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Meta-analysis and research on host–parasite interactions: past and future

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Abstract Host–parasite interactions are characterised by a lack of stable species-specific traits that limits generalisations one can make even about particular host or parasite species. For instance, the virulence, life history traits or transmission mode of a given parasite species can depend on which of its suitable hosts it infects. In the search for general rules or patterns, meta-analysis provides a possible solution to the challenges posed by the highly variable outcomes of host–parasite interactions. It allows an estimate of the overall association between any factor and its biological response that transcends the particulars of given host and parasite taxonomic combinations. In this review, we begin with a historical overview of the use of meta-analysis in research on the ecology and evolution of host–parasite interactions. We then identify several key conceptual advances that were made possible only through meta-analytical synthesis. For example, meta-analysis revealed the predominant association between rates of host and parasite gene flow and local adaptation, as well as an unexpected latitudinal gradient in parasite virulence, or parasite-induced host mortality. Finally, we propose some areas of research on host–parasite interactions that are based on a mature theoretical foundation and for which there now exist sufficient primary results to make them ripe for meta-analysis. The search for the processes causing variability in parasite species richness among host species, and the link between the expression of host resistance and the specificity of parasites, are two such research areas. The main objective of this review is to promote meta-analysis as a synthetic tool overriding the idiosyncrasies of specific host–parasite combinations and capable of uncovering the universal trends, if any, in the evolutionary ecology of parasitism.

Keywords Parasitism · Host manipulation · Immunity · Sexual selection · Virulence

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Introduction

By their very nature, host–parasite interactions are complex. Often, a parasite can exploit many alternative host species at a given stage of its life cycle, and a host can be used by many different parasite species. This lack of specificity and the intimate nature of the association between a parasite and its host mean that it is difficult to make generalisations even about particular host or parasite species. For example, a given level of virulence cannot be assigned to a parasite, since the same parasite species can cause very different fitness losses in different but closely related host species (Thomas et al. 1995; Jaenike 1996; Rutrecht and Brown 2009). Similarly, the size or fecundity achieved by a parasite, the transmission route it adopts, and whether or not it manipulates host behaviour all depend on which of its suitable hosts it infects (Moore et al. 1994; Poulin 1996a; Bauer et al. 2000), just as the responses of a host to infection or the fitness loss it incurs all depend on which of its suite of parasite species is afflicting it (Clayton and Tompkins 1994; Rauque et al. 2011). In addition, the outcome of host–parasite interactions can show complex spatial or seasonal dynamics and marked context-dependence, independent of the identity of the two antagonists (Thomas et al. 2002). Thus, there is no species-specific 'value' that can be assigned to any host or parasite species; the expression of most traits appears contingent on the identity of the antagonist and on a myriad of other factors. This substantial variability in the outcome of host–parasite interactions places challenging obstacles in the way of attempts to derive general rules or patterns.

Meta-analysis provides a possible solution to these challenges by allowing the formal combination of the results of independent studies to obtain an overall effect size, i.e., an estimate of the global strength of the association between a putative factor and its biological response (Arnqvist and Wooster 1995; Koricheva et al. 2012). Effect sizes found in each individual study, whether statistically significant or not, can be considered as independent estimates of the underlying association between factor and response, subject to random variation. If these independent estimates are combined with more weight given to more precise estimates based on larger sample sizes, then we can obtain a more reliable estimate of the overall effect size (Gurevitch et al. 2001; Gates 2002; Koricheva et al. 2012). Although meta-analysis has well-documented limitations (see Koricheva et al. 2012), it offers an appealing way to cut through the variability in results of studies of host–parasite interactions to uncover overall patterns that transcend the particulars of given host or parasite taxa.

Here, we first provide a historical look at the use of meta-analysis in research on the evolutionary ecology of host–parasite interactions, and identify several key advances made possible by meta-analytical synthesis. We then propose some areas of research on host–parasite interactions that have reached a stage (i.e., mature theoretical foundation and sufficient primary results) at which they are ripe for meta-analysis. Our main objective with this review is to highlight the advantages of meta-analysis as a synthetic tool to see beyond the idiosyncrasies of specific model systems and further our understanding of the complex interactions between hosts and parasites.

