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Review

Environmental Factors and Zoonotic Pathogen Ecology in Urban Exploiter Species

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Abstract: Knowledge of pathogen ecology, including the impacts of environmental factors on pathogen and host dynamics, is essential for determining the risk that zoonotic pathogens pose to people. This review synthesizes the scientific literature on environmental factors that influence the ecology and epidemiology of zoonotic microparasites (bacteria, viruses and protozoa) in globally invasive urban exploiter wildlife species (i.e., rock doves [*Columba livia domestica*], European starlings [*Sturnus vulgaris*], house sparrows [*Passer domesticus*], Norway rats [*Rattus norvegicus*], black rats [*R. rattus*] and house mice [*Mus musculus*]). Pathogen ecology, including prevalence and pathogen characteristics, is influenced by geographical location, habitat, season and weather. The prevalence of zoonotic pathogens in mice and rats varies markedly over short geographical distances, but tends to be highest in ports, disadvantaged (e.g., low income) and residential areas. Future research should use epidemiological approaches, including random sampling and robust statistical analyses, to evaluate a range of biotic and abiotic environmental factors at spatial scales suitable for host home range sizes. Moving beyond descriptive studies to uncover the causal factors contributing to uneven pathogen distribution among wildlife hosts in urban environments may lead to targeted surveillance and intervention strategies. Application of this knowledge to urban maintenance and planning may reduce the potential impacts of urban wildlife-associated zoonotic diseases on people.

Keywords: *Columba livia domestica*, Disease ecology, *Mus*, *Passer domesticus*, *Rattus*, Zoonoses

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INTRODUCTION

Human activity often leads to severe and large-scale environmental modifications, with cities representing an extreme example. Concurrent with exponential human population growth, the United Nations projects that pro- portion of urbanites worldwide will reach 66% by 2050 (2015). Cities are characterized by reduced biodiversity, while favoring specific free-ranging wild animal species (hereafter referred to as wildlife; Grimm et al. 2008). When classified by their responses to urbanization, ''urban ex- ploiters'' are wildlife species that depend on anthropogenic resources (i.e., food and habitat) and demonstrate peak abundance in urban core areas (McKinney 2006).

A subset of urban exploiter wildlife species flourishes in cities worldwide—rock doves (*Columba livia domestica*), European starlings (*Sturnus vulgaris*), house sparrows (*Passer domesticus*), Norway rats (*Rattus norvegicus*), black rats (*R. rattus*) and house mice (*Mus musculus*; McKinney 2006). Cities share similar environmental characteristics that favor these highly adaptive species: high-density hu- man populations, buildings and roads, heat island effects and fragmented vegetation (McKinney 2006). Also, global transportation, such as air travel, shipping and long-distance trucking, has provided the means for their introduction.

Besides effects on biodiversity and the environment, urbanization increases contact between certain wildlife species and people, creating the potential for zoonotic pathogen transmission. Most emerging infectious diseases are zoonotic, with a large proportion arising from wildlife (Jones et al. 2008). These emerging diseases in Asia–Pacific regions were 15 times more likely to arise from wildlife that are ecologically associated with people including rats and mice (McFarlane et al. 2012), leading to concerns over the sustained and frequent contact among people in cities and urban wildlife.

Environmental factors, particularly anthropogenic modifications, are strong drivers of zoonotic disease emergence (Daszak et al. 2001; Engering et al. 2013). Yet traditional host–pathogen studies often ignore environ- mental influences (Gortazar et al. 2014; Barrett and Bouley 2015), likely due to systemic complexity (Estrada-Pen˜a et al. 2014). An animal's environment may directly impact it with indirect influences on the pathogen(s) it carries, depending on the pathogen's characteristics and transmission route (i.e., direct, environmental and vector-borne).

For instance, abundant food resources contribute to good nutritional condition and enhanced immunity (Bradley and Altizer 2007). This may diminish pathogen load and persistence in the host, while enhancing reproductive success and population growth (Bradley and Altizer 2007). Other environmental factors that could influence pathogen ecology are land use, soil characteristics and floral and faunal biodiversity, including community composition among hosts (Estrada-Pen˜a et al. 2014; Barrett and Bouley 2015). Weather, including precipitation, humidity and temperature, as well as climate, may also influence pathogen ecology (Bradley and Altizer 2007).

Despite the dynamic nature of cities, investigations of environmental influences of zoonotic pathogens in this habitat are limited. A better understanding of how urban and other environments impact pathogen ecology will al- low us to track and reduce associated public health threats. This review: (1) examines and synthesizes knowledge of the environmental factors that influence the ecology and epidemiology of zoonotic microparasites (bacteria, viruses and protozoa) among globally invasive urban exploiter wildlife species and (2) provides directions for future studies.

