study, these results suggest that the net impact of TMIEs of fish on parasitism in *Daphnia* might be modest.

In our system, larger-bodied individuals are more susceptible to infection but less susceptible to predation by midge larvae. Given these strong links between body size, predation risk, and disease risk, we would predict a trade-off among genotypes between susceptibility to these two natural enemies, mediated by body size. A tradeoff in resistance to fish predation and parasitism was found in a different *Daphnia*-parasite system. In that system, the tradeoff was mediated by habitat use: genotypes that resided near the bottom of a pond avoided fish predation

313 but encountered more parasite spores, increasing disease risk (Decaestecker, De Meester &
314 Ebert, 2002).

315 If there is a tradeoff between susceptibility to midge larvae and the fungus in our system,
316 we might predict there would be evolutionary cycles driven by selection from predators and
317 parasites. For example, high intensity of predation by midge larvae would select for larger and/or
318 faster growing genotypes, increasing infection risk in the population and fueling a large disease
319 outbreak. That would then select for higher resistance, smaller bodies, and slower growth, which
320 would then render the population more susceptible to predation by midge larvae. We have
321 previously found evidence that fish predation rate influences epidemic size which, in turn,
322 influences evolution of resistance to disease (Duffy *et al.*, 2012). We plan to explore eco-
323 evolutionary dynamics in midge-*Daphnia*-parasite systems in the future.

324

325 7. Predator consumption of carcasses and/or spore spreading: Predators commonly consume free-
326 living stages of parasites (i.e., spores) or carcasses of infected individuals. If the parasite is
327 digested by the predator, this should decrease infection in the focal host population (Johnson *et*
328 *al.*, 2010; Bidegain *et al.*, 2016). However, in many cases, the parasite is not fully digested by the
329 predator, leading the predator to spread spores in the environment, increasing host exposure to
330 disease. In an example of predators reducing disease by consuming free-living parasites,
331 damselfly nymphs prey upon infectious stages of the trematode *Ribeiroia ondatrae*, reducing
332 infection prevalence in a focal amphibian host by approximately 50% (Orlofske *et al.*, 2012).
333 Conversely, faecal samples collected from scavengers (including jackals, hyenas, and vultures)
334 that preyed on the carcasses of anthrax-infected ungulates were found to frequently contain high
335 numbers of anthrax spores, suggesting that they could generate new foci of infection (Lindeque

& Turnbull, 1994).

Spore spreading might be particularly important in certain habitat types. For example, in stratified lakes, hosts that die from virulent effects of a parasite are likely to settle out of the water column before they release their spores. But, if a predator consumes infected hosts and releases the spores in the water column, those spores are then in close proximity to new hosts. Settling of dead hosts is likely to be common in many aquatic habitats (including lakes, oceans, rivers, and estuaries); standard disease models need to be extended to consider these habitats, especially given the potential economic and ecological importance of their parasites (Harvell *et al.*, 2004; Lafferty *et al.*, 2015; Bidegain *et al.*, 2016).

We are not aware of evidence of predators of *Daphnia* directly consuming spores from the water column or of them eating infected carcasses. However, we do know that they consume infected hosts. Fish only partially digest the spores contained in infected hosts: somewhat fewer spores are retrieved from *Daphnia* that have been fed to fish (vs. infected *Daphnia* that were not fed to fish), but there is no significant effect of fish gut passage on the infectivity of those spores (Duffy, 2009; Figures 4&5). However, it is likely that the effects of fish gut passage differ between different parasites (e.g., species that produce spores with thinner cell walls are likely to be impacted more strongly).

There is strong evidence for midge larvae spreading parasite spores in our system and for this increasing disease in our focal host. Midge larvae release spores when they regurgitate infected corpses, driving higher disease in experimental microcosms (Cáceres, Knight & Hall, 2009). Moreover, lakes with more midge larvae have more disease (Cáceres, Knight & Hall, 2009; Penczykowski *et al.*, 2014; Strauss *et al.*, 2016). Theory shows that the release of spores in the water column by this sloppy feeding is crucial for allowing disease outbreaks to occur in

359 stratified lakes (Cáceres, Knight & Hall, 2009; Auld *et al.*, 2014).

360 While we do not know of *Daphnia* predators that consume free-living stages of parasites
361 from the water column, we do know that daphniids can consume free-living stages of parasites of
362 other organisms. Daphniids feed on zoospores of fungi that infect diatoms (Kagami *et al.*, 2004),
363 the chytrid fungus *Bd* that attacks amphibians (Buck, Truong & Blaustein, 2011; Searle *et al.*,
364 2013; Hite *et al.*, 2016), viral parasites of frogs (Johnson & Brunner, 2014), and oomycete brood
365 parasites of copepods (Valois & Burns, 2016). Thus, *Daphnia* might promote "healthy herds" in
366 other host-parasite systems in their role as a key grazer in lake and pond food webs.

