Trends in Parasitology

CellPress

Opinion

Fast-lived Hosts and Zoonotic Risk

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Because most emerging human pathogens originate in mammals, many studies aim to identify host traits that determine the risk of sourcing zoonotic outbreaks. Studies regularly assert that 'fast-lived' mammal species exhibiting greater fecundity and shorter lifespans tend to host more zoonoses; however, the causes of this association remain poorly understood and they cover a range of immune and nonimmune mechanisms. We discuss these drivers in the context of evolutionary ecology and wildlife–human interactions. Ultimately, differentiating these mechanisms will require linking interspecific variation in life history with immunity, pathogen diversity, transmissibility, and zoonotic risk, and critical data gaps currently limit our ability to do so. We highlight sampling and analytical frameworks to address this gap and to better inform zoonotic reservoir prediction.

Highlights

More evidence exists for within-species associations between life history, immunity, and disease than between-species. Most comes from birds or a few mammal species.

Some studies support increased zoonotic risk in fast-lived species, but patterns are not consistent across studies and often come from relatively small datasets.

Large-scale investigations are hindered by incomplete characterization of life history traits across mammal taxa and by difficulties controlling for confounders.

Without immunoparasitological sampling regimes, studies cannot sufficiently explore links between life history, immunity, and zoonoses. Instead, between-host, exposure-related processes (biogeography, population dynamics, urban adaptation) could also shape zoonotic risk.

Researchers may incorporate information about life history's links with immunity and zoonosis into sampling regime design and outbreak preparedness.

Fast Life Histories as a Zoonotic Risk Factor

The search for zoonoses puts hosts front and center. Wild and domesticated mammals are the ultimate source of most emerging infectious diseases [1–3] so many analyses have sought to associate mammalian species traits with **zoonotic reservoirs** (see Glossary) [4–9]. To help guide sampling efforts and outbreak preparation, these species-level analyses seek to identify mechanisms that have driven outbreaks in wild and captive mammals and human populations, amid a tangle of phenotypic drivers, epidemiological factors, and sampling biases. To date, identified drivers includes phylogenetic effects [8,10,11], geographic distributions [4–6,8,10,12], interactions with humans [5,8], and host life history traits [4–9,11,12]. Having identified these patterns, the field is progressing towards understanding process (e.g., using phylogenetic effects as a proxy for receptor similarity), and therefore towards prediction. However, life history is an enduring exception.

Although a selection of studies have associated high zoonotic risk with components of mammalian life history [4–9] (see Table 1), **pace-of-life** fundamentally interacts with several covarying traits such as body size, behavior, and population dynamics (Figure 1). Consequently, there is little consensus about the underlying causes of life history–zoonosis associations, and potential explanations include host immunity, fine-scale population dynamics, covarying species traits, and unaccounted-for sampling biases (Figure 2, Key Figure). Although species with 'weedy' life history strategies have been proposed to hold greater roles in sourcing zoonotic pathogens for over a decade [13], with some supporting evidence (Table 1; [4–9]), we remain no closer to understanding the mechanism. Are fast-lived species truly responsible for hosting more pathogens, or for transmitting them to humans at a higher rate, and is immune variation ultimately responsible? Although this 'pace-of-life hypothesis' is commonly discussed, no studies provide evidence for a direct link from between-species life history variation through immunity, pathogen richness or **competence**, and zoonotic outbreaks. This lack of clarity is due to incomplete and inconsistently characterized life history data, alongside a dearth of experiments, immunoparasitological sampling regimes, and phylogenetic analyses aimed at untangling life history from other covarying traits.

Here, we critically assess the evidence for associations between host species' life history and the propensity to source zoonotic pathogens. We outline potential underlying mechanisms by which life history affects zoonotic risk, including not only immunity but also population dynamics,

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sampling effort, and contact with humans. Ultimately, we argue that any of these mechanisms can generate observed life history–zoonosis associations. Importantly, although more fine-scale immunoparasitological sampling across mammal species will inform the role of immunity in such associations, nonimmune traits, such as biogeography, population dynamics, and urban adaptation, are equally likely to underlie associations between fast life history and zoonotic risk. Lastly, we discuss sampling and analytical frameworks that will facilitate distinguishing these contrasting mechanisms to better inform zoonotic reservoir prediction.

Between-species Variation in Zoonotic Risk

Life history syndromes represent tradeoffs between fundamental aspects of an organism's fitness. The most notorious example is the *r*/K dichotomy, which originally represented species as prioritizing either reproduction (*r*-selected) or survival (K-selected) [14]. However, the simplistic *r*/K dichotomy has more generally been replaced by a more complex continuum between 'fast' and 'slow' life histories driven by allocation of energy in maintenance, development, or reproduction (Figure 1) [15–17]. Because reproduction and survival are the ultimate determinants of fitness, the fast–slow continuum covaries with many species' traits. Slow-lived species tend to be large and long-lived, investing relatively less in reproduction. In contrast, fast-lived species are small, invest more in reproduction, and have relatively shorter lifespans. Fast- and slow-lived species thus have large and small population sizes, respectively, owing to their different allocation to mass and reproduction [18–20]. Disease phenotypes likewise covary with life history, and particularly with reproductive allocation [21]; specifically, many studies have associated fast life histories with greater pathogen diversity and zoonotic risk (Table 1).