MATERIALS AND METHODS

A wide variety of wild animals occupy urban habitats, and the species assemblages vary depending on geographical location (e.g., coyotes [*Canis latrans*] in North America, rhesus macaques [*Macaca mulatta*] in India). For the broadest applicability and to consider those species that have the potential for prolonged and frequent contact with people, which may translate to increased risk of zoonotic pathogen transmission, we chose to limit this review to the species that are classified as urban exploiters with global distribution (i.e., rock doves, European starlings, house sparrows, Norway rats, black rats and house mice; McKinney 2006). From January to April 2016, we systematically searched Agricola, Web of Science, CAB Direct and JSTOR databases with keyword combinations of the following concepts: urban, environment, zoonotic and wildlife species (Supplemental Table 1). We selected studies from the English peer-reviewed scientific literature that considered zoonotic pathogens in their wildlife host along with environmental factors (e.g., weather, habitat). We excluded studies of pathogens

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that are not directly shed by animals (e.g., *Cryptococcus* spp. associated with pigeon feces), those in rural/natural areas without an urban component and those with low sample sizes (<25 individuals). We added references through citation searching and evaluated papers using a structured abstracting matrix and synthesis technique (Garrard 2014; Supplemental Table 2). Of the 1400 manuscripts identified in the search, we retained 69 that included 7 viral, 15 bacterial and two protozoal pathogens. Among the studies examined, approximately one-third occurred in North America (21/69; 30%) and most focused on rats (41/69; 59% [Supplemental Tables 3, 4]).

Table 1 summarizes the emergent themes. Most studies considered location as the primary environmental characteristic of interest. Among these, a subset compared specific habitat types, either within cities or among urban and non- urban locations. Season was an occasional environmental factor of interest. In contrast, few studies examined comparatively novel environmental factors (e.g., heavy metal exposure).

Pathogen Ecology Varies Among Locations

Varying Pathogen Prevalence by Location

Pathogen prevalence may have extreme variability, even over small geographical areas. This phenomenon is best demonstrated by mouse-associated pathogens. For example, the prevalence of *Toxoplasma gondii* in house mice in cities can range from 0 to 100% among houses and from 0 to 93% among blocks (Murphy et al. 2008). The prevalence of lymphocytic choriomeningitis virus (LCMV) can range from 0 to 50% among houses, from 0 to 23% among neighborhood streets and 4–13% among broader locations within the same city (Childs et al. 1992).

A study of rats in Vancouver, Canada, found that the prevalence of zoonotic pathogens (i.e., *Leptospira* spp., *Bartonella* spp., *Escherichia coli*, *Salmonella* spp., *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*) varied significantly between city blocks (Himsworth et al. 2013, 2014a, b, 2015a, b). The overall prevalence of *Leptospira* spp. was 11%, but ranged from 0 to 67% depending on the city block (Himsworth et al. 2013). Residual variation in prevalence after controlling for geographical clustering and covariates with multi-level multivariable modeling suggested that block characteristics, possibly microenvironmental features (e.g., land use, human refuse management) contributed to the variation. A different approach revealed that *Leptospira* spp. genomic equivalents shed by Norway rats in urine varied significantly by location, demonstrating that infected hosts and the amount of pathogen shed are geographically clustered (Costa et al. 2015).

The reasons for heterogeneous pathogen distribution were not investigated in these studies. Potential explanations include direct transmission among clustered hosts (Childs et al. 1992) and/or varied exposure to pathogens in the environment (Himsworth et al. 2015b). Environmental influences on both of these mechanisms require further investigation.

Varying Pathogen Genetic and Phenotypic Diversity by Location

Like prevalence, pathogen characteristics vary among locations, even on smaller scales. For example, Yokoyama et al. (2007) analyzed *Salmonella enterica* serovar Typhimurium isolated from rats captured in two buildings across the street from one another. Rats from each respective building had similar prevalences but were infected with genetically distinct clones (Yokoyama et al. 2007). A study of hepatitis E virus in Norway rats also identified genetic clustering over small geographical scales (<7 km among sampling sites; Johne et al. 2012). Antimicrobial-resistant (AMR) *E. coli* shows similar spatial heterogeneity (Allen et al. 2011; Sacrista´n et al. 2014), even within a neighbor- hood (Himsworth et al. 2015b). This suggests that exposure to antimicrobials or AMR *E. coli* may differ by site. Collectively, these studies provide evidence of barriers to pathogen spread and/or maintenance within the urban environment.