367

368 8. Fueling of spore production by predator-driven trophic cascades: Predators might fuel disease
369 via trophic cascades. Trophic cascades occur when predators reduce density of their prey
370 populations, leading to increases in density at the next lower trophic level (Pace *et al.*, 1999). If a
371 trophic cascade increases resource levels, it could increase parasite production in infected
372 prey/hosts. At present, we do not know of any evidence showing the full link of increased
373 predation driving increased resources driving increased parasitism. However, we know that, in
374 some systems, higher resource levels increase parasite production (Smith, 2007). For example,
375 increasing fructose in the diet of rats increased the number of eggs produced by a macroparasite,
376 and, five weeks after infection, mature parasite eggs were only found in rats that were fed high
377 fructose levels (Keymer, Crompton & Walters, 1983). However, sometimes higher resource
378 levels stimulate the host immune system, leading to reduced parasite production (Cressler *et al.*,
379 2014); sticking with examples from rodent-macroparasite systems, feeding mice high protein
380 diets decreased worm burdens 20-30 days post-infection (Michael & Bundy, 1992).

381 In the *Daphnia*-parasite system, we know that increasing resource levels increase

382 epidemic size, in part by increasing spore yield from infected hosts (Civitello *et al.*, 2015). This
383 argues that, if predators drive trophic cascades, this should fuel epidemics. Lakes with more
384 midge larvae have more algal resources for hosts (S.R. Hall, unpublished data), which is
385 consistent with a trophic cascade. However, we do not yet know whether this reflects a cascade
386 or an underlying productivity gradient. Thus, further work is needed to see if increased predators
387 increase resources and, as a result, increase disease.
388
389 Summary of impacts of predation on our *Daphnia*-parasite system: Fish reduce disease in
390 *Daphnia,* whereas midge larvae spread disease. In both cases, the predators influence disease via
391 several mechanisms that operate simultaneously. Fish prey highly selectively on infected hosts.
392 Fish also drive shifts in the community composition of competitors and predators in a way that
393 decreases disease risk for *Daphnia*. Thus, fish are healthy herds predators in our system. On the
394 other hand, midge larvae promote disease. One of the strongest, most consistent field patterns in
395 our system is a positive relationship between invertebrate predator density and disease (Figure 1)
396 (Cáceres, Knight & Hall, 2009; Penczykowski *et al.*, 2014; Strauss *et al.*, 2016). Midge larvae
397 spread disease via sloppy predation on infected hosts (Cáceres, Knight & Hall, 2009), and can
398 increase disease risk to our focal host by reducing the density of a key diluter host.
399 Future work is required to determine the relative strengths of the different mechanisms
400 and whether there are eco-evolutionary dynamics in the predator-*Daphnia*-parasite system. One
401 thing that is particularly needed is experiments that allow us to assess the impacts of multiple
402 mechanisms simultaneously. For example, our understanding of the net effects of predation on
403 disease in our system would benefit greatly from experiments that are done in stratified systems
404 (e.g., whole-water column bag enclosures) that contain fish, midge larvae, and *Ceriodaphnia*.

Ideally, these studies would manipulate not only fish predation rate, but also density of midge larvae and small-bodied diluter hosts. Such an experiment would allow us to directly test the direct and indirect effects of fish predators on disease in *Daphnia* and might help explain why the one prior experimental test of the role of fish predation on fungal disease in *Daphnia* did not find an effect (Duffy, 2007).

An interesting open question is whether and how global change will alter the influence of predators on disease in our system. One study has already considered direct impacts of temperature, finding that predators might be more effective at suppressing disease in a warmer world (Hall *et al.*, 2006). However, this temperature-driven increase in predation rate might be thwarted by changes in water clarity. Inland waters in much of Northeastern North America and Europe are becoming browner due to increased precipitation, land use change, and recovery from anthropogenic acidification (Williamson *et al.*, 2015). Selective predation can disappear in systems with high dissolved organic carbon, likely because infected hosts are less visible in darker water (Johnson *et al.*, 2006). Thus, at present, it is not clear whether fish will be more or less effective as healthy herds predators as lakes simultaneously become warmer and browner.

We have often used models to try to understand the different mechanisms by which predators can influence disease in their prey populations (e.g., Duffy *et al.*, 2005; Hall, Duffy & Cáceres, 2005; Hall *et al.*, 2006; Duffy & Hall, 2008; Cáceres, Knight & Hall, 2009; Auld *et al.*, 2014). We have created models that study one or a few specific mechanisms, but have not yet developed a model that synthesizes across all eight of these mechanisms. Our long-term goal is to take the models we have developed for different mechanisms and to use these as modules to create a more synthetic model. Among other things, having a synthetic model would allow us to better predict how global climate change will alter the influence of predation on diseases in our

system.

5.4 Conclusions:

Predators have the potential to suppress disease or to spread it, via a variety of mechanisms. At present, there is stronger evidence for some mechanisms than for others, though some of this likely reflects different amounts of research effort. Our hope is that the framework we lay out in this chapter for thinking about how predators influence disease via different mechanisms will motivate additional research on some of the mechanisms that have not been as well-studied. Such research is likely to help explain spatiotemporal variation in disease as well as inform management strategies.

