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Migratory animals feel the cost of getting sick: a meta-analysis across species

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Running title: How does infection alter animal migration?

Summary

1) Migratory animals are widely assumed to play an important role in the long-distance dispersal of parasites, and are frequently implicated in the global spread of zoonotic pathogens such as avian influenzas in birds and ebolaviruses in bats. However, infection imposes physiological and behavioural constraints on hosts that may act to curtail parasite dispersal via changes to migratory timing ('migratory separation') and survival ('migratory culling').
2) There remains little consensus regarding the frequency and extent to which migratory separation and migratory culling may operate, despite a growing recognition of the

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importance of these mechanisms in regulating transmission dynamics in migratory animals.

3) We quantitatively reviewed 85 observations extracted from 41 studies to examine how both infection status and infection intensity are related to changes in body stores, refuelling rates, movement capacity, phenology, and survival in migratory hosts across taxa.
4) Overall, host infection status was weakly associated with reduced body stores, delayed migration and lower survival, and more strongly associated with reduced movement. Infection intensity was not associated with changes to host body stores, but was associated with moderate negative effects on movement, phenology and survival.
5) In conclusion, we found evidence for negative effects of infection on host phenology and survival, but the effects were relatively small. This may have implications for the extent to which migratory separation and migratory culling act to limit parasite dispersal in migratory systems. We propose a number of recommendations for future research that will further advance our understanding of how migratory separation and migratory culling may shape host-parasite dynamics along migratory routes globally.

Keywords: disease ecology, migratory culling, migratory separation, host-pathogen dynamics, parasite ecology, pathogen dispersal, zoonoses

Introduction

Across the globe, billions of animals undertake long-distance migrations every year (Dingle 2014). These predictable mass-movements create ecological connections between otherwise isolated sites, with migrants transporting energy, nutrients, seeds and parasites throughout their journeys (Bauer & Hoye 2014; Viana, Santamaría & Figuerola 2016). In particular, migrants have been hypothesized to act as 'superspreaders' of infection (Fritzsche McKay &

Hoye 2016), because in addition to making long-distance movements, they also face increased exposure to parasites and pathogens (both referred to as 'parasites' henceforth; Figuerola & Green 2000; Leung & Koprivnikar 2016), and form dense aggregations that can promote transmission (Altizer, Bartel & Han 2011; Fritzsche McKay & Hoye 2016). Moreover, migration may render animals more susceptible to infection via changes to immune function (Owen & Moore 2008; Buehler, Tieleman & Piersma 2010). Together, these characteristics have led to the widely held assumption that migrants enhance the global transmission of parasites, including zoonotic pathogens such as Avian Influenza viruses, Ebolavirus and West Nile virus (Reed *et al.* 2003; Altizer, Bartel & Han 2011; Prosser, Nagel & Takekawa 2014). However, despite a number of powerful correlative studies that provide indirect evidence for migrant involvement in pathogen dispersal (e.g. Tian *et al.* 2015; Verhagen, Herfst & Fouchier 2015; Lycett *et al.* 2016), direct demonstration of transmission as a result of animal migration remains exceedingly rare (Ricklefs *et al.* 2005; Altizer, Bartel & Han 2011).

The scarcity of demonstrated parasite dispersal events by migrants has led to the suggestion that migrants may not universally enhance parasite transmission and dispersal. This concept is indirectly supported by some studies showing genetic differentiation of parasite strains along migratory routes (e.g. Park *et al.* 2015; Hill & Runstadler 2016), and only intermittent outbreaks of zoonotic diseases along migration corridors (e.g. Verhagen, Herfst & Fouchier 2015). Collectively, these findings have added to a growing body of ecological theory suggesting that migration may act to reduce parasite transmission (and thereby prevalence) within the population, via a number of distinct mechanisms (Loehle 1995; Krkošek *et al.* 2007; Altizer, Bartel & Han 2011; Shaw *et al.* 2016). Notably, the physiological and ecological constraints imposed by infection may result in behavioural changes that induce 'migratory separation', whereby infected individuals are delayed in their migration

phenology relative to uninfected counterparts, resulting in a period of spatial isolation and reduced transmission (Galsworthy *et al.* 2011; Bauer, Lisovski & Hahn 2016). In addition, the combined physiological demands of migration and infection may coalesce to permanently remove infected animals from the population via 'migratory culling' (Bradley & Altizer 2005). These two mechanisms are mediated by the effects of infection on host behaviour and, ultimately, survival.

The extent to which migratory separation and migratory culling act upon migratory populations is dependent on *how* infection affects migrants' physiology and behaviour, as well as the *degree* to which they are affected. For example, infection may impact the pre-migratory fuelling rate of the host (e.g. van Gils *et al.* 2007; but see Hoye *et al.* 2016), thereby reducing the body stores required to fuel migration (e.g. Altizer & Oberhauser 1999). Infection may also hamper host movement capacity (including endurance, stamina, and speed; Bradley & Altizer 2005; Sjöberg *et al.* 2009; Mages & Dill 2010). Such effects may accumulate throughout the migratory period to result in changes to migration phenology of the individual (Studds & Marra 2005) that lead to migratory separation across the population. Ultimately, changes to physiology, behaviour, and phenology may reduce host survival probability (Hostetter *et al.* 2011; Krkošek *et al.* 2013), thereby removing the host from the population either during (migratory culling) or (long) after infection. The degree to which infection alters each of these physiological and behavioural traits has important implications for the capacity of migrants to transport and transmit parasites along their migratory route (Galsworthy *et al.* 2011; Bauer, Lisovski & Hahn 2016), yet such effects are not well understood. Although the effects of infection have been examined in a number of individual host-parasite systems across migratory birds, fish and insects, the generality of these findings and the predictability of infection-induced changes to animal migrations across taxa has yet to be assessed.