The tendency for pathogen characteristics to vary among locations is not universal. Most *Chlamydia psittaci* isolates from European pigeons were genotypically similar, despite sampling several areas (Heddema et al. 2006; Gasparini et al. 2011; Geigenfeind et al. 2012). Birds may move great distances to share pathogens, but this result may also reflect limited genetic variation in this bacterium. Conversely, genetic diversity among birds, including spar- rows infected with West Nile virus, may be spatially dependent (Bertolotti et al. 2008). Genetic diversity was low at small scales (<1 km^2) but higher when sampling locations were >4 km apart, suggesting that distance is a limitation to pathogen transmission in this system. Al- though birds may move across

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greater geographical areas to share pathogens compared to rodents, the resulting consequences for pathogen diversity are likely dependent on the host home range size, as well as pathogen type and transmission routes.

Strengths and Limitations of Locational Studies

It is important to consider scale in urban wildlife studies (Estrada-Pen˜a et al. 2014). Scale(s) should fit the research question, animal home range size and urban geography and hierarchical arrangement (e.g., properties within blocks within neighborhoods within districts). The studies described above suggest that coarser scales may not represent pathogen distribution in complex urban environments or reflect public health risks. But coarse-scale studies can provide essential information. For example, the discovery that Seoul hantavirus caused hemorrhagic fever with renal syndrome (HFRS) in people stimulated cross-sectional studies in multiple cities in the 1980s. This research established the worldwide distribution and probable long- term carriage of Seoul hantavirus in rats, even though human clinical disease was primarily reported in Asian countries (Childs et al. 1985; LeDuc et al. 1985; Chen et al. 1986).

Studies that compare pathogen prevalence or characteristics among locations may identify a pathogen ''hot- spot'' that triggers public health interventions (Taylor et al. 2008). But these types of studies generally do not provide details or meaningful descriptions of habitat types or environmental features. Nor do these studies analyze the specific environmental features to understand whether these may contribute to differences. Therefore, studies that simply compare locations do not inform us about environmental mechanisms contributing to hotspot formation. Understanding the underlying factors, including those of the environment, which contribute to varying pathogen distribution is imperative to developing targeted surveillance and intervention strategies.

Pathogen Ecology Varies Among Habitat Types

Comparing Urban Habitats to Other Habitat Types

High densities of urban exploiter species and people in cities provide opportunity for prolonged and frequent contact between humans and animals, which may exacerbate the risk of zoonotic pathogen transmission. Thus, it is important to understand the differences between urban and other habitats, including agricultural, rural and natural areas (Brearley et al. 2013; Mackenstedt et al. 2015). Despite this, consistent trends in prevalence among different habitats are not evident. For example, the prevalence of *Bartonella* spp. in rats and mice was lower in urban sites compared to farms, harbor and suburban sites (Inoue et al. 2008; Hsieh et al. 2010). In contrast, Halliday et al. (2015) found a 60% prevalence of *Bartonella* spp. in urban black rats versus 13% in rats from a rural community. International trade in the urban location likely introduced rats, fleas and the *Bartonella* spp. they carry, while the rural site was more isolated (Halliday et al. 2015).

Avian pathogens also lack a distinct pattern. Although the prevalence of ticarcillin-resistant *E. coli* was higher in urban versus rural pigeons in one study (Sacrista´n et al. 2014), another found no pigeons carrying *Salmonella* spp. in 267 urban sites compared to 4% in 139 dairy farm sites (Pedersen et al. 2006). These studies attributed differences in prevalence to varying habitat exposures. Studies of West Nile virus (WNV) further highlight the complexity of habitat comparisons. Reisen et al. (2008) found the lowest WNV seroprevalence in birds (including house sparrows and pigeons) from locations near urban centers. Yet, in a different study, WNV seroprevalence was higher in urban sparrows but lower in urban pigeons compared to elsewhere (Reisen et al. 2006). Habitat type may also influence WNV genetic diversity, which was lower in birds in urban versus natural areas (Bertolotti et al. 2008).

Comparing Different Habitat Types Within Cities

Although studies have sampled animals in a variety of urban habitats, such as downtown/business areas, ports, commercial/industrial areas and near waste treatment plants (Jiang et al. 2008; Taylor et al. 2008;

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Wide´n et al. 2014), the most common approach is to compare residential areas to urban green spaces. Generally, pathogen prevalence is higher in animals in residential sites. For example, Norway rats and mice in residential areas were more likely to be seropositive for hantaviruses compared to those in urban parks (Childs et al. 1987a, b; Korch et al. 1989) or urban centers (Jiang et al. 2008). LCMV prevalence in house mice was higher in one residential area compared to other residential sites and urban parks (Childs et al. 1992). These studies suggest that habitat features in residential areas may favor the establishment and/or maintenance of rodent-borne viruses, assuming that ro- dents have small home ranges. Since these viruses are transmitted directly between hosts, the "dilution effect" may play a role in these habitat differences (Mills 2006). Natural areas and urban green spaces tend to support higher species diversity but lower densities of certain species; thus, pathogen transmission and prevalence may be reduced due to decreased contact among competent hosts.