Importantly, a single predator can have conflicting impacts on disease. For example, damselfly larvae had conflicting density- and trait-mediated indirect effects on a tadpole-trematode system, leading to no significant relationship between predator density and disease in tadpoles (Rohr *et al.*, 2015). Predators can also interact. In our system, fish are intraguild predators, preying on both midge larvae and *Daphnia*. This has meant that it sometimes has been difficult to disentangle healthy herds and predator spreader phenomena from field data collected on natural populations, given that the two predators tend to be negatively correlated and are predicted to have opposite effects on disease. Fortunately, path analysis can help us tease things apart in these situations (though there can still be issues when potential drivers strongly covary). Our recent synthetic analysis revealed that, in our system, a key way in which fish predation influences disease in *Daphnia* is by increasing the abundance of the diluter species *Ceriodaphnia* (Strauss *et al.*, 2016). We also know that fish predation decreases density of midge larvae (González & Tessier, 1997) and that midge larvae spread disease (Cáceres, Knight & Hall,

2009); thus, a second way in which fish predation might influence disease is via effects on midge density (Strauss *et al.*, 2016). The potential for a single predator to have multiple, opposing effects on disease, and for healthy herds predators and predator spreaders to interact, might help explain spatiotemporal variation in the impacts of predators on disease. Further research into the specific mechanisms by which predators influence disease – and the relative importance of those mechanisms in different ecosystems – should help us develop a better predictive understanding of how predators should influence disease in their prey.

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Box 5.1: Introduction to the *Daphnia*-parasite-predator system

Our work has centered around a system with one host, one pathogen, and two predators with contrasting effects on disease transmission. The focal host is *Daphnia dentifera*, which is one of the dominant grazers in stratified lakes in the Midwestern United States (Tessier & Woodruff, 2002), as well as a main food resource for planktivorous fish such as the bluegill sunfish (Mittelbach, 1981). The focal parasite is the fungus *Metschnikowia bicuspidata*, which is the dominant pathogen in many of our Midwestern study lakes (Duffy *et al.*, 2010; Hall *et al.*, 2010; Auld *et al.*, 2014; Penczykowski *et al.*, 2014). The fungus is highly virulent, reducing fecundity and lifespan and increasing fish predation risk (Duffy & Hall, 2008). The dominant vertebrate predator is the bluegill sunfish (*Lepomis macrochirus*), which is a visual predator. Bluegill are highly selective predators on infected hosts, presumably due to their increased opacity (Duffy *et al.*, 2005; Duffy & Hall, 2008) and serve as a healthy herds predator. The dominant invertebrate predator in our system are larvae of the phantom midge, *Chaoborus spp*. (Tessier & Woodruff, 2002; Strauss *et al.*, 2016). Midge larvae are gape-limited, tactile predators (Zaret, 1980; Pastorok, 1981). They do not feed selectively on infected hosts, but are "sloppy feeders", regurgitating infectious spores along with the corpses of infected hosts (Cáceres, Knight & Hall, 2009). As a result, they serve as predator spreaders. The effects of fish and midge larvae on disease arise from a variety of different mechanisms, as reviewed in the main text.

The main other species of hosts in our study lakes are *Daphnia pulicaria*, *Daphnia retrocurva*, and *Ceriodaphnia dubia* (Tessier & Woodruff, 2002; Strauss *et al.*, 2016). Importantly, all three of these hosts are much less susceptible to infection than *D. dentifera* and, as a result, serve as "friendly competitors", competing for algal food but also diluting disease (Hall *et al.*, 2009; Hall *et al.*, 2010; Cáceres *et al.*, 2014; Strauss *et al.*, 2015; Strauss *et al.*,

2016). In addition to the fungus *Metschnikowia*, daphniids in our study lakes also sometimes host other parasites, including bacteria, fungi, microsporidia, and oomycetes (Rodrigues *et al.*, 2008; Duffy *et al.*, 2010; Duffy, James & Longworth, 2015).

Table 1. Summary of the different mechanisms by which predators can influence disease in their prey populations and whether (and when) that mechanism should increase or decrease disease.

Mechanism	**Effect on disease**
1. Predator-driven reduction in host density	Can increase or decrease disease
2. Selective predation	Usually decreases disease, but can increase in specific scenarios
3. Predator-driven shifts in host demography or class structure	Can increase or decrease disease
4. Predator-driven shifts in competitor community composition	Can increase or decrease disease
5. Shifts in predator community composition	Can increase or decrease disease
6. TMIEs of predators & tradeoffs associated with predation	Can increase or decrease disease
7. Predator consumption of carcasses and/or spore spreading	Decreases disease if spores cannot survive predator consumption; can increase & spread disease if spores can survive consumption
8. Fueling of spore production by predator-driven trophic cascades	Increases disease if higher resources increase spore production; however, can decrease disease if resources stimulate immune responses in hosts

Chapter 5 Figure Legends

Figure 5.1. Densities of *Chaoborus* midge larvae in lakes that do and do not have epidemics of the fungus *Metschnikowia bicuspidata*. Figure reproduced from Cáceres et al. (2009), with permission.