The purpose of this study was to assess how infection status and infection intensity affect migration, with an overall aim of understanding the extent to which migratory separation and migratory culling may act to decrease parasite dispersal in migratory animals. Importantly, because migrants undertake predictable long-distance movements, both migrants and their parasites may have evolved particular adaptations to infection and host migration, respectively, that would alter host-parasite relationships in comparison to non-migratory hosts. We therefore quantitatively summarized the extent to which infection from a diverse range of parasites has been found to alter migratory performance in seasonal migrants that make spatially and temporally predictable migrations. We compiled standardized effect sizes for both infection status (Hedges' g) and infection intensity (Fisher's z) from the literature to assess, under a meta-analytical framework, how both these infection components are associated with changes to body stores, refuelling rates, movement capacity, migratory phenology, and survival, in migratory hosts. In addition to our findings, we propose recommendations for future research that will further advance our understanding of the extent to which migratory separation and migratory culling may shape host-parasite dynamics along migratory routes.

Material and methods

Study selection criteria

The following criteria were applied to select relevant articles:

1) The study had to be on a migratory species, of any taxa, that undertakes seasonal movements between one geographic region and another. A universal definition of animal migration has proved difficult to formulate (Dingle 2014). For the purpose of this study, we considered populations migratory if their movements took the form of spatially and temporally predictable, synchronous, persistent movements between regions; undistracted, at

least initially, by suitable resources or home ranges; on a much greater scale and of much longer duration than those arising in the animal's normal daily activities; and required distinct departure and arrival behaviours and energy reallocated to sustain the journey (Rankin 1985; Dingle & Drake 2007; Dingle 2014). We used this definition because parasite transmission is underpinned by both host susceptibility and host contact rate, and the prevalence in populations places selection pressure on individual behaviours (Altizer, Bartel & Han 2011). Therefore, individual- and population-level components of migration are central to understanding parasite transmission by migrants. Applying this logic, we included species and populations that were either obligate or partial migrants, regardless of whether these movements were completed by an individual or successive generations (i.e. migratory circuits; Dingle & Drake 2007). Species that make nomadic, dispersive, or irruptive movements (e.g. in response to variable rainfall patterns) were outside the scope of this study.

2) The study had to quantify infection status or intensity of infection for a given parasite, either directly (for instance via PCR amplification, microscopy, or visual detection; e.g. Sjöberg *et al.* 2009), or indirectly (for instance, physical disease symptoms; e.g. Hostetter *et al.* 2011). Experimental studies that implemented broad-scale parasite removal of gastrointestinal or ectoparasites were included (e.g. Krkošek *et al.* 2013), as well as studies that experimentally added parasites (e.g. Bradley & Altizer 2005).

3) The study had to assess a measure of performance related to migration, and either quantify differences between groups (e.g. infected/uninfected) or correlate the performance measure with infection intensity. Although there may be carry-over effects of reproduction on migration performance, we did not include studies that only quantified the effect of infection on reproduction because we considered it not directly related to migration performance and hence transmission potential.

4) The study had to have performed a frequentist statistical approach and provide all sample sizes, and either an exact *p* value or an effect size. In addition, the direction of the effect, even if reported non-significant, had to be clear. Studies were carried out during any life history stage of the host species and conducted either in the field or in controlled laboratory settings.

To find relevant articles the following search query was entered into Web of Science, on 2nd March 2017:

TOPIC: (infection or parasite or parasitised or parasitized or pathogen or parasitism or disease* or infected) AND (migration or migrant or migratory)TOPIC: (effect* or impact* or fitness or perform* or behaviour or behavior or survival or condition or cost* or phenology or mortality or arrival or departure).

Articles were filtered for year (after 1990), language (English), document type (article) and category (Supplementary file 1: Fig. S1). This refined 24,680 articles to 4445 articles. To target invertebrate studies, which are often not specifically noted as being migratory in articles, we reran the above query but replaced (migration or migrant or migratory) with (insect or invertebrate). This returned an additional 758 results. Eighteen potentially relevant articles were added to this list via screening references of known relevant articles. Therefore, a total of 5221 articles were manually screened for relevance, and 5080 of these were excluded immediately for not being on the relevant topic (e.g. brood parasitism, human migration, or known non-migratory species). The remaining 141 articles were read and either deemed to meet all four requirements (41 studies), or excluded with reasons (100 studies; Supplementary file 1 for list of excluded studies with reasons; Fig. 1 visualizes PRISMA flowchart for full study selection process).

Data extraction

Forty one studies met the study selection criteria outlined above (full list in Table S2). These studies investigated either multiple migratory host species, multiple parasites, or multiple performance traits, each of which were extracted as an observation (n = 99). Of these, 66 observations measured infection status (infected/uninfected), and 33 measured infection intensity.

For each observation we extracted the following four explanatory variables (details outlined in Table 1): 1) the performance trait measured (body stores, refuelling rate, movement, phenology, and survival); 2) parasite type (protozoa, mite, virus, and helminth); 3) life history stage at which performance was measured; and 4) study design (experimental or observational). All variables were classed as categorical.

Calculation of standardized effect sizes

We calculated all standardized effect sizes using the R package 'compute.es' (Del Re 2010), which converts presented effect sizes, *p*-values and sample sizes into standardized effect sizes. For observations that measured infection status (n = 66), we calculated the standardized effect size Hedges' *g* and its sampling-error variance. Hedges' *g* is defined as the number of standard deviations by which two groups differ (Hedges & Olkin 1986). Hedges' *g* was chosen over Cohen's *d* to calculate standardised effect size across studies because Hedges' *g* pools variance using $n - 1$ instead of n and thus provides an unbiased estimate for smaller sample sizes (Grissom & Kim 2012). For studies that measured the effect of infection intensity on performance, we calculated Fisher's z (Borenstein *et al.* 2009), which is calculated by converting Pearson's product-moment correlation coefficient *r* to the normally distributed variable *z*. Where insufficient information was available to compute standardised effect size from the text, figures (i.e., boxplots or scatterplots) in the respective publications were used to extract the relevant information using GetData Graph Digitizer software (seven observations across six studies). Authors were contacted to provide additional information on

sample sizes and analyses for two additional observations (Souchay, Gauthier & Pradel 2013; Sorensen *et al.* 2016).

