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Parasites destabilize host populations by shifting stage-structured interactions

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Abstract. Should parasites stabilize or destabilize consumer–resource dynamics? Recent theory suggests that parasite-enhanced mortality may confer underappreciated stability to their hosts. We tested this hypothesis using disease in zooplankton. Across both natural and experimental epidemics, bigger epidemics correlated with larger—not smaller—host fluctuations. Thus, we tested two mechanistic hypotheses to explain destabilization or apparent destabilization by parasites. First, enrichment could, in principle, simultaneously enhance both instability and disease prevalence. In natural epidemics, destabilization was correlated with enrichment (indexed by total phosphorous). However, an *in situ* (lake enclosure) experiment did not support these links. Instead, field and experimental results point to a novel destabilizing mechanism involving host stage structure. Epidemics pushed hosts from relatively more stable host dynamics with less-synchronized juveniles and adults to less stable dynamics with more-synchronized juveniles and adults. Our results demonstrate how links between host stage structure and disease can shape host/consumer–resource stability.

Key words: consumer-resource; Daphnia-Metschnikowia; *host–parasite; paradox of enrichment; stability; stage structure.*

Introduction

Why, how, and when do populations fluctuate? Empirical and theoretical studies have delineated a variety of mechanistic drivers of both stability (defined here as lower temporal variation in population density) and instability (higher temporal variation in population density). For example, the addition of a wide range of even minimal biological realism into consumer–resource models tends to generate instability via oscillations (Murdoch et al. 2003). The Rosenzweig-MacArthur model provides a canonical example, where higher carrying capacity or strong prey suppression destabilizes consumer–resource dynamics (Rosenzweig and MacArthur 1963, Murdoch et al. 2003). Yet, while well-known examples of consumer–resource cycling exist, most natural systems are more stable than simple models often anticipate (Murdoch et al. 2003, Jensen and Ginzburg 2005). This model–nature contrast suggests that our models lack crucial biology. Numerous mechanisms might explain this disconnect (reviewed by Roy and Chattopadhyay 2007) including both parasites and stage-structured consumer–resource dynamics.

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Theoretical work suggests that parasites could stabilize consumer–host interactions via disease-imposed mortality (Anderson and May 1978*a*, Hilker and Schmitz 2008, Hurtado et al. 2014, Cáceres et al. 2014; see Appendix S1 for an illustration). This intriguing possibility means that parasites, which are ubiquitous in natural ecosystems, may confer greatly underappreciated stability to their hosts. In this hypothesis (H1: *Disease Stabilized via Host Mortality*) virulence imposed on the host/consumer prevents severe overexploitation of the host's resource. Host/consumer mortality increases stability because it reduces peak (maximal) density of the host population and thus, the intensity of grazing pressure on the resource. The resource, then, is less severely depressed and more limited (and stabilized) by its own density dependence. Thus, our *a priori* prediction was that parasites should stabilize consumer–resource dynamics by elevating death rate (Fig. 1A, Appendix S1: Fig. S1). We looked for evidence of this hypothesis using a *Daphnia* consumer/host–fungal-parasite system. In field surveys and one of two experiments, death rates increased with large epidemics (as expected). Surprisingly, however, in the field survey and in both experiments, larger epidemics correlated with larger, not smaller, fluctuations of this consumer/host.