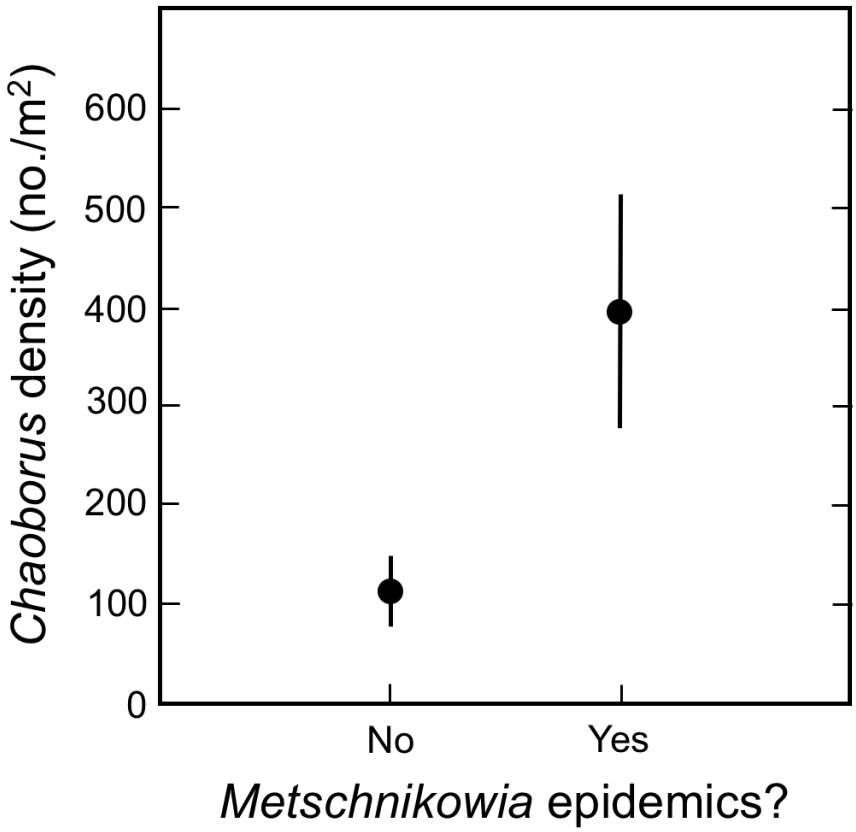
Figure 5.2. Conceptual summary of the eight different mechanisms by which predators can influence disease in our *Daphnia*-parasite system. Numbers on arrows correspond to the mechanisms in Table 1 and given below. Arrows showing infected hosts taking up spores and competitors eating algae were omitted for simplicity as they do not directly relate to any of the mechanisms discussed here.

