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SYNTHESIS

Host–pathogen interactions under pressure: A review and meta-analysis of stress-mediated effects on disease dynamics

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Abstract

Human activities have increased the intensity and frequency of natural stressors and created novel stressors, altering host–pathogen interactions and changing the risk of emerging infectious diseases. Despite the ubiquity of such anthropogenic impacts, predicting the directionality of outcomes has proven challenging. Here, we conduct a review and meta-analysis to determine the primary mechanisms through which stressors affect host–pathogen interactions and to evaluate the impacts stress has on host fitness (survival and fecundity) and pathogen infectivity (prevalence and intensity). We assessed 891 effect sizes from 71 host species (representing seven taxonomic groups) and 78 parasite taxa from 98 studies. We found that infected and uninfected hosts had similar sensitivity to stressors and that responses varied according to stressor type. Specifically, limited resources compromised host fecundity and decreased pathogen intensity, while abiotic environmental stressors (e.g., temperature and salinity) decreased host survivorship and increased pathogen intensity, and pollution increased mortality but decreased pathogen prevalence. We then used our meta-analysis results to develop susceptible–infected theoretical models to illustrate scenarios where infection rates are expected to increase or decrease in response to resource limitations or environmental stress gradients. Our results carry implications for conservation and disease emergence and reveal areas for future work.

KEYWORDS
environmental stress, epidemiological models, fecundity, infectivity, pollution, resource limitation, survival

INTRODUCTION

Accelerating anthropogenic impacts are modifying habitats and disrupting interactions between coevolved species (Barnosky et al., 2012), including host–pathogen dynamics, raising concern for human and animal health, biodiversity conservation and ecosystem structure and function (Allen et al., 2017; Gibb et al., 2020; Jones et al., 2008; Rohr et al., 2019; Wiethoelter et al., 2015). However, given the complexity and ubiquity of anthropogenic impacts, teasing apart the effects of perturbations on disease dynamics has proven difficult. A key to solving this challenge is identifying how human-induced stressors affect processes that mechanistically impact epidemiological dynamics, such as host survival and fecundity and pathogen infectivity (i.e., the ability of

a pathogen to establish an infection and replicate in a host).

Stressors affect transmission dynamics in three fundamental mechanistic ways. First, when stressors reduce host survival and fecundity, they reduce host density and, by extension, the transmission of density-dependent pathogens (McCallum et al., 2001). Second, host behavioural and immunological traits influence the acquisition, proliferation and dissemination of pathogens, a series of processes often summarized as host competence (Barron et al., 2015). Host competence may increase under stressful conditions that erode the immune response to pathogens (resource limitation or agrochemical exposure) (Knutie et al., 2017; Rohr et al., 2008). Third, stressors can have direct and indirect effects on pathogens. Host conditions can shape pathogen fitness by mediating intra-host resource availability and host immune response, as reviewed and modelled by Cressler et al. (2014). Pollution and environmental conditions may also negatively affect pathogens, especially in free-living stages (Pietrock & Marcogliese, 2003). Given that these three distinct mechanisms predict different outcomes, it is imperative to consider them collectively when examining stress-mediated effects on disease dynamics.

We aim to synthesize the current understanding of how human-induced stressors affect disease dynamics and consider the implications of these stressors for mitigating disease emergence and threatened species population declines. Here we define stress as any change that causes actual or perceived threats to the homeostasis of an organism (pathogen or host), precluding it from controlling fitness-critical variables (Del Giudice et al., 2018). We began by reviewing the literature to assess how stressors may affect host–pathogen interactions by altering (1) host density, (2) host defences and (3) pathogen infectivity. Further, we conducted a systematic search and meta-analysis of studies where host fitness (host survival and fecundity) and pathogen prevalence and intensity have been evaluated under benign and stressful conditions (low resources, adverse environmental conditions and pollution) for infected and uninfected hosts. Given that host defences and pathogen infectivity are rarely evaluated independently, we used infection prevalence and intensity to capture these two processes (hereafter infectivity). Specifically, we evaluated how different types of stressors affected host fitness and pathogen infectivity, if the fitness effects of stressors were more severe for infected versus uninfected hosts, and whether infectivity traits were more susceptible to stress than host fitness traits.

To further synthesize our results, we incorporated our empirical findings into two theoretical susceptible–infected (SI) models to elucidate scenarios where infection rates were expected to increase or decrease in response to the simultaneous trait changes (i.e., host fitness and pathogen infectivity) occurring over resource and environmental stress gradients. Our meta-analysis revealed similarly negative responses of infected and uninfected hosts to stressors and identified stressor type as a determinant of infection outcomes. Our results provide insights for predicting and mitigating the impacts of stressor–pathogen interactions on human and animal health, more relevant than ever as human-induced perturbations are a growing threat worldwide.

MECHANISTIC LINKS BETWEEN STRESSORS AND PATHOGEN TRANSMISSION

Stressors modulate host density

A key assumption of many infectious disease models is that contact rates between infected and uninfected individuals increase as population density increases (Anderson et al., 1986; McCallum et al., 2001). Therefore, if stressors negatively impact host fitness by restricting host population growth via reduced fecundity or increased mortality or emigration, pathogens will be less frequently transmitted and prevalence is expected to decline. This reasoning justifies culling campaigns, where infection rates are reduced or pathogens are extirpated by reducing host density below a critical transmission threshold (Lafferty & Holt, 2003; Prentice et al., 2019). Although, to our knowledge, no studies have explicitly evaluated the stressor–density–disease relationship, studies have shown that human pressures indirectly increase host–density thresholds, resulting in epidemics. For instance, overfishing of predatory lobsters (*Panulirus interruptus*) has led to dense purple urchin (*Strongylocentrotus purpuratus*) populations, and thereby more likely to experience urchin-specific bacterial (*Vibrio* spp.) epidemics (Lafferty, 2004). Similarly, although thermal stress increases the susceptibility of corals to disease, it only leads to white syndrome outbreaks where corals are at high density (Bruno et al., 2007).

Alternatively, stressors may contribute to increased local host density without increasing fecundity. For instance, behavioural responses to stressors, such as changes in migration patterns (Sánchez et al., 2020; Satterfield et al., 2018), foraging behaviours (Epstein et al., 2006) and aggregations in low-quality food-provisioned sites (intentional or unintentional) (Becker et al., 2015), have been associated with higher host density. Consequently, higher local density may intensify disease transmission via increased contact rates, as illustrated by theoretical models (Becker & Hall, 2014).

Disease transmission can also be sustained at low population densities. For instance, in social species, the frequency of social contact can govern disease epidemics independently of host density (Johnson et al., 2011; Rimbach et al., 2015; Rushmore et al., 2017). Given that density-independent transmission (e.g., sexual or vector-borne transmission) does not require a minimum host

density for parasites to invade a population (Hopkins et al., 2020), it is expected that a combination of stressors and pathogen infection would drive populations to extinction more frequently than density-dependent transmissions (de Castro & Bolker, 2005; Ryder et al., 2007).

Stressors may affect the fitness of infected and uninfected hosts differently. Infection increases sensitivity to other stressors, as infected hosts are more energetically constrained (Marcogliese & Pietrock, 2011). Such a combined effect of stress (warming temperatures) and infection (e.g., *Vibrio coralliilyticus*) may be responsible for the rapid global coral reef decline (Maynard et al., 2015). Despite many examples of synergistic tolls that stressors and pathogens have on host fitness (Crain et al., 2008), few have tested whether stressors have a differential impact on the fitness of infected compared to uninfected hosts (Beldomenico & Begon, 2016; Marcogliese & Pietrock, 2011).

Stressors constrain host defences

Hosts invest resources to defend themselves from pathogens via behavioural or physiological mechanisms. While avoidance behaviour is less understood (Buck et al., 2018), physiological mechanisms, such as infection resistance or disease tolerance, are well documented (Råberg et al., 2007, 2009; Svensson & Råberg, 2010). Resistance mechanisms control parasite growth and reproduction, reducing infection intensity, while tolerance reduces or compensates for infection-induced pathology without reducing pathogen burden (Boots, 2008; Medzhitov et al., 2012). Although resistance limits pathogen replication while tolerance does not, leading to different disease implications (Schneider & Ayres, 2008), both strategies have high energetic requirements, and hosts should only elicit them if parasite infections reduce their fitness (Ayres & Schneider, 2009; Cumnock et al., 2018). Consequently, trade-offs exist between immune response and other energetically costly physiological processes, such as reproduction and growth (Lochmiller & Deerenberg, 2000), in both vertebrates (Gustafsson et al., 1994) and invertebrates (Schwenke et al., 2016). Furthermore, there is recent evidence that trade-offs between reproduction and immune function exist at the transcriptomic level and may be conserved across animals (Rodrigues et al., 2021). Given these trade-offs, host defence may be compromised under stressful conditions (Gervasi et al., 2015; Sheldon & Verhulst, 1996).