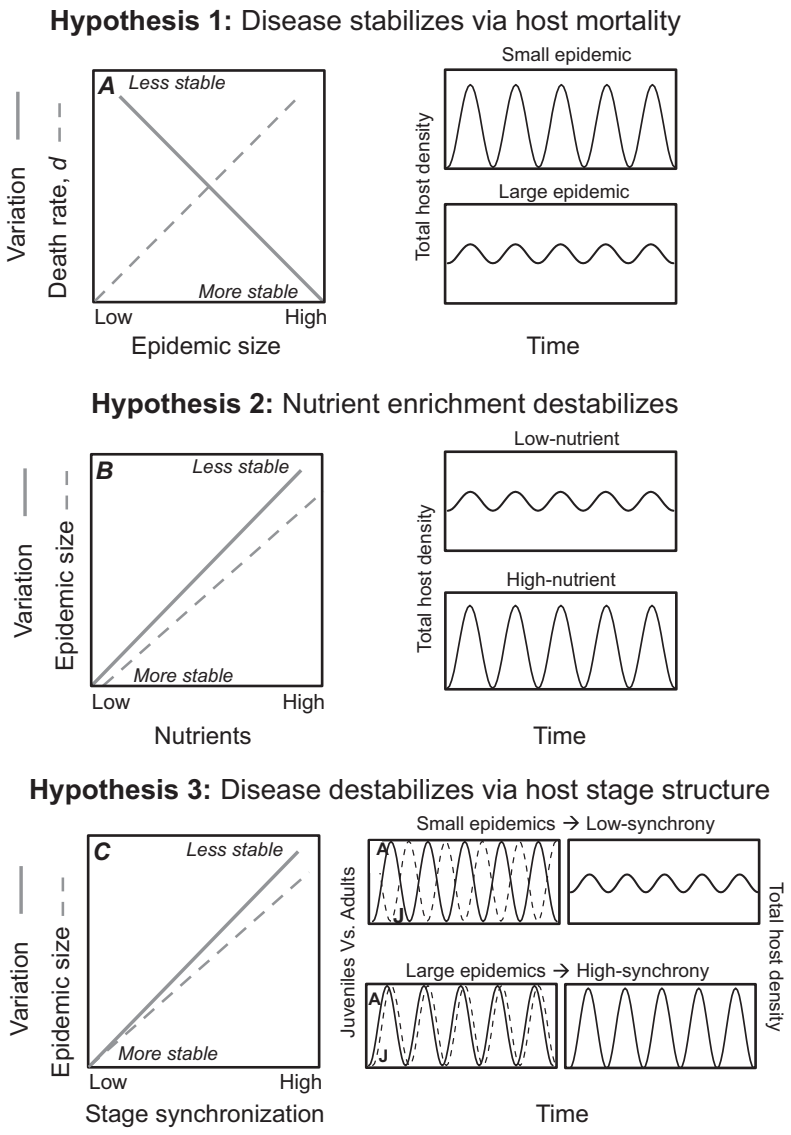

FIG. 1. Three potential drivers of stability in consumer-host populations. The left column illustrates hypothesized relationships between stability (here, more temporally variable populations are less stable) and three potential drivers: death rate, epidemic size, nutrients, and host stage structure. The right column illustrates the temporal dynamics underlying the overall changes in variation. (*A*) *Disease Stabilizes via Host Mortality* (H1): increased mortality from disease should stabilize host populations (higher mortality reduces over-exploitation by consumer/hosts). As epidemic size increases, mean per capita death rate should increase, thereby enhancing stability. (*B*) *Nutrient Enrichment Destabilizes* (H2): nutrient enrichment should destabilize (i.e., increase variation in) consumer/host populations. Consequentially, low nutrient systems have smaller amplitude cycles while high-nutrient ones have large amplitude. Higher nutrient systems could also have larger disease epidemics, creating a spurious stability-disease link. (*C*) *Disease Destabilizes via Host Stage Structure* (H3): as juvenile (J) and adult stages (A) become more synchronized, consumer-host dynamics become more variable (i.e., less stable).

What, then, could explain how disease can destabilize host dynamics? Other models predict that parasites can destabilize host dynamics via various mechanisms, including parasite-induced reductions in host fecundity (Anderson and May 1978*b*, Greischar and Lively 2011), arrested development of the parasite (Dobson and Hudson 1992), Allee effects in the underlying host demography (Hilker et al. 2009), or prolonged environmental residence time of indirectly transmitted parasites (Sharp and Pastor 2011). None of these mechanisms fit the natural history of our focal planktonic disease system (e.g., our parasite does depress fecundity, though not severely enough to trigger host–parasite oscillations; see Auld et al. 2014). Therefore, we investigated two, alternative mechanisms that are more germane to the natural history of our focal system involving nutrient enrichment (H2: *Nutrient Enrichment Destabilizes*) and host stage structure (H3:

Disease Destabilized via Host Stage Structure). To test and resolve these competing hypotheses, we coupled field data with field enclosure and indoor mesocosm experiments.

The "nutrient enrichment destabilizes" hypothesis (H2) revolves around a potentially spurious correlation. In the field survey, an apparent link between disease and destabilization could be driven by a productivity gradient (nutrient supply; Fig. 1B). Nutrient enrichment can increase epidemic prevalence and/or intensity by increasing host density (Anderson and May 1992, Power et al. 2011, but see Civitello et al. 2013 and Appendix S1), transmission (Krist et al. 2004, Beldomenico and Begon 2010), or propagule production (Seppälä et al. 2008, Hall et al. 2009*a*, Tadiri et al. 2013). Simultaneously, higher nutrients could destabilize the host/consumer–resource system via the paradox of enrichment (Rosenzweig and MacArthur 1963, Murdoch et al. 2003, Sharp and Pastor 2011; Fig. 1B, Appendix S1: Fig. S1). This destabilizing force might overwhelm any stability conferred by parasite-mediated mortality. Thus, enriched systems might have larger epidemics and greater overall enrichment-driven instability. To disentangle these two potential impacts of enrichment on disease, we directly manipulated productivity and disease in an experiment.

The alternative hypothesis (H3: disease destabilizes via host stage structure) fuses causal connections between disease, stage structure, and stability. Competition for shared resources arises commonly between juvenile and adult life stages of consumers (Miller and Rudolf 2011, de Roos and Persson 2013). Without disease, these competitive interactions can strongly determine the stability of consumer–resource dynamics (McCauley et al. 1999, de Roos and Persson 2013). Stage-structured theory tells us why: asymmetric competition between life stages causes juveniles and adults to cycle out-of-phase with each other (involving development-time and fecundity-based mechanisms: Fig. 1C). The temporal asynchrony of juveniles and adults creates a numerical effect whereby total host density (juveniles + adults) varies less (Fig. 1C, "low-synchrony"). Alternatively, more symmetric competition between life stages can cause juveniles and adults to cycle in-phase (Fig. 1C, "high-synchrony"). Here, the consumer should show larger variation in total density, potentially exacerbating the destabilizing effect of resource overexploitation (in less stable, high-synchrony cycles). These types of stage-structured interactions are well known for *Daphnia* (de Roos and Persson 2013). Parasites may potentially reduce the asymmetry of competition between life stages by inflicting stronger virulent effects on otherwise competitively dominant adults (Hall et al. 2007, DeMott et al. 2010, see *Discussion*). Such a parasite-mediated alteration of competition could push consumer/hosts from more stable, "low-synchrony" juvenile–adult cycles before epidemics to "high-synchrony" juvenile–adult cycles during epidemics. This parasite-mediated shift should increase variation in total host density, potentially interacting with and elevating consumer–resource instability.

Here, we use a field survey and our two mesocosm experiments to evaluate all three hypotheses. As stated above, using both field data and mesocosm experiments, we reject that disease stabilizes via host mortality (H1). The second hypothesis, nutrient enrichment destabilizes (H2), is partially supported by field data, but rejected by a lake enclosure experiment that factorially manipulates parasites and nutrients. Finally, our third hypothesis, disease destabilizes via host stage structure (H3), is supported robustly by field data, the same lake enclosure experiment, and an indoor mesocosm experiment that manipulates parasites (though not nutrients). The lakes and experiments varied in many ways from each other (e.g., the role of predators, competitors, inedible resources, etc.). Nonetheless, they all support the same mechanism. Thus, while disease might stabilize consumer–resource dynamics in other systems, here fungal disease destabilized its *Daphnia* host by undermining the stabilizing effects of low-synchrony stage-structured cycles.