Investigations into species-level drivers generally examine a suite of taxonomic and phenotypic traits to investigate whether they explain (zoonotic) pathogen diversity [5,8,9] or the probability of hosting a known zoonosis [4,6,7]. Notably, fast-lived species of bats and rodents host more (zoonotic) viruses [5,11,12] and tick-borne pathogens [6], bats with relatively greater reproductive output are more likely to host filoviruses [4], and fast-lived primates are more likely to host Zika virus [22]. The most comprehensive broad-scale analysis to date found that mammalian reservoir species generally exhibit fast life history traits [9]. The evidence supporting the pace-of-life hypothesis is therefore diverse in terms of both host and pathogen taxa.

Nevertheless, there is conflicting evidence for pace-of-life effects on zoonotic risk. For example, although bats with more litters per year (a fast-lived trait) have more zoonotic viruses, the same was true of bats with greater longevity and smaller litters (both slow-lived traits), and this same study found no pace-of-life effects in rodents [12]. Another study uncovered no associations between longevity and pathogen diversity in carnivores and primates, and long-lived ungulate species instead harbored more pathogens [23]. These examples indicate that many life history drivers of pathogen diversity and zoonotic risk have multiple potential mechanisms: in the case of longevity, while short-lived (fast) species should exhibit greater competence, longer-lived species accrue more **exposure** events, increasing their pathogen diversity. Similarly, domestic mammals are generally slow-lived, but are some of the most prominent zoonotic hosts given their proximity to humans and consequent sampling biases [8]. Evidence is also mixed when focusing solely on body size, which is fundamentally confounded with life history [18,19,24,25]. For example, larger, rather than smaller, mammals tend to host ebolaviruses [7]. The allometric scaling of pathogen diversity and competence is complex and hard to generalize, but smaller species are not universally associated with greater zoonotic ability [24]. Given that body size – and corresponding traits such as population dynamics and ranging behavior – correlate strongly with other life history traits, life history is not a silver bullet for explaining species' reservoir status.

Glossary

Between-host: refers to processes that are defined by interactions between individuals, often driving pathogen exposure.
Biogeographic: of or related to large-scale patterns of biological diversity across space, originating from evolutionary history and geological processes.
Competence: a host's ability to host and transmit a pathogen to other hosts, often of another species.
Exposure: the process of encountering a pathogen, or the rate at which this happens.
Immunoparasitology: a regime or scientific enterprise that involves both the host's immune system and some measure of disease (primarily infection status or pathogen intensity).
Pace-of-life: the tendency of a host species to prioritize reproduction versus survival; fast pace-of-life implies prioritizing reproduction and is associated with a short life.
Reservoir: the animal species that hosts a given pathogen in natural contexts and can transmit it to other animal species.
Spillover: the transmission of a pathogen from one species to another – often used specifically to describe zoonotic transmission from an animal to a human.
Susceptibility: a host's propensity to become infected with a pathogen once exposed.
Zoonotic: refers to a pathogen that can be transmitted from animals to humans.

Table 1. Studies that Investigated Between-species Effects of Mammalian Life History Variation on Pathogen Diversity, Zoonotic Risk, and Immune Variation

Pathogen	Hosts assessed	Traits assessed	Effects	Refs
Filovirus	Bats	Many traits using boosted regression trees	Faster reproduction increased probability of hosting filovirus	[5]
All viruses	Rodents	Many traits using boosted regression trees	Faster reproduction increased probability of hosting zoonoses	[4]
All viruses	Mammals	Geography – could not include reproduction due to missing values	Overlap with humans increased proportion zoonotic viruses	[8]
Borrelia burgdorferi, WNV, EEEV	Rodents (nine species)	Life history, morphology	Fast life history increased competence	[47]
Borrelia burgdorferi, WNV, EEEV	Rodents (nine species) (same data as Huang *et al.* [47])		Fast life history increased competence, but population density competed	[6]
Zaire Ebola virus	Mammals	Life history, morphology	Larger species more likely to host Zaire ebolavirus	[7]
All zoonotic pathogens	Mammals	Life history principal components analysis (PCA)	Faster life history PCA loading associated with reservoir status	[9]
All zoonotic viruses	Bats and rodents	Life history PCA	In bats: greater zoonotic diversity with smaller litter, greater longevity, and more litters per year. Nothing in rodents	[12]
All zoonotic viruses	Bats and rodents (same data as Luis *et al*. [12])	Life history PCA	Same as Luis *et al*. [12]	[11]
Zika virus	Primates	Many life history traits (machine learning)	Earlier age at first reproduction and shorter reproductive intervals more likely to host ZIKV	[22]
Immunity	Rodents (three species)	Species identity (a priori life history classification)	Mice have greater constitutive but weaker adaptive immunity than slower-lived chipmunks and squirrels	[41]
Immunity	*Peromyscus* mice (six species)	Reproductive traits	Immune variation axis not associated with reproduction	[40]
Immunity, richness of all pathogens	Ungulates, carnivores, and primates	Longevity, body mass	Longevity associated with increased pathogen richness in ungulates	[23]
Immunity	Rodents (37 species)	Testes mass, body mass	White blood cell counts did not correlate with promiscuity	[43]

