TITLE: Scaling effects of temperature on parasitism from individuals to host–parasite systems

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ABSTRACT

Parasitism is expected to change in a warmer future, but whether or not warming leads to substantial increases in parasitism remains unclear. Understanding how warming effects on parasitism in individual hosts (e.g., parasite load) translates to effects on population-level parasitism (e.g., prevalence, R_0) remains a major knowledge gap. We analyzed the temperature dependence of parasitism at both host and population levels in eight empirical mosquito-borne host–parasite systems and found a very strong positive correlation between the thermal optima of individual- and population-level parasitism. By contrast, we did not find a significant correlation in five empirical environmentally-transmitted host–parasite systems. Likewise, parasitism thermal optima were close to host performance thermal optima in mosquito-borne systems but not in environmentally-transmitted systems. We then adapted and simulated simple models for both transmission modes and found a similar pattern to the empirical systems: thermal optima in mosquito-borne systems were more strongly correlated across scales compared to environmentally-transmitted systems. Generally, our results suggest that information on the temperature-dependence, and specifically the thermal optimum, at either the individual- or population-level should provide a useful—though not quantitatively exact—baseline for predicting temperature dependence at the other level in mosquito-borne parasite systems. By

contrast, environmentally-transmitted parasitism may operate by a different set of rules, suggesting the need for trait-based studies of temperature-dependence at individual and population levels in these systems.

INTRODUCTION

Climate change is causing organisms to increasingly face temperatures warmer than their optima for physiological performance. These changes in temperature can alter species interactions (Kordas et al., 2011; Thomas and Blanford, 2003), and there is growing evidence that climate change has impacted interactions between individual hosts and their parasites as well as parasite dynamics and outbreaks in host populations (Ben-Horin et al., 2013; Bruno et al., 2007; Claar and Wood, 2020; Harvell et al., 2019; Koelle et al., 2005; Lafferty and Mordecai, 2016; Rohr et al., 2011). Predicting the effects of temperature and changing climate on infectious disease is an urgent priority (Altizer et al., 2013), yet research tends to focus on the level of either an individual host's biology or of host populations, but rarely both.

Understanding how individual-level interactions between hosts and parasites scale to the population level is key for mitigating disease (Fenton, 2008). Indeed, host–parasite interactions span multiple levels of biological organization, from individual cell biology, physiology, and immunology to population dynamics and dispersal among populations, and bridging these levels is an important research area (Handel and Rohani, 2015). Crucially, each of these processes and the traits that underlie them may be temperature dependent. However, whether or not the effects of temperature on individual-level parasitism (e.g., on parasite load) typically match the effects of temperature on population-level parasitism (e.g., on parasite prevalence or on the basic reproduction number, R_0) remains an open research gap, as does whether differences in the host–parasite system should affect how thermal effects scale between levels. Understanding the effects

of temperature on both individuals and populations is critical for disease prevention and mitigation efforts as the world warms because if the effects are similar across levels of organization, we can leverage observations of the thermal dependence of parasitism at one level to inform predictions in more complex systems. However, if effects of temperature differ across biological scales, using observations on the thermal dependence at one level to extrapolate to the other could provide erroneous predictions for how warming will affect disease in a system.

Beyond exploring how the optimal temperature for parasitism scales across levels, comparing the thermal optima for parasitism to that of the uninfected host can provide a more holistic view of how warming should affect a host–parasite system. One potential framework for doing this is the thermal mismatch hypothesis (Cohen et al., 2017). This hypothesis predicts that parasitism is maximized at temperatures away from the host's optimum—i.e., parasitism peaks at cool temperatures for warm-adapted host species and at warm temperatures for cold-adapted species—at both the host individual and host population levels (Cohen et al., 2019a, 2019b, 2017). Thermal mismatches were first documented in amphibian–chytrid fungus (*Batracochytrium dendrobatidis*, *Bd*) systems at both the individual and population levels (Cohen et al., 2017). More recently, Cohen et al. (2020) analyzed >2000 host–parasite combinations at the population level and found evidence for population-level thermal mismatches: hosts from cool climates had increased disease prevalence at warm temperatures and vice versa. However, outside of amphibian–*Bd* systems, it is unclear whether systems with thermal mismatches at the population level will also exhibit thermal mismatches at the individual level. How the optimal temperatures for individual- and population-level parasitism compare to the optimal temperature for the host may mediate how climate change will affect host–parasite interactions: decreased host performance at warmer temperatures could either be compounded by increasing parasitism or mitigated by decreased parasitism.

Here, we tested whether there is empirical and theoretical evidence to support the idea that the temperature dependence of parasitism at one level (individuals) approximates temperature dependence at a higher level (populations). First, we surveyed the literature and identified thirteen systems that report temperature dependence of parasitism and host performance at multiple levels. Each system was either vector-borne or environmentally-transmitted, and we hypothesized that thermal optima may scale differently in these two types of systems. We therefore re-analyzed the data separately to test for significant correlations in thermal optima (T_{opt}) across levels in both types of systems. Next, we compared thermal optima of individual- and population-level parasitism to the thermal optimum of host performance in these thirteen systems to test whether the thermal mismatch hypothesis holds across levels in these systems. Finally, we generated and simulated simple temperature-dependent models for vector-borne and environmentally-transmitted parasite systems to test our hypotheses that transmission mode and underlying trait relationships affect how T_{opt} scales. Our findings provide a first step towards finding general rules for how warming temperatures will affect parasitism across biological levels of organization in different types of host–parasite systems.

OVERVIEW OF THERMAL OPTIMA AND PARASITISM

Obtaining, summarizing, and comparing thermal responses across levels of organization can be difficult and sometimes unfeasible. Fortunately, most thermal response curves, which project a continuous relationship between a focal trait or process and temperature, have a characteristic non-linear shape with a single optimal temperature at which performance is maximized (the thermal optimum, or T_{opt})(Angilletta, 2006; Huey and Kingsolver, 1989; Huey and Stevenson, 1979). In this study, we therefore focus on and compare thermal optima, as these data are more widely available for many host–parasite systems than full thermal response curves.

Though it does not represent the complete thermal response as a TPC would, T_{opt} is a useful metric for comparison both across levels of organization and among taxa because it determines the range of temperatures at which warming has a positive effect on parasitism (for $T < T_{opt}$) versus a negative effect (for $T > T_{opt}$). Other metrics, such as thermal breadth and the minimum and maximum temperatures that allow survival and growth (known as critical thermal minima and maxima), would provide additional information about how climate change could affect host–parasite interactions at the margins of thermal tolerance.