There are exceptions to the trend toward increased prevalence in animals sampled in residential areas. For instance, rats in an informal settlement and business district in Durban, South Africa, had equal prevalence of *T. gondii* and *Leptospira* spp. (Taylor et al. 2008). These are protozoal and bacterial pathogens, respectively, that are mainly transmitted indirectly, while viruses trended toward higher prevalence in residential areas. Thus, habitat influences may vary depending on the pathogen type and mode of transmission.

Shipping ports provide another exception, as they tend to support high pathogen prevalence and diversity. Norway rats near a port in Yangon, Myanmar, were more often seropositive for *Yersinia pestis* compared to non-port sites (Brooks et al. 1977). Comparably, mice and rats near a port had higher serogroup diversity among *Leptospira* spp. isolates compared to elsewhere (Romero-Vivas et al. 2013). Importation of animals possibly introduced novel serogroups to this focal area. These and other studies (Anholt et al. 2014) indicate that shipping ports may sustain higher pathogen diversity and prevalence than elsewhere in cities through periodic animal and pathogen introductions.

Strengths and Limitations of Habitat Studies

Uncovering associations between pathogen prevalence and habitat types may be particularly useful for targeted interventions, predictive modeling and surveillance (Mills and Childs 1998). While some urban habitats (e.g., ports) may support hosts with high pathogen prevalence and diversity, there are no clear trends when comparing cities to other habitats. Pathogen ecology in urban exploiter species may differ from their non-urban counterparts, a difference that also occurs among a wider range of wildlife hosts (Brearley et al. 2013). But large-scale studies that dichotomize urban versus other habitats may oversimplify environmental complexity along the urban–rural gradient and thus influences on pathogen ecology (Beninde et al. 2015). Studying specific habitat types within cities (i.e., urban green spaces, residential neighborhoods, industrial areas) may be more insightful than arbitrary locations since habitats may be comparable between cities, and thus, findings may be more generalizable. Future research should focus on specific details of these habitats to explain differences.

Disadvantaged Urban Areas are Associated with Increased Pathogen Prevalence

There is an apparent association between disadvantaged urban areas including low-income areas, slums and refuse dumps, and increased pathogen prevalence in urban exploiter species. For example, rats from areas in Lyon, France, with dense human populations and low average incomes were more likely to be infected with *Leptospira* spp. compared to less populated, higher-income areas (Ayral et al. 2015). Although this study found no correlation between capture success (a proxy for population density) and pathogen status, a more robust approach would have been to include population density as a predictor and/or potential confounding variable. Also in Lyon, all rats carrying hepatitis E virus originated in a low-income area, with none testing positive from elsewhere, including a green space, waste treatment facilities and a peri-urban area (Wide´n et al. 2014). This study did not control for the effects of population density. Income might be functioning as a proxy for true causal factors (Ayral et al. 2015). These may include microenvironmental characteristics found in areas with low income and high human population density, such as building disrepair and inadequate refuse management.

Urban slums may be sites of increased pathogen prevalence among rats and mice. Rats from a shantytown in Buenos Aires, Argentina, were more likely to be seropositive for hantaviruses compared to

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rats from other locations, including urban parks and residential areas (Cueto et al. 2008). Taylor et al. (2008) identified two ''hotspots'' for *Leptospira* spp. and *T. gondii* in rats and mice in Durban, South Africa, one of which was an informal settlement. But the association between high prevalence and disadvantaged areas is not always consistent. Muñoz-Zanzi et al. (2014) found the lowest *Leptospira* spp. prevalence among rats and mice sampled from urban slums compared to villages.

There is also evidence that garbage, a prominent feature of disadvantaged urban areas (Satterthwaite 2003), may also be associated with high pathogen prevalence. For instance, Norway rats originating from dumps had higher *Leptospira* spp. (Hathaway and Blackmore 1981) and Seoul hantavirus (Jiang et al. 2008) prevalence versus other sites, including natural areas and suburbs. High population density of rats in dumps may contribute to higher pathogen prevalence (Hathaway and Blackmore 1981). In addition to location and season, Gargiulo et al. (2014) examined the effect of a waste emergency on the prevalence of enteric zoonotic pathogens in pigeons. Prevalences were significantly higher in pigeons from municipalities in which a waste emergency had occurred during the study period. Human refuse is a major food source for urban wildlife (McKinney 2006) so collectively, these findings suggest that research into this association may uncover a causal relationship leading to novel approaches to zoonotic pathogen control.

Strengths and Limitations of Studies in Disadvantaged Urban Areas

There are only a few studies that include disadvantaged urban areas as an environmental characteristic. And these studies examined a variety of pathogens, so the association with increased prevalence is tenuous. If true, the phenomenon that these areas support higher proportions of zoonotic pathogen-carrying animals is a double tragedy exacerbated by an increased likelihood of infestations (Feng and Himsworth 2014; Johnson et al. 2016). Thus, people in these areas may be at an increased risk of zoonotic diseases (Oliveira et al. 2013). This important area for future re- search should seek to understand the causal mechanisms underlying this perceived association. For example, does poor municipal hygiene contribute to increased pathogen prevalence independent of host population density?