Stressors may modulate host defensive mechanisms against infections. Malnutrition can impair immune function by reducing T-cell-mediated immune response (Alonso-Alvarez & Tella, 2001), toxicants can immunocompromise a host (Caren, 1981) or upregulate host immunity (Pölkki et al., 2012), and extreme temperature variation can impair immunity, leading to species declines (Rohr & Raffel, 2010). Owen et al. (2021) showed that food-deprived robins (*Turdus migratorius*) developed higher West Nile Virus titres and were infectious longer than robins fed normally. Similarly, amphibians exposed to pesticides have experienced eosinophil recusation (a resistance mechanism) and associated increases in trematode infections and subsequent limb malformations (Kiesecker, 2002). Conversely, infection tolerance in Galapagos mockingbirds (*Mimus parvulus*) has been impaired by climatically induced food stress, exhibiting lower fledging success in dry years (when resources were scarce) compared to wet years due to the inability to compensate for the costs of parasitic fly nest infestations (McNew et al., 2019). These examples show that host susceptibility to infections and/or pathogen transmission may increase under stressful conditions.

Pathogens are affected by stressors as well

Pathogens can be affected by stressors directly or indirectly through their hosts. It is critical to distinguish these mechanisms, as each may affect host populations differently. By definition, pathogens rely on host resources to grow and reproduce (Casadevall & Pirofski, 2002); therefore, pathogens compete for resources with host physiological processes that mediate disease outcome (i.e., reproduction, growth and immune defence; Cressler et al., 2014). Direct manipulation of immune responses by pathogens has been documented (Maizels & Yazdanbakhsh, 2003; Schmid-Hempel, 2008), but pathogens may also outcompete host immune responses through direct resource consumption (Cressler et al., 2014). For example, in a *Daphnia*–fungal parasite system, more resources equate to greater epidemics due to both higher *Daphnia* reproductive rates (i.e., host density-driven) and higher infection intensity (Civitello et al., 2015), suggesting that food stress lowers parasitism in the *Daphnia*–fungal parasite system.

On the other hand, a common sickness behaviour, reduced food consumption, may be an adaptive host response (Ayres & Schneider, 2009; Exton, 1997; Murray & Murray, 1979). Parasite-mediated anorexia can improve host health and recovery (Wang et al., 2016), much like fever (Kluger et al., 1996). Anorexia appears to intensify with higher levels of parasite exposure or intensity (as reviewed by Hite et al., 2020); however, the advantages or disadvantages of anorexia depend on nutrient stores and quality and ambient conditions (Becker et al., 2015; Hite et al., 2020; Johnson et al., 2010; McKenzie & Townsend, 2007). Sometimes a low-quality resource may be inadequate for the host while sufficient for the pathogen (Dallas & Drake, 2014) or lead to fewer resources for the parasite (Hall, Knight, et al., 2009; Hall, Simonis, et al., 2009; Kyriazakia et al., 1998). Conversely, hosts may increase food intake to compensate for energy lost fighting infections [i.e., resource compensation hypothesis (Christe et al., 1996)]. As a result, high-resource diets

may increase host tolerance to infections by reducing resource competition between hosts and parasites without negatively affecting parasite fitness (Knutie et al., 2017), with possible implications for the evolution of pathogen virulence (Hite et al., 2020).

Environmental stressors may also directly impact pathogens at environmental stages (Riggs et al., 1987). Fluctuating environmental conditions and pollutants can negatively affect pathogens (Pietrock & Marcogliese, 2003). For instance, deviations from temperature and salinity optima can reduce survival and lifespan in free-living helminths (Measures, 1996; Pechenik & Fried, 1995), and, in turn, reduced longevity decreases infective periods. Similarly, elevated nitrate concentrations can reduce free-living spore survival, which may counteract the effects of increased intensity within *Daphnia* (Dallas & Drake, 2014). Even when pathogens survive stressors, their capacity to infect hosts could be affected. For instance, metals can impact sensory receptors of environmental stages of parasites, such as cercariae, impairing their ability to locate, recognize and infect hosts (Ghandour & Webbe, 1975; King & Higashi, 1992; Morley et al., 2002).

Finally, differential effects of stressors on directly versus indirectly transmitted pathogens (i.e., vector-borne or intermediate hosts) may lead to divergent outcomes (Hopkins et al., 2020). For instance, Studer et al. (2010) showed that temperature affects the many steps of the transmission process of the trematode *Maritrema novaezealandensis*. Although increased temperatures favoured cercarial emergence and transmission from the first intermediate snail host (*Zeacumantus subcarinatus*) and development within their second intermediate amphipod host (*Paracalliope novizealandiae*), warmer temperatures increased amphipod mortality, creating a bottleneck for pathogen transmission in the trophically transmitted part of the trematode's life cycle. Similarly, qualitative differences between aquatic and terrestrial systems, due to life history differences and the greater taxonomic diversity of aquatic parasites and hosts (Byers, 2021; Harvell et al., 2002; McCallum et al., 2004), may result in divergent disease outcomes. For example, environmental transmission dominates aquatic systems (Lafferty, 2017), making pathogens more susceptible to the direct effects of stressors.

META-ANALYSIS

We conducted a systematic literature search and meta-analysis to evaluate the impacts of three broad types of environmental stressors on disease dynamics. First, we confirmed that pathogen exposure in laboratory studies typically negatively affects host fitness. We then proceeded with our main meta-analyses, focused on two specific questions: (Q1) were stressor fitness effects more severe for infected versus uninfected hosts? and (Q2) was infectivity more susceptible to environmental stress than host fitness traits? To address these questions with data from primary studies, we used infection intensity and prevalence as proxies for infectivity and survivorship and fecundity as proxies of host fitness.

Literature survey and study selection

To identify studies that evaluated the effects of environmental stressors on infectivity and host fitness traits in host–parasite systems, on February 9th of 2021, we conducted a systematic literature search in Web of Science using the following search terms: (parasit* OR pathogen* OR disease) AND (environment* OR temperature OR pollution OR resource OR provision* OR toxi* OR contamination) AND (infection OR load OR yield OR resistance) AND ("birth rate" OR "death rate" OR surviv* OR mortality OR reproduct* OR fecundity). We limited our search to journal articles published in English between 2010 and 2020 and scanned the titles and, if relevant, abstracts of all 20,684 hits. This initial screening effort was split and carried out by two experienced independent reviewers (AVS and BW). We identified ten additional studies from references to selected studies. One experienced reviewer or two student reviewers further examined articles documenting the effects of environmental stressors on infectivity and host fitness.

We classified stressors into three groups: (1) environmental factors, which can vary naturally but are also subject to human-induced perturbation (hereafter "endogenous environment"); (2) the presence or quantity of chemical pollutants (hereafter "chemical pollution") that lead to negative expected outcomes for hosts; and (3) resource availability for hosts (hereafter "resource limitation"). Although, in natural systems, these stressors often overlap (e.g., increased temperature can alter resource availability), we included studies where only one stressor was evaluated to facilitate the interpretation of our results. We excluded studies if stressful and control environments differed due to additional antagonistic biotic interactions (e.g., presence of predators or competitors) or by the presence of substances purposely used as therapeutic interventions on infected hosts (e.g., chlorine as water treatment). Furthermore, we limited our search to studies with animal hosts and excluded studies on parasitoid infections (Figure 1).