Materials and Methods

Host-parasite system

Our hosts, *Daphnia dentifera* (hereafter "hosts") become infected while foraging by inadvertently consuming spores of the virulent fungal parasite (*Metschnikowia bicuspidata;* hereafter "fungus" (see Hall et al. 2007). The fungus can substantially reduce host growth (R. M. Penczykowski et al. *unpublished manuscript*), fecundity, and survival (Hall et al. 2009*a*,*b*). Hosts do not recover from infection and, upon death, release spores into the environment to infect new hosts. Resource quantity and quality drive parasite virulence in this system: assimilation rate, host reproduction rates, spore production within hosts, and subsequently, host mortality all increase with increasing resources (quality [Hall et al. 2009*a*], quantity [Hall et al. 2009*b*]).

Field survey

We first used field patterns from natural epidemics to examine potential links between disease and host dynamics. We sampled 15 lakes in southwestern Indiana (USA) weekly throughout the epidemic season (approximately July through the first week of December 2010). These lakes span a total phosphorous (TP) gradient from low nutrient (oligotrophic) to higher nutrient (eutrophic): a range of 4–54 μg P/L (Penczykowski et al. 2014). At each visit, we collected hosts with two replicate plankton samples using a Wisconsin net (13 cm diameter, 153 μm mesh; towed bottom to surface). We estimated infection prevalence

and densities of each host stage (i.e., juvenile vs. adults). Host stages are easily identified under the microscope based on the presence of a brood chamber. At each visit, we also collected integrated epilimnetic water samples to estimate an index of lake productivity, total phosphorous (TP).

Lake enclosure experiment

We used data from two experiments to evaluate the three hypotheses. In the first experiment (lake enclosures), we factorially manipulated nutrient levels and parasite exposure in large, whole-water-column mesocosms in University Lake during the epidemic season (early September–late October 2011). We suspended polyethylene enclosures (depth 6 m, diameter 1 m) with screen (1 mm) lids from wooden rafts in a randomized block design (see Appendix S2 for supplemental methods). We stocked enclosures with sieved (80 μm) lake water and added lake-collected hosts (initial density of *D. dentifera*: ~5000 *Daphnia*/m^2) on 6 September. Two days later (8 September), we began the nutrient treatments by initiating low- (in situ lake conditions: 10 μg P/L, 400 μg N/L) and high- (30 μg P/L, 750 μg N/L) nutrient levels. Five days later (13 September), we inoculated one-half of the enclosures with a single fungal isolate (3.6 spores/mL). Each productivity × parasite treatment was replicated eight times for a total of 32 enclosures and maintained for 40 days post spore inoculation (approximately seven *Daphnia* generations). We maintained nutrient levels with twice each week additions of $NaNO_3$ and K_2HPO_4 (assuming a 5% instantaneous daily loss/settling rate; Civitello et al. 2013). We collected nutrient and host samples twice per week at night and estimated infection prevalence, host density variation (during epidemics), death rates, and stage synchronization during the epidemics (outlined in *Metrics* sections).

Indoor mesocosm experiment

In the second, indoor-mesocosm experiment, we isolated the effect of disease on host stability and stage synchronization. We used 50-L mesocosms stocked with high-hardness COMBO (Baer and Goulden 1998) and lab-reared high-quality algae, *Ankistrodesmus falcatus* (initial density: 1.0 mg dry mass/L) maintained at 21°C on a 16:8 light : dark photoperiod. On 7 June, we established host populations with approximately equal proportions of 11 genotypes (total initial density: 25 individuals/L). Twenty days later (27 June), we inoculated one-half of the tanks with fungal spores (5.6 spores/mL). Both treatments (i.e., with and without fungal spores) were replicated five times for a total of 10 mesocosms and maintained for 74 days (~10 host generations) post spore inoculation. We maintained nutrient levels as previously outlined (20 μg P/L, 300 μg N/L; a midrange of the low- and high-nutrient treatments of the lake enclosure experiments). We sampled twice per week to estimate infection prevalence, variation in host density, death rates, and stage synchronization during the epidemics, as outlined in *Metrics* section.

Metrics: epidemic size, host variation, death rate, productivity, and stage synchronization

Using data from the field survey and two experiments, we calculated several metrics. These metrics, and the specific hypotheses that they test, include the following.

Epidemic size (all three hypotheses).—We visually diagnosed infection status of live hosts per lake-date ($n \geq 400$) or sampling date (n = entire sample) using a dissecting scope at 20–50× magnification (Hall et al. 2009*a*). We then estimated epidemic size in each population by integrating infection prevalence (proportion infected) through time. This integrated prevalence metric (units of proportion × days) quantifies the size of epidemics varying in length and shape (Van der Plank 1963). Integrated prevalence strongly correlates with mean infection prevalence in the field (Pearson correlation, $r = 0.91$, $P < 0.0001$), and in the experiments (lake enclosures, $r = 0.99$, $P < 0.0001$; indoor mesocosms, $r = 0.99$, $P < 0.0001$).

Host variation (all three hypotheses).—To index destabilization, we calculated the standard deviation of ln-transformed total host densities (McCauley and Murdoch 1990). Higher values imply more destabilization (i.e., less stability). In the lake survey, we used a change (Δ) in variation index to account for underlying background variation in host populations before epidemics began. First, we calculated the standard deviation of ln-transformed total host densities in the pre-epidemic period (August–September) and then again during epidemics (October–December). The start date of epidemics was defined as the Julian day when lakes had >1% infection prevalence. Since start date was fairly uniform, we use the mean start date among lakes to separate pre- vs. during-epidemic periods. Then, we subtracted the pre-epidemic variation value from the during-epidemic variation value. Host populations that became less stable (more variable) during the epidemic season would show positive Δ values. In the experiments, we quantified disease-mediated destabilization by directly comparing parasite-addition and parasite-free treatments.