While existing studies are suggestive, and some biologically reasonable arguments support relationships between pace-of-life and zoonotic risk (see following text), interpreting mechanism from such studies remains challenging; instead, we suggest that a careful study of the actual mechanistic drivers of a relationship between life history and zoonotic risk is needed. Most often, authors suggest that associations between fast life history and zoonotic risk emerge from a generalized weaker immune response, which increases pathogen diversity or competence, facilitating pathogen transmission to humans. In the following text, we discuss the evidence for this mechanism.

Life History Variation and Immunity

The study of life history–immunity relationships has a storied past. From the foundation of ecoimmunology, reproductive allocation has been theorized as a principal determinant of between-individual variation in immunity [26]. Generally, fast-lived individuals are expected to mount weaker immune responses, rendering them less able to repel pathogens. First, allocating to reproduction requires resources that are then unavailable for immunity [17,26–28]. Second, prioritizing reproduction leads to a reduction in survival [28–30]. Reduced longevity in turn means a more dispensable soma, so fast-lived hosts are less motivated to maintain their health, as they are unlikely to live long regardless.

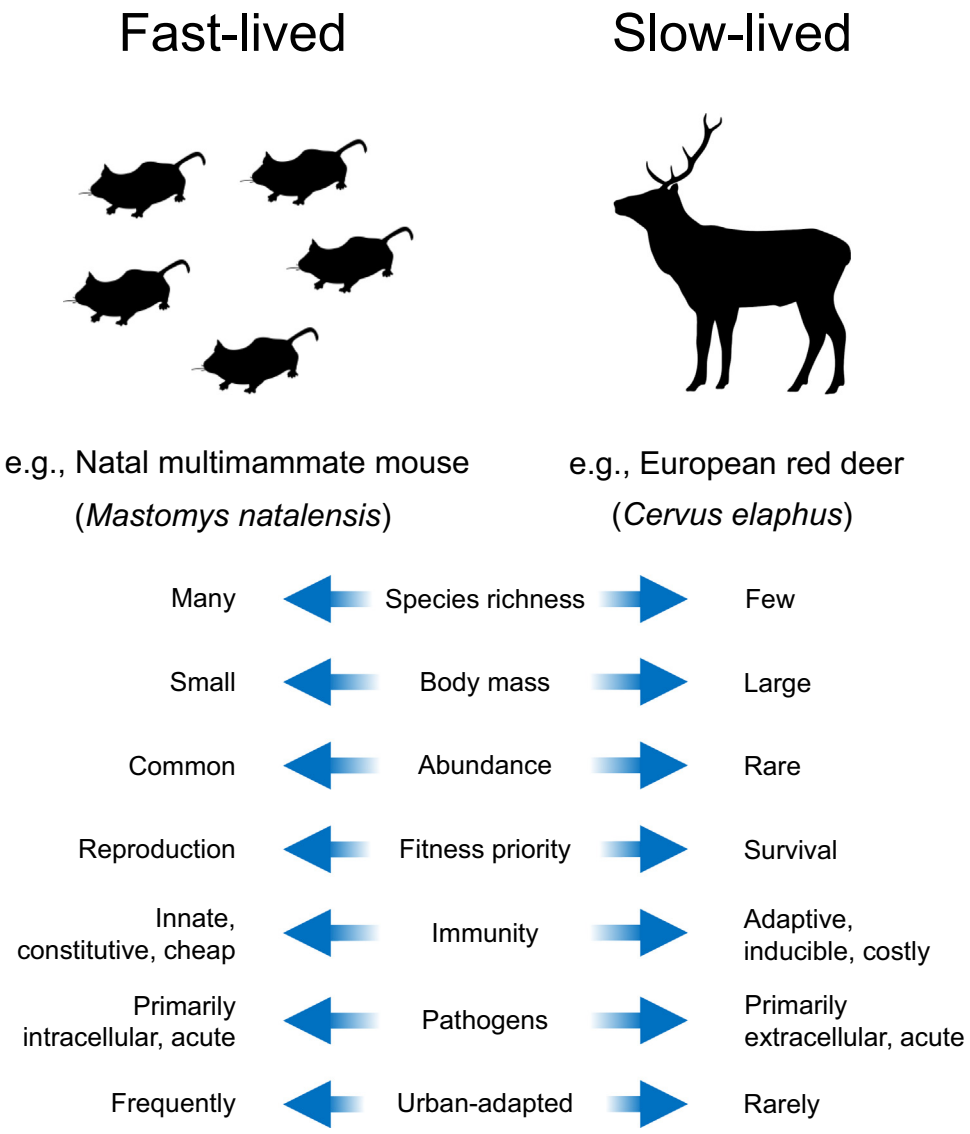

Figure 1. Fast- and Slow-lived Species are Hypothesized to Differ Predictably in a Wide Variety of Fundamental Traits. Fast-lived species (i.e., those that prioritize reproduction over survival) also tend to be smaller, more abundant, and are more commonly urban-adapted. All such traits might affect their propensity to host and source zoonoses. Silhouettes are taken from phylopic.org.