Seasonality and Weather Effects on Pathogen Characteristics in Wildlife Hosts

There are no overall trends between season and weather with pathogen prevalence among urban exploiter species. For instance, a study of rats from Cyprus revealed that seasonal effects are pathogen dependent (Psaroulaki et al. 2010). The prevalence of *T. gondii* and *Leishmania infantum* was highest in summer; there were no seasonal associations with *Coxiella burnetii* or *Bartonella henselae*.

Studying Seoul hantavirus infection in Norway rats, Klein et al. (2002) found no association between prevalence and season, temperature or photoperiod in a 5-year study. Childs et al. (1987a) identified new infections in every season, establishing year-long virus transmission. Using a virus-carrying index (i.e., combination of rodent density and virus-carrying rate) among rodents (primarily Norway rats), Guan et al. (2009) identified a lag in the effects of temperature, precipitation and humidity on virus-carrying index and subsequently, human incidence of HFRS over 16 years. This suggests that weather factors have a major indirect effect on human disease by influencing pathogen dynamics in reservoir hosts. Collectively, these studies hint that weather and seasonal influences on hantavirus trans- mission in cities are complex and require further study, yet are potentially important factors that may influence prevalence in urban rat hosts and disease risk to people.

The absence or inconsistency of seasonal/weather effects such as with *C. psittaci* prevalence in urban pigeons (Heddema et al. 2006; Geigenfeind et al. 2012) and some pathogens in rats may be attributed to the complex effects of weather on hosts, vectors and environmental pathogens. Year-long contact among urban animals may facilitate direct pathogen transmission regardless of season or weather (Klein et al. 2002). Impervious surfaces (e.g., concrete, asphalt) collect moisture in otherwise dry locations, facilitating pathogen survival in the environment and creating microhabitats for pathogen transmission. Shelter provided by buildings and other built structures may reduce the effects of precipitation on transmission and pathogen survival in the environment. Cities are also warmer and experience diminished seasonality compared to adjacent areas. This urban ''heat island effect'' may influence pathogen ecology (Bradley and Altizer 2007). Warm cities may prevent environmentally transmitted pathogens and vectors

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from freezing. But hot cities may actually decrease pathogen survival in the environment and may impede vector transmission (e.g., flea-transmitted *Y. pestis*, the causative agent of plague; Cavanaugh 1971). Abundant food resources that are available year-round may support high populations of urban exploiters and the pathogens they harbor (McKinney 2006). Finally, seasonal effects likely vary by geographical location (i.e., four seasons vs. wet/dry season climates). These and other features of the urban environment add to the complexity of understanding pathogen ecology in cities.

Strengths and Limitations of Seasonal and Weather Studies

Relatively few high-quality studies have examined the effects of season and weather on pathogen carriage in urban exploiter hosts. This is an important knowledge gap to fill. There is evidence that seasonality and weather may influence the prevalence of infection in other animals (e.g., *Leptospira* spp. in dogs; Lelu et al. 2015) and zoonotic diseases in people (e.g., leptospirosis; Benacer et al. 2016). Future studies should follow the example of Guan et al. (2009), by including a lag period for weather factors prior to animal capture since infections likely occur at undetermined time points prior to sampling, when weather conditions differed. Multi-year studies of seasonal effects and weather are preferable to single-year studies due to the ability to replicate the exposure. Public health professionals could use this information to develop predictive models, surveillance and host control strategies, develop public awareness campaigns, and devise additional measures to reduce the risk of human infections (Mills and Childs 1998). Since climate change may impact cities worldwide (Lau et al. 2010), knowledge about the influence of meteorological factors on zoonotic pathogens in urban wildlife is increasingly important.

Other Environmental Characteristics

A range of environmental characteristics may influence pathogen–host dynamics. For example, a unique study of *Y. pestis* in rodents considered building material (i.e., brick, wood or thatch) and indoor versus outdoor trapping location, finding that most seropositive rats were indoors within wooden structures (Brooks et al. 1977). This difference likely reflects where rats live in this community but also emphasizes the risk of potential zoonotic transmission within indoor environments.

Another rare study approach involved measuring soil pH while assessing *Leptospira* spp. in rodents in an informal settlement of Durban, South Africa (Taylor et al. 2008). Soil pH throughout the study area was optimal for *Leptospira* spp. survival outside of hosts. Finally, a study of heavy metal exposure in pigeons (proposed to reflect local environmental contamination) found that birds with low zinc levels in feather samples were more likely to be infected with *C. psittaci* (Gasparini et al. 2014). Zinc may interact with the immune system or directly with the pathogen to cause this association (Gasparini et al. 2014). Overall, these studies demonstrate how researchers can incorporate environmental features beyond location and habitat to generate novel hypotheses that stimulate further research.