We included only experimental studies with hosts exposed to or infected by parasites under laboratory conditions. We only included studies if infected hosts were exposed to stressful and control treatments, and both host fitness (fecundity and/or survivorship) and pathogen infectivity (prevalence and/or intensity) were reported from the same experiment (i.e., the same pool of individuals divided between stressful and control treatments) at matched timepoint(s) (Figure 1). For example, if a study reported infection intensity at 24 and 72 h post-infection

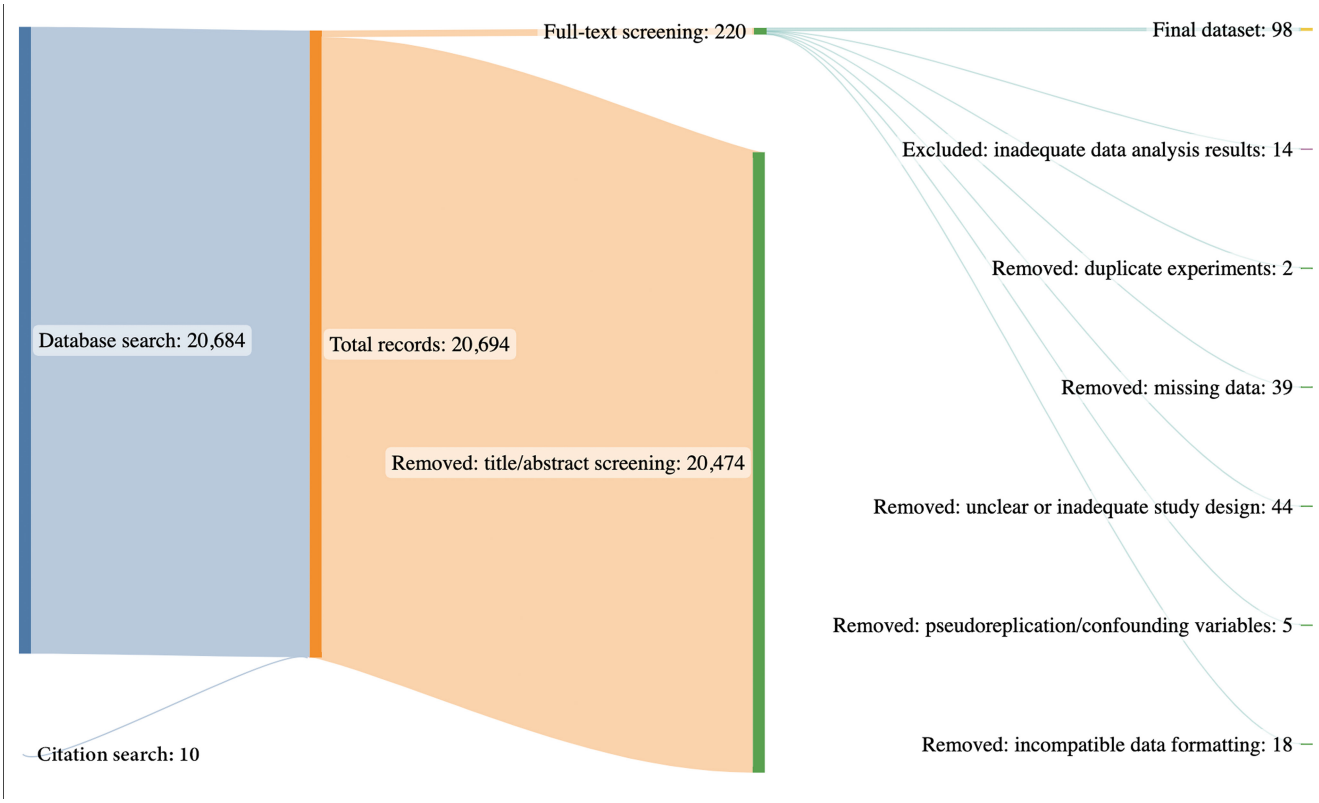

FIGURE 1 PRISMA diagram documenting our study screening for inclusion and exclusion for the meta-analysis. Each stage of the data collection process is highlighted with different coloured pipes (blue: literature search; orange: title/abstract screening; green: full-text screening).

(hpi), but survivorship was only recorded at 72 hpi, we used 72 h data. If a study recorded both fitness and infectivity at multiple time intervals, we included all matched intervals in the data collection. We accounted for the non-independence of these effects and their sampling errors in the random structure of our statistical models (see sections *Meta-analyses* and *Publication bias*). Studies were further excluded for pseudoreplication, missing sample size information, or when estimates were reported without associated errors (Figure 1).

Data collection and transformations

We obtained primary literature data directly from the main text, tables, supporting material or raw data files whenever available. Otherwise, we digitized data from figures using PlotDigitizer (https://plotdigitizer.com). Stressor effects were standardized to unbiased mean differences (Hedge's *g*) from both continuous and discrete variables (Hedges, 1981). For continuous variables, we obtained the mean and standard deviation (SD) of fitness traits and infectivity metrics in environments with different exposures to stressors. If SD was not reported, an error estimate (standard error [SE], 95% confidence interval [CI], or Wald's CI) was converted to SD, assuming normality. If a study reported median instead of mean ($n = 13$ effects in four studies), we estimated the mean following Hozo et al. (2005). If dispersion was only reported as a data range or interquartile range ($n = 8$ effects in one study and $n = 5$ effects in three studies, respectively), we approximated SD (Lajeunesse, 2013; Wan et al., 2014). The mean and SD of the response variables were then used to calculate standardized mean differences (*d*) and their variances.

Many studies ($n = 67$) used discrete variables to quantify infection prevalence and/or survivorship. In these cases, we calculated odds ratios between environmental treatments and estimated variances (Rosenberg et al., 2013). In cases where at least one category had no observations (e.g., no survival in polluted treatment), we applied Yate's continuity correction to avoid dividing by zero (Yates, 1934). Log odds ratios were then converted to *d*, and variances of log odds ratios were converted to variances of *d*, assuming a continuous logistic distribution underlies each discrete trait (Hasselblad & Hedges, 1995). Finally, we estimated Hedge's *g* and its variance by applying sample size correction *J* to all values of *d* and their variances (Hedges, 1981).

Most experiments ($n = 108$) contrasted host fitness traits and infectivity across three or more environmental treatments or in more than one-time intervals. For example, a control group could be compared to two levels of chemical pollution or at both 24 and 48 hpi. In these

cases, stressor effects and sampling errors were not independent, as they shared a control group or time baseline. To account for correlated sampling errors between these effects, we computed covariances in sampling errors between effects in multiple-comparison designs following Viechtbauer (2010). We included these variance–covariance matrices in our statistical analyses (see below). For a few experiments ($n=8$) where large covariances between effects and small sample sizes resulted in variance–covariance matrices with negative eigenvalues (i.e., not positive definite), we adjusted covariance estimates to produce the nearest positive definite matrix using the R package *Matrix* (Douglas & Maechler, 2021). As an alternative approach to estimating sampling error covariances, we adjusted fixed effect coefficients using the robust variance estimator (RVE) (Hedges et al., 2010), as implemented in the R package *clubSandwich* (Pustejovsky, 2020). Here, we focus on results with estimated covariances and show results under the RVE in Data S1.

Moderators

Our first analysis aimed to determine whether pathogen exposure in selected studies led to reduced host fitness without environmental stressors. For this analysis, we used the response trait category (fecundity or survivorship) as the only moderator and included only data from hosts in control (i.e., no environmental stress) conditions. We then focused on the effects of environmental stressors on host–pathogen dynamics and examined three factors that could moderate the magnitude of these effects. For Q1, we considered infection status (infected and uninfected), stressor type and response trait (fecundity and survivorship) as moderators. We were specifically interested in whether infection status amplified any negative fitness consequences of stressors. As mentioned above, stressors were of three types: (1) endogenous environmental factors (e.g., temperature, humidity, salinity, dissolved oxygen and habitat structural complexity); (2) chemical pollution by toxins or synthetic compounds typically derived from pesticides or herbicides; and (3) resource limitation (restricted access to food or specific nutrients, like nitrogen and phosphorus). For response traits, fecundity was typically recorded as the total number of offspring, whereas survivorship was reported as proportion alive, number alive and, sometimes, time to death.

In Q2, we focused exclusively on infected individuals under the abovementioned criteria. We investigated stressor type and response trait as moderators. We aimed to contrast the effects of stress on fitness versus infection responses. We, therefore, included two additional response traits as infectivity proxies: infection intensity and prevalence. Prevalence was always reported as the number or percentage of infected individuals. Infection intensity was often quantified in different ways for different types of pathogens, for example, (log) copy number for viruses, colony-forming units for bacteria, mean number of cercaria for helminths and spore counts for fungi. To compare the relative sensitivity of fitness and infectivity, and because prevalence and infection intensity represent the opposite of host defence, signs of unbiased, standardized mean differences were flipped. By doing so, a positive effect size reflects greater defence and a beneficial outcome for hosts, whereas, for fitness traits, a positive sign indicates higher survivorship or fecundity.