There is a wealth of evidence for within-species links between life history and immunity. For example, a meta-analysis of clutch size manipulations in birds demonstrated substantially weaker inducible immune responses resulting from greater reproductive allocation [27]. Similar examples exist in fish [31], bats [32], ungulates [33], and many insects [34]. Additionally, while reproduction is the most-cited tradeoff in this context, similar evidence exists for other costly traits such as exercise [35]. This rationale extends to sex differences in immunity and infection, which are often attributed to males' riskier (i.e., faster) life history strategies [36,37], and likewise to between-species comparisons [38–41]. However, within-species evidence does not necessarily extrapolate to between-species differences; between-species relationships are more complex and harder

Key Figure

Pathways to Pace-of-life Syndromes

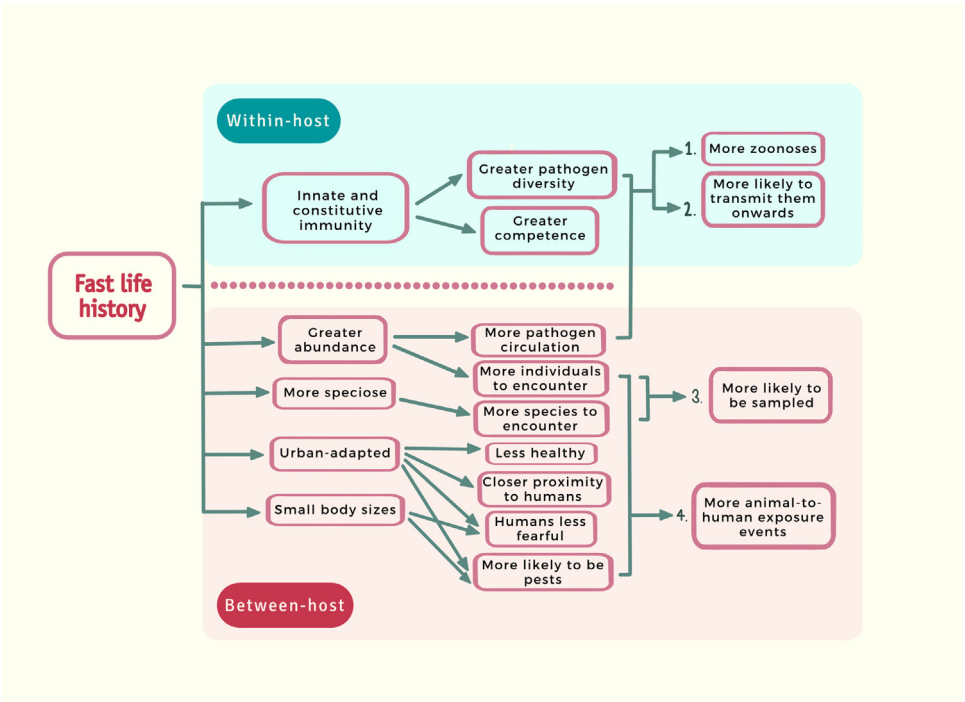

Figure 2. A variety of immune and nonimmune traits could drive fast-lived species' greater propensity to source zoonoses. Arrows represent causal relationships between fast life history and such traits. Numbers 1–4 on the right-hand side are outcomes that might increase actual or perceived zoonotic risk. Most attention in the literature has been paid to within-host (immune) processes rather than between-host (exposure-driving) processes.

to quantify, being fraught with coevolutionary caveats and scaling difficulties [18,39], and there are far fewer examples.

Fast-lived species are predicted to invest relatively more in nonspecific and inflammatory immune defenses at the expense of adaptive and especially antibody-mediated defenses [38–40,42]. In support of this claim, one study found higher antibody levels and weaker constitutive immunity in slower-lived rodent species (chipmunks and squirrels) than in mice [41]. This example highlights that, especially at the between-species level, fast life history and reproductive allocation provoke different rather than weaker immunity. Consequently, fast-lived species are asserted to primarily host more intracellular and acute pathogens, while pathogens of slow-lived hosts are more likely extracellular and chronic [42]. Moreover, there is substantial conflicting evidence for hypothesized pace-of-life effects: one study found no association between reproduction and immunity across six *Peromyscus* species [40]; there was no association between promiscuity and leukocyte concentration across 37 rodent species [43]; and a larger study incorporating ungulates, primates, and carnivores found no association between longevity and leukocyte counts [23].

If life history fundamentally shapes between-species variation in immune defense, the ramifications for zoonotic risk could be far-reaching. First, immunological differences could

produce greater **susceptibility**, allowing these species to host a greater diversity of pathogens, a proportion of which will have zoonotic potential (Figure 2). Second, distinct immune phenotypes could increase hosts' capacity to maintain pathogens within their populations [44,45] – or, third, into greater capacity to transmit pathogens to other species (i.e., competence) [24,46]. Competence is difficult to quantify but varies predictably with species' body mass for certain pathogens. For example, smaller mammal species are more competent for rabies virus [24] and several tick-borne pathogens [6,47]. As such, reproduction–immunity interrelationships are a well-theorized reason to explain why fast-lived species are more often a source of zoonoses.