History of meta-analyses of host–parasite interactions

In the early to mid-1990s, as the use of meta-analysis spread rapidly among behavioural and evolutionary ecologists (Arnqvist and Wooster 1995; Koricheva et al. 2012), some of the very first applications of this new tool addressed outstanding questions regarding host-parasite interactions. Indeed, in behavioural ecology, the first appearance of ‘meta-analysis’ in either the title or abstract of articles published in some of the leading journals in the field was in studies linking parasitism with host behaviour, i.e., in *Animal Behaviour* (Poulin 1994), *Behavioral Ecology* (Côté and Poulin 1995), and *Behaviour* (Hamilton and Poulin 1997). Therefore, research on host–parasite interactions has led the way in the adoption of meta-analysis by evolutionary ecologists.

To determine whether this early trend continued over time, we performed a search of the ISI Web of Science® database to compare how frequently meta-analysis has been applied to host–parasite research versus research on other areas of behavioural and evolutionary ecology. We used the following search string to identify studies of host–parasite interactions that have used meta-analytical approaches: ‘(metaanaly* or meta-analy*) and (parasit* or pathogen* or disease*) and (ecolog* or evolut* or behav*)’. The title and abstract of all studies retrieved by this search were examined individually to eliminate obviously spurious or irrelevant hits, most of which pertained to human health research not concerned with ecological or evolutionary questions. To obtain comparative data on all studies regardless of whether or not they focused on parasitism, we performed a second search using the same keywords as above but without the terms in the middle parentheses (i.e., without parasit* or pathogen* or disease*). This second search yielded thousands of hits; although these numerous studies might not all relate to behavioural and evolutionary ecology in a strict sense, they nonetheless capture the temporal change in the use of meta-analysis in the broader field outside host–parasite studies. These searches may exclude studies that have used meta-analytical methods without identifying them as such, but should still provide a clear indication of contrasting temporal trends, if any.

The results indicate that evolutionary ecologists in general and those working specifically on host–parasite interactions have expanded their use of meta-analytical methods at roughly the same rate over the past two decades (Fig. 1). Although the absolute numbers of studies involved are vastly different, the relative increase in articles using or mentioning meta-analysis follows very similar cumulative functions for both all studies in behaviour, ecology, or evolution, and for only those dealing with host–parasite interactions. Therefore, at least in terms of how frequently it has been used, meta-analysis has served to synthesize research results on host–parasite biology to the same extent as in other areas of evolutionary ecology. Interestingly, the number of meta-analytic studies has been rising sharply

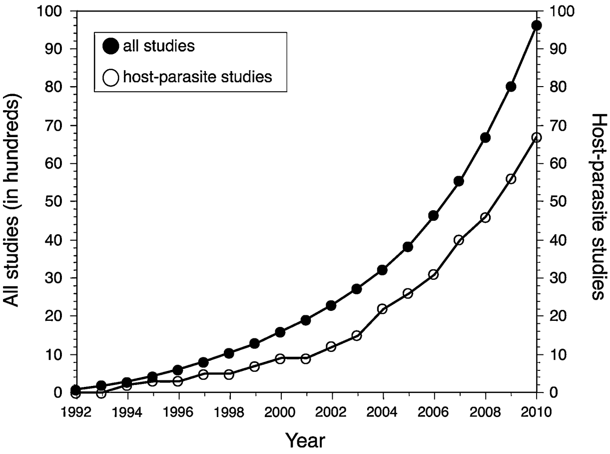

Fig. 1 Cumulative number of articles published in the past two decades using a meta-analytical approach, or mentioning meta-analysis in their abstract or keywords, based on a search of the ISI Web of Science® database. The data are shown for all studies in the area of behaviour, ecology and evolution, and for the subset of studies dealing specifically with host–parasite interactions. Note the different y-axis scales

in recent years, an indication of the method's appeal. Below, we summarize some of its main contributions to our understanding of the complex interactions between hosts and their parasites.

Main insights from meta-analysis

Some authors label their syntheses as meta-analysis even if they do not apply any standard meta-analytical techniques or alternative methods that are roughly equivalent. Conversely, other authors employ meta-analytical approaches without identifying them as such. Here, we consider a study to be a meta-analysis if it uses statistical methods to combine evidence, i.e., results, from several earlier studies or independent analyses that address a common hypothesis or test a common prediction, whether or not its authors have called it a meta-analysis. In general, this normally involves calculating a measure of effect size for each original study or analysis, allowing a weighted average effect size to be estimated. The meta-analyses of host–parasite interactions we retained are listed in Table 1 and the main ones are discussed below. We do not pretend that this list is exhaustive; however, we feel it includes all major contributions to the field that are founded on rigorous meta-analytical synthesis.