We complemented these main models for Q2 with two additional moderators in separate analyses. We investigated whether the transmission environment (terrestrial or aquatic) or transmission mode (direct or indirect) modulates the effects of environmental stressors on infectivity and host fitness responses. For hosts that occupy different environments across life stages, we categorized transmission environments based on the life stage of hosts exposed or infected in each study, which was typically the most susceptible life stage to the target pathogen. We classified pathogen transmission as "indirect" if it met one of three conditions: (1) pathogen required an ecologically distinct intermediate host to complete its life cycle; (2) pathogen was transmitted between ecologically similar hosts via vectors; or (3) pathogen could survive independently of the host during the free-living stage. Otherwise, pathogens were considered to have "direct" transmission between ecologically similar hosts.

Meta-analyses

We analysed effect sizes (Hedge's *g*) for Q1 and Q2 with multi-level meta-analytic (MLMA) models, fitted in R v 4.1.2 (R Core Team, 2013) and using the package *metafor* version 3.0-2 (Viechtbauer, 2010). We employed a model selection approach based on the Akaike Information Criterion (AIC) to identify the most important moderators explaining heterogeneity in effect sizes and the most parsimonious model (Arnold, 2010). This required first fitting the full model and all reduced models via maximum likelihood (ML) estimation. For Q1, the full model included the moderator variables infection status, fitness trait, stressor type and all their interactions. The full model for Q2 included response trait, stressor type and their interaction.

All models accounted for the non-independence of effects and sampling errors measured in the experiment. Models also included observation-level random intercepts, so residual variation within studies could be estimated. Full and reduced models (including the intercept-only model) were compared using the "dredge" function of the R package *MuMIn* v 1.43.17 (Bartón, 2023). The highest-ranking model based on small sample size corrected AIC (AICc) was then refitted via restricted maximum-likelihood (REML) estimation

to interpret moderators and evaluate publication bias and heterogeneity.

We report meta-analytic mean estimates and 95% confidence intervals for the effects of moderators in the final models. Meta-analysis results were plotted using the R package *orchaRd* (Nakagawa et al., 2021). We tested the significance of statistical contrasts between fitness and infectivity response variables in Q2 using Wald-type chi-square tests, computed with the function "anova".

Heterogeneity

We estimated the proportion of heterogeneity relative to sampling error (I^2; Higgins & Thompson, 2002) and partitioned it into between-study heterogeneity and within-study heterogeneity (Nakagawa & Santos, 2012). Current formulations of I^2 do not accommodate sampling-error covariances for multivariate meta-analytic models. We, therefore, fitted simpler models with only observation-level variances to estimate I^2. While this is not ideal, we note that the meta-analytic effects of moderators accounting for sampling-error covariances are robust to these simpler models after adjustment with RVE (see Data S1).

Publication bias

Following Nakagawa et al. (2022), we relied on two complementary approaches to assess small study effects, which may result from publication bias. First, we visualized the relationship between effect sizes and precision (SE) using funnel plots. To do this, we re-fitted selected models as random effect models and computed residual effect sizes conditional on experiment, observation and factor level for factors included as moderators in the main analyses. These conditional residuals have the advantage of taking some within-experiment non-independence into account, but they still make unlikely assumptions about sampling variances (Nakagawa et al., 2022).

We, therefore, complemented funnel plots with a two-step, modified Egger's test for multilevel meta-analysis (Nakagawa et al., 2022). In the first step of this test, the SE of effect sizes is included as the only moderator in a meta-regression with the same random effect structure as our main MLMA analyses. A significant slope of this moderator means that studies with low precision tend to report either more negative or more positive effects than studies with higher precision. Therefore, if the SE slope is different from zero, the second step of the test is to fit a meta-regression with the variance of effect sizes as the only moderator. The intercept of this second meta-regression is then a more appropriate estimate of the overall meta-analytic effect (Stanley & Doucouliagos, 2014). Because we uncovered evidence consistent with publication bias in Q1 and Q2, we tested the robustness of the meta-analytic effects of moderators by fitting a multi-level meta-regression (MLMR) with variance in addition to the moderators of interest for each question in our study (see Data S1).

Summary of the literature survey

Our final data set included 98 studies and 891 effects (Figure 1), where 384 were included for Q1 and 686 for Q2. While most studies reported results from a single experiment, 21 studies included two to four experiments, resulting in a total of 122 experiments. Host taxa included arthropods ($n=20$ species, classes Brachiopoda, Copepoda, Insecta and Malacostraca), molluscs ($n=13$ species, classes Bivalvia and Gastropoda), fish ($n=13$ species), amphibians ($n=21$ species) and several vertebrates species (two bird, one reptile and one mammal) (Figure S1a). Parasite taxa comprised viruses ($n=37$), bacteria ($n=14$), fungi ($n=6$), parasitic animals ($n=13$, helminths and myxozoan) and protozoans ($n=8$) (Figure S1b).

Q1: Fitness effects of stressors on infected and uninfected hosts

After confirming that pathogen infections in the surveyed literature reduce host fitness (Figures S2 and S3, Table S1), we asked if the effects of stressors on fitness are modulated by infection status (Q1). The lowest AICc model for Q1 included stressor type, response trait and their interaction as moderators (Table S2). Our data, therefore, do not support differential effects of environmental stressors between infected and uninfected hosts (Figure S4). The interaction between stressor type and response trait resulted primarily from a relatively strong negative effect of resource limitation on fecundity (Table S3; Figure 2) and a relatively strong negative effect of endogenous environmental stressors on survivorship (Table S3; Figure 2). Pollution also negatively affected survivorship (Table S3; Figure 2), but this effect was contingent on the results of low-precision studies (see Evidence of publication bias). These contrasting effects of the three stressor types were qualitatively similar if the RVE was used instead of modelling sampling-error covariances (Figure S5). Differences in effect sizes both within ($I^2=40.42\%$) and between ($I^2=53.41\%$) experiments contributed to relatively high total heterogeneity ($I^2=93.83\%$).

Q2: Sensitivity of host fitness and infectivity responses to stress

We contrasted the fitness and infectivity effects of stressors on infected hosts. The full model, including