Statistical analyses

The aim of this study was to estimate host migration responses to both infection status and infection intensity, for each migratory performance trait (host body stores, refuelling rates, movement capacity, phenology, and survival probability), within a meta-analytic framework. Put simply, this involved adding extracted effect size of infection on the measured performance trait (either Hedges' *g* or Fisher's *z*) as the response variable within a mixed-effect meta-model, and the performance trait measured (body stores, refuelling rates, etc.) as the predictor variable, and weighting each data point within the model by the study's statistical power (sample size). We built two 'optimum' meta-regression models (described below) that estimated host responses to infection: one for observations that measured infection status (predicting Hedges' *g*), and one for those that measured infection intensity (predicting Fisher's *z*). Because Hedges' *g* and Fisher's *z* cannot be compared to each other, we conducted analyses for each type of infection measure separately.

Model selection

We selected the optimal meta-regression models by applying biological principles and by model selection based on lowest AICc (corrected Akaike's Information Criterion; Burnham & Anderson 2004). For observations that measured infection status, we tested which explanatory variables should be retained as covariables by comparing AICc values of candidate meta-regression models predicting migration responses to host infection status, constructed from a global model of Hedges' *g* against all four ecologically relevant variables outlined above (categories and sample sizes in Table 1). Candidate models were compared using the glmulti package (Calcagno & de Mazancourt 2010). Each candidate model was

allowed a maximum of two variables from the global model to avoid over-parametrization, and all models additionally included study ID and host phylogeny as random effects.

For observations that measured intensity, sample sizes were quite small (n = 33), therefore we applied univariate meta-models predicting Fisher's z as a function of each of the four explanatory variables, as well as the null model. Study ID and phylogeny were again included as random effects. The model retaining performance trait best explained variation in Fisher's z (AICc values: 45.1, 55.5, 57.7, 58.6, 67.4 for models retaining the variables trait, no variables (null model), parasite type, study design, and host life history stage, respectively). Therefore we present a simple meta-regression model with trait as the only explanatory variable as our optimum model predicting Fisher's *z*.

Model construction

All meta-models compared during the model selection process were built using the rma.mv function in package Metafor (Viechtbauer 2010). When building any meta-model, observations were weighted automatically by the inverse of the variance of the effect size, so that large studies (with small sampling-error variance) were given more weight than small studies (Gurevitch & Hedges 1999). However, due to eight observations that measured infection status having particularly small variances (due to very large sample sizes in the tens of thousands), we ran our analyses with variance capped at 0.01 (i.e. could not go below 0.01). This ensured that the weighting was not excessively biased towards these observations (weighting plots for final model predicting Hedges' *g* with and without capped variance provided in Fig. S4). Rerunning the final model for infection status (described in more detail below) without capped variance did not alter model results, but produced a model that had much higher heterogeneity (i.e. variance in true effects, as opposed to sampling variance; I^2 = 89% compared to 18%; Table S5 & Fig. S6 for uncapped model estimates). In addition, excluding points that are capped, and rerunning the model with uncapped variances produced

a model very similar to the model with capped variances, providing further evidence that the model is robust to changes in model weighting methods. We also checked model fit by plotting fitted and residual values for final meta-models. Although four outliers were identified in the model estimating host response to infection status (the four most negative points in Fig. 3), excluding these points made almost no difference to the model due to their small sample sizes, and therefore low weighting in the model. Finally, excluding studies on the Monarch butterfly, which had small sample sizes, did not alter model results, effect sizes or interpretation, therefore we retained these points in all models.

Accounting for dependency

To account for correlations in effect sizes as a result of data points being extracted from the same study or from phylogenetically similar host species, we included study ID and host phylogeny as random effects in all models. To control for phylogeny, we created a phylogenetic tree of all host species (Fig. S3) using the *rotl* package (Michonneau, Brown & Winter 2016) in R version 3.2.3 (R Core Team 2013). Because *rotl* does not calculate branch lengths for trees, we estimated these using the compute.brlen function within the R *ape* package (Paradis, Claude & Strimmer 2004). A correlation matrix of phylogenetic relatedness between any two host species was then constructed using *ape*'s vcv function. This correlation matrix was incorporated into all meta-regression models, within Metafor, so that phylogenetic relatedness between any two host species could be accounted for as a random effect.

For the analysis of infection status (n = 66), we randomly excluded 14 observations that used the same animals to measure the same trait (e.g. a study that analysed the effect of two different strains of parasite on survival of the same group of host animals), to avoid excessive dependency. Therefore the meta-analysis on infection status had a final sample size of 52 observations. Excluding these points did not significantly alter model results. However, we

retained data points that used the same host animals to measure separate traits (e.g. the effect of infection on survival and condition of the same group of animals) to maintain sample sizes. To account for this type of dependency, we also analysed the traits separately to ensure pooling data did not bias results, and present these models with their individual I^2 values (Higgin *et al.* 2003). We present total I^2 (per cent of observed variation estimated to be due to true heterogeneity in effects, opposed to sampling variation or error), and how much of this heterogeneity is attributed to study and host phylogenetic effects.

For analysis of observations that measured infection intensity (n = 33), excluding points that used the same animals to measure the same trait (n = 6) did not change the model, therefore we included all data. However, we noted that dependency between observations cannot be fully accounted for due to the limited number of studies that data could be extracted from (n = 13), and therefore we present this model without drawing strong conclusions, and as a reference point for future studies. As with observations measuring infection status, we also analysed each trait separately for comparison. For full transparency, we visualized the data distribution amongst studies in Fig. 4b.

Results

Of the 41 studies included in our analyses, 27 were on avian hosts, 10 on fish, and 4 on the long distance migratory Monarch butterfly (*Danaus plexippus*). No studies involving mammalian or reptilian migrants fit the criteria for inclusion in the study.