Some meta-analyses of host–parasite interactions, although not generating important new insights per se, have nonetheless provided much-needed global assessments of the existing empirical support for important theoretical predictions. For instance, Hamilton and Zuk (1982) hypothesised that parasites were driving forces behind the evolution of secondary sexual characters. Within species, this would mean that heavily-infected males should be less showy than healthy conspecifics; across species, in contrast, we should expect more elaborate secondary sexual characters in species exposed to higher levels of parasitism, because selection for males that advertise their health and for choosy females would have been stronger in those species than in related species exposed to lower infection levels. After the publication of several independent tests of these predictions, meta-analyses revealed a general agreement between results and theory, while identifying the host and parasite taxa and the type of secondary sexual traits for which the effect is strongest (Hamilton and Poulin 1997; Møller et al. 1999; Garamszegi 2005). While some aspects of the Hamilton and Zuk hypothesis remain contentious (see Clayton 1991; Møller et al. 1999), meta-analysis has at least served to evaluate the global empirical support it received from independent studies.

In other cases, meta-analysis can support the existence of patterns expected not from theory, but from known physiological mechanisms. Consider, for example, the known immunosuppressive effect of androgen hormones like testosterone (Grossman 1985; Zuk and McKean 1996; Klein 2004). The expected outcome of this coupling between male hormones and immunity should be, all else being equal, a greater susceptibility of males than females to parasitic infections. A global male-bias in parasitic infections has indeed been demonstrated by separate meta-analyses that have also pointed out the combinations of host and parasite taxa where the bias is strongest (Poulin 1996b; Schalk and Forbes 1997), and identified exceptions or the role of additional factors such as the host's mating system (McCurdy et al. 1998; Moore and Wilson 2002). Interestingly, a meta-analysis also showed that immune activation following parasite infection suppresses testosterone levels (Boonekamp et al. 2008), adding a further twist to the interrelationships between infection, immunity, hormones and sex. The link between immunity and oxidative stress provides a second example of this type of contribution from meta-analysis. The observation that

Table 1 Summary of major findings of meta-analysis applied to research on the evolutionary ecology of host–parasite interactions

General theme and central question	No. of independent effect sizes	Measure of effect size*	Main finding	Reference
Local (and general) adaptation				
Is local adaptation affected by a parasite's host range, i.e., by its host specificity?	32	Item-response effect size	Parasites with broad host ranges are less likely to demonstrate local adaptation than host-specific ones	Lajeunesse and Forbes (2002)
Do parasite infectivity and host resistance show local adaptation in snail-trematode interactions?	32	Hedges' d	Parasites are better at infecting sympatric hosts than allopatric ones; asexual host populations are more resistant to infection than sexually-reproducing ones	Lively et al. (2004)
Do relative migration rate, relative generation time and virulence affect local parasite adaptation?	57	Cohen's w	Parasites with higher migration rates than their hosts show local adaptation; no effect of generation time or virulence	Greischar and Koskella (2007)
Do parasite species traits such as gene flow rate or generation time affect local parasite adaptation?	29	Performance ratio	Parasites with higher gene flow rates than their hosts show local adaptation	Hoeksema and Forde (2008)
Is outcrossing rate in plants related to the number of fungal pathogen species that attack them?	7	Correlation coefficients	There is a significant positive association between outcrossing rate and fungal pathogen richness	Busch et al. (2004)
Manipulation of host behaviour				
Does parasitism influence host behaviour?	114	Hedges' d	Nematodes have greater effects on host activity level and microhabitat choice than other helminths	Poulin (1994)
Do published estimates of the effects of parasites on host behaviour decrease over time?	137	Hedges' d	Estimates of the effects of parasites on host behaviour correlate negatively with their year of publication	Poulin (2000a)
Do published estimates of parasite-induced increases in transmission rate decrease over time?	14	Biased predation	Estimates of parasite-induced boosts in transmission rate correlate negatively with year of publication	Poulin (2000a)
Host social behaviour				
Does host group size correlate with individual infection levels by parasites?	21	Correlation coefficients	Group size correlates positively with infection by contagious parasites, negatively for mobile parasites	Côté and Poulin (1995)