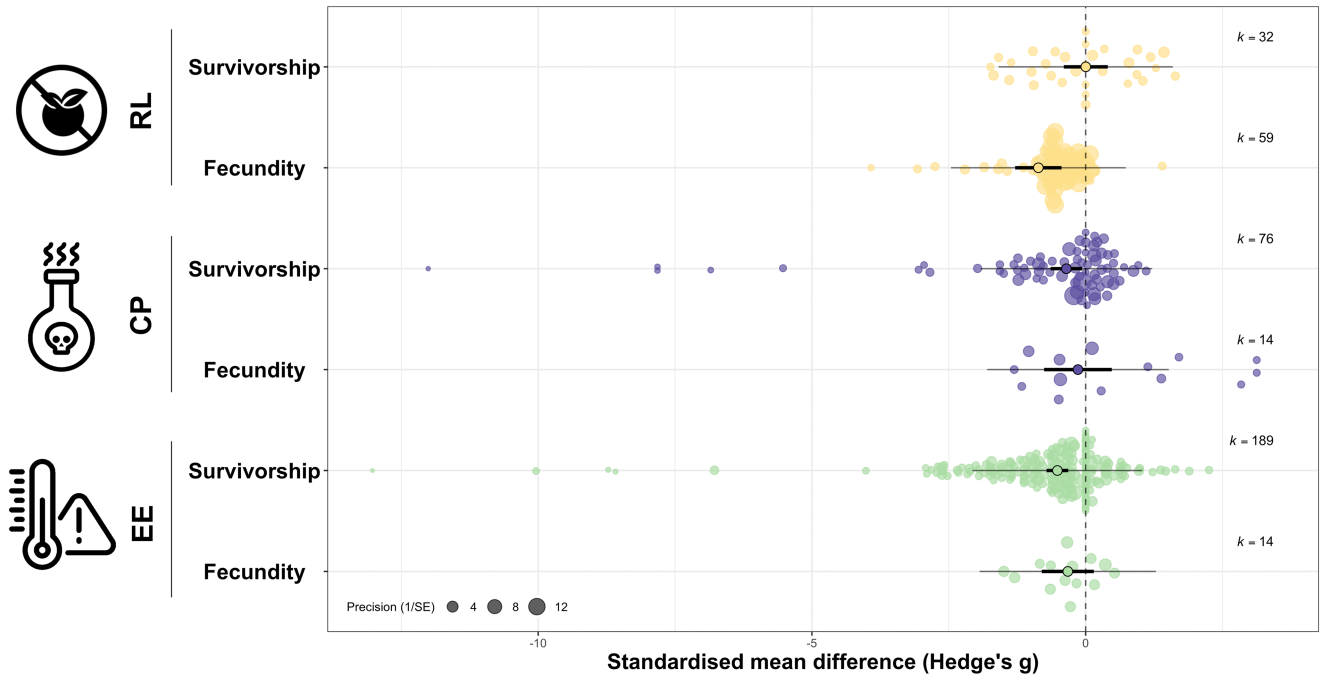

FIGURE 2 Orchard plot for the best multi-level meta-analytic (MLMA) model of the effects of environmental stressors on host fitness traits. The model includes two factorial moderators: stressor type, coded as "endogenous environment" (EE), "chemical pollution" (CP) and "resource limitation" (RL) and fitness response trait ("fecundity" or "survivorship"). Nodes in the same colour show the effects of the same stressor. The overall mean effect sizes (Hedge's *g*) for each combination of stressor and response trait are shown as circles with black border lines. 95% confidence intervals are represented by the thick black bars, and prediction intervals are represented by the thin bars. The number of effects for each category (*k*) is given in parentheses. Circle size is proportional to effect size precision.

stressor type, response trait and their interaction, had the lowest AICc score (Table S4). In this model, the interaction arose not only due to the differential sensitivity of fecundity and survivorship responses to stressor type but also because the direction of infectivity responses only aligned with fitness responses for endogenous environmental stressors (Table S5; Figure 3). Effects of resource limitation differed between response variables (fecundity vs. intensity: $p < 0.001$; fecundity vs. prevalence: $p = 0.006$; survivorship vs. infection intensity: $p = 0.010$; and survivorship vs. prevalence: $p > 0.05$). When resources were limited, not only was host fecundity reduced (as noted in Q1), but infection intensity was also reduced (Table S5; Figure 3). In contrast, chemical pollution impacted survivorship more than either proxy of infectivity (survivorship vs. infection intensity: $p = 0.024$, survivorship vs. prevalence: $p = 0.018$). We found that pollution decreased both host survival and pathogen prevalence (Table S5). Finally, perturbation of the endogenous environment tended to decrease host survival and increase pathogen intensity, both of which had negative consequences for host fitness and health (Table S5; Figure 3, all infectivity vs. fitness contrasts $p > 0.05$; however, survivorship vs. prevalence: $p = 0.057$).

We obtained a similar pattern of interaction among stressors and fitness and infectivity responses when the RVE was used to account for the non-independence of sampling errors (Figure S6). Despite these contrasting effects of moderators, heterogeneity remained high (total $I^2 = 90.26\%$), both between ($I^2 = 64.11\%$) and within ($I^2 = 25.15\%$) experiments.

The effects of stressors on host fitness and infectivity traits also depended on the environment and mode of pathogen transmission. While the negative effect of resource limitation on host fecundity was consistent in both environments, resource limitation only lowered pathogen intensity for aquatic hosts (Table S6, Figure S7). Similarly, chemical pollution reduced pathogen prevalence, and endogenous environmental stressors reduced host survivorship and increased infection intensity in aquatic but not terrestrial hosts (Table S6, Figure S7). For host–pathogen systems with indirect transmission modes, resource limitation decreased host fecundity and pathogen intensity, and chemical pollution reduced host survival and pathogen prevalence (Table S7, Figure S8). While the effects of endogenous environmental stressors were generally consistent between transmission modes, mortality was more pronounced in hosts exposed to pathogens through direct transmission (Table S7, Figure S8). Although our results show potential distinctions and similarities between environments and transmission modes, we note that most effects were from aquatic (495 of 686) and indirect transmission (509 of 686) systems, possibly biasing our findings towards these systems.

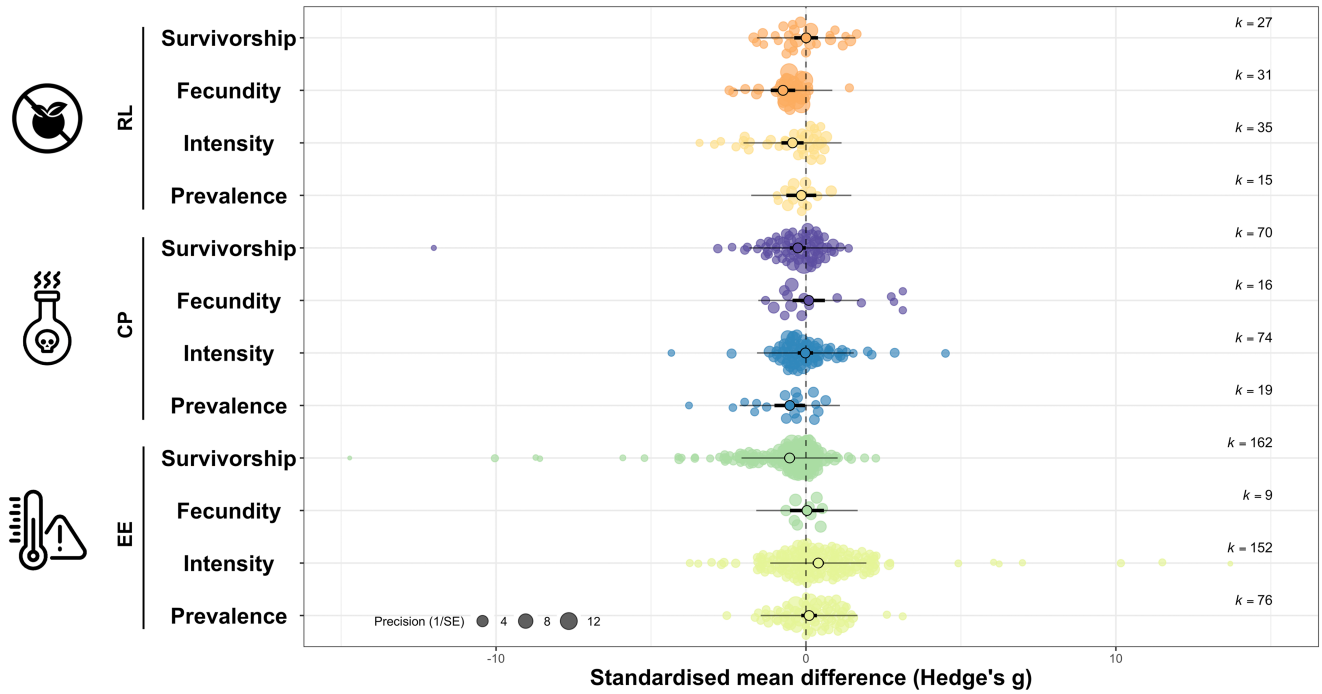

FIGURE 3 Orchard plot for the best multi-level meta-analytic (MLMA) model of the effects of environmental stressors on host fitness traits and infectivity. The model includes two factorial moderators: stressor type, coded as "endogenous environment" (EE), "chemical pollution" (CP), and "resource limitation" (RL) and response trait ("prevalence", "intensity", "fecundity" or "survivorship"). Negative effect sizes imply reduced fecundity, survivorship, infection prevalence, or intensity. Nodes in the same colour show effects of the same stressor on the same category of the response variable (fitness or infectivity). The overall mean effect sizes (Hedge's *g*) for each combination of stressor and response variable are shown as circles with black border lines. 95% confidence intervals are represented by the thick black bars, and prediction intervals are represented by the thin bars. The number of effects for each category (*k*) is given in parentheses. Circle size is proportional to effect size precision.