Despite the focus on mammals in zoonotic risk studies, most cross-species studies on life history–immunity relationships have examined birds. Across Neotropical birds, natural antibody levels were greatest in species with slow life histories (i.e., longer incubation periods), whereas fast-lived species (i.e., larger clutch sizes) had greater complement activity (i.e., innate defense) [38]. European bird species with longer incubation periods also had more lymphocytes (i.e., B and T cells) [48]. Cell-mediated immune response, a component of adaptive defense, was also greatest in bird species with larger body mass and longer nesting and incubation periods, supporting these life history and immunological axes [39]. Across avian species, fast-lived hosts also tend to more easily transmit *Borrelia burgdorferi* to larval ticks, but competence does not vary strictly according to pace-of-life [49]. Unfortunately, relationships between pace-of-life and immunity have received nowhere near the same scrutiny in mammals: the mammalian studies we cite are taxonomically limited and used relatively small sample sizes. As such, the evidence is weak, contradictory, and limited mainly to birds. Instead, other potential mechanisms may explain associations between life history and zoonotic risk.

Life History Traits and Nonimmune Processes

Although most studies reporting associations between pace-of-life and zoonotic risk attribute them to variation in immunity, an animal's immune system is only one determinant of its disease burden [6,24,26,50]. Instead, many **between-host** processes could also underlie relationships between a species' life history strategy and its role in spreading zoonotic pathogens to humans [24]. Due to ecoevolutionary tradeoffs and physical constraints, life history fundamentally covaries with body size, behavior, and biogeography [5,17–19,24]. For example, large adults have large offspring, which require a long gestation period [19,20]. Similarly, because they are small and have high reproductive output, fast-lived species have greater richness and abundance than slow-lived mammals (Figures 1–3). For example, rodents account for almost half of all mammals (42% of species in the PanTHERIA dataset [51]; Figure 3) and typically obtain large and highly fluctuating population sizes. All such traits could impact pathogen prevalence and zoonotic risk. For example, one study in rodents found that species' population density was actually a better predictor of reservoir competence than life history itself, suggesting between-host processes could be at play [6].

Based on first principles, population dynamics of fast-lived species could profoundly alter their pathogen landscape without requiring any role of immunity. Their large population sizes could facilitate transmission for density-dependent pathogens, enabling greater persistence [52]. Additionally, fast-lived species are also more likely to have multiple reproductive bouts per year, introducing influxes of susceptibles into the host population that can facilitate persistence of pathogens [53] such as filoviruses, lyssaviruses, and coronaviruses [54–56].

Fast-lived species are not only more abundant but more diverse. Hyperdiverse groups of broadly fast-lived species – most notably rodents – have many close phylogenetic relatives,