The thermal optima of parasitism could either match or differ across biological levels of organization. First, we may expect a match between optimal temperatures for parasitism at the individual and population levels because processes across the two levels can be linked (Ewald, 1983; Frank, 1996; Handel and Rohani, 2015; Mideo et al., 2011). For example, if the rate-limiting process for population-level parasitism directly depends on a temperature-dependent metabolic rate of the host and/or parasite, then the outcome of individual host–parasite interactions may also depend on temperature (such as if transmission rates scale with individual parasite load (McCallum et al., 2017)) and the effects of temperature on individual-level parasitism may propagate directly to the population level (Anderson and May, 1979). Indeed, trait-based models have shown that temperature-dependence of underlying traits can cause the basic reproduction number R_0—a key metric in determining if a parasite will or will not cause an epidemic in a host population—to vary with temperature in both vector-borne and environmentally-transmitted parasite systems (Molnár et al., 2013b; Paaijmans et al., 2009; Tesla et al., 2018). From this perspective, the thermal optima of parasitism at the two levels are unlikely to be independent in many systems.

On the other hand, temperature may not have the same effects across levels, even in cases where population-level parasitism is dependent on the dynamics of individual-level parasitism.

Indeed, in research on the effects of anti-parasite treatments, models and field experiments have shown that treatment effects on individual hosts do not necessarily lead to equivalent effects in host populations (Fenton, 2013; Pedersen and Antonovics, 2013). The process of parasite transmission among hosts can potentially decouple population dynamics of hosts and parasites from dynamics within host individuals, particularly if the traits that shape the transmission process are temperature dependent (e.g., temperature-dependent activity rate; Casey, 1976). If the thermal optima of traits that affect transmission are much higher or much lower than that of individual-level parasitism, we may expect the thermal optimum of population-level parasitism to be pulled away from the individual-level optimum towards those of transmission-related traits.

One potentially important factor for determining how the temperature-dependence of parasitism scales is the parasite transmission mode. Parasites can be transmitted through the environment, directly (host-to-host), via a vector (often an arthropod such as a mosquito or tick), or through other modes. Vector-transmitted parasites depend on the vector's ability to successfully transmit the parasite into the host, thereby potentially linking the individual and population levels because parasite growth within the vector can increase the chance of successful transmission (Ohm et al., 2018). Additionally, parasites are often considered to be less virulent within their vectors compared to within their hosts (Wilson et al., 2017), better allowing the parasite to grow within the vector while not greatly diminishing the vector's ability to survive and contact hosts (though see Hu et al., (2008) and Cator et al., (2015) for examples of parasites affecting vector fecundity and behaviour, respectively). By contrast, environmentally-transmitted parasites are not dependent on either a vector or host's ability to contact other hosts. This means that once a parasite is released into the environment, its ability to survive (and in some systems grow and move) and eventually contact a new host will depend only on its own temperature-dependence. This may lead to a disconnect between the optimal temperature for the parasite

within the host (which depends on both host and parasite temperature-dependence) and population-level transmission and parasitism.Directly-transmitted parasites may fall somewhere in the middle of this spectrum, in which parasites are not dependent on a vector but are also not in the environment long enough for their own temperature-dependence to play a large part.

RESULTS

Empirical systems

The thirteen empirical systems we analyzed demonstrated a range of thermal optima for individual-level parasitism (11.8°C – 29.3°C) and population-level parasitism (14.7°C – 29.1°C)(Table 1). We found that population-level parasitism T_{opt} was significantly positively correlated with individual-level parasitism in mosquito-borne systems (Fig. 1a; Pearson correlation = 0.974; 95% CI: 0.860 - 0.995; n = 8). We found a non-significant, positive trend in the environmentally-transmitted systems, for which we had a lower sample size (Fig. 1b; Pearson correlation = 0.522; 95% CI: -0.667 - 0.962; n = 5). All eight mosquito-borne systems exhibited thermal optima at individual and population levels that were within 2.5°C of each other, while only one of the five environmentally-transmitted systems exhibited optima that were within 2.5°C across levels (Fig. 1, Table 1). The largest difference across levels appeared in the *D. magna–O. colligata* system in which individual-level parasitism peaked at a temperature that is 7°C cooler than the peak for population-level parasitism. Nine of the thirteen systems exhibited higher thermal optima for population-level parasitism than individual-level parasitism, though in most cases this difference was small (Fig. 1; points above the dashed 1:1 line).

