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From superspreaders to disease hotspots: linking transmission across hosts and space

Sara H Paull[1*], Sejin Song[1], Katherine M McClure[1,2], Loren C Sackett[1], A Marm Kilpatrick[2], and Pieter TJ Johnson[1]

Since the identification and imprisonment of "Typhoid Mary", a woman who infected at least 47 people with typhoid in the early 1900s, epidemiologists have recognized that "superspreading" hosts play a key role in disease epidemics. Such variability in transmission also exists among species within a community and among habitat patches across a landscape, underscoring the need for an integrative framework for studying transmission heterogeneity, or the differences among hosts or locations in their contribution to pathogen spread. Here, we synthesize literature on human, plant, and animal diseases to evaluate the relative influence of host, pathogen, and environmental factors in producing highly infectious individuals, species, and landscapes. We show that host and spatial heterogeneity are closely linked and that quantitatively assessing the contribution of infectious individuals, species, or environmental patches to overall transmission can aid management strategies. We conclude by posing hypotheses regarding how pathogen natural history influences transmission variability and highlight emerging frontiers in this area of study.

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In November of 2002, doctors in the Guangdong Province of China began noticing unusual pneumonia cases that were later identified as the beginning of an epidemic of severe acute respiratory syndrome (SARS). The virus that causes SARS, which ultimately infected over 8000 people and killed 774, spread from a Hong Kong hotel when infected hotel guests began traveling across the globe (WHO 2003). One of those infected was a flight attendant, who was ultimately linked to more than 100 SARS cases in Singapore (WHO 2003). Encapsulated within this account lies a key phenomenon that influences disease dynamics: heterogeneity in transmission among individuals and across space. The risk of infection varies by location (eg hotels), by behavior (eg air travel), and especially among individuals.

In a nutshell:

- Diseases of plants, domestic animals, wildlife, and humans display transmission heterogeneity across individuals, species, and environments
- Heterogeneity among hosts can be caused by variability in host behavior, environmental exposure, host and pathogen genetics, and patterns of co-infection
- Spatial heterogeneity can result from variable host densities and environmental characteristics
- Quantitatively estimating host and spatial transmission heterogeneity and understanding their connections can aid in the development of cost-effective, targeted management strategies

Individuals who are responsible for a disproportionate number of transmission events, such as Typhoid Mary and the flight attendant carrying the SARS virus (Leavitt 1996; WHO 2003), are characteristic of many infections in both humans and animals (Lloyd-Smith *et al.* 2005; Hudson *et al.* 2008). This underscores the importance of understanding transmission heterogeneity, defined as variability in the contribution of specific hosts or locations to overall rates of pathogen spread. Failure to recognize and incorporate heterogeneity into epidemiological models can result in poor estimates of rates of disease spread and outbreak probabilities, and represent a missed opportunity for effective disease control strategies (Lloyd-Smith *et al.* 2005). Transmission heterogeneity also occurs between different species and across landscapes, and host and spatial transmission heterogeneity can interact positively, with each facilitating heterogeneity in the other. A better understanding of such linkages may enhance our ability to identify the hosts and environments that contribute disproportionately to transmission. In this paper, we consider the causes of, consequences of, and linkages between transmission heterogeneity across individuals, species, and locations. We suggest mechanisms for how pathogen transmission mode may influence transmission heterogeneity across hosts and space, and we advocate a quantitative approach that will allow researchers and managers to determine the magnitude of transmission heterogeneity across hosts, species, and environments (Panel 1). Finally, we offer future research directions (Panel 2) that could provide a framework for understanding and managing transmission heterogeneity.

[1]*Department of Ecology and Evolutionary Biology, University of Colorado, Boulder, CO* [*]*(sara.paull@colorado.edu);* [2]*Department of Ecology and Evolutionary Biology, University of California, Santa Cruz (UCSC), Santa Cruz, CA*