Table 1 continued

General theme and central question	No. of independent effect sizes	Measure of effect size*	Main finding	Reference
Host sexual selection				
Is male showiness associated with parasite load within given species?	18	Hedges' *d*	The expression of secondary sexual traits is largely reduced in parasitised males compared to controls	Hamilton and Poulin (1997)
Is male showiness associated with parasite load within given species?	55	Correlation coefficients	The expression of secondary sexual traits does not correlate with infection levels, except possibly in fish	Hamilton and Poulin (1997)
Is male showiness associated with parasite load across different host species?	45	Correlation coefficients	Host species exposed to higher levels of parasitism have more showy males (particularly among birds)	Hamilton and Poulin (1997)
Is male showiness associated with either parasite load or the strength of immune responses within given host species?	69	Correlation coefficients	Males with few parasites and/or strong immune responses have more showy secondary sexual traits	Møller et al. (1999)
Are various bird song characteristics correlated with levels of parasitism?	27	Effect size correlations	Performance-related characteristics (e.g., song rate) are affected by infection, but not other song traits	Garamszegi (2005)
Sex bias in infection				
Are male hosts more heavily parasitized than females among vertebrates?	295	Hedges' *d*	Male vertebrates have higher helminth prevalence, particularly nematodes in birds and mammals	Poulin (1996b)
Are male hosts more heavily parasitized than females among vertebrates?	169	Hedges' *d*	Male vertebrates have higher intensity of helminths, particularly nematodes in mammals	Poulin (1996b)
Do helminth parasites achieve larger sizes in male vertebrate hosts than in females?	34	Hedges' *d*	Nematodes, but not cestodes, achieve a larger size in male hosts than in female ones.	Poulin (1996c)
Are male hosts more heavily parasitized than females among mammals?	145	Corrected vote-count	Male mammals harbour more protozoan and arthropod (but not helminth) parasites than females	Schalk and Forbes (1997)
Are male birds more heavily parasitized than females by blood parasites?	35	Hedges' *d*	*Haemoproteus* prevalence was higher in breeding females than males, even in polygynous species	McCurdy et al. (1998)
Are parasite infections more prevalent in male arthropod hosts than in females?	61	Hedges' *d*	There was no overall sex bias in parasite infections of arthropods	Sheridan et al. (2000)

Table 1 continued

General theme and central question	No. of independent effect sizes	Measure of effect size*	Main finding	Reference
Is the intensity of parasite infections higher in male arthropod hosts than in females?	31	Hedges' *d*	There was no overall sex bias in parasite infections of arthropods	Sheridan et al. (2000)
Are male hosts more heavily parasitized than females among mammals?	355	Hedges' *d*	Male mammals harbour more helminth and arthropod (but not unicellular) parasites than females	Moore and Wilson (2002)
Host immunocompetence				
Does the strength of non-specific immune responses correlate with survival in birds?	12	Correlation coefficients	Immune function has a moderate-to-large positive effect on bird survival	Møller and Saino (2004)
Is immunocompetence compromised by high levels of testosterone in vertebrates?	36	Hedges' *d*	High testosterone levels do not reduce immunity (after controlling for multiple studies on same species) but increase ectoparasite infections	Roberts et al. (2004)
Does immune activation suppress testosterone levels in birds and mammals?	14	Correlation coefficients	Immune activation strongly reduces testosterone, whether infection is by live pathogens or antigens only	Boonekamp et al. (2008)
Does greater reproductive effort lead to reduced immune responses and increased parasite infections in birds?	66	Correlation coefficients	Greater reproductive effort generally reduces immune responses and increases parasite infections, though results depend on methods used	Knowles et al. (2009)
Does induction of an immune response cause oxidative stress in birds?	49	Correlation coefficients	Immune response causes moderate oxidative stress but has stronger effects on oxidative status markers	Constantini and Møller (2009)
Parasite virulence and host mortality				
What is the effect of *Plasmodium* infection on the survival of mosquito vectors?	24	Correlation coefficients	Mosquito survival more likely reduced in long-term studies or in unnatural vector-parasite combinations	Ferguson and Read (2002)
Do arboviruses reduce the survival of their mosquito vectors?	33	Correlation coefficients	Arboviruses generally reduce mosquito survival, especially alphaviruses or viruses with horizontal transmission	Lambrechts and Scott (2009)
What factors correlate with parasite virulence in bird hosts measured as nestling mortality?	117	Correlation coefficients	Parasite-induced nestling mortality higher at lower latitudes and in bird species with open nests	Møller et al. (2009)