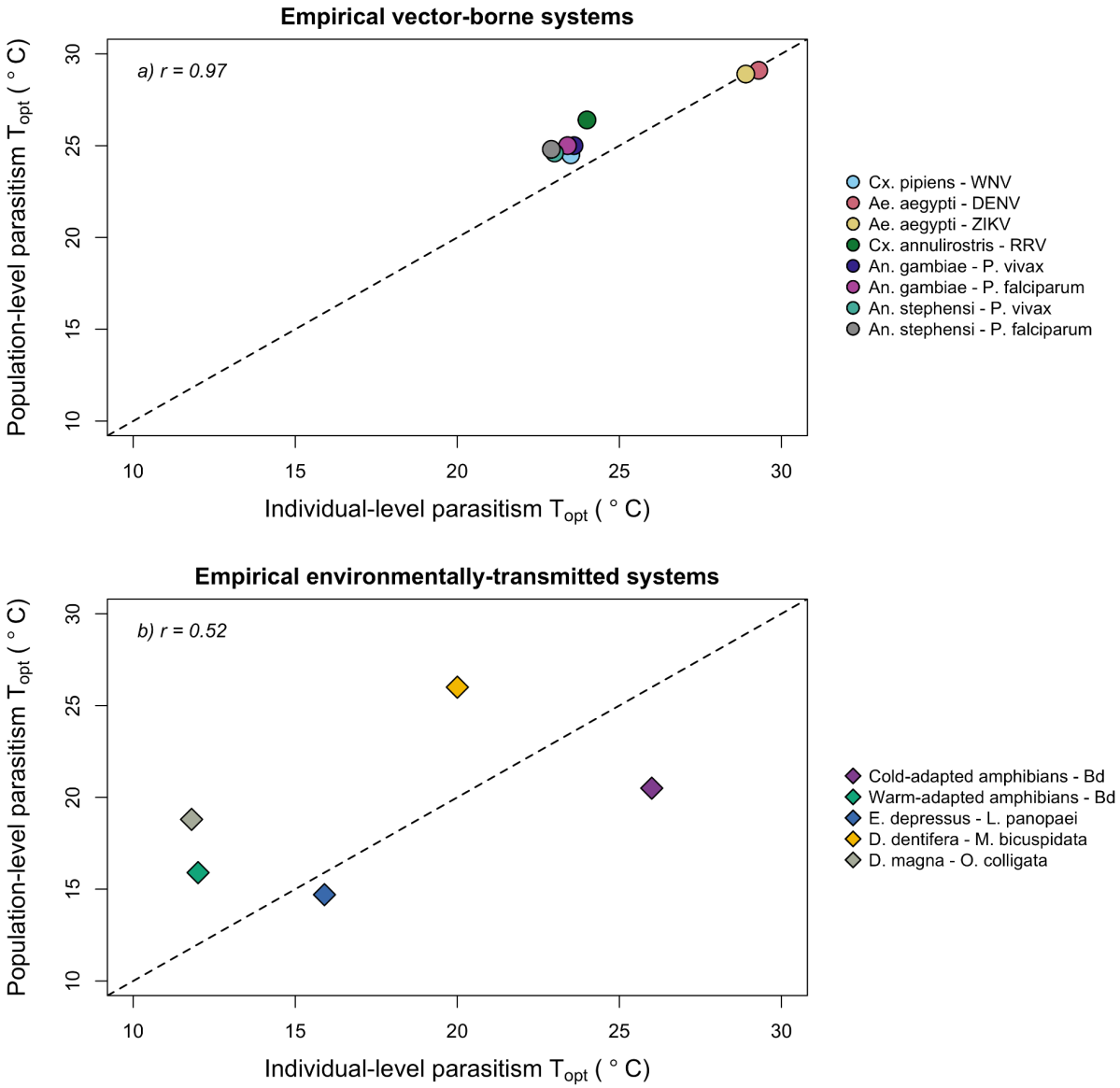

Figure 1. The thermal optima of population-level parasitism are significantly positively correlated with the thermal optima of individual-level parasitism in mosquito-borne but not environmentally-transmitted systems. We found a significant, positive correlation between population-level parasitism thermal optima (T_{opt}) and individual-level parasitism T_{opt} in mosquito-borne systems (a; Pearson correlation = 0.974; 95% CI: 0.860 - 0.995; n = 8), and a non-significant, positive relationship in environmentally-transmitted systems (b; Pearson correlation = 0.522; 95% CI: -0.667 - 0.962; n = 5). Nine of the thirteen systems exhibited higher thermal optima for population-level parasitism than for individual-level parasitism (i.e., fall above the dashed 1:1 line).

Next, we compared the thermal optima of parasitism at both levels to T_{opt} for host performance (Fig. 2). If a system was situated at the origin in Fig. 2, it would have individual-level parasitism, population-level parasitism, and host performance maximized at the same temperature (i.e., no thermal mismatches exist). Displacement from the origin represents parasitism peaking at temperatures away from where host performance peaks (i.e., thermal mismatches at one or both levels). We found that over half (7/13) of the systems were situated close to the origin (arbitrarily defined here as within Euclidian distance of 2.5°C, represented by the circle in Fig. 2). However, all seven of these are mosquito-borne parasite systems, with the only mosquito system exhibiting strong thermal mismatches being *Cx. pipiens*–West Nile virus, in which both infected days and R_0 peak at temperatures nearly 10ºC higher than host performance (Fig. 2). The cold adapted amphibian–*B. dendrobatidis* system was also situated in the far upper-right quadrant (Fig. 2), showing strong thermal mismatches at both levels of parasitism. Two systems showed cold-temperature mismatches at both levels: the crab *E. depressus–L. panopaei* and warm-adapted amphibian–*B. dendrobatidis* host–parasite systems. The zooplankton *D. dentifera–M. bicuspidata* system exhibited a thermal mismatch at cold temperatures at the individual level but no mismatch at the population level. Finally, the zooplankton *D. magna–O. colligata* system showed a distinct pattern of differing thermal mismatches across levels (Fig. 2): individual-level parasitism was maximized at a lower temperature than host performance while R_0 peaked at a higher temperature than host performance. None of the thirteen systems showed positive individual-level mismatches but negative population-level mismatches; therefore, the lower-right quadrant of Fig. 2 is empty. The six systems that exhibited thermal mismatches generally supported our hypothesis that if mismatches occured they would be at both levels and in the same direction, as more of these

systems were situated in the upper-right or lower-left quadrants of Fig. 2 compared to the upper-left or lower-right quadrants.