Effect of infection status on migration

Thirty five studies, encompassing 52 observations, measured how infection status affected performance. Of these, parasites were found to have a negative effect on a performance trait in 69% of observations, and a positive effect in 27% (the remainder were neutral (i.e. Hedges' *g* equalled zero; Fig. 2a). In total, only 24 observations (42%) reported significant effects ($p <$

0.05; Fig. 2a). A negative rank correlation between variance and effect size showed the largest (negative) effect sizes came from the studies with least precision (Kendall's τ = -0.21, p = 0.008), indicative of some publication bias towards negative effects (Fig. 2b). However, this relationship was driven by three points with particularly negative effects and small sample sizes (Fig. S7). These points had low weights within the meta-models, and therefore had little influence on model outcome.

The null model predicting the effect of infection status on overall performance across observations (n = 52) predicted an overall Hedges' *g* of -0.21 ± 0.07 SE (Z = -2.7, *p* = 0.006). This model had an I^2 of 56% (i.e. 56% of variance was attributed to true heterogeneity, as opposed to sampling variance). Of this heterogeneity, 28% was attributed to within-study clustering, and 28% was attributed to clustering by host phylogeny. Model comparison on the basis of AICc found that trait was the only strong predictor of Hedges' *g* (Table 2). Comparison of variable importance values (equal to the sum of the weights for candidate models in which the variable appeared) for all explanatory variables found that migration trait was the most important predictor of Hedges' *g* (trait = 0.8, study design = 0.2, host life history stage = 0.1, parasite type = 0.05). Our optimum model predicting Hedges' *g* therefore included trait only, controlling for study ID and host phylogeny as random effects. This model predicted a Hedges' *g* (equal to the number of standard deviations between infected and uninfected groups) of -0.13, -0.15, -0.49, -0.17 and -0.10 for body stores, refuelling, movement, phenology, and survival, respectively (Table 3a for model statistics; Fig. 3a visualizes model estimates for each trait). Infection had a significant negative effect on each trait except refuelling rate (for which there were just five observations), and infection status had a significantly more negative effect on movement than other traits (Fig. 3a). Traits were also modelled separately (with no covariates) to ensure independence and to explore heterogeneity for each trait (Table 3b, Fig. 3b). Null models of each trait showed very similar

effect estimates but heterogeneity was variable, with estimates for survival being the most precise with lowest I^2, and those for movement being the least precise with highest I^2.

Effect of infection intensity on migration

We calculated effect size Fisher's *z* for 33 observations from 13 studies. Of these, 71% reported a negative effect and 23% a positive effect, with 57% in total reported significant (Fig. 2c). A funnel plot of the null model predicting Fisher's *z* indicated no evident publication bias (Fig. 2d).

The null model across observations, estimated a negative Fisher's z correlation of -0.14 between infection intensity and migratory performance, with performance decreasing with increased infection intensity. However, this model had high heterogeneity (I^2 = 67%; of which 23% attributed to within-study effects, and 44% was attributed to host phylogenetic effects), suggesting very variable effects of infection intensity on performance across studies. Adding trait as an explanatory variable found that intensity was positively but weakly associated with host body stores, and negatively associated with movement, phenology and survival (Fisher's *z* = 0.05, -0.16, -0.27, and -0.24, respectively; Table 4a, Fig. 4a). This model had an I^2 of 73% (of which 40% was attributed to within-study effects, and 33% was attributed to host phylogenetic effects). Modelling each trait separately demonstrated similar results (Table 4b; Fig 4b). However, these data should be treated with caution, due to the small sample sizes and non-independence arising from data points being extracted from relatively few studies (Fig. 4b).

Discussion

Parasite infection has the potential to impose physiological constraints on migratory hosts that may act to reduce parasite prevalence, either by culling infected hosts or temporarily separating them from uninfected counterparts. By quantitatively reviewing the available

literature and accounting for study power, we provide evidence that parasite infection is indeed associated with behavioural changes that may alter migratory performance and consequently parasite transmission. Host infection status was associated with lower body stores, reduced movement capacity, delayed migration phenology, and lower rates of survival, although the estimated effects on most of these traits, except movement, were relatively weak. Moreover, we found that the intensity of the infection may also be important in predicting host response to infection, with increased intensity negatively associated with host movement, phenology, and survival. Although sample sizes were small, there was no relationship between infection intensity and body stores. Such modest effects of infection on host performance traits may provide some explanation for half of all observations reporting no significant effect of infection on performance traits. Although such small effects may still be biologically (and epidemiologically) relevant, sample sizes must be high to reliably and consistently detect such differences.

Effect of infection on movement

Across studies, infection status was found to curtail host movement capacity, with infected hosts tending to have poorer physical endurance (Bradley & Altizer 2005; Kocan *et al.* 2006), have slower movement speeds (Bradley & Altizer 2005), and move shorter distances (Sjöberg *et al.* 2009; Altizer *et al.* 2015). Infection intensity was also associated with negative effects on movement, although sample sizes were too small to be conclusive. Reduced movement is a common sickness behaviour, and may facilitate a more rapid recovery from acute infection by reducing energy expenditure (Hart 1988). However, the cost-benefit trade-offs for such behaviours are dependent on ecological context (Adelman & Martin 2009), and such movement effects may not manifest during non-stressful periods (e.g. van Dijk *et al.* 2015; Bengtsson *et al.* 2016). This may explain the particularly high heterogeneity (i.e. variance in true effects, as opposed to sampling variance) in the model that

predicted host movement response to infection status (I^2 = 64%; Table 3b), which suggests the effect of infection on host movement may be subject to context. Critically, however, the majority of studies assessed here measured movement *outside* of the migratory period. Given the physiological demands of active migration, it remains to be seen whether the negative effects of infection reported during sedentary periods remain, or are increased, during periods of active migration. Although the specific conditions under which such effects manifest are still unclear, evidence from a number of taxonomic groups suggests that movement behaviour of migrants can be compromised whilst infected, which has the potential to reduce pathogen dispersal over long distances (Galsworthy *et al.* 2011; Bauer, Lisovski & Hahn 2016).