Table 1 continued

General theme and central question	No. of independent effect sizes	Measure of effect size*	Main finding	Reference
Is parasite-induced mortality affected by host or parasite taxon, parasite life cycle stage or environmental conditions?	59	Survival odds ratio (log)	Host mortality higher for certain host or parasite taxa, and higher at lower latitudes	Robar et al. (2010)
Does parasite infection affect the host's resting metabolic rate?	22	Hedges' *d*	Overall, parasitism has no significant effect on host metabolism, though its effects in specific systems can be important	Robar et al. (2011)
Parasite sex ratio and life-history differences between sexes				
Do male and female schistosomes differ in life history strategies at any stage of their life cycle?	61	Hedges' *d*	Some differences (male cercariae more infective, female cercarial output and survival higher) exist between schistosome sexes	Boissier et al. (1999)
Is schistosome sex ratio correlated with worm burden in the mammalian definitive host?	616	Weighted proportions	Generally, the more individual worms infect a host, the more male-biased their sex ratio, in all mammal host species tested	Boissier and Moné (2001)
Parasite biogeography and community ecology				
Does the mean abundance of parasites (fleas and gamasid mites) decrease with increasing distance from their centre of maximum abundance?	22	Correlation coefficients	Mean abundance of parasites generally decreases as a function of distance from the locality where it peaks	Krasnov et al. (2008)
Is the abundance of a parasite species (gamasid mites) influenced by the overall abundance and diversity of the parasite community it belongs to?	29	Correlation coefficients	The abundance of given mite species was generally positively correlated with the combined abundances of all other co-occurring mite species	Krasnov et al. (2009)
Is the proportion of shared parasite species proportional to the phylogenetic relatedness among fish host species?	5	Correlation coefficients	Similarity in parasite faunas decays exponentially, but not strongly, with increasing phylogenetic distance between host species	Poulin (2010a)
Transmission success and patterns of infections				
Which factors influence the relationship between host size and intensity of parasitic infections among conspecific fish?	76	Correlation coefficients	Larger fish do not invariably harbour more parasites, with some exceptions (e.g., trematode metacercariae, gnathiid isopods)	Poulin (2000b)

Table 1 continued

General theme and central question	No. of independent effect sizes	Measure of effect size*	Main finding	Reference
Does the uptake of microfilariae from infected humans by mosquito vectors follow density-dependence?	16	Linear mixed effects model	Uptake of microfilariae is density-dependent, but to an extent that varies among mosquito genera	Snow and Michael (2002)
Is the development of microfilariae inside mosquito vectors subject to density-dependence?	20	Model fitting	The form of the function between development and intensity depends on which mosquito genus is used	Snow et al. (2006)
Can the absence of a dilution host (deer) result in a change in tick density?	22	Hedges' *d*	Absence of deer led to lower tick densities in large exclosures but to higher densities in small ones	Perkins et al. (2006)
What factors influence the establishment rates of parasitic nematodes in sheep?	87	Linear model	Establishment depends on host breed and age, infection dose and infection procedure, etc.	Gaba et al. (2006)
Does temperature affect the multiplication rate of trematode cercariae inside their snail intermediate host?	21	Temperature coeff. (Q_{10})	Cercarial output increases with temperature more sharply than expected from basic metabolic processes	Poulin (2006)
What factors affect infection success by trematode cercariae in experimental conditions?	145	% infection success	Infection success decreased (weakly) with increasing dose, and was also affected by host traits and experimental procedures	Poulin (2010b)
What factors affect infection success by trematode metacercariae in experimental conditions?	106	% infection success	Infection success decreased with increasing dose, and was also affected by host taxon and/or body size	Poulin (2010c)

* The measures used by different authors may deviate slightly from the one indicated. Thus, Hedges' *d* (Hedges and Olkin 1985) here represents any difference between two average values that has been corrected for either, or both, sample sizes and variance. See original studies for details

immune cells like phagocytes and lymphocytes kill pathogens by releasing pro-oxidant compounds suggested that mounting an immune response might increase oxidative stress for the host, an expectation confirmed by meta-analysis (Constantini and Møller 2009).