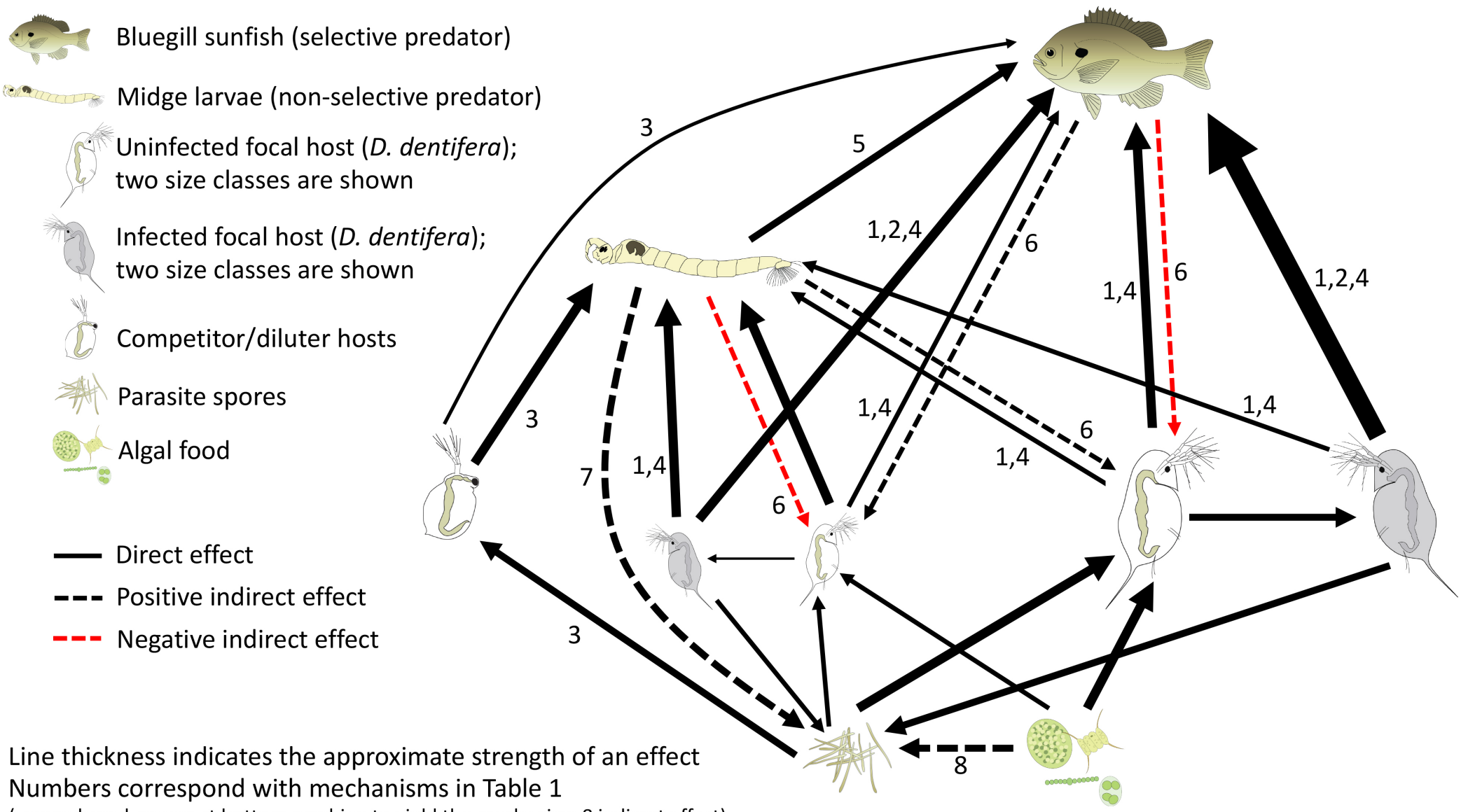
Figure 5.3. Selectivity of bluegill sunfish on *Daphnia* infected with the fungus *Metschnikowia bicuspidata*, an unnamed oomycete, and the bacterium *Spirobacillus cienkowskii*. Data were collected by analyzing the gut contents of fish collected in lakes at dawn, compared with the infection prevalence in hosts in the lake at the same time. In each case, the comparison was between infected or uninfected hosts. We used Chesson's alpha which compares the availability of a prey type (in this case, a host infected with a particular parasite) and the selection of that prey type. 0.5 indicates neutral selectivity (shown by a dotted line); the strength of selectivity for a prey type increases as alpha increases towards 1. Data on *D. dentifera* and *D. retrocurva* are from Duffy & Hall (2008) and unpublished data collected by M.A. Duffy in 2002-2003. Data on *D. pulicaria* are from Johnson et al. (2006). Points are jittered slightly along the x-axis. Inset figure shows the transparent body of an uninfected *D. dentifera*.

Figure 5.4. Recovery of parasite spores after passage through a fish gut. Data are shown for control infected *Daphnia* that were not fed to a fish and for *Daphnia* that were fed to a fish. In the experiment done on the fungus *Metschnikowia* (reported in Duffy 2009), spores were retrieved from fish fecal pellets and from the water in the beaker where the fish had been feeding. In the experiment done on the bacterium *Pasteuria* (collected by S.K.J.R. Auld and M.A. Duffy), we only collected the fish fecal pellet and did not attempt to quantify spores released into the water. In the *Metschnikowia* study, the median for control *Daphnia* was ~72,000 spores/*Daphnia*, whereas, after combining the data from the fish fecal pellets and water, it was 35,000 spores/*Daphnia* for those fed to fish. For *Pasteuria*, the median was ~1,438,000 for control *Daphnia* and ~964,000 for those fed to fish. At present, we don't know how many spores are in the water column during epidemics or how much of an impact on disease these reductions in spore yield would be predicted to have. However, for the bacterium *Spirobacillus cienkowskii,* we know that spore concentrations in the water column can exceed 4000 cells/mL; moreover, there was a linear relationship between spore density at the sediment-water interface on one sampling day and the prevalence of infection in *Daphnia* one week later (Thomas *et al.*, 2011).