Death rate (H1: disease stabilizes via host mortality).—To estimate death rate (d) of host populations, we used the egg ratio method (Edmondson 1968). To implement the egg ratio method in the field survey, we recorded infection status and the number of eggs in the brood chamber of adults using a stratified sampling approach: we counted 20–50 uninfected adults and 0–40 infected adults. We then calculated a weighted average

of the egg ratio in the uninfected and infected classes. To convert egg ratio to an instantaneous birth rate (b), we used temperature-based relationships during each sampling date (Edmondson 1968) after measuring water temperature with a multiprobe (see Appendix S2 for further details). Then, we calculated instantaneous population growth rate, r, as the difference in ln-transformed host densities between sampling visits, $\ln(N_{s+1}) - \ln(N_s)$, divided by the time between samples, $t_{s+1} - t_s$. We estimated death rate for each sampling date as $d = b - r$. Then, we calculated mean death rate during epidemics (from October to December in the field survey, or following parasite addition in the experiments). We followed a similar procedure for calculating d in experiments (see Appendix S2 for details on the temperature-based calculations of birth rate).

Total phosphorous (TP), a productivity index (H2: nutrient enrichment destabilizes).—We averaged total phosphorous (TP) to characterize underlying productivity status of each lake (pre-epidemic period) or field enclosure. We estimated TP with standard acid-molybdate colorimetric assays following persulfate digestion (APHA 1995) on a spectrophotometer (UV-1700; Shimadzu Scientific Instruments, Columbia, Maryland, USA).

Stage synchronization (H3: disease destabilizes via host stage structure).—To characterize synchronization of host stages, we ln-transformed juvenile and adult densities and calculated cross-correlation coefficients at lag zero (McCauley et al. 1999). Then, we Fisher-transformed the cross-correlation coefficients to help linearize them (Cox 2008). High coefficients mean strong juvenile–adult stage synchronization (in phase), whereas low coefficient values show unsynchronized (out of phase) juvenile–adult dynamics.

Statistical analyses

For the field analyses, we used linear regression and ln-transformed variables to better approximate normality and equalize variances. For the lake enclosure experiment, we detected no block effects. Thus, we used two-way ANOVAs, sequentially dropping nonsignificant terms (results were similar with and without dropping nonsignificant terms). For the indoor mesocosm experiment, we used separate unpaired one-sided t tests to test our hypotheses that epidemics decreased stability, increased death rate, and increased stage synchronization of hosts. We used R (R Development Core Team 2012) for all statistical tests.

Results

We first use data from the field survey to test hypotheses 1–3. Then, we test them with results from the two experiments. Finally, we synthesize these results in the *Discussion*.

Field survey

As epidemic size increased, host populations became less stable relative to the before-epidemics period (i.e., Δ host variation correlated positively with epidemic size: $n = 15$, $r = 0.590$, $P = 0.020$, Fig. 2A). H1: *Disease Stabilizes via Host Mortality* Death rate was higher during larger epidemics ($n = 15$, $r = 0.563$, $P = 0.028$, Fig. 2B). However, host populations in lakes with higher death rates became less stable during epidemics ($n = 15$, $r = 0.586$, $P = 0.021$, Fig. 2C). Consequently, disease did not stabilize consumer/host–resource systems by increasing per capita death rate, d (Hilker and Schmitz 2008, Hurtado et al. 2014, Cáceres et al. 2014; Appendix S1). H2: *Nutrient Enrichment Destabilizes* Total phosphorous (TP) was correlated with higher prevalence of disease ($n = 15$, $r = 0.521$ $P = 0.046$, Fig. 3A) and a greater change (Δ) in host stability ($n = 15$, $r = 0.568$, $P = 0.027$, Fig. 3B) during the epidemic season. However, prior to epidemics, host stability (standard deviation of ln-transformed host density) and TP were not correlated ($n = 15$, $r = 0.018$, $P = 0.949$), as a paradox of enrichment-type destabilization mechanism would anticipate. Thus, the field data create a first problem for the "nutrient enrichment destabilizes" idea. H3: *Disease Destabilizes via Host Stage Structure* Larger epidemics correlated with an increase in synchronization of juvenile and adult host densities (during epidemics, relative to pre-epidemic season; $n = 15$, $r = 0.570$, $P = 0.026$ Fig. 3C). Therefore, host stability decreased (or, variability increased) as juvenile and adult dynamics become more synchronized during epidemics ($n = 15$, $r = 0.824$, $P = 0.0002$, Fig. 3D).

An example illustrates changes in stability of host density and stage structure before vs. during epidemics within a single lake (Downing Lake; Fig. 4). Host density shifted from more stable (host variation [standard deviation] = 0.36) to less stable (host variation [standard deviation] = 0.51) during the epidemic season (Fig. 4A; Δ host variation = 0.15). Concurrently, juvenile and adult stages of the host shifted from less synchronized (cross-correlation coefficient (cc) = −0.66) to more synchronized (during epidemic, cc = 0.67) dynamics over the course of the epidemic season (Fig. 4B; difference of Fisher-transformed cross correlations, Δ cc = 1.59).

Lake enclosure and indoor mesocosm experiments

Both population-level experiments showed that disease significantly reduced host population stability and shifted host stage structure. We describe results from both experiments in parallel. Mean prevalence in the lake-enclosure experiment was 13% (integrated prevalence = 4.76) in the high-nutrient treatments and 12% (integrated prevalence = 4.14) in the low-nutrient treatments (Fig. B1c). In the indoor mesocosm experiment, mean prevalence was slightly higher (18%). H1: *Disease Stabilizes via Host Mortality* (Fig. 5A–D).