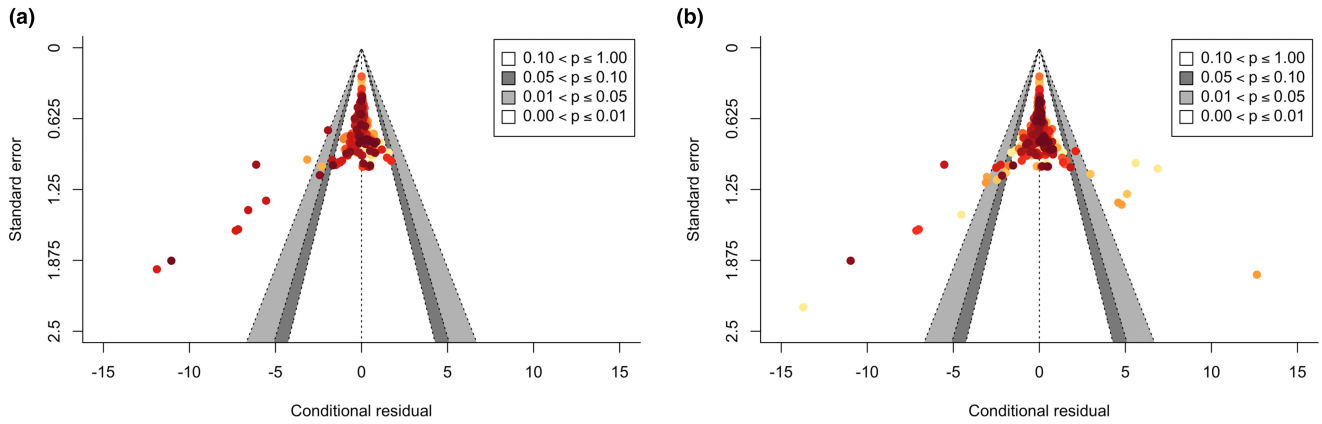

FIGURE 4 Funnel plots showing the relation between precision (SE) and conditional residuals of the effects of environmental stressors on (a) fitness and (b) fitness and infectivity responses in animal hosts. Dark and light grey areas show bounds of 90% and 95% CIs for conditional residuals given the SE. Circles represent individual effects and are coloured by precision, with dark red representing greater precision.

Evidence of publication bias

More negative effects of stressors in studies with lower precision suggest that publication bias may partially explain our results for Q1 and Q2 (Figure 4). We confirmed these negative relationships between effect size and precision using a two-step modified Egger's test (Table S8). We thus adjusted meta-analytic estimates for analyses in Q1 and Q2 by including variance as an additional moderator in both models.

Some results in Q1 differed qualitatively after adjusting for small study effects. Specifically, the effects of endogenous environmental stressors and pollution became non-significant when variance was included as a moderator (Table S9, Figure S9). Moreover, the effect of resource limitation on survivorship changed direction after the

small-study adjustment. However, we note that this effect was indistinguishable from zero in both unadjusted and adjusted models and was based on few studies (n=8).

In Q2, our qualitative results remained essentially unchanged after adjusting for publication bias. Overall, the effects of endogenous environmental stressors reduced host survival and increased both infectivity traits (Table S10, Figure S10). As in our primary analysis, resource limitation in the adjusted model negatively affected fecundity, but the meta-analytic effect on intensity was marginally non-significant (Table S10). Finally, the negative impact of chemical pollution on host survival and prevalence in our primary analysis (Table S5; Figure 3) became indistinguishable from zero in the adjusted model (Table S10, Figure S10). However, we caution that this result was based on a relatively small number of experiments (n=9).

INTEGRATING EMPIRICAL RESULTS INTO EPIDEMIOLOGICAL MODELS

When considering the effects of stress on infected host fitness and infectivity, responses varied depending on stressor type. Environmental stress decreased host survivorship and increased infection intensity; pollution decreased host survival and pathogen prevalence; and limiting resources decreased host reproduction and pathogen intensity.

We integrated the best-supported relationships from our meta-analysis into mathematical models to evaluate the net impact of these simultaneous effects of stressors on host–pathogen interactions. We built two dynamic SI models: an SI-Resource model following the framework of Civitello et al. (2018), where key processes (i.e., host reproduction and pathogen transmission) could depend on resource availability (Box 1), and an SI-Environmental gradient model following the framework of Lafferty and Holt (2003), where key processes (i.e., host survivorship and pathogen transmission) could depend on an abiotic environmental factor (Box 2). Because our meta-analysis suggested no proportional difference between uninfected and infected hosts for survival or reproduction, we incorporated this result by including a common parameter for the strength of these effects on both groups (Boxes 1 and 2).

We used the models to determine equilibria of disease prevalence as a function of resource availability and environmental stress gradients, using the numerical integration function "lsoda" in the R package *deSolve*

BOX 1 SI-Resource model

Susceptible (S) and infected hosts (I) are foraging on available resources (R), while resources grow logistically. Hosts require resources to reproduce, as determined by the conversion efficiency (e, births per unit of resource) and foraging rate (f_M). From our meta-analysis results, limited resources affected host reproduction (decreased fecundity) of both susceptible and infected hosts. However, infected hosts reproduce at a lower rate than susceptible hosts (ρ, relative fecundity of I compared to S). Hosts die at a background death rate (d), but infected hosts have increased mortality due to the pathogen (ν, virulence). Hosts become infected at a transmission rate (β_M). To determine how fast traits rise with resource availability, we use the half saturation reproduction constant (h_r) and the half saturation transmission constant (h_t) as part of the Type II functional response. The latter increases as hosts are more sensitive to resource availability. Resources grow at a growth rate (r) and have a carrying capacity (K). Parameters used in our simulations: e=0.5, f_M=0.1, ρ=0.25, d=0.01, ν=0.04, β_M=0.01, h_r=4, h_t=varies (0, 1, 2, 4, 8), r=1, K=10.

$$\frac{dS}{dt} = \underbrace{ef_M\frac{R}{h_r+R}\times(S+\rho I)}_{\text{Births}} - \underbrace{\beta_M\frac{R}{h_t+R}SI}_{\text{Transmission}} - \underbrace{dS}_{\text{Deaths}}$$

$$\frac{dI}{dt} = \underbrace{\beta_M\frac{R}{h_t+R}SI}_{\text{Transmission}} - \underbrace{(d+\nu)I}_{\text{Increased mortality}}$$

$$\frac{dR}{dt} = \underbrace{rR\frac{1-R}{K}}_{\text{Resource growth}} - \underbrace{f_M\frac{R}{h_r+R}SI}_{\text{Resource removal}}$$

BOX 2 SI-Environmental stress gradient model

Susceptible hosts (S) grow logistically and have a density at which the birth rate (b) hits zero from competition (K, carrying capacity). As an assumption of relative change, transmission rate (β) and background death (d) are sensitive to environmental stressors (E), β_E and d_E, respectively. From our meta-analysis results, environmental stress (and pollution) affected survival, regardless of infection status. However, infected hosts (I) reproduce at a smaller rate than susceptible hosts (ρ, relative fecundity of I compared to S) and have increased mortality due to the pathogen (ν). Parameters used in our simulations: $b=0.5$, $K=10$, $\beta=0.01$, $d=0.01$, $E=$varies (0–1), $\beta_E=$varies (−8, −4, −2, 0, 2, 4, 8), $d_E=2$, $\rho=0.25$, $\nu=0.04$.

$$\frac{dS}{dt} = \underbrace{b(S+\rho I)\left(1-\frac{S+I}{K}\right)}_{\text{Births}} - \underbrace{\beta e^{(\beta_E E)} SI}_{\text{Transmission}} - \underbrace{d e^{(d_E E)} S}_{\text{Deaths}}$$

$$\frac{dI}{dt} = \underbrace{\beta e^{(\beta_E E)} SI}_{\text{Transmission}} - \underbrace{(d+\nu) e^{(d_E E)} I}_{\text{Increased mortality}}$$

(Soetaert et al., 2010). We examine different scenarios in which fecundity and infectivity, or background death and infectivity, had different sensitivities to either resource (Box 1) or environmental stress gradients (Box 2), respectively. We simulated epidemiological dynamics of each model across a gradient of either resource availability or environmental stress, then plotted equilibrium infection prevalence and host density against such gradients for each model (Figure 5).

Model predictions

Using our dynamical models (Boxes 1 and 2), we evaluated whether the patterns of trait sensitivity to stressors we documented in the meta-analysis reduce or increase infection prevalence across stress gradients and how stressors ultimately impact host population densities. The SI-Resource model predicts that a decrease in resource productivity decreases infection prevalence (Figure 5a), in part because host densities also decrease with limited resources (Figure 5c). Once a pathogen establishes itself in a population, there is stabilizing feedback, where pathogens suppress host density, increase resources and further increase transmission (Figure S11). Therefore, in all scenarios of sensitivity of pathogen transmissibility to resources (smaller values of the half-saturation transmission constant (h_t) increase the sensitivity of transmission rate (β) to resources), the model reaches the same prevalence equilibrium. However, although population density also stabilizes, impacts on host density are different for each scenario: populations more sensitive to resources available will reach smaller population sizes compared to less sensitive populations (Figure 5c).