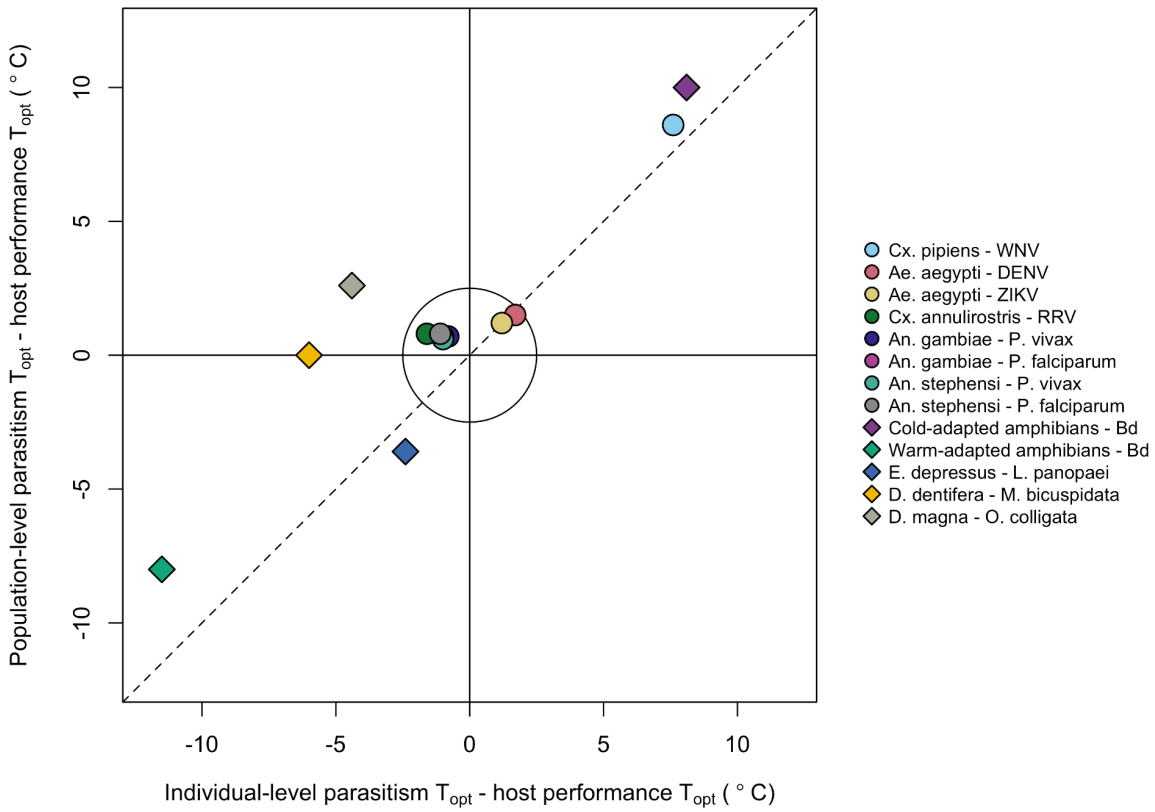

Figure 2. Thermal matches and mismatches tended to be correlated across levels of biological organization. The difference between T_{opt} of population-level parasitism and host performance (y-axis) is plotted against the difference between T_{opt} of individual-level parasitism and host performance (x-axis) for thirteen host–parasite systems. Systems situated at the origin had population-level parasitism, individual-level parasitism, and host performance all maximized at the same temperature (i.e., no thermal mismatches exist), while displacement from the origin represents parasitism peaking at temperatures away from where host performance peaks (i.e., thermal mismatches at individual or population levels). All seven of the systems situated close to the origin (within Euclidian distance of 2.5°C, represented by the black circle) were mosquito-borne parasite systems (circles; in contrast to environmentally-transmitted systems: diamonds).

Simulated systems

We developed and simulated temperature-dependent models to understand how differences in transmission mode or the relationships between traits affect the scaling of T_{opt} at the individual-level (measured as infected days and parasite load for mosquito-borne and environmentally-transmitted systems, respectively) to the population-level (measured as R_0) for mosquito-borne and environmentally-transmitted parasites. Mirroring the empirical results, the simulated mosquito-borne parasite systems showed a significantly stronger positive correlation between individual- and population-level T_{opt} in system (Fig. 3a; Pearson correlation = 0.681; 95% CI: 0.646 - 0.713; n = 1000) compared to any of the three environmentally-transmitted parasite scenarios (Fig. 3b-d). These patterns are qualitatively similar to those found in the empirical systems (Fig. 1), though for both transmission modes, the empirically observed correlations were stronger than those generated in model simulations. This suggests that organismal constraints on thermal performance across traits in empirical systems may strengthen the correlation between thermal performance of different traits and subsequently of parasitism across multiple scales.

The strength of correlation in environmentally-transmitted systems differed significantly depending on the number of relationships between individual-level parasitism and transmission-related processes. Of the three scenarios, we observed the strongest correlation in host–parasite systems in which both parasite shedding rate and the number of parasites released after host death were proportional to parasite load (Fig. 3b; Pearson correlation = 0.412; 95% CI: 0.359 - 0. 462; n = 1000). Systems in which the number of parasites released after host death—but not shedding rate—was proportional to parasite load exhibited a weaker but still significant positive correlation (Fig. 3c; Pearson correlation = 0.257; 95% CI: 0.198 - 0.314; n = 1000). Systems in

which neither of these rates or quantities were proportional to parasite load exhibited no correlation in T_{opt} across scales (Fig. 3d; Pearson correlation = 0.003; 95% CI: -0.059 - 0.065).