In using meta-analytical approaches, it is often important to consider moderator variables explicitly once heterogeneity is identified in the data. Moderator variables can affect the magnitude of effect sizes observed. In the examples above, and many others, important moderator variables include the taxa of host or parasite species being considered, age of hosts, and whether or not results are based on experimental or correlational studies. It is also imperative to consider alternative explanations that might become subjects of their own meta-analysis. We provide one example. The argument that the male-biased parasitism seen in many vertebrates is androgen-mediated has considerable support (Klein 2004). This explanation is one based on the theory of life history trade-offs. However, a problem in applied ecology is that males often also harbour greater concentrations of certain contaminants than do females of the same species (Ackerman et al. 2007; Burger 2007). The conventional wisdom is that females depurate contaminants to eggs or embryos whereas males lack this excretion route. One can see that the generality of this finding becomes important especially if it occurs in those species also showing male biases in parasitism. Contaminants, like androgens, have been seen as potentially immunosuppressive. This example illustrates how important it is to examine the influence of moderator variables to tease out their underlying effects from those of focal predictors.

Meta-analysis, like other analytical approaches, realises its true potential when it (i) provides decisive general evidence in favour of one hypothesis over another, or (ii) uncovers previously unknown empirical patterns and thus provides new insights into host–parasite interactions. We see at least two major insights of this kind emerging from the meta-analyses summarised in Table 1. First, two separate meta-analyses concluded that parasites with higher rates of migration or gene flow than those of their hosts are more likely to demonstrate local adaptation, i.e., achieve higher infection success in sympatric hosts than in allopatric ones (Greischar and Koskella 2007; Hoeksema and Forde 2008). Theory on host–parasite coevolution was previously divided into two alternative sets of models making different predictions on whether high or low rates of parasite gene flow would favour local parasite adaptation (Lively 1999). On the one hand, many models predicted that local adaptation would be facilitated by high rates of parasite migration or gene flow among populations, since this would introduce new alleles on which local selection can act (Gandon et al. 1996; Gandon 2002; Gandon and Michalakis 2002). On the other hand, a different set of models predicted that high gene flow rates would swamp local selection and cause the genetic homogenisation of populations over time, either leading to local maladaptation or at least preventing local adaptation (Slatkin 1985; Holt and Gomulkiewicz 1997; Lenormand 2002). After years of empirical studies producing highly variable outcomes, the meta-analyses of Greischar and Koskella (2007) and Hoeksema and Forde (2008) provided convincing global evidence favouring the former set of models, resolving an ongoing debate and setting the stage for further progress in this field.

Second, two recent meta-analyses based on different sets of primary studies have uncovered a latitudinal gradient in parasite-induced mortality, with parasite virulence and associated host mortality increasing toward lower latitudes (Møller et al. 2009; Robar et al. 2010). Although some earlier authors had suggested the possibility of such a latitudinal trend (e.g., Møller 1998), its strength and generality were surprising. Numerous earlier studies have focused on the possibility that parasite species diversity follows the same latitudinal gradient observed for many taxa of free-living organisms (see Rosenzweig 1995). However, these have produced such highly inconsistent results (e.g., Poulin 2001; Lindenfors et al. 2007; Bordes et al. 2010; Dunn et al. 2010) that there is at present no solid evidence that parasite diversity peaks at lower latitudes. The meta-analyses of Møller et al. (2009) and Robar et al. (2010) demonstrate that although the diversity of parasites may not be higher in the tropics, their effects on hosts are greater. It is clear that future meta-analyses examining determinants of virulence will have to consider studies done in the tropics and temperate regions, explicitly. The notion that biotic interactions are more important factors for population and community ecology in the tropics than in temperate or polar areas is an old one (MacArthur 1972). The more stable and higher temperature at lower latitudes may have direct impacts on the survival and infectivity of parasite transmission stages (Pietrock and Marcogliese 2003). Whatever the explanation for the pattern, the net outcome suggested by meta-analysis is that parasitism may be a stronger selective force in the tropics, driving processes ranging from host population dynamics to the evolution and rates of diversification of host lineages.