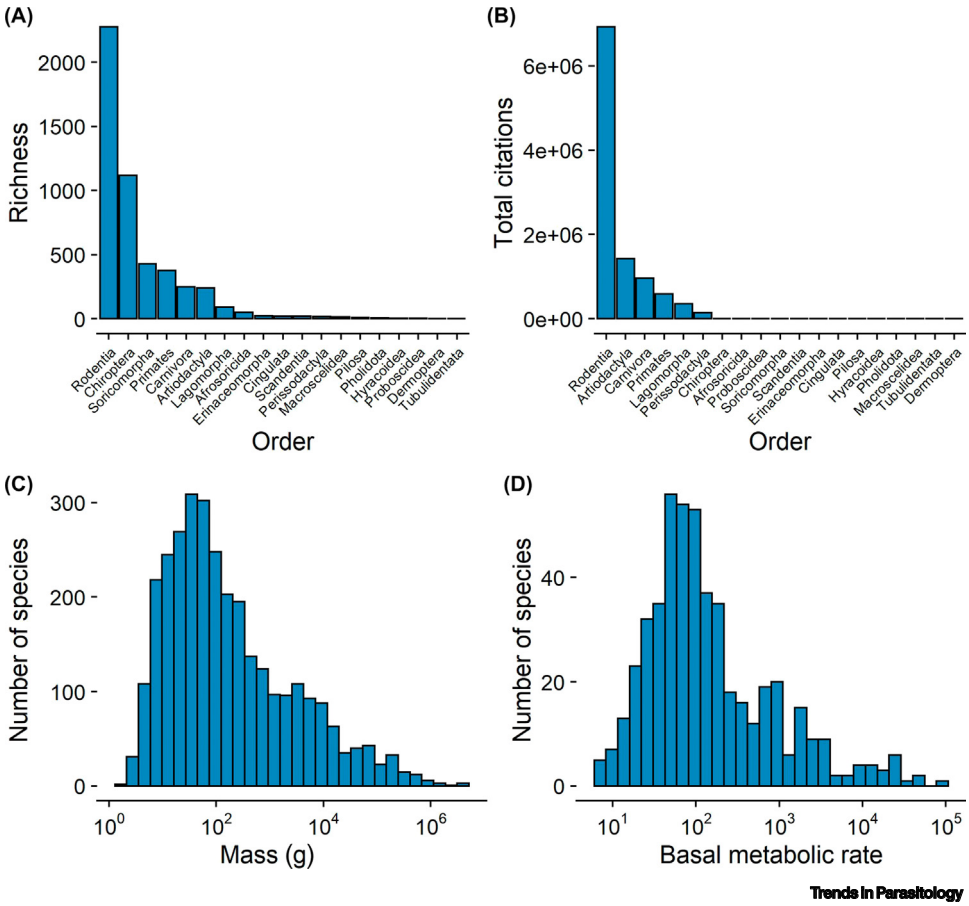

Figure 3. Most Species are Rodents, Small, and/or Short-lived. As represented with the PanTHERIA dataset [51]. Fast-lived orders of mammals, specifically rodents, have more species (A) and have been more well-cited (B). Similarly, most species have small body sizes (C) and short lives (D). Because more species exhibit fast than slow life histories, null or 'neutral' sampling processes could drive associations between fast life history and zoonotic risk because humans are more likely to come into contact with fast-lived species. In panel C, the x axis is on the log scale.

which also increases their centrality in the overall viral sharing network [10]. If this densely connected sharing network corresponds to a larger population of susceptible hosts, and thus greater transmission and maintenance, then greater pathogen diversities may result, of which a certain proportion will have zoonotic capacity. Similarly, a recent analysis demonstrated that speciose groups may source more zoonoses simply through their high species richness [57] – although questions remain about the disproportionate virulence of bat viruses [58,59]. Divining the role of such **biogeographic** (or 'neutral') processes in determining patterns of zoonotic **spillover**, relative to species' traits, will be an important frontier in disease ecology in the coming years [10].

Weedy Species in Human Landscapes

Fundamentally, species with fast life histories could source more zoonoses because they host more pathogens or transmit them more efficiently (as outlined previously), or because they more regularly come into contact with humans. While the first two are most likely determined by immunity, the latter could emerge from a wide range of traits. For example, greater richness and abundance of fast-lived species could not only facilitate pathogen persistence but also produce more individual animals for humans to contact.

Alongside their greater abundance and richness, fast-lived mammal species may also thrive better in anthropogenic environments [60,61], putting them in closer proximity to humans and potentially rendering them more likely to transmit zoonotic pathogens. As well as facilitating resilience in degraded and fragmented habitats, fast life history more readily permits range expansions into novel environments [62,63]. Fast-lived species, especially dietary generalists, can also more readily benefit from abundant anthropogenic foods, which can further increase population size [64,65]. These elevated host densities could amplify contact between wildlife and humans, which may also be facilitated by anthropogenic resources (e.g., rodents with household refuse [66]) and greater tolerance of urban-adapted species towards humans [67]. Anthropogenic habitats can also increase pathogen transmission in their resident wildlife. For fast-lived dietary generalists, elevated population sizes from access to urban resources can facilitate pathogen persistence [68,69]. Additionally, exposure to toxicants or crowding stress in urban environments can impair wildlife health, increasing susceptibility [70]. Such elevated density and susceptibility could operate synergistically to increase exposure and competence. Thus, urban populations of fast-lived species may simultaneously exhibit greater infection prevalence and intensity, greater transmission capacity, and more frequent interactions with humans. This combination of processes could lend fast-lived urban species to function as potent reservoirs for pathogens of all transmission modes; to take a notable example, rat-borne pathogens include those transmitted by direct contact (hantaviruses [71]), fomites (*Leptospira* [72]), and arthropod vectors (plague [73,74]). All such pathogens are facilitated by rats' physical proximity to humans [73,75], and the same could be true of many urban-adapted (and likely fast-lived) species.

These and other between-host processes are potentially important drivers of zoonotic risk, and over ecoevolutionary time they could have led fast-lived mammals to transmit more zoonotic pathogens to humans – without requiring fast-lived species to be immunologically different from slow-lived species. Unfortunately, critical data gaps currently prevent weighing their roles against that of immunity. To successfully contrast these hypotheses will require comprehensively linking between-species life history variation with immune variation (e.g., as has been done in birds [38]), and then onwards with pathogen diversity and zoonotic risk. This will likely require high-resolution immunoparasitological sampling regimes. No sampling regimes have yet been able to do so; even in within-host frameworks, the number of studies that simultaneously link life history variation with immunity and pathogens is small, such that the role of immunity in mediating reproduction–parasitism tradeoffs remains uncertain [27,33]. Ultimately, identifying whether immunity or between-host processes are responsible for shaping observed patterns of zoonotic propensity in fast-lived species is important for prioritizing future research. For example, further study of the 'special' nature of fast-lived immunity could be of secondary importance if neutral or exposure-driving processes – or simply close proximity to humans – are more responsible for these species' roles in hosting zoonotic pathogens. Regardless of which is responsible, this knowledge can be funneled towards the design of sampling regimes to better catalog pathogen diversity and identify risky hosts [76].