Directions for Future Research

Study Quality

Study quality is a major limitation of research on environmental influences on zoonotic pathogens in urban exploiter species and may result in erroneous conclusions. Thus, the true impact of the themes identified in this review remains unclear. This research field would benefit from approaches that use epidemiological principles when feasible. Animals should be collected using randomized, systematic sampling to avoid selection bias that may result from convenience/purposive sampling in sites with high animal densities. Sites could be repeatedly sampled over time (i.e., longitudinal and repeated cross-sectional studies) to analyze the impact of environmental characteristics. Alternatively, multiple sites of a particular habitat type or that have variable environmental characteristics of interest could be systematically sampled in cross-sectional studies (e.g., systematic trapping of an entire neighborhood). Aspects of host and parasite ecology (e.g., representative demographic groups, pathogen transmission routes) should inform study design. To understand the reservoir dynamics of multi-host pathogens, studies need to consider the potential hosts in a given location, which may include both wild and domestic species (Haydon et al. 2002).

Studies should also follow reporting guidelines (Sargeant et al. 2016) and add confidence intervals when possible. For instance, studies should include sufficient methodological detail to enable replication and describe results by species/location/habitat rather than aggregating data, which may hinder

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interpretation. Maps greatly enhance clarity of methods and findings. Researchers should use statistical analyses such as multivariable modeling that account for confounding/interacting variables (e.g., sex, species and age) and data that may be autocorrelated in space, time or by social grouping (e.g., rat in a burrow, pigeons in a flock). As well, researchers should use sample size calculations that account for autocorrelated data to

design studies with adequate statistical power (Dohoo et al. 2009). Consistent and systematic approaches to study de- sign, analysis and results will enhance comparability across studies and may result in more definitive conclusions.

Impact of the Urban Environment on Pathogen Ecology

Studies have considered a range of potential environmental factors that may influence pathogen ecology in urban exploiters—location, habitat, soil pH (Taylor et al. 2008), human socioeconomic data (Ayral et al. 2015) and heavy metal exposure (Gasparini et al. 2014). There are also missed opportunities when assessments are limited to associations between environmental factors and animal abundance, but exclude comparisons among these environmental factors and pathogen prevalence (e.g., Mun˜oz- Zanzi et al. 2014). It would be beneficial if future studies included a range of relevant biotic and abiotic environmental factors that may influence pathogen ecology in ci- ties (Fig. 1).

It is also possible that the variation and themes identified in this review are not related to the environment but rather to other factors, including host population structure, pathogen transmission dynamics and genetics. Until there are standardized, high-quality studies at smaller scales that take into account features of the microenvironment, it will be difficult to tease out these factors. Table 2 contains suggested areas of future research to uncover the mechanisms and factors contributing to uneven pathogen distribution in cities.

Conclusions

Knowledge of zoonotic pathogen ecology in urban wildlife, particularly urban exploiter species, is essential to assessing the risks of transmission to people in this age of emerging infectious diseases. The upstream environmental effects on pathogen ecology are an important component to risk evaluation. A key finding in this review is that pathogen prevalence consistently varies by location and habitat type. Future research should seek to explain this variation by exploring environmental and other factors. The apparent increased tendency for animals carrying zoonotic pathogens to originate in residential and disadvantaged urban areas is troubling and also warrants further investigation. The relationships between environmental characteristics such as seasonality, weather and others are far more tenuous with no clear trends identified in the current literature. Well-designed epidemiological and ecological studies would inform and strengthen these conclusions.

Urban environments could be important drivers of zoonotic pathogen ecology. Research that considers causal relationships between environmental factors and pathogen ecology is essential for designing evidence-based surveillance and intervention strategies. It would also provide fundamental information that may help mitigate public health risks through urban maintenance, planning and design. Ultimately, the results may provide a comprehensive approach to cultivating healthy urban landscapes.

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Compliance with Ethical Standards

Conflict of interest

The authors declare that they have no conflict of interest.