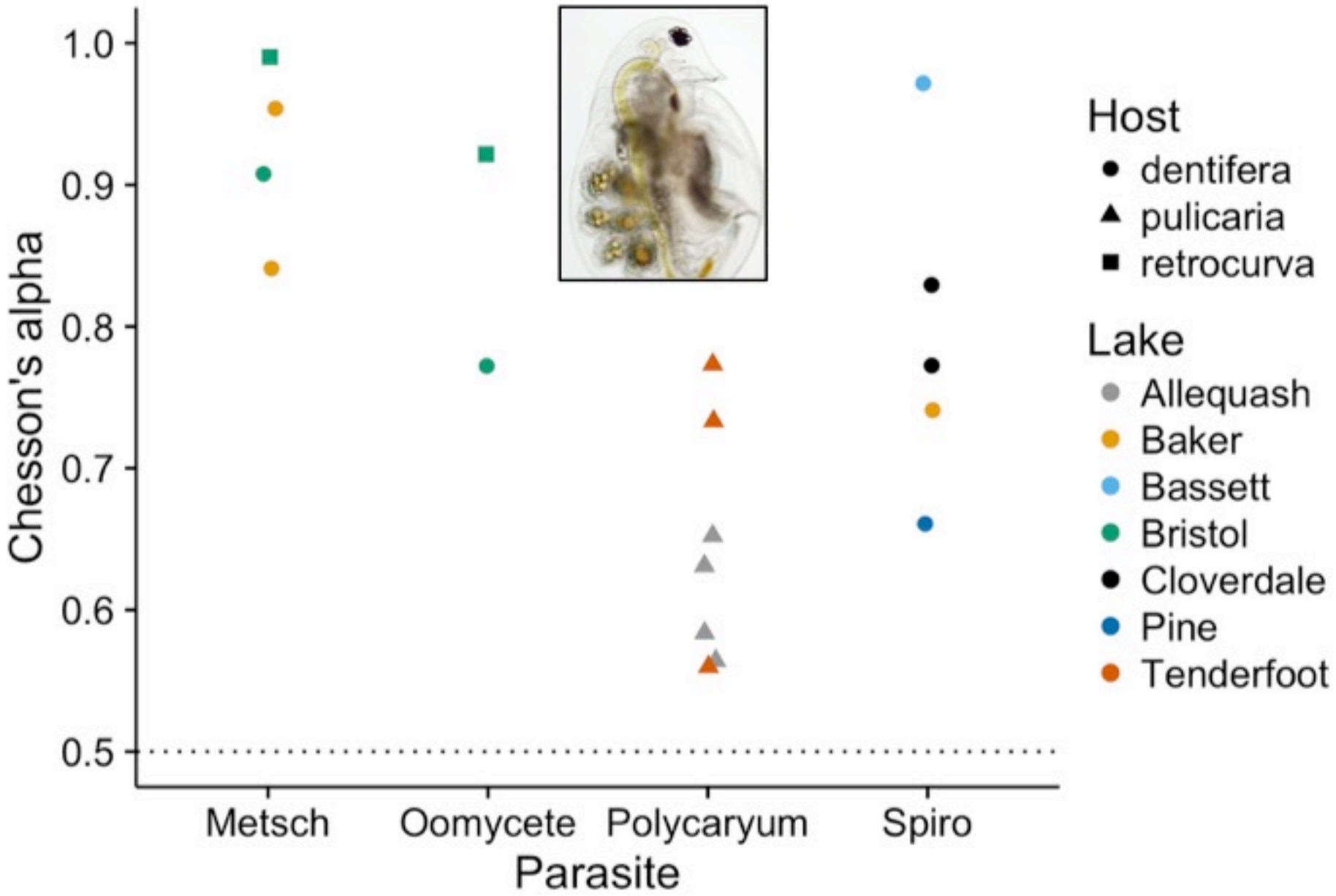
Figure 5.5. Spores of both the fungus *Metschnikowia* and the bacterium *Pasteuria* remain viable after passage through bluegill sunfish guts. Data are shown for spores from control *Daphnia* that were not fed to fish (black bars) and for spores retrieved from fish fecal pellets (gray bars). These spores were used in infection assays, where individuals were exposed to a set spore dose for 24 hours. "Control" and "fish" treatments received the same spore dose. In the *Metschnikowia* experiment, both treatments were exposed to 500 spores/mL; for *Pasteuria,* both treatments were