Effect of infection on phenology

Given that infected migrants were found to have poorer endurance and displace over shorter distances, we expected this to translate to altered migration phenology. However, in contrast to the effects on movement capacity, infection was associated with only slight delays in the phenology of migratory movements (a difference of 0.17 standard deviations between infected and uninfected groups). The discord between the effect sizes for the movement and phenology traits may be partly explained by the strong association in the literature between certain host-parasite systems and certain performance traits (see Figure S8 for distribution of parasite types and host taxa across traits). For example, studies assessing phenology are primarily based on avian blood parasite systems, whereas those assessing movement capacity have focused on avian influenza viruses in birds, as well as parasitized fish and monarch butterflies. This provides little opportunity to compare different performance traits within the same infection systems. In addition, avian blood parasites may be distinct from other pathogens in that they often result in chronic, life-long infections of low intensity, and these infections are often symptomless once the host survives the initial acute infection (Zehtindjiev *et al.* 2008). The impact of these low-level chronic infections may differ

substantially from both acute infections and intense life-long infections (such as the protozoan parasite *Ophryocystis elektroscirrha* infecting Monarch butterflies). This is supported by our finding that increased infection intensity was associated with a significant negative effect on host phenology where data was available (Fig. 4). Critically, although our results suggest that chronic infections may have a minor, yet significant, negative effect on phenology, this may be an underestimate of the true effect given the scope and design of current studies.

Effect of infection on survival

Infected migrants tended to have lower survival probability compared to those that were uninfected, although effect sizes were again quite small. These estimates appear relatively robust, with a number of large-scale studies reporting significant, albeit relatively small effects of experimental removal of parasites prior to migration on annual survival (Brown, Brown & Rannala 1995; Krkošek *et al.* 2013; Souchay, Gauthier & Pradel 2013). Observational studies found similarly mild or non-existent effects of infection during active migration on annual survival (Hostetter *et al.* 2011; Maxted *et al.* 2012), providing only limited evidence for migratory culling. This is reflected by the very low heterogeneity in the model that predicts the effect of infection status on host survival (I^2 = ~0%), supporting consistent and robust effect sizes across studies and host taxa. Overall, this suggests that hosts may survive chronic or short-term infections over their migrations, particularly if hosts have evolved some degree of pathogen tolerance (Medzhitov, Schneider & Soares 2012), including reduced movement behaviour. However, such short-term (within-season) tolerance may be at the expense of long-term fitness, with the strongest negative effect of infection on migrants reported to date being the reduced lifespan of great reed warblers (*Acrocephalus arundinaceus*) chronically infected with avian malaria (Asghar *et al.* 2015). This long-term study suggests that chronic infection may cause a series of within-season effects, so small as

to be undetectable, that nevertheless accumulate and eventually impair lifetime fitness. Importantly, the small effects of infection on survival reported here do not preclude the probability of mortality being higher for novel or high intensity infections encountered during migration (in which case infected individuals may be culled before they are included in a study). However, our results do suggest that if an individual survives initial infection, then annual survival may not be substantially reduced.

Study strengths, limitations, and requirements for future work

This study provides an important foundation for improving our understanding of how parasites affect migratory hosts. However, we concede that there are many variables that could influence the effect of infection on migratory performance that we were not able to consider. The limited number of observations across a range of host-parasite systems means that many factors, such as parasite type, host species, and migratory strategy, as well as various aspects of study design, could not be controlled for as effectively as we would have wished. Nevertheless, the effect size estimates reported here are robust to changes in model structure (e.g. modelling traits together or separately, or using capped or uncapped sample-error variances), suggesting that given the available data, the results are reliable.

Several key questions remain outstanding in our understanding of how parasites affect animal migrations. Notably, there is very little understanding of how infections affect hosts during the migratory period – which is of paramount importance for our understanding of pathogen transmission. Finer-scale data on movements of individuals over the course of migration are needed in order to reliably evaluate this, requiring large-scale tracking studies gathering repeated, longitudinal data for individuals with a known infection history. Importantly, because it is often impossible to know exactly when infection took place, experimental studies may be needed to reduce this uncertainty (Beldomenico & Begon 2010). Infection intensity is also a critical component that need to be more specifically considered in future

studies. This meta-analysis provides evidence that intensity may be important when assessing the effect of infection on host migration performance traits, although the strength of the relationships between host susceptibility, infection intensity, and migration performance remains unclear. Critically, although immune function has been demonstrated to shift over the course of the migratory cycle (Buehler *et al.* 2008; Hegemann *et al.* 2012), it is still uncertain how this relates to an individual's infection history and how it manifests in terms of susceptibility to infection and transmission potential (Fritzsche McKay & Hoye 2016; van Dijk & Matson 2016). In addition, the scope of host-parasite systems under study needs to be considerably expanded. Strikingly, there is little research on the impact of infections on migratory mammals (although this is increasing, e.g. Mijele *et al.* 2016; Mysterud *et al.* 2016), despite the renowned migrations of mammals such as ungulates and whales, and evidence for the transmission of zoonotic pathogens by migratory bats (Leroy *et al.* 2009; Ogawa *et al.* 2015). Lastly, considering our results here, future studies addressing these questions should ensure statistical power to detect small effect sizes (e.g. power analyses for complex models; Johnson *et al.* 2015). Studies with insufficient sample sizes are likely to either not detect or misrepresent true patterns, obscuring overarching ecological mechanisms. Ultimately, it will be critical to assess the consequences of any measured effects in terms of both parasite transmission and host population dynamics, as even small effect sizes may have profound ecological effects (Asghar *et al.* 2015; Bauer, Lisovski & Hahn 2016).

Conclusions

This meta-analysis provides evidence for moderate negative effect of infection status on host movement, and weaker negative effects on host phenology and survival, which may have implications for the extent to which migratory separation and migratory culling act to limit parasite dispersal. Critically, such effects are still likely to have important implications for parasite dispersal, limiting (but not precluding) the potential for migrants to disperse parasites

long distances, even when long term impacts on phenology and survival are small. We also show that infection intensity may be important in determining this relationship between infection and host migration performance. However, this meta-analysis also highlights several gaps in our collective understanding of the impact of infection on animal migrations. Future studies redressing these gaps are sorely needed to fully comprehend how migrants alter pathogen transmission and dispersal globally.