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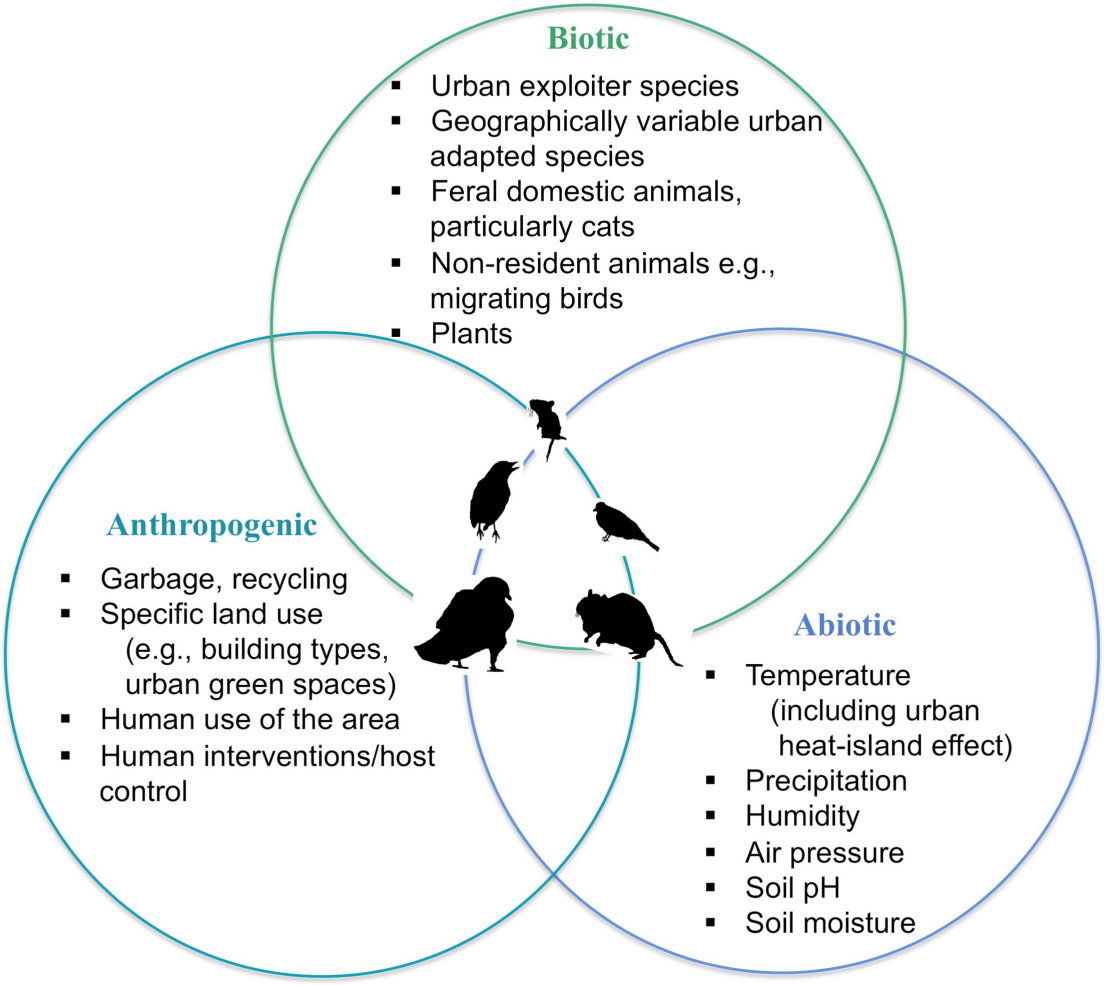

Figure 1. Examples of abiotic, biotic and anthropogenic factors that may influence zoonotic pathogens in urban wildlife.

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Tables

Table 1. Summary of Emergent Themes

- Pathogen prevalence and other characteristics vary by location and habitat of hosts for reasons that are poorly understood
- Rats and mice in residential sites may have higher prevalence of viral pathogens compared to elsewhere
- Rats and mice in disadvantaged urban areas may have higher prevalence of pathogens compared to elsewhere
- Urban shipping ports may be sites of high pathogen prevalence and diversity
- ere are no consistent trends for seasonal and weather effects

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Table 2. Summary of Future Research Directions

Category	Suggestion
Study Design	• Account for host and pathogen ecology including transmission routes • Use randomization, sample size calculations, multivariable modelling and other applicable epidemiological techniques to maximize the validity and utility of study results • Draw on expertise from other disciples such as urban ecology, ecohealth, disease/ecologic modelling and urban planning to systematically study the associations between environmental characteristics and zoonotic pathogens in their hosts • Sample indoor and outdoor environments • Examine season, meteorological and climatological factors with various lag intervals over multiple years to identify underlying weather patterns associated with pathogens in hosts and to inform predictive models • Conduct longitudinal studies to determine if associations with environmental features are consistent over time • Expand research to include multi-pathogen and urban-adapted hosts and the zoonotic pathogens they carry • Include representative cities from around the world and across varied climatic regions
Interventions	• Prospective studies are needed that modify the urban environment to assess if these interventions result in meaningful change in zoonotic pathogen prevalence • Consider the effects of meteorological factors in the context of climate change • Target interventions to pathogen "hot spots" rather than broad-sweeping population control schemes • Funding bodies (public health, wildlife, environmental) need to recognize and support urban wildlife studies through long-term funding