Overall, the meta-analyses listed in Table 1 have each provided either a solid empirical foundation or a source of new hypotheses that will fuel further research into the evolutionary ecology of parasitism. There have been other meta-analyses of host–parasite interactions, but these typically fall outside the scope of evolutionary or behavioural ecology, unless they are seen as testing alternative explanations for observed patterns (e.g., sex biases in parasitism). For instance, meta-analyses have been employed to assess the effect of pollution on parasite infections, host susceptibility, and/or the sensitivity of parasites to pollutants with respect to their potential use as bioindicators of environmental impact (Blanar et al. 2009; Rohr and McCoy 2010; Vidal-Martinez et al. 2010). Meta-analysis has also been used to compare the effects of pathogens, parasitoids and predators as biocontrol agents against weeds and animal pests (Stiling and Cornelissen 2005). These studies provide further examples of the potential of meta-analysis as a synthetic tool.

Current grounds for meta-analytical approaches

As illustrated above, meta-analysis can extract general patterns from a set of messy and variable results, to identify likely cause-and-effect relationships and pinpoint additional variables that are also influential. Several other aspects of host–parasite interactions could benefit from similar rigorous synthesizing. Here, we identify three areas that seem ripe for meta-analysis.

First, the search for the determinants of variability in parasite species richness among host species has gone on for decades without obvious progress. Several host species traits, such as body size, longevity, metabolic rate, diet, population density, social behaviour or geographic range size have been proposed as important factors influencing the colonization of hosts by parasite species and the latter's subsequent persistence over evolutionary time. For instance, large-bodied host species might provide more resources for the coexistence of more parasite species than related but smaller hosts, and host species with vast geographic ranges might overlap with more other species from which they can acquire parasites than their relatives with more restricted ranges. Recent examples of attempts to identify key determinants of parasite species richness include studies across mammal species (Nunn et al. 2003; Torres et al. 2006; Bordes et al. 2007; Lindenfors et al. 2007), bird species (Clayton and Walther 2001; Arriero and Møller 2008) and fish species (Luque and Poulin 2008; Randhawa and Poulin 2010). However, the results of most of these studies are highly variable and characterized by low r^2 values (Poulin 1997, 2004). In other words, a given host trait correlates with parasite species richness in some studies but not others, and when it does, it explains only a small fraction of the variance in richness across different host species. These studies provide the necessary information for the estimation of effect sizes for each presumed predictor, in the form of partial regression or correlation coefficients. Meta-analysis could therefore be used to make sense of the variable outcomes of individual studies and identify the circumstances (e.g., which host or parasite taxa, which continent, etc.) under which a particular factor exerts a key influence on the evolution of species-rich parasite assemblages.

Second, the expression of resistance to parasites in relation to the degree of host specificity of those same parasites would prove a fruitful avenue for meta-analysis. In a similar vein, the importance of host specificity to testing for local (mal)adaptation was demonstrated by Lajeunesse and Forbes (2002). There are likely hundreds of studies that measure host resistance to parasites and do so in relation to a whole series of intrinsic and extrinsic factors (such as host age, host diet, parasite developmental stage, or temperature).

Expression of host resistance is thought to make sense in terms of trade-off theory (parasite resistance is, after all, costly). However, host specificity is likely equally, or more, important than actual costs of resistance in determining the expression of resistance (cf. Schmid-Hempel and Ebert 2003). Presumably, a parasite that evolves to evade one host species' immune system might, at the same time, fail to evade immunity of another, or several other, host species. This idea of a recognition trade-off underpins work by Nagel et al. (2010a), that has shown that resistance to parasitic mites is seen in host species when the parasite species is a generalist. Host resistance to a specialist parasite is expressed less often and only when parasite intensity is high (Nagel et al. 2010b). This work is promising, but still in its infancy. We feel that researchers should be able to get indices of host specificity for a reasonable subset of those studies examining expression of host resistance. There are a number of indices of host specificity (see Poulin et al. 2011) that could also prove useful as moderator variables in meta-analyses on other topics.