Modeling and defining transmission heterogeneity and superspreading

Epidemiologists typically determine whether a pathogen can invade a host population by using the basic reproductive number (R_0). This value represents the average number of new infections caused by an infectious individual in an immunologically naïve host population (Anderson and May 1991). Subsequent work has shown that the intensity of macroparasitic infections (eg worms per individual) generally follows a negative binomial distribution with high skew (Shaw and Dobson 1995), with more highly infected individuals potentially being responsible for more transmission events. A later study proposed the "20/80" rule and showed that, in a variety of disease systems, 20% of hosts were responsible for at least 80% of transmission events (Woolhouse *et al.* 1997). Thus, models allowing for heterogeneity in the distribution of the expected number of new infections an infectious individual produces (rather than using a single mean value, R_0) have transformed the epidemiological modeling of diseases by taking into account changes in disease dynamics that result from such heterogeneities (Lloyd-Smith *et al.* 2005). Importantly, heterogeneous transmission also occurs in cases where amplification host species or environmental "hotspots" contribute disproportionately to disease transmission within a community or landscape (Figure 1). Thus, one of the major goals of this paper is to extend the same principles that underlie host transmission heterogeneity to understand landscape variability in disease risk.

Extreme cases of transmission heterogeneity have been referred to as "superspreading events". A useful definition for a superspreading event, proposed by Lloyd-Smith *et al.* (2005), is when an infected host causes a greater number of secondary infections than the *n*th percentile of the

Panel 1. Quantifying transmission heterogeneity and its importance for management

Two key challenges for optimizing disease control are quantifying the magnitude of transmission heterogeneity across hosts and space and identifying key individuals or hotspots for targeted control efforts. Heterogeneity among individuals can be quantified by comparing the variability among individuals to that expected by chance. When transmission events can be observed directly (eg through contact tracing), one approach is to estimate the effective reproductive number, R_{eff} (the average number of new infections resulting from an original infection) for a population, and then to compare the number of secondary infections caused by individuals to a Poisson distribution with mean R_{eff} (Lloyd-Smith *et al.* 2005).

This conceptual approach can be extended to expected transmission contributions by subsets of hosts (identified by traits such as gender, age, and species). Prospective transmission among host subsets can be described by modified who-acquires-infection-from-whom (WAIFW) and *R* matrices (Anderson and May 1985; Diekmann *et al.* 1990; Dobson and Foufopoulos 2001). Each element of the *R* matrix describes transmission among one pair of host groups as the product of the mean infectious contact rate and the mean infectious period. The sum of each row quantifies the expected number of cases, summed across all groups, caused by an infectious individual in a given group, and thus determines the importance of that host group in pathogen invasion.

For a vector-borne pathogen, WAIFW and *R* matrices include one row for vector-to-host transmission and one column for host-to-vector transmission. If vertical transmission is absent, all other elements in the matrix are zero (Dobson and Foufopoulos 2001). As a result, the contribution of each host group *j* to initial amplification can be written as

$$R_{0,j} = \frac{f_j^2 C_j}{N_j} \qquad \text{(Eq 1)}.$$

Here, f_j is the fraction of vectors feeding on host species *j*, N_j is the fraction of the total host community represented by host species *j*, C_j is the competence (including susceptibility, infectiousness, and infectious period) of host group *j*, and R_0 is the sum across all *j* groups multiplied by the square of the vector biting rate and vector abundance. The importance in amplification, A_j, of each host group relative to its abundance is then $A_j = (R_{0,j}/R_0)/N_j$. To determine whether a host group is likely to be a superspreader at the *n*th percentile requires determining whether the observed value of A_j is unlikely given an expectation of $A_j = 1$ and the measurement error associated with estimating $(R_{0,j}/R_0)$ and N_j. This entails determining the probability of observing the estimated value of A_j by comparing it to the ratio of two distributions that have identical means equal to N_j but possibly different variances as determined by the measurement error of $(R_{0,j}/R_0)$ and N_j. The most appropriate distribution for N_j and $(R_{0,j}/R_0)$ for this comparison will be an important problem for further study, but one possibility is to use beta distributions, which are flexible and vary between 0 and 1. For non-vector-borne pathogens, a priori quantification of importance is much more challenging because empirically measuring the infectious contact rate among hosts is difficult. If possible, identifying measurable surrogates for infectious contact rates would aid discovery of host traits that are correlated with contact rates.

Quantifying spatial heterogeneity and identifying the importance of hotspots relative to purely stochastic variation can follow the same methodology. Doing so requires defining the quantity of interest – the density of transmission events, the density of all infected hosts, or the density of infected hosts of one group or species. Subsequently, a hotspot at the *n*th percentile can be described if the quantity (eg number of transmission events) in that area divided by the fraction of the landscape of interest represented by that area (a number between 0 and 1) is greater than the *n*th percentile of the appropriate ratio of distributions as described above.