Data Accessibility

Data and all R code described in this article are available to download at https://doi.org/10.5281/zenodo.1001820 (Risely 2017).

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Author Statement

BH conceived idea; all authors contributed to study design; AR collected and analysed the data, and lead writing the MS. All authors contributed critically to the drafts and gave final approval for publication. No authors have any conflict of interests in regards to this study.

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Tables

Table 1) The four ecologically relevant variables included in the meta-analysis, including their categorical levels, description, and sample size (total N = 52 for infection status, N = 33 for intensity). In addition, the sample sizes for the taxonomic order of host species is included. Phylogenetic relationships are controlled for as a random effect.

Variable	Level	Description	N Status	N Intensity
Trait	Body stores	Measures include: body mass, condition index, fat score, growth rate	15	7
	Refuelling	Measures include: plasma triglyceride concentration, feeding rate, mass change	5	0
	Movement	Measures include: distance travelled, speed, physical endurance, dynamic body acceleration	9	4
	Phenology	Measures include: spring arrival, spring departure, stop-over arrival, staging time	9	16
	Survival	Measures include: annual survival, migration survival, lifespan, survival probability	14	6
Parasite type	Protozoa	Parasites include: haemoparasites, Ichthyophonus spp, Ophryocystis spp	28	18
	Viruses	All viruses in this study were on Avian Influenza viruses	13	1
	Mites	Ticks and mites	6	12
	Helminths	Cestodes and nematodes	4	2
Life history stage	Breeding	Host sampled at their breeding grounds	19	19
	Non-breeding	Host sampled at their non-breeding grounds	10	1
	Migration	Host sampled during migration	21	6
	Laboratory	Experiment in a laboratory	2	7

Study design	Observational	Study was observational	42	26
	Experimental	Study involved experimentally adding or removing parasites	10	7
Host phylogeny	Passeriformes	Songbirds	22	18
	Coraciiformes	Bee-eaters	1	0
	Charadriiformes	Shorebirds	1	0
	Salmoniformes	Salmon and trout	6	3
	Anguilliformes	Eels	1	3
	Clupeiformes	Herring	1	0
	Lepidoptera	Butterflies	3	6

Table 2) Top ten competing candidate models constructed from a global model of all four variables predicting standardized effect size (Hedges' *g*; ES) of infection status, ranked by corrected Akaike's Information Criterion (AICc).

	Model	AICc	ΔAICc	Weight
1	ES ~ Trait	41.0	0.0	0.60
2	ES ~ Trait + Study design	43.5	2.5	0.17
3	ES ~	44.4	3.4	0.11
4	ES ~ Life history stage	46.1	5.1	0.05
5	ES ~ Study design	46.6	5.6	0.04
6	ES ~ Study design + Life history stage	48.1	7.1	0.02
7	ES ~ Trait + Parasite type	48.6	7.6	0.01
8	ES ~ Parasite type	50.3	9.3	0.01
9	ES ~ Parasite type + Study design	52.4	11.4	0.00
10	ES ~ Parasite type + Life history stage	53.0	12.0	0.00

Table 3) Model statistics for a) the full model predicting the effect of infection status on different migratory traits; and b) each trait modelled separately. All models account for study ID and host phylogeny as random effects, and the residual heterogeneity that these factors are estimated to account for are included under I^2 (study) and I^2 (phylo), respectively.

a)	Variable	Level	Estimate	S.E.	Z	Lower 95% CI	Upper 95% CI	*P*	I^2 (total)	I^2 (study)	I^2 (phylo)	N
		Intercept	-0.13	0.06	-2.06	-0.24	-0.01	**0.04**	17.7	0.0	17.7	52
		(Body stores)	-	-	-	-	-	-	-	-	-	15
	Trait	Refuelling	-0.02	0.16	-0.11	-0.32	0.29	0.91	-	-	-	5
		Movement	-0.36	0.10	-3.69	-0.56	-0.17	**<0.001**	-	-	-	9
		Phenology	-0.04	0.07	-0.58	-0.18	0.10	0.56	-	-	-	9
		Survival	0.03	0.06	0.52	-0.09	0.15	0.60	-	-	-	14
b)	Model											
	1	Body stores	-0.12	0.07	-1.72	-0.27	0.02	0.09	31.9	1.9	30.0	15
	2	Refuelling	-0.13	0.15	-0.84	-0.42	0.17	0.400	0	0	0	5
	3	Movement	-0.47	0.16	-2.84	-0.79	-0.14	**0.005**	67.7	67.7	0	9
	4	Phenology	-0.20	0.09	-2.23	-0.37	-0.02	**0.026**	40.9	40.9	0	9
	5	Survival	-0.10	0.04	-2.68	-0.17	-0.03	**0.007**	0	0	0	14

Table 4a) Model statistics for the meta-regression model predicting the effect of infection intensity (Fisher's *z*) on migration trait (n = 33). **Table 4b)** shows model statistics for each trait modelled separately. Model estimates for all models below are visualized in Fig. 4a and b.

Variable	Level	Estimate	S.E.	Z	Lower 95% CI	Upper 95% CI	P	I^2 (total %)	I^2 (study)	I^2 (phylo)	n
a) Trait	Intercept (Body stores)	0.05	0.09	0.60	-0.12	0.23	0.55	73.1 -	39.4 -	33.7 -	33 7
	Movement	-0.21	0.13	-1.60	-0.46	0.05	0.11	-	-	-	4
	Phenology	-0.32	0.08	-4.19	-0.47	-0.17	**<0.001**	-	-	-	16
	Survival	-0.29	0.08	-3.63	-0.45	-0.13	**<0.001**	-	-	-	6
b)											
	Body stores	0.02	0.05	0.35	-0.08	0.12	0.72	12.7	0	12.7	7
	Movement	-0.19	0.07	-2.63	-0.32	-0.05	**0.008**	0	0	0	4
	Phenology	-0.26	0.18	-1.41	-0.62	0.10	0.15	88.8	40.9	47.9	16
	Survival	-0.15	0.05	-2.95	-0.25	-0.05	**0.003**	20.1	0	20.1	6

Figures

Figure 1) PRISMA flowchart of article selection process and sample sizes.