Epidemics significantly reduced host population stability (increased variation) in the lake enclosures (E effect, $F_{1,25} = 9.24$, $P = 0.005$, Fig. 5A) and in the indoor mesocosm experiment ($t = -29.04$, df = 10.50, $P < 0.0001$, Fig. 5B). There was no relationship between epidemics (E effect, $F_{1,24} = 0.01$, $P = 0.92$, Fig. 5C), nutrients (N effect, $F_{1,23} = 1.44$, $P = 0.24$), or their interaction (E × N, $F_{1,22} = 1.53$, $P = 0.23$) on per capita death rate of hosts in the lake enclosure experiment. Disease, however, clearly increased per capita death rate of hosts in the indoor mesocosm experiment ($t = -2.20$, df = 7.83, $P = 0.03$, Fig. 5D). Note that host per capita death rate was considerably higher in the lake enclosure experiment (Fig. 5C) compared to the indoor mesocosm experiment (Fig. 5D). Thus, neither experiment supports H1. H2: *Nutrient Enrichment Stabilizes* Neither nutrients (N effect, $F_{1,24} = 0.32$, $P = 0.58$, Fig. 5A) nor the epidemic × nutrient interaction (E × N, $F_{1,23} = 1.09$, $P = 0.31$) destabilized host dynamics. Furthermore, nutrients did not significantly increase disease prevalence (Fig. B1c). Thus, the field enclosures did not support H2. H3: *Disease Destabilizes via Host Stage Structure* (Fig. 5E–H). In the lake enclosures, disease ($F_{1,25} = 8.23$, $P = 0.007$, Fig. 5E), not nutrients ($F_{1,24} = 0.0005$, $P = 0.98$) nor their interaction ($F_{1,23} = 0.20$, $P = 0.66$), shifted host stage structure into more synchronized juvenile–adult dynamics. This synchronizing effect of disease was more pronounced in the indoor mesocosm experiment ($t = -23.56$, df = 16.56, $P < 0.0001$, Fig. 5F). In this experiment, juveniles and adults without disease were more strongly asynchronous compared to those in the lake enclosure experiment. Together, the indices of stability and stage structure illustrate that disease destabilized systems by increasing variation in total (summed) host density and by shifting host stage-structured interactions (Fig. 5G,H).

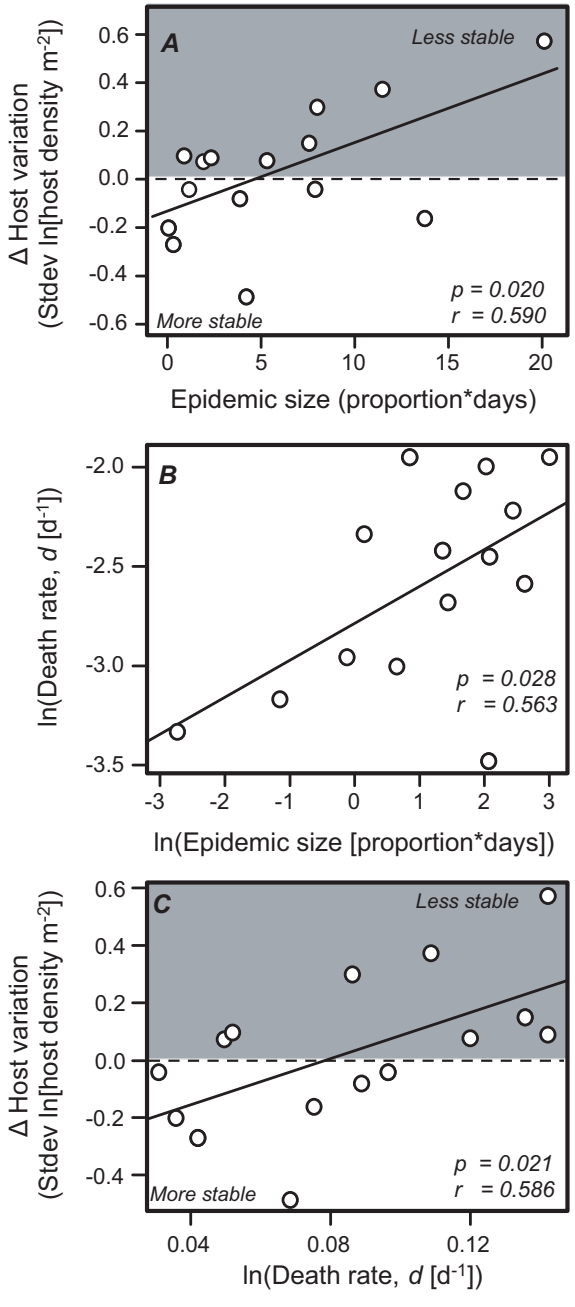

Fig. 2. Patterns of stability of zooplankton hosts, size of fungal epidemics, and instantaneous per capita death rates estimated from a survey of 15 Indiana (USA) lakes in 2010. *Disease Stabilizes via Host Mortality* (H1): (*A*) Host populations became less stable during vs. before epidemics during large disease outbreaks. Here, the "Δ Host variation" metric compares the difference in the standard deviation of ln-transformed host density calculated for before and during epidemic periods; larger values indicate increased destabilization (see text). (*B*) Mean per capita death rate was higher during larger epidemics, as anticipated (see Fig. 1). However, (*C*) host populations suffering higher mortality rates were less stable. Gray shading indicates positive change in consumer-host variation, i.e., hosts became less stable during epidemics (gray zones).

Discussion

What drives pronounced spatiotemporal fluctuations in population abundances? Existing disease theory offers the compelling possibility that parasites may provide greatly underappreciated stability to their hosts (Appendix S1; Hilker and Schmitz 2008, Hurtado et al. 2014). In this "disease stabilizes via host mortality" hypothesis (H1), virulence imposed on the host/consumer prevents severe overexploitation of the host's resource. Released from severe predation, the resource becomes more limited by its own stabilizing, negative density dependence rather than grazing. As far as we know, this hypothesis has not been tested yet. Thus, we looked for the stabilizing effect of death rate on host/consumer–resource cycling using a case study of *Daphnia* and a virulent fungal parasite. In field surveys and one of our population-level experiments, we saw that host death rate increased with