Managers can benefit substantially from understanding the relative contribution of host groups and hotspots to transmission because recognizing heterogeneity could enable highly targeted control. The cost-effectiveness of targeted control, however, rests on the costs of identifying and controlling hotspots or key transmission individuals relative to the costs of broader, untargeted control.

expected distribution of new infections arising from a single infection, assuming homogeneous transmission potential across hosts. Lloyd-Smith *et al.* (2005) used an example of 99th percentile superspreading events, but their definition allows for versatility across disease systems and contexts. The powerful influence of rare events (or "black swans") drawn from the tail of probability distributions has similarly been recognized in other aspects of ecology (eg invasion, disturbance, dispersal) as well as in geology (eg meteorite impact) and the social sciences (eg war, financial market collapse; Mack *et al.* 2000; Taleb 2007; Whitten 2010).

Individual transmission heterogeneity

Transmission heterogeneity across individuals is often characterized by variability in contact rates with other potential hosts, duration of infectiousness, or parasite shedding rates (Figure 2; Lloyd-Smith *et al.* 2005; Hudson *et al.* 2008; Hawley and Altizer 2011). Traits such as host age, sex, body condition, and genetics can influence all three of these characteristics by affecting host susceptibility, immune responses, or social behavior (Wilson *et al.* 2001; Altizer *et al.* 2003; Hudson *et al.* 2008; Beldomenico and Begon 2010). For instance, experimental manipulations in birds and rodents have shown that males can be important drivers of population-level infection rates, and that elevated testosterone levels can suppress the immune response while increasing host contact rates (Ferrari *et al.* 2004; Mougeot *et al.* 2005; Grear *et al.* 2009).