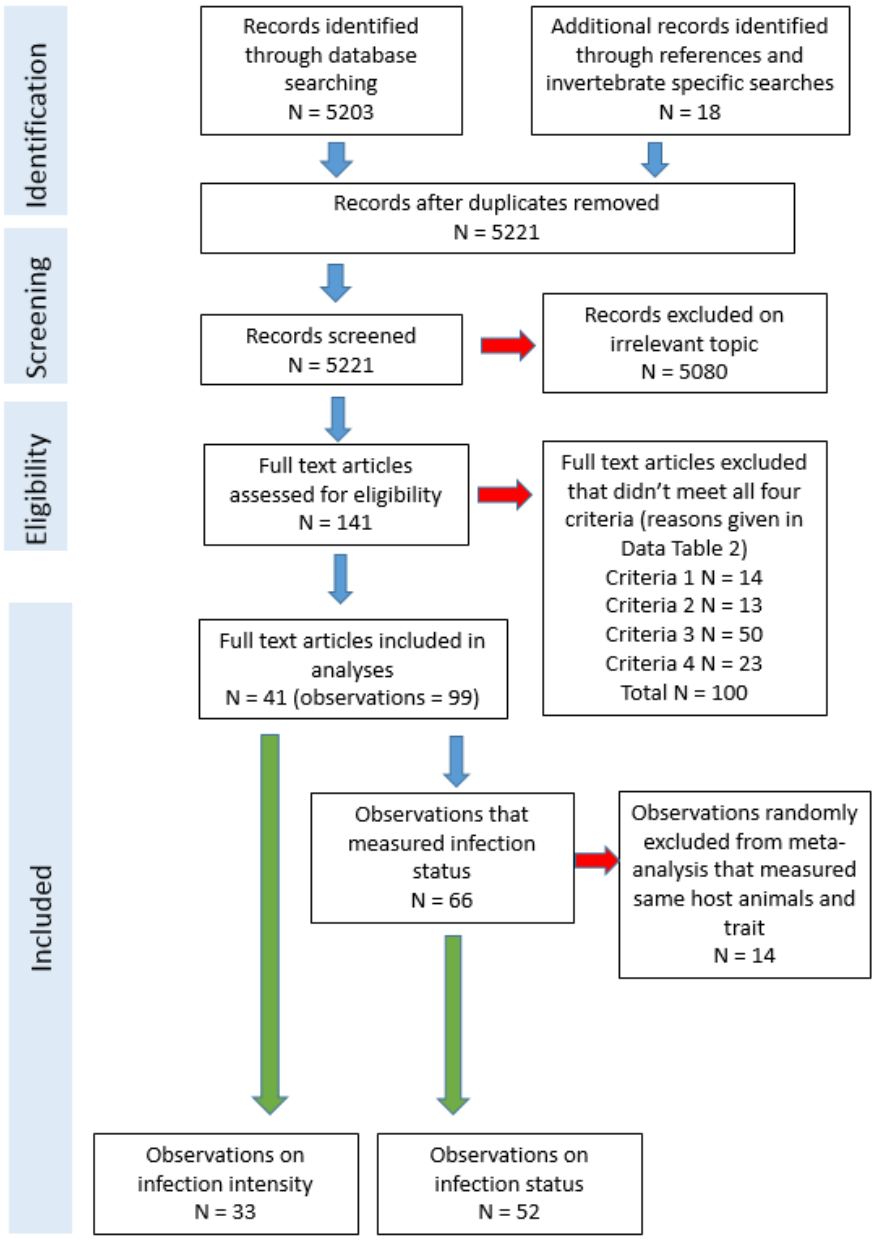

Figure 2a) Forest and b) funnel plots of Hedges' *g* values and their variances for observations measuring the effect of infection status on five different migratory performance traits (n = 52). Six points on the left outside of the white triangle of the funnel plot indicate some minor publication bias towards negative results; c) Forest and d) funnel plots of Fisher's *z* values and their variances for observations measuring the effect of infection intensity on four performance traits (n = 33; no observation measured effect of intensity on refuelling). For forest plots: square size is proportional to the weights used in the meta-analysis. Asterisks indicate observations that were reported statistically significant. Triangles indicate variances that were capped at 0.01 for analyses (variances for these points are close to zero).