Future Directions

Apart from further motivating high-resolution **immunoparasitology**, how can our understanding of pace-of-life syndromes inform future sampling and analysis? Although studies generally imply that fast-lived species are most responsible for zoonotic spillover, this information alone can have low value in terms of actionability, for at least two reasons. First, many sampling regimes already target relatively fast-lived groups of animals such as rodents. Second, because most species (and most individual animals) are small and fast-lived (Figure 3), all else being equal, most sampling regimes will capture more fast- than slow-lived animals when sampling broadly. This was the case with a shotgun sampling approach looking to identify Ebola virus reservoirs,

which captured mostly small, fast-lived species [77]. An important priority for future zoonotic research should be to distinguish 'active' life history effects from such biogeographic (or 'neutral') processes: that is, more species and more individuals of each species producing more zoonoses by increasing sampling frequency and exposure. For analytical approaches, one recommendation is to include pseudoabsences (species for whom there are no known zoonotic records): because there are more fast- than slow-lived species (Figure 3), the number of fast-lived species with zero observed zoonoses may be proportionally larger. Systematically excluding these zeroes could skew associations with life history, risking false positives. Some studies only examine hosts with one or more known pathogens (e.g., [8]), partly because this avoids collecting additional species trait data for the pseudoabsences. This latter possibility will only be remedied by more even coverage of life history data across the mammal phylogeny (see following text).

Apart from weighing the importance of species-level drivers against neutral phylogeographic processes, future investigations should also aim to sample evenly across the mammal class, especially when looking to account for confounding effects of other covarying traits such as body mass. These analyses must be carried out using methods that control for phylogenetic dependence to successfully and confidently identify the causal factors [18,19,25]. Issues of phylogenetic scale can complicate such analyses [78]. For example, do we expect differences in zoonotic risk between entire orders of mammals or between species within the same family? Given possibly confounding effects of taxonomy (e.g., bats and rodents differ not only in life history but also in flying ability), controlling for taxonomic variation by sampling within host clades may be more likely to detect true pace-of-life effects. This problem is further compounded when we consider differences in slope between groups: what if pace-of-life effects are more severe in one taxon than in others? These phenomena are difficult to anticipate a priori and, as yet, our sparse and unevenly distributed data are poorly suited to answering them. Fortunately, modern methods are increasing the ease of phylogenetically controlled comparative analyses [79], and some approaches may allow us to more easily identify the phylogenetic scale of pace-of-life effects [80]. Potential solutions include (i) comprehensive sampling and comparisons both within and between broad clades [4,5]; (ii) flexibly dividing the phylogeny using statistical approaches to identify multiple important phylogenetic scales in reservoir analyses [80]; and/or (iii) pairing species that are ecologically similar except in life history (i.e., sister clades).

An overarching solution to the problem of conducting balanced, scale-robust phylogenetic analyses is to use greater swathes of the mammal tree: one of the greatest obstacles to confidently testing the pace-of-life hypothesis and differentiating competing mechanisms has been the relatively narrow selection of included species (Table 1; but see [9]). An unfortunate hurdle to pan-mammalian analyses of life history traits is their incomplete characterization across the phylogeny; for example, in the expansive PanTHERIA dataset, 35% of species have no known body mass, 54% no known litter size, and 89% no known metabolic rate [51]. Worse, these missing values are unevenly distributed across the tree: for example, longevity is known for 44.8% of carnivores, but only 8.7% of rodents [51]. The consequences of this sparsity are tangible: a prominent analysis of pan-mammalian zoonotic risk was precluded from examining life history traits because their representation in mammal databases was too sparse [8]. To remedy such gaps, some studies use machine learning-based imputation of life history traits [9,22] and/or take analytical approaches that can account for missing values [4,5]; however, this approach risks losing power and ignoring important variation, depending on the quantity and bias of the missing data. In the future, fundamental life history research will play a vital role in correcting these data sparsities – for example, making use of primary data sources such as museum collections [81]. This endeavor will facilitate a wider range of statistical approaches, allowing researchers to more comprehensively test associations between life history, immunity, and zoonotic pathogens.

Such sparsities in life history data affect not only trait availability per species but also the robustness of species-level information. Although comparative analyses often rely on species means, traits can vary substantially within species [82]. This lack of repeatability can introduce bias, as data quality will be driven by sample size; species means derived from few observations will be less reliable than those from large samples [83]. As fast-lived species will generally obtain larger population sizes, and thus be more easily sampled than slow-lived species, hosts with a slower pace-of-life may display high intraspecific variance that introduces additional bias into analyses of life history–zoonosis associations. Alongside greater trait data coverage at the intraspecific and interspecific level, solutions at the analytic level include weighting by sample size (or explicit measures of within-species variance when available, such as standard deviation or the coefficient of variation) in phylogenetic comparative analyses [79] or using phylogenetic mixed models on individual-level data to explicitly account for such variation [79]. Importantly, the former would also help better link within- and between-species scales of the life history–zoonosis relationship.