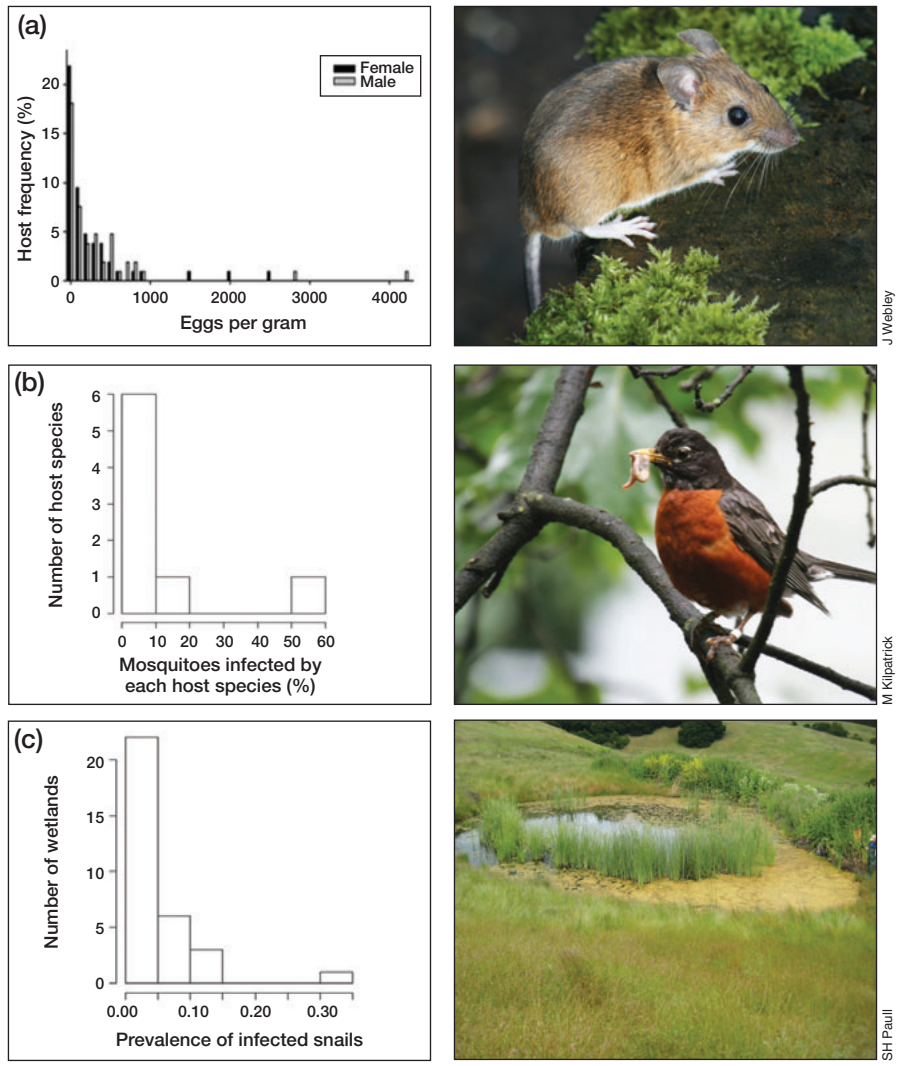

Figure 1. *Aggregated distributions of factors influencing transmission potential across hosts and space. (a) A few yellow-necked mouse (*Apodemus flavicollis*) individuals released most of the total eggs of the nematode* Heligmosomoides polygyrus *(modified with permission from Ferrari* et al. *2004). (b) American robins (*Turdus migratorius*) infected a much greater percentage of mosquitoes with West Nile virus than did other bird species, and more than would be expected from their relative abundance (data from Kilpatrick* et al. *2006). (c) A few ponds have very high percentages of snails infected with the trematode* Ribeiroia ondatrae *(Johnson unpublished data).*

An emerging research frontier in disease ecology involves identifying the relative contributions of host, pathogen, and environmental characteristics in transmission heterogeneity among individuals. Factors such as genetic differences in host resistance or parasite virulence and genotype–environment interactions can lead to individual transmission heterogeneity. For example, experimental inoculations of bay laurel (*Umbellularia californica*) leaves with *Phytophthora ramorum*, the fungal pathogen that causes sudden oak death syndrome, showed that individual trees varied substantially in their genetic susceptibility to the pathogen (measured by mean lesion area; Anacker *et al.* 2008). However, field observations revealed that disease levels (measured as number of symptomatic leaves per tree) at the plot scale were primarily associated with local environmental differences in temperature and precipitation rather than with genetic differences among hosts (Anacker *et al.* 2008). The distribution of pathogens or vectors within the environment may also be a factor influencing host burdens and, by extension, transmission heterogeneity (Brunner and Ostfeld 2008). For instance, when parasites are clumped together rather than scattered evenly across the environment, individuals that happen to encounter the areas with higher parasite densities are likely to experience higher infection intensities as a result.

Intriguingly, other parasites and microorganisms co-occurring within hosts can also influence the distribution of transmission rates across individuals (Hudson *et al.* 2008; Lloyd-Smith *et al.* 2008). For instance, host differ-

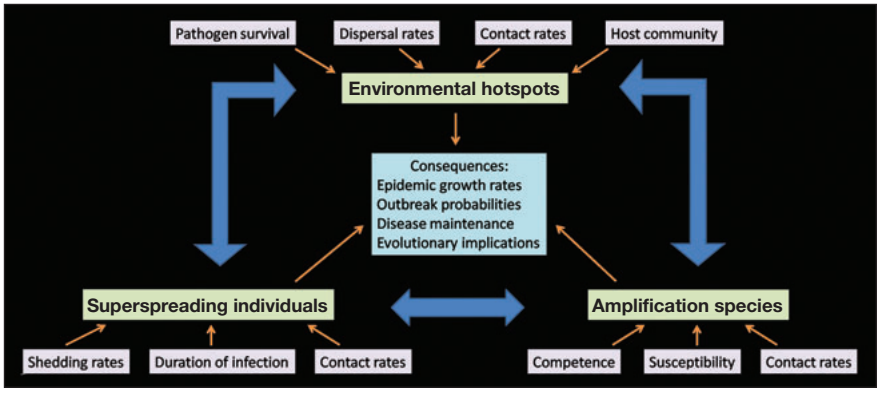

Figure 2. *Conceptual diagram illustrating causes (purple boxes) and consequences (blue box) of transmission heterogeneity (green boxes), as well as connections across hosts and space (large blue arrows). Here, "contact rate" refers to contacts between either two host species or a host and vector; "dispersal" refers to the movement of a pathogen from one environmental patch to another; and "host community" refers to the density of hosts and their collective reservoir potential. Many of the consequences of, and linkages between, heterogeneity at multiple scales remain to be discovered (Panel 2).*