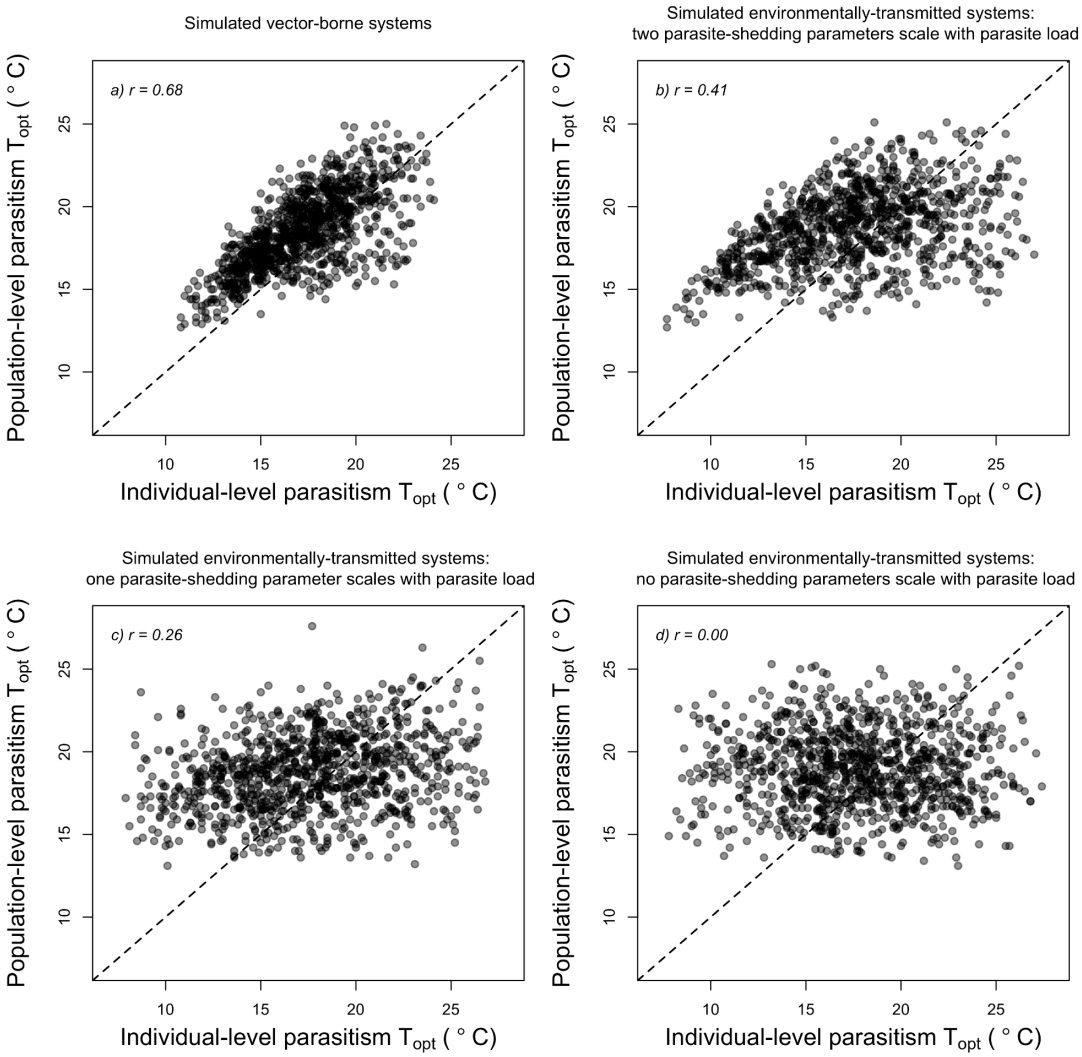

Figure 3. The strength of correlation in simulated systems between thermal optima of individual- and population-level parasitism differs across transmission mode and the number of relationships between individual-level parasitism and transmission processes. Simulated mosquito-borne parasite systems exhibited a stronger positive correlation (a) than environmentally-transmitted parasite systems (c-d).The strength of correlation in environmentally-transmitted systems differed significantly depending on the number of relationships between individual-level parasitism and transmission-related processes (b-d). Dashed black lines represent the 1:1 lines.

DISCUSSION

To predict how warming temperatures will affect parasites and their hosts, we need to understand how effects of temperature on parasitism scale across levels of biological organization, as well as whether this differs systematically across different types of systems. Moreover, understanding how these effects on parasitism compare to thermal effects on uninfected hosts can offer a more complete lens into how climate change will affect host fitness. In our examination of empirical systems, we found a significant positive relationship between parasitism T_{opt} at individual- and population-levels in mosquito-borne but not environmentally-transmitted systems (Fig. 1). Additionally, while individual- and population-level parasitism both peaked at temperatures away from the host optimum in some systems, supporting the thermal mismatch hypothesis, these were almost exclusively environmentally-transmitted, and not vector-transmitted, parasites (Fig. 2), suggesting that thermal mismatches may be more common in certain types of host–parasite systems. Our model also showed how differences in transmission mode and underlying relationships between individual-level parasitism and transmission-related processes can substantially alter the expected relationship between the thermal optima of parasitism in individual hosts and host populations (Fig. 3). Generally, our results suggest that information on the temperature-dependence, and specifically the thermal optimum, at either the individual- or population-level should provide a useful—though not quantitatively exact—baseline for predicting temperature dependence at the other level in mosquito-borne parasite systems, and that caution should be taken when extrapolating thermal dependence between levels, particularly in environmentally-transmitted parasite systems.

We found a significant positive correlation between T_{opt} of population-level parasitism and T_{opt} of individual-level parasitism in the eight mosquito-borne systems (Fig. 1a), suggesting that the effects of warming on parasitism may often be in the same direction across levels in

these types of systems. This is likely because temperatures that allow the parasite to best grow within the vector—while not causing it severe damage—will correspond with temperatures where transmission to humans is high. We did not find a significant correlation in the five empirical environmentally-transmitted systems, though the observed trend across this small number of systems was also positive (Fig. 1b). We may intuitively expect environmentally-transmitted systems to exhibit a relationship that is both positive but not as strong as that observed in vector-borne systems, for several reasons. First, we may expect the positive relationship because quantities and rates at the individual level can still correlate with transmission rates in environmentally-transmitted systems, for example the amount of parasites shed into the environment can increase with individual parasite load (McCallum et al., 2017). However, once parasites have entered the environment, their survival (and potentially growth and movement) is no longer dependent on the host temperature responses that help determine individual-level parasitism. Instead, the environmental parasite's ability to contact and infect a new host will depend on its own temperature-dependent rates in the environment, potentially its new host's movement or contact rates, and in some cases the parasite's ability to behaviourally thermoregulate (Molnár et al., 2013a). Taken together, for parasites that must travel through the environment rather than transmit via a vector, the temperatures that maximize individual-level parasitism may be decoupled from those at which transmission within populations peaks.

Population-level parasitism tended to peak at slightly warmer temperatures than individual-level parasitism in the majority of systems (Fig. 1), meaning that these systems may experience small temperature ranges in which warming leads to increases in population-level parasitism but decreases in individual-level parasitism. In the mosquito-borne systems, this pattern may be because biting rate—a driver of host contact—usually has one of the highest optimal temperatures of all measured traits (Mordecai et al., 2019, 2017, 2013; Shocket et al.,

2018; Villena et al., 2020), thereby shifting R_0 to higher temperatures. The greatest differences in T_{opt} were observed in the zooplankton *D. magna–O. colligata* system, the cold-adapted amphibians–*B. dendrobatidis* system, and the zooplankton *D. dentifera–M. bicuspidata* system (Fig. 1, Table 1). It is difficult to definitively parse out the causes of T_{opt} differences in the two amphibian systems since individual-level *Bd* parasitism was measured on either one or two frog species in the lab while population-level prevalence by the same parasite was synthesized across many field studies encompassing 235 host species (Cohen et al., 2017; see Materials and Methods for more details). However, the *D. magna–O. colligata* system can provide an illuminating example. Contact rate in this host–microsporidian parasite system is maximized at 30.1°C (Kirk et al., 2019). This is nearly 20°C warmer than T_{opt} for individual-level parasitism (11.8°C) and is thus one of the key factors that pulls the thermal optimum of R_0 away from individual-level parasitism T_{opt} to a warmer temperature (18.8°C), illustrating how processes such as contact rate can decouple individual- and population-level temperature dependence.

The thirteen systems analyzed here represent only a small slice of the diversity of host–parasite systems that exist. However, some of the trends found in thermal trait biology may be common in other systems, as temperature-dependent metabolic rates are often conserved across systems, and traits can vary accordingly with metabolic rates (Brown et al., 2004; Dell et al., 2011; Molnár et al., 2017). For example, if, as observed in these systems, traits that drive contact across systems (e.g., biting rate, filtration rate, movement rate) tend to exhibit higher thermal optima than traits that determine individual-level parasitism, our finding that population-level parasitism T_{opt} is typically warmer than individual-level parasitism T_{opt} may be common. More empirical work measuring thermal responses of traits related to parasite transmission in other types of host–parasite systems, such as those with helminth or bacterial parasites—both of which have been shown to be affected by climate (Ben-Haim et al., 2003; Ben-Horin et al., 2013;

Mignatti et al., 2016)—as well as other types of vectors (e.g., ticks, sandflies) and transmission modes can help to broaden our perspective on the scaling of parasitism from individuals to populations in light of climate change.