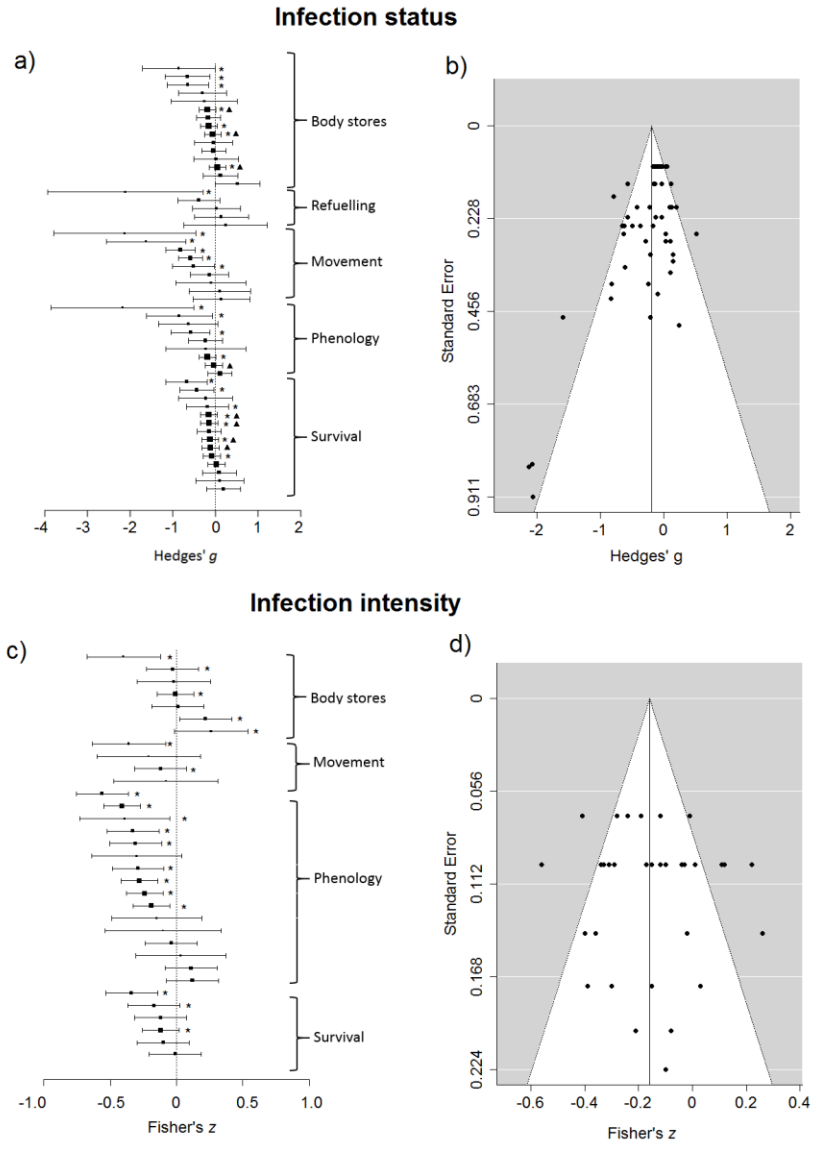

Figure 3) Estimated effect sizes (Hedges' *g*), standard errors (shaded grey) and 95% confidence intervals (whiskers) extracted from a) the optimum model that predicts effect size of infection status on performance trait (Table 3a); and b) estimated effect sizes from models where each trait is modelled separately (Table 3b). Boxplots are overlayed with raw data (circles) with the size of the circle proportional to its weight within the model (i.e. larger circles represent larger sample sizes). Colours represent host phylogeny by order (a) and parasite type (b).

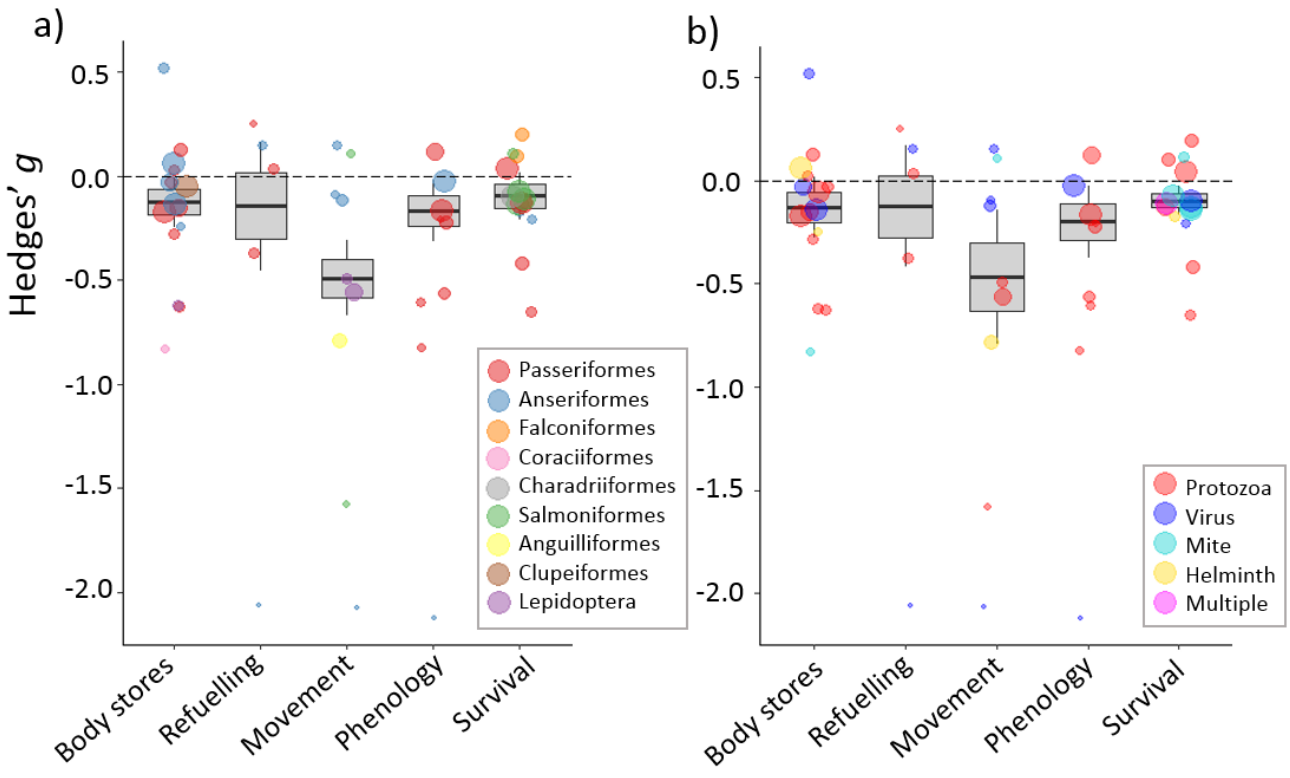

Figure 4) Estimated effect sizes (Fisher's *z*), standard errors (shaded grey) and 95% confidence intervals (whiskers) extracted from a) the meta-model predicting the effect of infection intensity on performance trait (Table 4a); and b) when each trait is modelled separately (Table 4b). Boxplot overlayed with raw data (circles) with the size of the circle proportional to its weight within the model. Colours represent the parasite type (a), and the study the data was collected from (b).