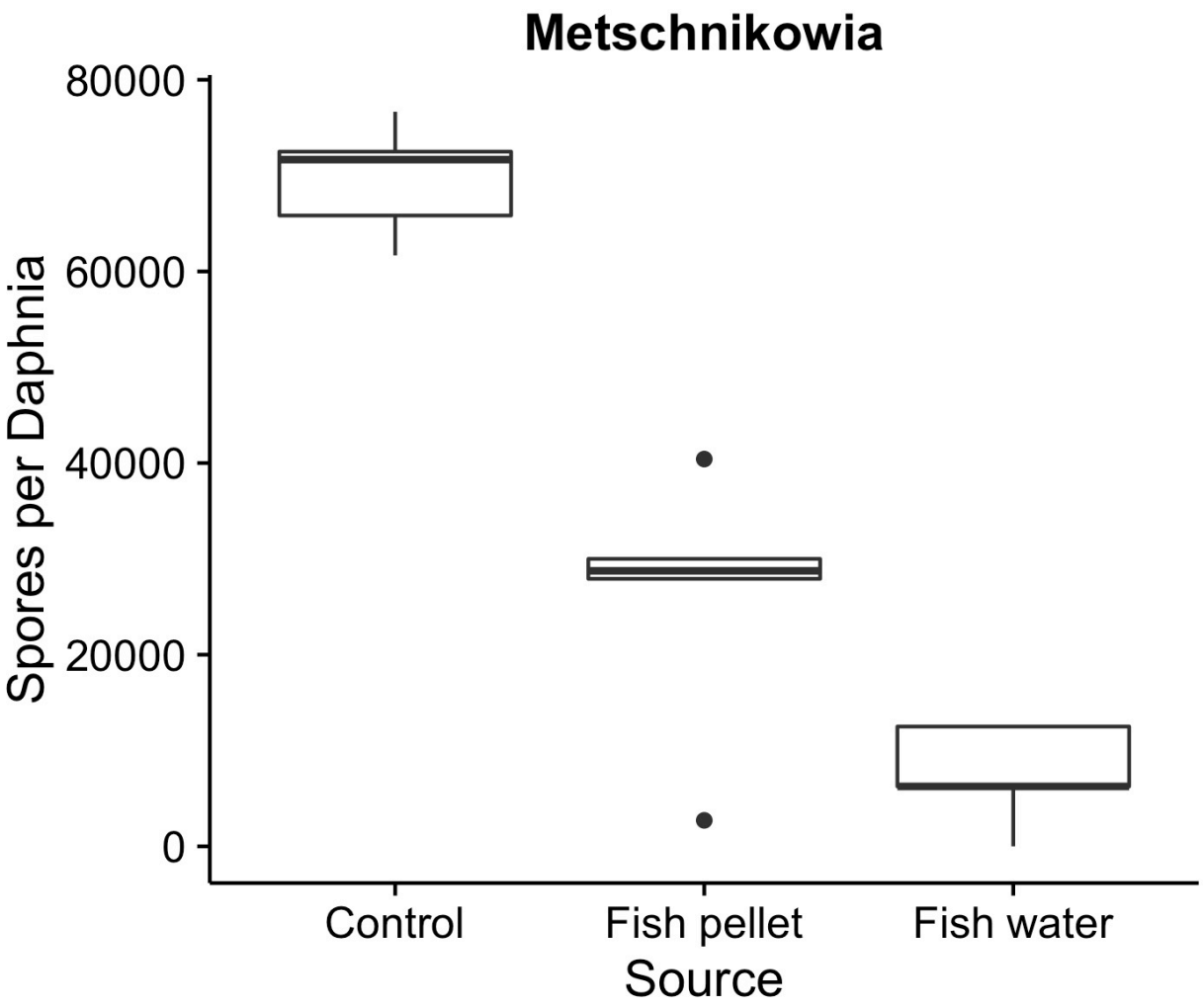
exposed to 2000 spores/mL. *Metschnikowia* data are from Duffy (2009). *Pasteuria* data are unpublished data collected by S.K.J.R. Auld and M.A. Duffy.

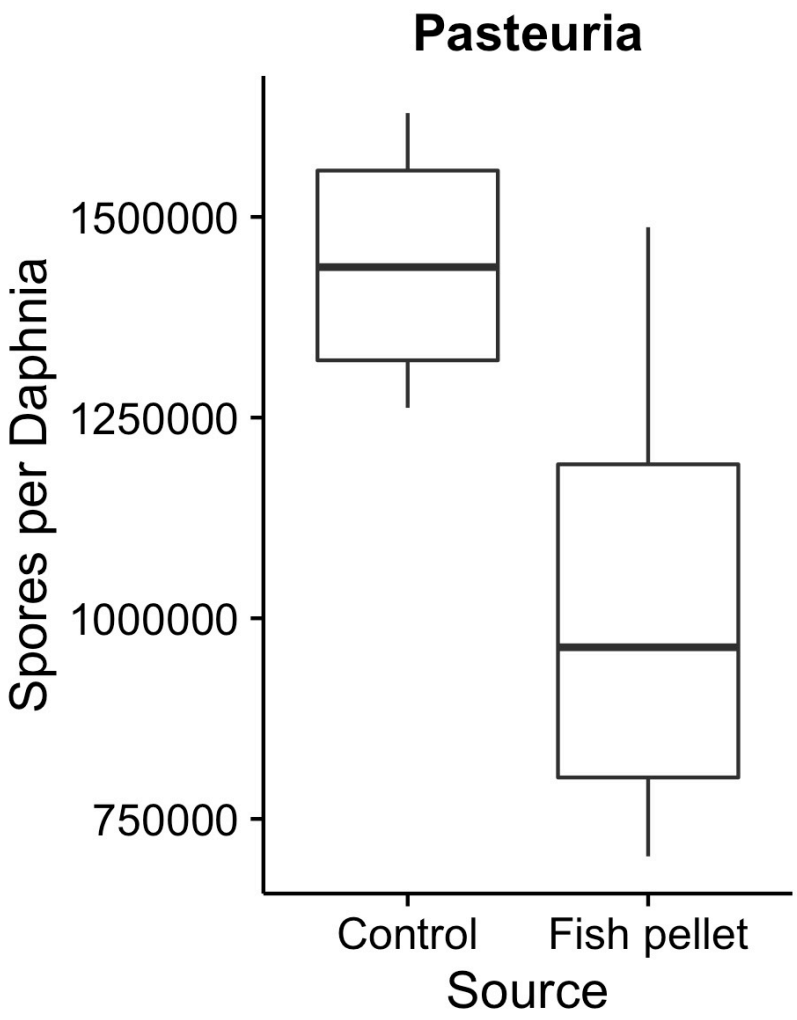

Chaoborus density (no./m^2)
600
500
400
300
200
100
0
No
Yes
Metschnikowia epidemics?