Our model simulations showed that differences in transmission mode or the number of relationships between individual-level parasitism and transmission-related processes such as parasite shedding rate can affect the scaling of T_{opt}. We found a stronger correlation in mosquito-borne systems (Fig. 3a) compared to environmentally-transmitted systems (Fig. 3b-d), qualitatively similar to the patterns found in empirical systems (Fig. 1). The quantitative correlations observed were weaker than for the empirical observations, which was not surprising since our models only seeked to describe hypothetical mosquito-borne and environmentally-transmitted host–parasite systems with trait thermal responses drawn at random, ignoring any correlations in thermal responses among traits that are likely to occur in most biological systems. Our model also showed that systems that have more relationships between individual-level parasitism (e.g., parasite load) and processes that affect transmission (e.g., parasite shedding rate) will exhibit stronger scaling of parasitism T_{opt} (Fig. 3b-d). This intuitive result suggests that knowledge of how transmission-related processes do or do not depend on individual-level parasitism in a system can help predict whether the temperature-dependence of parasitism should scale in that system.

The thermal mismatch hypothesis (Cohen et al., 2020, 2019a, 2019b, 2017) has been proposed as an approach for understanding the effects of climate change on host–parasite systems, predicting thermal mismatches in which T_{opt} for parasitism occurs at temperatures away from host T_{opt} due to larger organisms (hosts) generally having narrower thermal breadth than smaller organisms (parasites; Rohr et al., 2018). While empirical evidence shows that thermal mismatches do occur at the population level across many animal systems (Cohen et al., 2020),

the novel hypothesis we tested here is that thermal mismatches at the individual level will correspond with similar thermal mismatches at the population level. Of the five non-mosquito systems we explored—including the two amphibian–*Bd* systems investigated previously—parasitism tended to peak at temperatures away from the host's optimum in each, meaning that these systems experience thermal mismatches at one or both levels. Our hypothesis was that most systems experiencing thermal mismatches would fall in the upper-right or lower-left quadrants of Fig. 2, rather than the upper-left or lower-right, and we found that this was generally the case. Evidence for thermal mismatches occurring at either level was weak in the mosquito–parasite systems. Seven of eight mosquito–parasite systems were situated close to the origin (Fig. 2), suggesting that parasitism and host performance are maximized at close to the same temperatures and that thermal mismatches do not occur at either level. Notably, when testing for thermal mismatches at the population level, Cohen et al. (2020) also found that thermal mismatch effects were strongest in systems without vectors (or intermediate hosts). Why we observed this pattern in mosquito systems will require further investigation in different vector-borne systems, though it may be related to parasites often causing relatively little harm to their vector (Wilson et al., 2017).

To better understand how temperature affects parasitism and to make better predictions for how climate change will affect host–parasite interactions across biological levels, we highlight two important research directions. First, when possible, studies that use experiments to investigate effects of temperature at the individual level can also be used to parameterize simple models of population-level parasitism (a 'bottom-up' approach). Second, field studies investigating population-level parasitism under different climate or weather conditions, often undertaken by measuring the proportion of individuals infected, should also aim to record measures of individual-level parasitism (a 'top-down' approach). The best direct measure would

be to record parasite load or an analogous metric measuring the parasite on or within the host, but in cases where this is not possible, indirect measures such as host condition may still be informative. Greatly expanding our repertoire of empirical information on different host–parasite systems is critical for understanding the consequences of climate change for human, domestic species, and wildlife disease.

Many studies have investigated the effects of temperature on parasitism (reviewed, for example, in Altizer et al., 2013; Claar and Wood, 2020; Lafferty, 2009; Lafferty and Mordecai, 2016; Marcogliese, 2008; Rohr et al., 2011), though often at only one of either the individual or population levels. Our findings build upon these studies by emphasizing that how temperature affects individual-level parasitism can scale up to affect parasite transmission, prevalence, and the potential for epidemics in host populations, though not always in a 1:1 manner. More broadly, tying together more theory and empirical results to provide general predictions for how climate change will affect parasitism from individuals to ecosystems in a diverse range of hosts and parasites remains an urgent priority as accelerating climate change makes potentially catastrophic temperature increases of > 2°C increasingly likely by 2050.

MATERIALS & METHODS

Empirical systems

We sought to test hypotheses related to the scaling of thermal optima of both hosts and parasites in empirical systems. We searched for systems for which measures of individual-level parasitism (e.g., parasite load within or on the host (number of parasites), parasite growth rate on or in the host (d^{-1})), population-level parasitism (e.g., the basic reproduction number R_0, prevalence (infected hosts/total hosts)), and host performance (e.g., lifetime reproduction (offspring)) were

estimated across multiple (minimum 4) temperatures, allowing us to identify T_{opt} for each of the measures. We identified thirteen systems that matched these requirements (Table 1): four mosquito–virus systems (Mordecai et al., 2013, 2017; Shocket et al., 2018; Shocket et al., 2020; Tesla et al., 2018); four mosquito–malaria parasite systems (Villena et al., 2020); two *Daphnia*–parasite systems (*D. magna–O. Colligata*, Kirk et al., (2020, 2018), *D. dentifera–M. Bicuspidata*, Shocket et al., (2018); two amphibian–*B. dendrobatidis* (*Bd*, the causative agent of chytridiomycosis) systems (Cohen et al., 2017); and one crab–rhizocephalan barnacle parasite system (*E. depressus–L. Panopaei*, Gehman et al., (2018)). The parasites in these systems are all either vector-transmitted (n=8) or environmentally-transmitted (n=5). While the mosquito systems are mainly studied with respect to human disease, here we leverage the rich data on their thermal dependence to explore thermal scaling of the mosquito–parasite interaction, which in turn affects transmission to humans and is of major concern for its potential response to climate change (Patz et al., 1995; Zhou et al., 2004).

Host performance, individual-level parasitism, and population-level parasitism were measured using different metrics in different systems (Table 1; Supporting Information). We report a single host T_{opt} value for eleven of the systems, but two host T_{opt} values (individual and population) for the amphibian systems. This is because individual-level parasitism for cold-adapted and warm-adapted amphibians was measured in the lab across one and two host species, respectively (Cohen et al., 2017), but the thermal response of population-level parasitism was reported as *Bd* prevalence in the field as a function of environmental temperature for 235 surveyed species, where cold- and warm-adapted amphibians were categorized as those at locations where 50-year mean temperature was <15°C or >20°C, respectively (Cohen et al., 2017). We therefore used separate T_{opt} values for our individual-level host performance

(measured as thermal preference in the lab) and population-level host performance (measured as the mean climatic temperature experienced in the field across surveyed species).