Third, there are many recent studies, with more on the way, on how infection by one parasite species influences the likelihood of host infection by another parasite of the same or different species (Cox 2001). This avenue of research is not surprising given the widespread occurrence of multiple genotypes and species of parasites within individual hosts. Understanding factors that favour evolution to facilitate or to hinder co-infection will likely prove important for understanding determinants of host infracommunities, host pathology and parasite growth and development. Here, these phenomena should best be studied with experimental infections and appropriate controls. Once a sufficient number of single studies are done (we have reached that time), researchers can use meta-analysis to determine which parasites or life history traits of parasites are more likely to favour an increase or decrease in host susceptibility to further infection.

Other research areas have either reached, or are about to reach, a stage where their theoretical foundation is well established and sufficient primary results have accumulated for meta-analysis. For example, research on the effects of climatic variables on parasite transmission, infectivity or virulence has exploded in recent years, and meta-analysis may be the only way to make sense of the highly variable results generated by this research (Lafferty 2009). Faced with the inconsistent results typical of much research on host–parasite interactions, the potential of future meta-analyses simply cannot be overstated.

Looking ahead

The complex and intrinsically variable research findings on host–parasite interactions have been, and will continue to be, subjected to meta-analysis in order to extract general trends and make sense of variable outcomes. To date, this approach has either provided completely novel insights or uncovered empirical regularity from seemingly incongruent results. We can expect further advances in our understanding of host–parasite interactions as we harness the full potential of meta-analysis.

For example, meta-analysis can be combined synergistically with other methods to shed further light on research outcomes. Indeed, another synthetic approach has played a major role in the development of ecological and evolutionary parasitology. The comparative approach, which is grounded on comparisons of trait values across species instead of effect sizes across studies, can also be used to uncover global trends in host–parasite interactions. In simple terms, the comparative approach consists in testing for statistical associations between values for two or more traits across different species, while correcting for non-independence due to shared ancestry among related species (Harvey and Pagel 1991). It has been used widely to test hypotheses about the evolution of parasite diversity and life history strategies (Poulin 1995; Morand 1996; Morand and Poulin 2003), as well as hypotheses about the impact of parasitism on host sexual selection, investment in immune organs or mortality (Read 1987; Read and Harvey 1989; Chandler and Cabana 1991; John 1995; Sorci and Møller 1997; Morand and Poulin 2000). Recent methodological advances now allow meta-analysis and comparative analysis, the two most influential synthetic approaches that have been applied to host–parasite research, to be combined into a unified framework (Adams 2008; Lajeunesse 2009; Hadfield and Nakagawa 2010). One of the main sources of contingency in research outcome still plaguing meta-analysis in ecology and evolution, that due to phylogenetic effects, can now be overcome.

It is also important to reiterate that meta-analysis combines *past* studies with variable approaches and outcomes: this is both its strength and a weakness. Its strength is that it reveals general patterns that allow researchers to prioritize their own particular studies. For example, another study showing male biases in parasitism of breeding birds or mammals might be viewed reasonably as “incremental” science. A study examining whether the same biases occur often, outside of the breeding season or a study that delves into the mechanisms producing such patterns likely would be more informative and useful. Furthermore, the meta-data that accompany meta-analyses, if made public, can allow researchers to identify species or questions or exceptions not yet studied or explored. The weakness of meta-analyses, in addition to the fact that they may suffer from Type II errors due to small sample sizes (Arnqvist and Wooster 1995), is that they do not necessarily allow for strong inference. The collection of studies upon which meta-analysis is based have variable methods and outcomes. Therefore, failure to demonstrate the importance of a moderator variable might occur in meta-analysis, despite the fact that some studies have supported its effect. Individual studies range in quality from weak to strong; quality here refers to the reliability of the evidence provided by a study, even if the criteria used to assess quality remain subjective (Lajeunesse 2010). One of the challenges with meta-analysis is that both strong and weak individual studies get equal weight (there is no epistemiological weighting by strength of inference). Finally, meta-analysis combines past studies, but in this age of social media, researchers might be organized to conduct very similar, if not identical, studies concurrently. Discussions of approaches and methods could take place before actual tests and before publication. The results of such combined strong tests could be analysed with a rigorous meta-analysis and help fill the void between individual studies with particular methodologies and vast collections of studies with multiple and variable ones. The benefits of this kind of coordination prior to meta-analysis would be particularly evident for research on host–parasite interactions, where approaches and methods are currently borrowed from disciplines ranging from ecology to veterinary medicine.

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