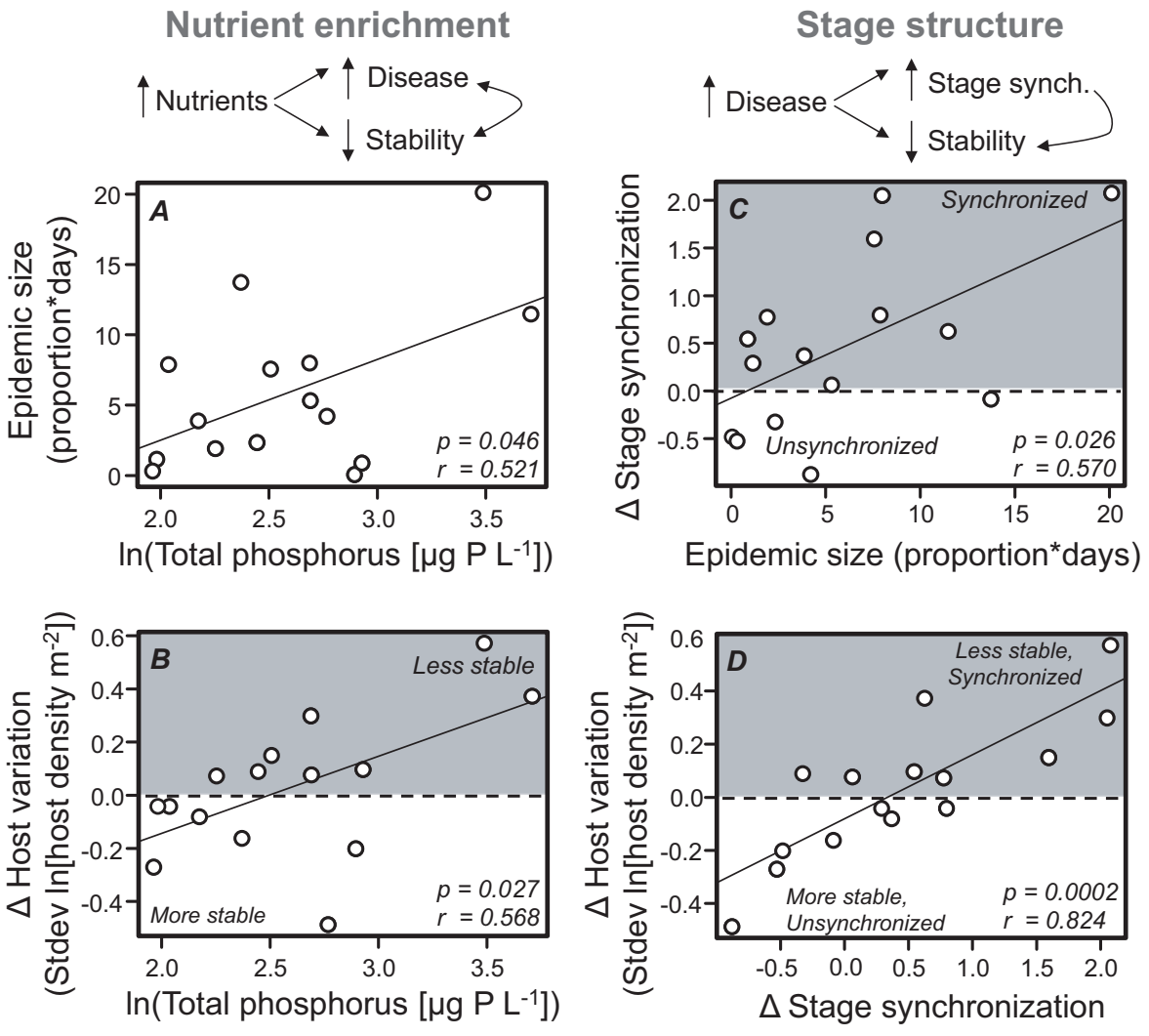

FIG. 3. Two competing hypotheses that link disease to destabilization of host populations. (*A and B*) *Nutrient Enrichment Destabilizes* (H2). Both (*A*) disease prevalence, indexed as epidemic size (see text) and (*B*) change (Δ) in host variation during vs. before epidemics (see Fig. 2) positively correlated with total phosphorous (TP, an index of lake productivity) during the epidemic season. (*C* and *D*) *Disease Destabilizes via Host Stage Structure* (H3). (*C*) During larger epidemics, juvenile and adult dynamics become more synchronized relative to before epidemics (illustrated by the change [Δ] in the synchronization index [Fisher-transformed, lag-zero cross-correlation]). (*D*) Host variation increased as juvenile and adult dynamics become more synchronized. Gray shading (panels *B–D*): host populations became less stable (more variable) during epidemics (gray zone of each panel).

disease prevalence. However, increased death rate did not stabilize host dynamics: larger epidemics were correlated with larger, not smaller, fluctuations of the host/consumer.

Why did enhanced death rate not stabilize host dynamics in this plankton system? At least two possibilities emerge. First, an underlying environmental driver, such as ecosystem productivity, could increase both instability and disease prevalence, creating a correlation between epidemic size and instability (H2: *Nutrient Enrichment Destabilizes* Nutrient enrichment increases epidemic severity in a broad array of disease systems (Johnson et al. 2010, Becker et al. 2015). Thus, this enrichment-based disease-instability correlation might arise commonly. Our results, however, did not support this hypothesis. First, on the stability end, we expected to see a strong TP–host-variation signature before epidemics began. Yet, our lake surveys revealed no evidence for enrichment-mediated destabilization of host populations before epidemics. Second, we found no experimental support for this hypothesis (perhaps as anticipated by our model; see Appendix S1). A three-fold TP enrichment (Fig. B1a) did not significantly elevate host density, even in the disease-free controls (Fig. B1b), or disease prevalence (Fig. B1c). Furthermore, TP enrichment did not destabilize host dynamics in the experiment. While much greater enrichment gradients might create a joint