While we were generally constrained to use whichever metric of parasitism or host performance was reported in each study, we had access to thermal response data for several different metrics in the mosquito–parasite systems. We chose to use the number of infected days as our measure of individual-level parasitism in these eight systems because it is a composite metric reflecting the effect of temperature on parasite development rate within the mosquito, vector competence (the mosquito's ability to acquire and transmit the parasite), and mosquito survival. We were also interested in how this choice affected our findings of how closely T_{opt} of individual-level parasitism matched T_{opt} of population-level parasitism and T_{opt} of host performance. Generally, using vector competence as a metric of individual-level parasitism gave similar results to our main metric of infected days, but parasite development rate tended to exhibit higher T_{opt} values than the other two metrics (Fig. S3). The Supporting Information contains further details on both our model and the methods used to analyze the empirical systems.

We hypothesized that thermal optima in vector-borne systems may scale differently from individual-level parasitism to population-level parasitism compared to thermal optima in environmentally-transmitted systems. We therefore separated the thirteen systems by transmission mode and tested for a significant correlation in vector-borne systems (n=8) and in environmentally-transmitted systems (n=5) by comparing population-level parasitism T_{opt} to individual-level parasitism T_{opt} using the *cor.test* function in the R package *stats* (R Core Team 2020; method = *pearson*). In some of these systems, metrics used to calculate individual-level parasitism T_{opt} are also a subset of the metrics used to calculate population-level parasitism T_{opt}. For example, the thermal response of mosquito mortality rate is one of several components used

to calculate individual-level parasitism in mosquito–parasite systems, and also one of many components used to calculate population-level parasitism in the same systems. As a result, observed thermal optima for population-level parasitism are not independent from observed thermal optima for individual-level parasitism. While this may affect the interpretation of the observed correlation across systems, we argue that the partial dependence of population-level parasitism on what occurs at the individual-level is biologically realistic for many systems.

Next, using the same systems, we compared T_{opt} for individual- and population-level parasitism to T_{opt} of host performance to determine whether parasitism generally peaked at temperatures away from host thermal optima as predicted by the thermal mismatch hypothesis (Cohen et al., 2019a, 2019b, 2017), whether thermal mismatches at the individual level corresponded to thermal mismatches at the population level, and whether these results were dependent on transmission mode.

TABLE 1. Thermal optima of parasitism and host performance for thirteen host–parasite systems. The first eight systems are vector-borne, and the last five systems are environmentally-transmitted.

Host – parasite system	Measure of host performance	Measure of individual-level parasitism	Measure of population-level parasitism	Host performance T_{opt} (°C)	Individual-level parasitism T_{opt} (°C)	Population-level parasitism T_{opt} (°C)	Reference
Culex pipiens – West Nile virus	Adult reproduction weighted by lifespan	Infected days	R_0↟	15.9	23.5	24.5	Shocket et al. 2020
Aedes aegypti - dengue virus	Adult reproduction weighted by lifespan	Infected days	R_0	27.6	29.3	29.1	Mordecai et al. 2017
Aedes aegypti - Zika virus	Adult reproduction weighted by lifespan	Infected days	R_0	27.7	28.9	28.9	Tesla et al. 2018
Culex annulirostris – Ross River virus	Adult reproduction weighted by lifespan	Infected days	R_0	25.6	24.0	26.4	Shocket et al. 2018a
Anopholes gambiae - *Plasmodium*	Adult reproduction weighted by lifespan	Infected days	Transmission suitability	24.4	23.6	25.0	Villena et al. 2020
Anopholes gambiae - *Plasmodium*	Adult reproduction weighted by lifespan	Infected days	Transmission suitability	24.4	23.4	25.0	Villena et al. 2020
Anopholes stephensi - *Plasmodium*	Adult reproduction weighted by lifespan	Infected days	Transmission suitability	24.0	23.0	24.6	Villena et al. 2020
Anopholes stephensi - *Plasmodium*	Adult reproduction weighted by lifespan	Infected days	Transmission suitability	24.0	22.9	24.8	Villena et al. 2020
Cold-adapted amphibians - *Batrachochytriu*	Temperature preference for individuals; mean	Parasite growth rate on host	Prevalence	17.9 (10.5) †	26.0*	20.5	Cohen et al. 2017
Warm-adapted amphibians - *Batrachochytriu*	Temperature preference for individuals; mean	Parasite growth rate on host	Prevalence	23.5 (23.9) †	12.0*	15.9	Cohen et al. 2017
Eurypanopeus depressus - *Loxothylacus panopaei*	Uninfected host survival	Parasite lifetime reproduction	R_0	18.3	15.9	14.7	Gehman et al. 2018
Daphnia dentifera - *Metschnikowia*	Uninfected intrinsic growth rate	Spore load	R_0	26.0*	20.0*	26.0	Shocket et al. 2018b
Daphnia magna – *Ordospora colligata*	Lifetime reproduction	Spore load	R_0	16.2*	11.8*	18.8	Kirk et al. 2018, 2020

* T_{opt} for these values was determined as the temperature at which the measure was maximized along a range of discrete experimental temperatures, rather than from a continuous thermal performance curve, as is the case for each other value in the table. For discrete temperature range used, see Supporting Information.

† The first number listed is individual-level host T_{opt}. The number in parentheses is population-level T_{opt}.

↟ R_0 is the basic reproduction number of the parasite in the host population.

Simulated systems

To investigate how different features of a host–parasite system can affect the thermal scaling of parasitism and the observed correlations in T_{opt}, we developed several temperature-dependent models. This allowed us to link temperature-dependent quantities or processes that occur within individuals (and therefore individual-level parasitism) to a key metric of population-level parasitism (the basic reproduction number, R_0) under different assumptions. Our aim was to investigate whether differences in transmission mode and assumptions regarding trait relationships could result in different patterns in the relationship of thermal optima in parasitism across levels, rather than to exhaustively explore all potential outcomes. As such, these models are not meant to represent specific host–parasite systems, but instead represent a generalized mosquito-borne parasite system and a generalized environmentally-transmitted parasite system under specific thermal biology assumptions.