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Supplemental Tables

Table 1. Details of the keywords used in the search process

Concept*	Search Terms
Urban	urban* OR city OR cities OR municipal* OR suburban OR exurban OR residential OR metropol* OR "human-modified landscapes"
Environment	ecosystem* OR landscape* OR ecolog* OR habitat* OR management OR harbourage OR environment* OR abiotic OR biotic OR climate* OR precipitation OR weather
Urban wildlife species**	
Columba liva domestica	"rock dove" OR "rock pigeon" OR "Columba livia" OR "feral pigeon*" OR pigeon* OR "columba livia domestica"
Passer domesticus	"house sparrow*" OR "Passer domesticus"
Sturnus vulgaris	"European starling*" OR "Sturnus vulgaris"
Mus musculus	mice OR mouse OR "Mus musculus" OR "Mus domesticus"
Rattus sp.	*"Rattus norvegicus"* OR *"Rattus rattus"* OR "black rat" OR "Norway rat" OR "brown rat" OR "roof rat" OR rat OR rats
Zoonotic pathogens	
Columba liva domestica	Salmonell* OR "Escherichia coli" OR "E. coli" OR "Chlamydophila psittaci" OR "Histoplasma capsulatum" OR Aspergill* OR "Candida parapsilosis" OR "Cryptococcus neoformans" OR chlamyd* OR histoplasmosis OR cryoptococcosis OR zoono* OR "zoonotic disease"
Passer domesticus	"west nile virus" OR Salmonell* OR "E. coli" OR "Escherichia coli" OR "Buggy creek virus" OR arbovirus* OR zoono* OR "zoonotic disease"
Sturnus vulgaris	Salmonell* OR "Chlamydophila psittaci" OR chlamyd* OR "E. coli" OR "Escherichia coli" OR "Histoplasma capsulatum" OR histoplasmosis OR "west nile virus" OR zoono* OR "zoonotic disease"
Mus musculus	lymphocytic choriomeningitis OR Arenavir* OR salmonell* OR "E. coli" OR "Escherichia coli" OR zoono* OR "zoonotic disease" OR rickettsialpox OR "Rickettsia akari" OR "scrub typhus" OR "tsutsugamushi disease" OR "Orientia tsutsugamushi" OR "rat-bite fever" OR "Streptobacillus moniliformis"
Rattus sp.	Bartonell* OR leptospir* OR "Weil's disease*" OR Salmonell* OR "Escherichia coli" OR "E. coli" OR Yersin* OR plague OR "Streptobacillus monilliformis" OR "rat bite fever" OR "Haverhill fever" OR Rickettsia OR typhus OR "murine typhus" OR Campylobacter* OR "hepatitis E virus" OR hantavirus* OR "hemorrhagic fever with renal syndrome" OR "Seoul hantavirus" OR "Seoul virus" OR zoono* OR "zoonotic disease*"

* Concepts were combined with the Boolean operator AND
** Keywords for each species and its respective pathogens were searched together

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Table 2. Details of the topics used to create a structured abstracting matrix

Category	Topics
Study design	Species, non-urban exploiter species included, number in study, zoonotic pathogen(s), dates, study design, study objective, study location
Methods	Diagnostic test(s), number of sampling sites, sampling technique (e.g., selection criteria for sampling sites, sample size calculation), statistical analysis
Environmental factors	Was environmental component primary or secondary, scale, description of environmental factors, consideration for disease in people & domestic animals, weather factors
Results	Overall prevalence, range of prevalence, inclusion of a map & description, environmental factors associated with pathogen in host, habitat type with highest prevalence, weather factors associated with pathogen in host, reason for distribution, varying pathogen characteristics by location
Study quality	Subjective assessment of quality & relevance

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Table 3. Details of the systematic search results

Species*	Number of papers in initial search**	Number retained for final review***
Mus musculus	285	12
Columba liva domestica	257	13
Rattus sp.	478	41
Passer domesticus	205	2
Sturnus vulgaris	175	1
	Total: 1400	**Total: 69**

* papers that evaluated multiple species were included in the count for the main species in the study.
** limited to peer-reviewed scientific literature written in English and excluding relevant reviews
*** Studies retained for final review included consideration for zoonotic pathogens in their host and had an environmental component to the study (e.g., weather, geographical location). We excluded studies that focused exclusively on identifying zoonotic pathogen in a host without regard for environmental influences. We also excluded studies of pathogens that are not directly shed by animals (e.g. *Cryptococcus* spp. associated with pigeon feces), those in rural/natural areas without an urban component and those with low sample sizes (<25 individuals).

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Table 4. Summary of continental location of studies considered in the review

Continent	Number (%) *n* = 69
Africa	3 (4.3)
Asia	16 (23.2)
Europe	19 (27.5)
North America	21 (30.4)
Oceania	1 (1.4)
South America	9 (13.0)