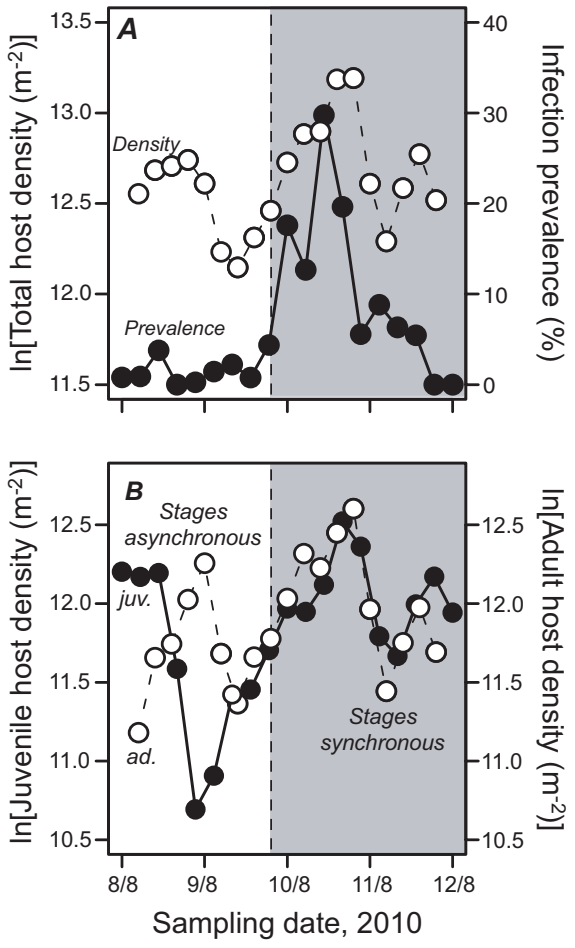

FIG. 4. An example illustrating changes in stability of host density and stage structure before vs. during epidemics in Downing Lake (dashed line represents the beginning of the epidemic). (*A*) Density of zooplankton host, *Daphnia dentifera* (dashed line, open symbols) and prevalence of infection by a virulent fungal parasite, *Metschnikowia bicuspidata* (percentage of hosts infected; solid line, filled symbols). Host density shifted from more to less stable during the epidemic season. (*B*) Concurrently, juvenile and adult stages of the host shifted from less to more synchronized dynamics over the course of the epidemic season. Gray shading indicates epidemic season. Data were smoothed using three-point running averages for presentation purposes only.

productivity–disease–stability correlation, our results do not support this hypothesis.

Instead, disease destabilized hosts by changing stage-structured dynamics (H3). In the field survey and both experiments, epidemics pushed hosts from relatively stable dynamics in which juveniles and adults cycle asynchronously, to less-stable dynamics with highly synchronized juvenile–adult cycles. Our proposed underlying mechanism synthesizes stage-structured consumer–resource ecology and stage-dependent epidemiology. First, *Daphnia*–algal systems behaved more stably, with more asynchronous juvenile–adult dynamics, before epidemics began. The likely mechanism involves competition for poor-quality resources. Competitive asymmetries arise due to differences in resource use between stage classes (Nelson et al. 2005, McCauley et al. 2008, de Roos and Persson 2013). In particular, juvenile assimilation efficiency and growth suffer greatly when resources are poor quality (i.e., digestion resistant; DeMott et al. 2010), like those in lakes before epidemics begin (Hall et al. 2009*a*). Such asymmetries can catalyze asynchronous juvenile–adult dynamics (de Roos and Persson 2013). However, disease could equalize these competitive differences between juveniles and adults. Competitively superior adults experience both higher exposure to parasites and higher infection prevalence than juveniles (Hall et al. 2007). Thus, adults suffer higher per capita mortality during epidemics. Additionally, adults tend to depress their foraging rates more than juveniles when exposed to spores (J. L. Hite et al., *unpublished manuscript*), and infected adults reduce their foraging rates even further (R. M. Penczykowski et al., *unpublished manuscript*). Thus, through several parasite-inflicted forms of virulence (on survival and/or foraging), the adult class could lose its competitive advantage over juveniles once epidemics begin. By predominantly infecting adults, the fungus might place juveniles and adults on more equal competitive footing and shift host populations into more synchronized cycling and less stable host dynamics. This mechanism, however, needs further theoretical and empirical development in the future.

Our particular stage structure-stability mechanism adds to growing evidence that host stage structure matters for disease more broadly. Strong links between host stage structure and disease have arisen when epidemiological traits depend on host body size, such as foraging rates (e.g., insect–virus ([Grenfell 1988, Dwyer 1991]; insect–pathogens [Briggs and Godfray 1995]); snail–trematode [Krist et al. 2004]) or host surface area (e.g., fish–ectoparasites [Cable and van Oosterhout 2007]; amphibian chytrid [J. L. Hite et al., *unpublished manuscript*]). Other mechanisms also link host stage structure to disease. For example, some life stages are much more vulnerable to infection, regardless of body size, or are more crucial to propagule production than others. Thus, ignoring stage-specific differences in key epidemiological traits could undermine management strategies in, for example, malaria (Barclay et al. 2012), Lyme disease (Caraco et al. 2002), childhood diseases (e.g., chickenpox; Keeling and Rohani 2008), and amphibian chytridiomycosis (Briggs et al. 2010). Regardless of the particular mechanism, host stage structure plays a pivotal role in various epidemiologically important traits. However, it remains unknown if those trait differences reverberate onto population dynamics and stability of hosts in other systems.