The temperature-dependent mosquito-borne disease model (Eq. 1) describes how the basic reproduction number, R_0, varies with temperature as a function of several temperature-dependent rates and probabilities. R_0 is a commonly-used metric that represents the number of new infections one infected host should cause in a fully-susceptible population: without stochasticity, $R_0 > 1$ should lead to an epidemic and $R_0 < 1$ should lead to parasite extirpation. Our mosquito-borne model was adapted from a temperature-dependent model for dengue from Mordecai et al., (2017), and similar models have been used to describe R_0 as a function of temperature for malaria and other mosquito-borne diseases (Mordecai et al., 2013; Paaijmans et al., 2009; Shocket et al., 2020; Villena et al., 2020):

$$R_0(T) = \left(\frac{a(T)^2\, bc(T)\, e^{-\mu(T)/PDR(T)}\, EFD(T)\, p_{EA}(T)\, MDR(T)}{N\, r\, \mu(T)^3} \right)^{1/2} \qquad \text{Eq. 1}$$

Here, a is per-mosquito biting rate, bc is vector competence, μ is adult mosquito mortality rate, PDR is parasite development rate, EFD is the number of eggs produced per female per day, p_{EA} is egg-to-adult survival probability, MDR is immature development rate, N is density of humans, and r is human recovery rate. Following empirical patterns found across mosquito-borne disease systems (reviewed in Mordecai et al., 2019), we modeled biting rate, parasite development rate, eggs production rate, and mosquito development rate using Brière functions (Eq. 2, as described below), and vector competence, egg-to-adult survival probability, and lifespan using concave-down quadratic functions. Mosquito mortality rate μ was set to 1/lifespan.

The Brière function (Eq. 2) is an asymmetrical unimodal function that is often used to describe thermal performance in biological systems (Briere et al., 1999), where c is a positive rate constant, T_{min} and T_{max} are the minimum and maximum temperatures, respectively, T is temperature, and $B(T)$ is set to 0 when $T > T_{max}$ or $T < T_{min}$.

$$B(T) = cT(T - T_{min})(T_{max} - T)^{1/2} \qquad \text{Eq. 2}$$

The quadratic function (Eq. 3) is a similarly concave-down function that takes three parameters (positive rate constant c, T_{min} and T_{max}) but is symmetrical rather than asymmetrical.

$$Q(T) = -c(T - T_{min})(T - T_{max}) \qquad \text{Eq. 3}$$

To best align with the metrics available from the empirical systems, our metrics for individual-level and population-level parasitism in the mosquito-borne parasite systems are infected days and R_0 (Eq. 1), respectively. Infected days is a function of parasite development rate, vector competence, and mosquito survival (see Supporting Information for additional details on how this is calculated).

We developed the environmentally-transmitted parasite model (Eq. 4) to represent a system in which parasites are shed into the environment throughout the life of an infected host as well as when the host dies. Parasites in the environment can die or infect a susceptible host.

$$R_0(T) = \left(\frac{\chi(T)\,\sigma(T)\,S(T)}{\theta(T)}\right)\left(\frac{\lambda(T)}{\mu(T)+\alpha(T)} + \omega(T)\right) \qquad \text{Eq. 4}$$

Here, $\boldsymbol{\chi}$ is *per capita* contact rate between susceptible hosts and parasites in the environment, σ is probability of infection after contact, S is susceptible host density at equilibrium in a disease-free population, θ is parasite mortality rate in the environment, $\boldsymbol{\lambda}$ is parasite shedding rate from an infected host, μ is host background mortality rate, α is host parasite-induced mortality rate, and ω is the number of parasites released into the environment upon host death. To approximate equilibrium susceptible host density (S), we assumed that S is equal to the ratio of host birth rate to background mortality rate. We also assumed that α was proportional to the number of parasites within the host.

We hypothesized that if processes related to environmental parasite transmission were dependent on parasite load within the host, we would observe stronger correlations in T_{opt} across scale. We therefore simulated the environmentally-transmitted model under three different assumptions. First, we assumed that both parasite shedding rate ($\boldsymbol{\lambda}$) and the number of parasites released into the environment upon host death (ω) were each proportional to parasite load (i.e., individual-level parasitism). Next, we assumed that only the number of parasites released after host death (ω) was proportional to parasite load. Finally, we assumed that neither of these rates or quantities were proportional to parasite load.

We modeled the temperature dependence of parasite load (and therefore parasite-induced mortality rate), parasite shedding rate, parasites released after host death, and probability of infection using the quadratic function (Eq. 3), and contact rate and birth rate as Brière functions

(Eq. 2). We modeled the thermal response of background host mortality rate (μ) and parasite mortality in the environment (θ) using concave-up quadratic functions where mortality is minimized at the thermal optimum and increases at cooler and warmer temperatures, as mortality often shows relatively symmetrical responses across temperature (Angilletta, 2009; van der Have, 2002). The thermal response of susceptible host density (S) is a function of the thermal responses of birth rates and background host mortality rates. Our metrics for individual-level and population-level parasitism in the environmentally-transmitted parasite systems are parasite load (Eq. 3) and R_0 (Eq. 4), respectively.

We simulated 1000 mosquito-borne parasite systems and 1000 environmentally-transmitted parasite systems under each of the three assumptions (n = 3000 total) by randomly drawing different thermal response function parameters $\{c, T_{min}, T_{max}\}$ for each temperature-dependent trait in Eqs. 1, 2, 3, and 4. For both Brière and concave-down quadratic functions, T_{min} was drawn from a uniform distribution between 0-10, T_{max} was equal to T_{min} plus a value drawn from a uniform distribution between 15-35, and the rate constant c was drawn from a uniform distribution between 0.5-1.3. Similarly, for the concave-up quadratic function that describes background host mortality rate and parasite mortality rate in the environment in Eq. 4, we drew parameter a from a uniform distribution between 0.0008-0.0009, b from a uniform distribution between 0.02-0.03, and c from a uniform distribution between 0.1-1. Thermal responses were scaled to realistic magnitudes for each temperature-dependent trait (e.g., all thermal responses for the contact rate parameter were scaled by a factor of 0.0005). See Supporting Information for more detail and Figs. S1-S2 for examples of the simulated thermal responses.

To test our hypotheses that 1) observed T_{opt} correlations would differ between mosquito-borne (Eq. 1) and environmentally-transmitted parasite systems (Eq. 4), and 2) observed T_{opt}

correlations would differ between environmentally-transmitted parasite systems under different trait relationship assumptions, we estimated the correlation between population-level parasitism T_{opt} and individual-level parasitism T_{opt} using the *cor.test* function in the R package *stats* (R Core Team 2020; method = *pearson*) for each of the four cases.

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COMPETING INTERESTS

The authors declare no competing interests.

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