The SI-Environmental stress gradient models revealed that population density decreases regardless of the effects of stress on host susceptibility due to increased mortality. But it exponentially decreases host populations when the transmission rate is sensitive to the environmental factor (Figure 5b,d). Specifically, when stress increases host susceptibility (i.e., greater values of β_E), infection prevalence will increase rapidly (Figure 5b), but at the cost of increasing host mortality (Figure 5d). Therefore, infection prevalence will reach its maximum at an intermediate stress level but will drop as population densities are too low to sustain transmission. In contrast, as transmission is more negatively affected by stressors (i.e., pathogens are negatively affected by stressors), infection prevalence will quickly reach zero with increasing environmental stress (Figure 5b). But as stress increases and persists, populations will decline after pathogen extirpation (Figure 5d). Importantly, our models suggest that high pathogen prevalence and/or stressors can result in host population extinction.

Our models illustrate that the consequences of stress gradients on disease can depend on the sensitivity that host traits, such as births and deaths, and shared host–pathogen traits, such as transmission (i.e., β), have to stressors. Interestingly, and consistent with Lafferty and Holt (2003) simulations, our models showed that increased environmental stress generally decreased disease, mainly driven by host density reductions. Although stress can make hosts more likely to become infected at the individual level, at the population level, negative impacts on host survival and reproduction may be

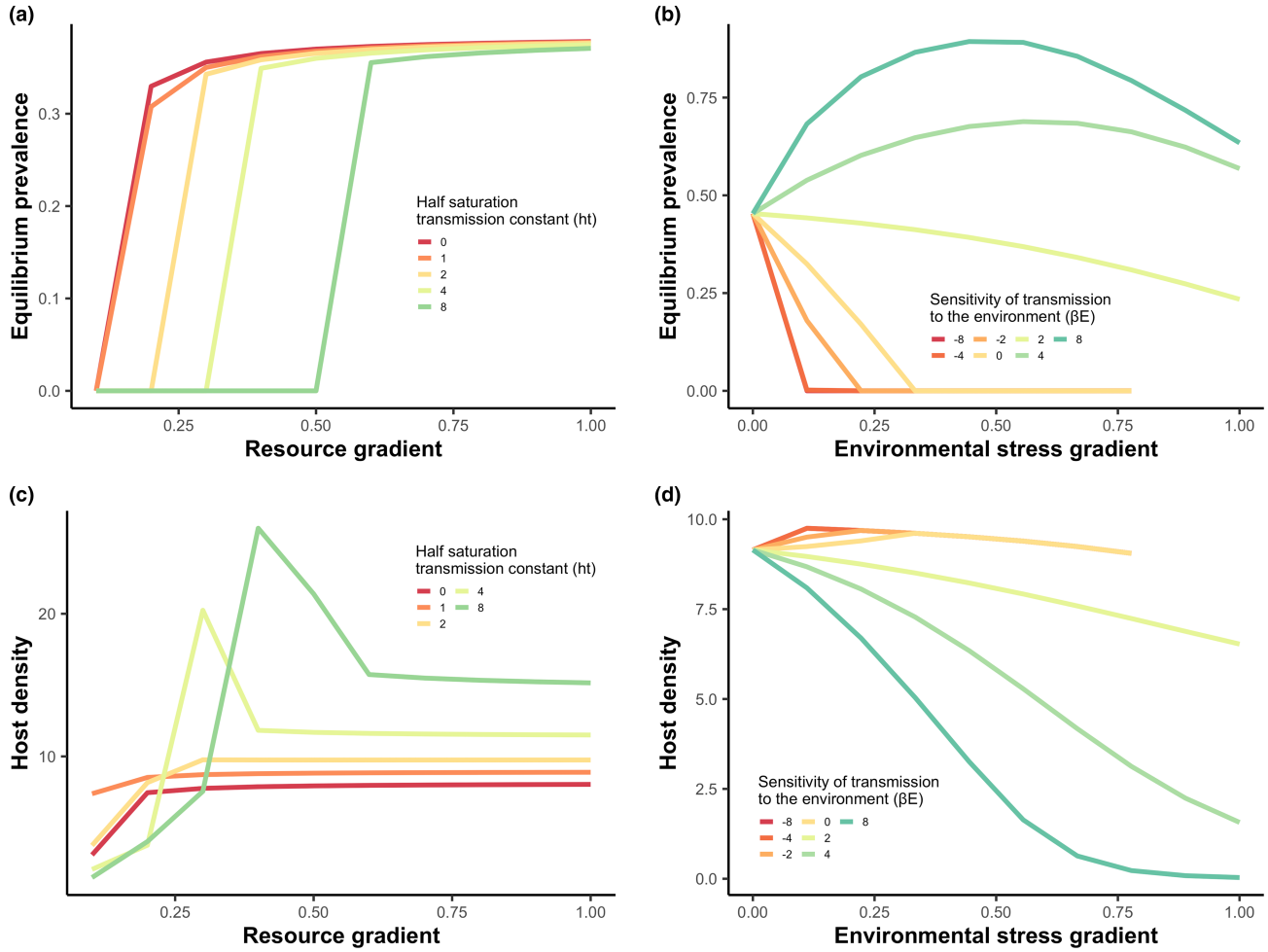

FIGURE 5 Contrasting outcomes for equilibrium prevalence (a, b) and host density (c, d) from hypothetical epidemiological models that illustrate dynamics that rise when fitness traits (survival and fecundity) and infectivity (transmission rate) vary with stressors, as demonstrated by our meta-analysis results. (a) and (c) are simulation outcomes of the SI-Resource model. The half-saturation transmission constant (h_t) determines the transmission rate (β) response to resource availability, where a greater value of h_t makes the β less sensible to resources, and vice versa. (b) and (d) are simulation outcomes of the SI-Environmental stress model. In the model, β could have different sensitivities to environmental factors (β_E), ranging from positive to negative. For parameters used in each model simulation, see Boxes 1 and 2, respectively.

driving pathogen and host local extinctions (Lafferty & Holt, 2003).

DISCUSSION

Stressor type modulates host fitness and infectivity in different ways

Our meta-analysis documented the dominant effects of stressors on host fitness and pathogen infectivity. Interestingly, we found that infected and uninfected hosts had proportionally similar sensitivity to stressors in relation to survival and fecundity. Furthermore, stressor type determined host fitness and pathogen infectivity outcomes. Although we found that resource limitation decreased host fecundity and pathogen intensity, other authors have described positive, negative and unimodal relationships across animal taxa. For example, Cressler et al. (2014) found that as invertebrates increased their resource uptake, they increased their pathogen intensity, whereas increased resource consumption decreased pathogen intensity in vertebrates. They argued this differential response could be due to distinct immune systems and body sizes (Cressler et al., 2014). Contrary to their results, we found that both vertebrate and invertebrate hosts (which represented most of our data) reproduced less and carried a lower pathogen burden when facing limiting resources. One possible explanation is that hosts invest resources in immune defence at the cost of reproduction. In support of this hypothesis, it has been proposed that illness-mediated anorexia may enhance immune function by acting as a "master switch" that reduces investment in other physiological processes (Hite et al., 2020). For example, Cumnock et al. (2018) showed that malaria-infected mice reduced their food intake and switched from burning sugar (glycolysis)

to fats (ketosis), which influenced host tolerance to infections. Alternatively, resource limitation could negatively affect pathogens, decreasing their capacity to reproduce within hosts. Lastly, resource-limited hosts are often smaller and may carry fewer pathogens, reducing pathogen intensity. This has been reported in the snail-Schistosome system, where smaller snails carry fewer parasites (Civitello et al., 2022). Moreover, in *Daphnia* populations, food shortages reduced body size, with subsequent reductions in the spore loads of a microsporidian parasite (Pulkkinen & Ebert, 2004).

Regarding endogenous environmental stressors, we found that stressed hosts survive less but have higher pathogen intensity. Coping with fluctuating abiotic environments can be energetically demanding for hosts, and human activities may exacerbate the frequency and severity of naturally occurring fluctuations. For example, temperature variation occurs naturally, but climate change makes it unpredictable or more drastic (Harvell et al., 2002; Marcogliese, 2008). When stressed, hosts may not resist infections (increasing pathogen proliferation) and/or compensate for damage done by the pathogen (tolerating infection), as seen when higher temperatures increase coral (*Gorgonia ventalina*) susceptibility to fungus (*Aspergillus sydowii*) while also increasing fungal growth and virulence (Ward et al., 2007).