Our proposed stage-structure-based mechanism joins several other mechanisms that can stabilize or destabilize hosts during epidemics. For instance, strong virulence on fecundity is predicted to destabilize host dynamics (Anderson and May 1978*b*, Greischar and

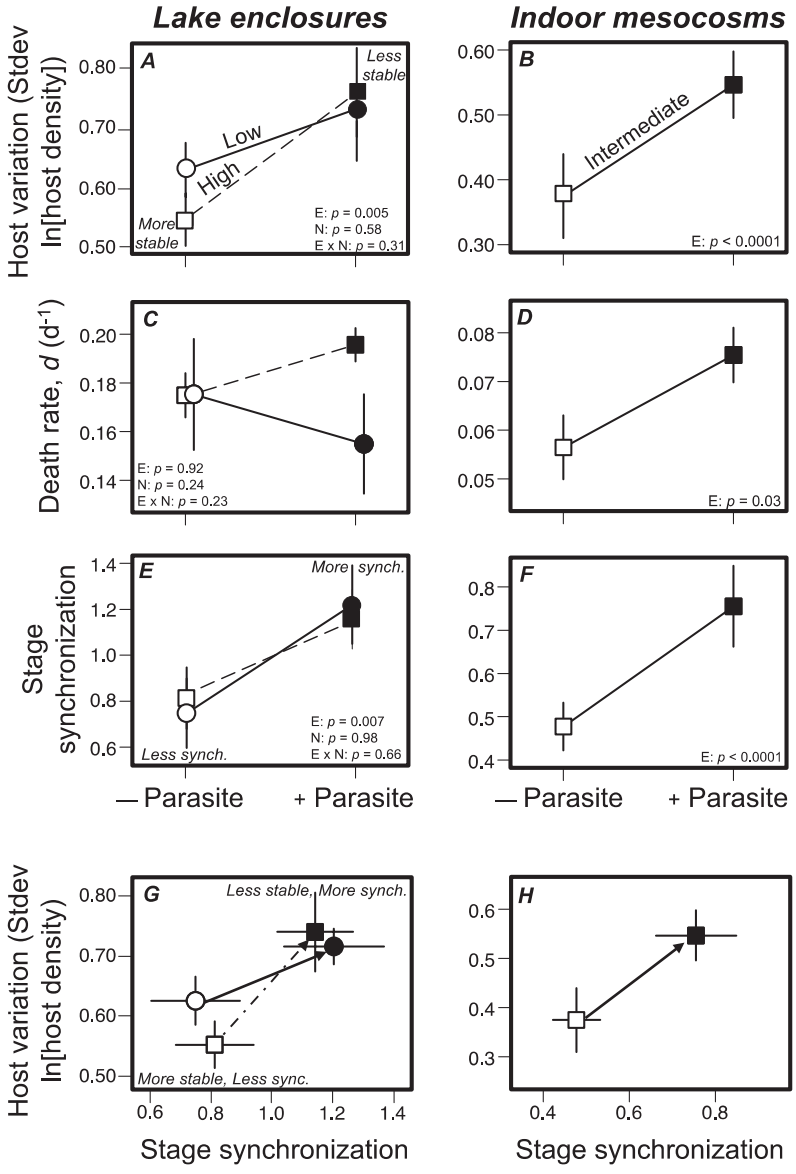

FIG. 5. Tests of the three hypotheses using two experiments. Left column (A, *C, E, G*) A lake enclosure experiment. Right column (*B, D, F, H*) An indoor mesocosm experiment. Solid symbols are + parasite treatments and open symbols are – parasite treatments. Stability indices: (*A*) Disease, not nutrients, significantly reduced host population stability (standard deviation of ln-transformed host density; higher, positive values denote increased variability and less stability) in the enclosure experiment (low nutrients, circles and solid line; high-nutrients, squares and dashed line); (*B*) disease also destabilized hosts at intermediate nutrients in the mesocosm experiment. Death rates: (*C*) Neither nutrients or disease increased death rate of hosts in the lake enclosures. (*D*) Disease, however, clearly increased host death rate in the mesocosms. Stage synchronization: (*E*) In the enclosure study, disease, not nutrients, shifted host stage structure into more synchronized juvenile–adult dynamics (index of stage synchronization [Fisher-transformed, lag-zero cross-correlation]). (*F*) This destabilizing effect of disease was more pronounced in the smaller mesocosm experiment (note the scale difference in *E* and *F*). (*G* and *H*) Synthesis: disease destabilized systems by increasing variation and by shifting host stage structure. *P* values of ANOVA are presented with E indicating epidemic effects, N indicating nutrient effects, and E × N indicating their interaction.

Lively 2011), as was recently proposed for a castrating bacterial parasite, *Pasteuria ramosa*, that sterilizes its *Daphnia* hosts early in infection (Auld et al. 2014). This destabilization mechanism remains unlikely here because fungal infection does not dramatically decrease host fecundity severely enough to trigger host–parasite oscillations (Auld et al. 2014). Additionally, Allee effects can interact with infection and induce pronounced instability and even drive hosts extinct (via violent cycles involving homoclinic bifurcations; Hilker et al. 2009). Third, arrested development in the parasite can destabilize host populations (Dobson and Hudson 1992).

These three destabilizing mechanisms (or others) may apply to other host–parasite systems. However, based on the natural history of the *Daphnia*–fungus system, we have no evidence that these known mechanisms apply here. Instead, our experimental and field results point to a new destabilizing mechanism: disease-mediated changes in competitive interactions between juveniles and adults.

This study grappled with discordance between existing theory and observations from natural populations. Based on recent models of host–resource–parasite systems (Hilker and Schmitz 2008, Cáceres et al. 2014, Hurtado et al. 2014, Appendix S1), we anticipated that disease-induced mortality should stabilize our focal *Daphnia* consumer/host–algae system. This mortality-based mechanism might help explain why natural systems often seem more stable than predicted by consumer–resource models without disease (e.g., Murdoch et al. 2003, Jensen and Ginzburg 2005). However, in our system, larger epidemics made host populations fluctuate more, not less. Stage-structured consumer–resource theory provides a mechanistic framework to understand this result (McCauley and Murdoch 1990, Nelson et al. 2005, de Roos and Persson 2013). Disease should shift host–resource systems from more stable, "low-synchrony" cycles when virulence inflicted by parasites equalizes competitive performance of adult and juvenile host classes. The converse result could arise, of course: disease could shift host–resource systems away from larger, "high-synchrony" cycles if parasites create competitive asymmetries between host classes (de Roos and Persson 2013, Orlando et al., *unpublished manuscript*). These results highlight that links between intraspecific host variation and consumer resource ecology can yield key insights into disease dynamics and help us understand why, how, and when populations fluctuate.

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