More generally, life history itself is a multivariate, shifting concept, having evolved from a dichotomy between *r*- and K-selected species to the current fast–slow continuum [14–17]. As such, 'pace-of-life' is only a proxy for a multitude of underlying species traits used to identify risk factors. Analytic approaches thus increasingly use multivariate methods, such as principal components analysis, to capture the complex nature of life history variation more so than independent traits such as fecundity or lifespan alone [9,12,40,69]. Importantly, by projecting numerous life history-relevant traits into multivariate space, such methods may ultimately help facilitate cross-taxa comparisons, given that single life history traits may have conflicting definitions or standard quantification between groups of animals.

Unlike comparative analyses of zoonotic status, which can capitalize on binary pathogen data (e.g., a host's infection compatibility), comparative studies of immune variation use primarily continuous and highly diverse data such as cell counts or antibody titers [84]. In mammals, studies have used readily obtainable data on concentrations or proportions of white blood cells [23,43], although such measures have restricted insights into immune function [85]. One challenge of functional measures, such as those gained from microbial killing assays, is that they require species-level optimizations [86]. Interspecific comparisons thus require standardizing conditions across species (e.g., the same dilution factor [40,87]), or explicitly comparing the optimization process across species (e.g., the dilution curve for microbial killing) [88]. The increasing accessibility of RNA-Seq and transcriptomic datasets can also facilitate targeting specific immune genes for expression across multiple species of interest [89,90]. Such approaches have generally facilitated tests of pace of life and immunity in other taxa, such as birds [39]; however, to inform the pace-of-life hypothesis, these would have to be further linked with zoonotic pathogen diversity, as we outline in the previous text.

Similarly, another aspiration of future pace-of-life studies should be to look beyond the mammal tree: while current work on zoonotic hosts is dominated by a focus on mammals, mammalian and avian orders may not vary substantially in the fraction of their pathogens that are zoonotic [57]. Further examining pace-of-life patterns in birds and other vertebrates might give important context to findings in mammals, as well as providing actionable insights for zoonotic prediction and prevention. Expanding empirical evidence on life history and zoonotic reservoirs into bird orders may be especially informative given the role that such species play in vector-borne diseases such as Lyme borreliosis and West Nile encephalitis [91]. Initial syntheses suggest that within-host traits such as competence are predictable across avian phylogeny or life history axes [24,49,92]. Additionally, as mentioned in the preceding text, many of the key insights into species-level tradeoffs between reproduction and immunity have been in birds, and many

immune assays have been adapted across avian species [38,39]. In pursuit of a life history–immunity–zoonosis link, researchers could build on the pre-existing wealth of immunological data in avian life history studies, setting a precedent for mammals and furthering our understanding of species-level zoonotic risk in birds.

Concluding Remarks

Our call for greater characterization and analysis of life history effects goes against the tide of popular opinion. A recent analysis of shifting themes in ecology identified life history as dead last in a list of 46 topics, having dropped an average of ten ranks per decade for the last three decades [93]. This decrease is indicative, the authors suggest, of a general falling-out-of-fashion of classical ecological concepts that focus on the individual scale, in favor of global matters of increasing importance or molecular processes that are increasingly manipulable in the bioinformatics age, or phenomena that cross multiple scales of biological organization. In contrast, the enduring popularity of the hypothesized link between life history traits, immunity, and zoonosis – and its nevertheless inconclusive evidence – is indicative of the importance of maintaining such foundational empirical research. Without life history data, much of our knowledge concerning zoonotic risk factors would have been impossible to develop [4–9], and many of our open questions would be impossible to address (see Outstanding Questions). Furthermore, the field is beginning to produce large-scale efforts to predict patterns of zoonotic disease for applied purposes [94–97], but these models require trait data to perform well, and especially to predict out-of-sample [95]. Just as the known mammal virome is limited in scope [98,99], data on species-level drivers of host–pathogen associations are prohibitively limited, and ensuring that these research agendas remain afloat will be a pressing need in a time of ever-increased scrutiny for disease ecologists. Harnessing such trait data will allow us to better identify the drivers of life history–zoonosis associations, establishing a better mechanistic understanding of the drivers of zoonotic risk.

Outstanding Questions

How general is the finding that species with faster life histories host more (or more virulent) zoonoses?

Is the cause of this association life history or reproductive output itself, or merely other covarying traits such as body size, population dynamics, or biogeography?

What is the role of immunity in driving life history–zoonosis associations, and how do its impacts compare to between-host processes?

Does between-individual or between-population variation in life history bear the same relationship with zoonotic risk as it does between-species?

How well can the effects of life history be extracted from those of other covarying phylogenetic traits and taxonomic clustering?

How do we account for sampling bias directed at smaller, more widespread, or more abundant species?

Are fast-lived species better at interacting with human-adapted environments, and does this fact exacerbate zoonotic risk?

If fast-lived species more commonly source zoonoses in urban environments, is this due to their increased pathogen diversity, competence, or contact with humans?

At what taxonomic scale does life history variation affect zoonotic risk?

Is pace-of-life a driver of zoonotic risk in nonmammalian host taxa?

Is host pace-of-life a driver of zoonotic risk homogeneous across pathogen groups?

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