Finally, we found hosts exposed to pollutants had higher mortality but lower pathogen prevalence. However, we note that these results must be interpreted cautiously, given that the experimental studies included in our meta-analysis intentionally used sub-lethal toxin doses. Low prevalence may be due to hosts dying before replicating and transmitting the pathogen. This result is consistent with mechanistic models of how toxicants influence pathogen transmission, showing that infection prevalence was lower in more contaminated landscapes due to high host mortality (Sánchez et al., 2020). Although pollution can decrease parasitism if infected hosts suffer more than uninfected hosts from pollutant exposure, our analysis showed that hosts are equally sensitive to toxins regardless of infection status. Alternatively, parasites could also be negatively affected by pollution. For example, mortality increased in infected hosts as zinc concentration increased, but parasite burden peaked at intermediate zinc concentrations in a fish–parasite system (Gheorgiu et al., 2006). A follow-up study revealed that both parasite lifespan and fecundity were also negatively affected by zinc (Gheorgiu et al., 2007).

Implications for biodiversity conservation and disease transmission

While there are many examples of human activities conspicuously causing wildlife population declines (Dirzo et al., 2014), more subtle disruptions of host–pathogen interactions can also impact population dynamics. The worldwide amphibian decline constitutes an important example. Although mass amphibian mortalities have been linked to chytrid fungus infections (Lötters et al., 2009), the pathogen alone is not sufficient to cause ongoing declines (Alford et al., 2007; Rollins-Smith et al., 2011; Scheele et al., 2019). Global warming, another culprit of population declines, degrades amphibian conditions (Reading, 2007), increasing susceptibility to the fungus (Cohen, Civitello, et al., 2019; Cohen, McMahon, et al., 2019; Cohen et al., 2020; Garner et al., 2009; Rollins-Smith et al., 2011). In the wild, when pathogens are highly virulent, sick individuals are seldom found, probably due to reduced survivorship and diminished activity when ill. However, sick or dead individuals are conspicuous at infrequent times, such as the beforementioned amphibian mass mortality events (Lötters et al., 2009). As sick animals become more abundant, they could be more commonly detected, indicating an ongoing population decline (green lines in Figure 5b,c) (Beldomenico & Begon, 2016). It is important to note that other strategies to monitor and manage wildlife diseases exist, like targeted surveillance on single species that dominate transmission (Charlier et al., 2022; Streicker et al., 2013).

Effects of multiple stressors (e.g., environmental stressors plus infection) can perpetuate cycles where hosts in poor condition may not respond adequately to infection (e.g., reduced infection resistance or tolerance), further reducing their condition and increasing susceptibility to stressors and additional infections (Beldomenico & Begon, 2016). As most known pathogens are multi-host (Woolhouse et al., 2001), such cycles could affect population- and community-level dynamics (Beldomenico & Begon, 2016). For example, Lafferty and Holt (2003) showed a positive association between stress and disease because transmission did not decrease as a specific host population became rare (as in our models with a single species), posing a threat to other species. White-nose syndrome, an emerging fungal disease in bats, constitutes another notable example. While the disease has severely decimated some bat species populations, other sympatric and closely related species have been largely unaffected while sustaining transmission (Cheng et al., 2021; Langwig et al., 2012, 2016).

Although most of the taxa examined (arthropods, molluscs, amphibians and fish) are not commonly associated with zoonotic events, insights are gained by identifying generalities across taxa and comparing them with other systems. For instance, we found that pathogen intensity increased in hosts exposed to environmental stressors, suggesting negative implications for public health. Under stressful conditions, individuals could become superspreaders, amplifying pathogen transmission potential and disease risk (Faust et al., 2017; Gervasi et al., 2015; Lloyd-Smith et al., 2005). Consequently, they could increase intra- and inter-species transmission and pose a risk for spillover to humans and domesticated

animals (Faust et al., 2018; Plowright et al., 2017). For example, nutritional stress has been identified as a primary risk factor for Hendra virus infection in flying foxes (*Pteropus* sp.), leading to spillover events that affected livestock and humans (Becker et al., 2023; Eby et al., 2023; Plowright et al., 2015).

Future directions and concluding remarks

Our analyses included only experimental studies, with hosts exposed to a single parasite species and a single stressor. This approach, although easier to interpret and valuable to tease apart stressor effects in host–pathogen interactions, is difficult to translate to the natural world, where populations are likely exposed to multiple pathogens and a combination of stressors. When considering co-infections, for instance, stressors may compromise one arm of immune defence, making hosts more vulnerable to pathogens that require such a response. For example, food restriction increased levels of eosinophils in capybaras (a Th2 immune response) and consequently reduced nematode burden (where resistance relies on the Th2 response), but coccidian infection intensity increased due to an inadequate Th1 immune response (Eberhardt et al., 2013). Future studies should use a combination of field and laboratory experiments to perturb processes that covary with stressors to determine how and why results vary when comparing laboratory and real-world conditions.

As a next level of complexity, host–pathogen systems do not occur in isolation, and some other biotic stressors and interactions can indirectly affect disease dynamics. For example, hosts compete for resources with other species and are consumed by predators. Consequently, stressors can affect other community members in ways that could enhance or negate epidemiological effects on hosts and pathogens (Strauss et al., 2015, 2016). Furthermore, most known pathogens infect multiple host species (Woolhouse et al., 2001), but some host species are disproportionately responsible for parasite transmission (Haydon et al., 2002). Generally, ecologically resilient species exhibit fast life histories and invest less in immune defence compared to more disturbance-sensitive species (Johnson et al., 2012; Pap et al., 2015; Previtali et al., 2012), predicting that resilient species will have insufficient immune response to prevent pathogen replication and transmission, resulting in higher transmission rates. Therefore, future research is sorely needed to evaluate the effects stressors have on different host species and their relative contribution to community disease transmission.

Moreover, combining experimental and modelling approaches is needed to move beyond associational patterns towards a mechanistic understanding of how stressors affect hosts and pathogens due to the common occurrence of multiple simultaneous stressors. Approaches are available for incorporating stressors into epidemiological models, such as examining variation in R_0, the basic reproductive number of a parasite (Anderson & May, 1991). Pinpointing when and how stressors increase or decrease R_0 is crucial to understanding their roles in infectious disease dynamics. Though multiple mechanisms (including changes in host contact rates and per-contact probability of transmission) are often subsumed in the transmission parameter β, these need not be fixed, as we have illustrated with our models. The same applies to birth and death rates and even to pathogen virulence, given that variation in host immune defences alters per-contact transmission probabilities and the duration of the infectious period. As a next step, integrating a series of models with empirical results will inform the generality of predicted patterns.

Finally, our study highlights the need to expand empirical research at the interface of stress and infectious disease in highly relevant systems for zoonotic disease emergence. The studies included in our meta-analysis had low coverage of vertebrates and terrestrial systems, yet terrestrial vertebrates such as rodents and bats have been linked repeatedly to zoonotic diseases affecting humans and livestock (Han et al., 2016; Luis et al., 2013). However, only one rodent study provided sufficient data to be included in our meta-analysis (Eze et al., 2013).

As anthropogenic activities continue to alter ecosystems in ways that facilitate disease emergence worldwide, we must consider stressor effects on disease dynamics. Our findings improve our understanding of this interplay and provide insights for predicting and mitigating the impacts of stressor–pathogen synergies on human, animal and planetary health.

AUTHOR CONTRIBUTIONS

Amanda Vicente-Santos conceived the study. Amanda Vicente-Santos, Beatriz Willink, David J. Civitello and Thomas R. Gillespie designed the project and plans for data collection. Amanda Vicente-Santos, Beatriz Willink and Kacy Nowak collected data. Amanda Vicente-Santos, Beatriz Willink, Kacy Nowak and David J. Civitello analysed the data. Amanda Vicente-Santos, Beatriz Willink and David J. Civitello designed figures and tables with inputs from all authors. Amanda Vicente-Santos and David J. Civitello conceived and created the models. Amanda Vicente-Santos, Beatriz Willink and Thomas R. Gillespie drafted the manuscript. All authors revised and edited the manuscript for intellectual content.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Data and code are available from the Dryad Digital Repository (https://doi.org/10.5061/dryad.zw3r228cd).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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