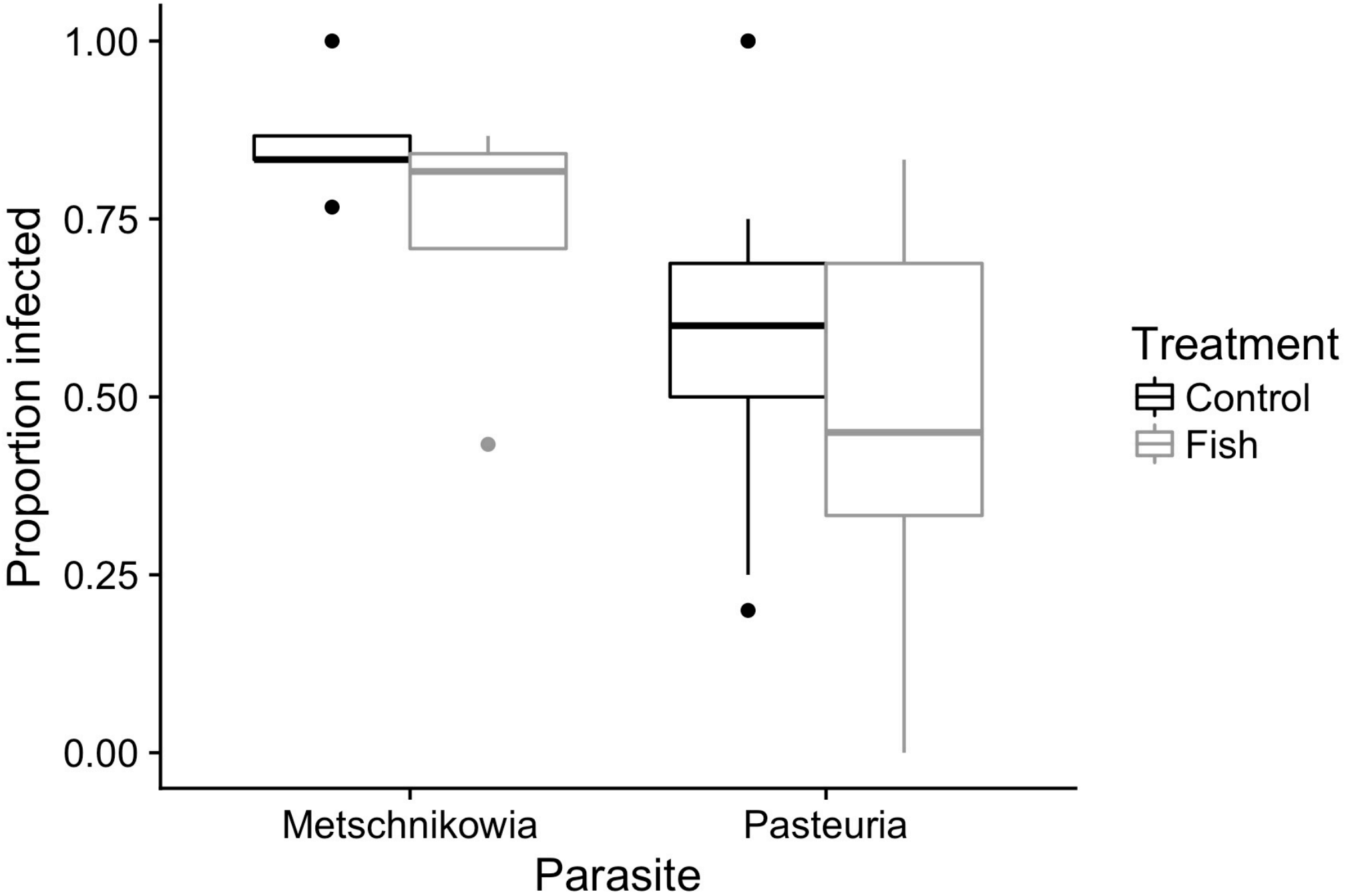


Line thickness indicates the approximate strength of an effect
Numbers correspond with mechanisms in Table 1
(unnumbered arrows at bottom combine to yield the mechanism 8 indirect effect)


1.0
0.9
0.8
0.7
0.6
0.5
Chesson's alpha
Metsch
Oomycete
Polycaryum
Spiro
Parasite
Host
dentifera
pulicaria
retrocurva
Lake
Allequash
Baker
Bassett
Bristol
Cloverdale
Pine
Tenderfoot


Metschnikowia
80000
60000
40000
20000
0
Spores per Daphnia
Control
Fish pellet
Fish water
Source


Pasteuria
1500000
1250000
1000000
750000
Spores per Daphnia
Control
Fish pellet
Source


1.00
0.75
0.50
0.25
0.00
Proportion infected
Metschnikowia
Pasteuria
Parasite
Treatment
Control
Fish