ences in intestinal microbiota can determine whether individual mice shed high levels of pathogens in their feces (Lawley *et al.* 2009). Additionally, immune system trade-offs in response to different types of pathogens (eg microparasites versus macroparasites) can increase the duration and intensity of infection in individuals harboring multiple pathogen types (Graham *et al.* 2007; Telfer *et al.* 2010; Hawley and Altizer 2011). Co-infection may also reduce transmission potential as a result of cross-immunity and the contact-reducing behaviors of infected hosts (Rohani *et al.* 2003; Hawley and Altizer 2011). Determining the impact of co-infections on transmission is an important direction for further research.

Quantifying individual transmission heterogeneity can help direct disease management strategies (Panel 1). When individuals that contribute disproportionately to transmission can be identified from infection levels or transmission studies such as contact tracing, targeted control efforts can be considerably more effective at preventing and containing outbreaks than random control (Woolhouse *et al.* 1997; Lloyd-Smith *et al.* 2005). Even more effective control is possible when individuals with the potential for disproportionate transmission can be predicted before infecting others (Lloyd-Smith *et al.* 2005; Hudson *et al.* 2008), for example based on host characteristics such as weight or sex (eg Perkins *et al.* 2003). However, identifying superspreaders may be costly in terms of time and effort, highlighting the need for methods to calculate the cost-effectiveness of reducing R_0 via targeted versus untargeted population-level controls.

Species-level transmission heterogeneity

In addition to intraspecific heterogeneity described above, many pathogens infect multiple host species, in which contact rates and pathogen transmissibility vary, leading to differences between species in their contribution to disease transmission (Woolhouse *et al.* 2001; Haydon *et al.* 2002). Interspecific variability in transmission is a function of host susceptibility, contact rates with vectors or other hosts, and host competence, which is the efficiency with which a host produces and transmits a pathogen (Figure 2; Kilpatrick *et al.* 2006; Brisson *et al.* 2008; Cronin *et al.* 2010). For instance, American robins (*Turdus migratorius*) are competent hosts for West Nile virus (WNV), and are more frequently fed upon by WNV-transmitting mosquitoes relative to their abundance. As a result, robins may infect 24–71% of WNV-

Panel 2. Outstanding questions about host and spatial transmission heterogeneity

Several outstanding research questions remain before a theory can be developed that integrates our understanding of transmission heterogeneity across hosts and space. A combination of models for well-parameterized systems, field surveys, and experimental tests of different management strategies (when ethical) will offer insight into these questions.

Causes of transmission heterogeneity:

- To what extent is transmission heterogeneity caused by stochastic processes as opposed to inherent qualities of the individual, species, or environment?
- Are the identities of individuals and locations that are responsible for large numbers of transmission events temporally stable?

Consequences of transmission heterogeneity:

- Does the cause of transmission heterogeneity (eg high contact rates, shedding rates, long duration of infection) influence the strength of the heterogeneity or the co-evolutionary implications?
- How do the consequences of transmission heterogeneity for disease dynamics (epidemic growth rates and probability of pathogen extinction) vary across individuals, species, and space?
- How frequently do hosts and environments with the highest contact rates form isolated sub-networks that lead to reduced disease risk in those outside the network?
- How does transmission heterogeneity influence co-evolution between hosts and parasites?

infected vectors at a site, despite representing only 1–8% of the avian hosts (Kilpatrick *et al.* 2006).

Identifying hosts that amplify pathogen transmission ("amplification hosts") is a key priority for effective management of multi-host diseases. For vector-borne diseases, it has been hypothesized that hosts that infect more vectors are associated with an "r-selected" (eg rapid turnover) life-history strategy (Cronin *et al.* 2010). For example, experimental exposure of six grass species to barley yellow dwarf virus suggested that plants with a "quick return" phenotype (eg high levels of nitrogen and phosphorus, as well as high metabolic rates in leaves) had increased host susceptibility, competence, and vector population sizes, most likely because their leaves offered more resources for vector and pathogen growth and generally had fewer defenses (Cronin *et al.* 2010). Such hosts enhance the population of infected vectors, increasing infection risk for co-occurring host species. Species that tend to have high population densities or show highly social behavior may also be at increased risk of contracting pathogens for which transmission is dependent on host density, resulting from higher contact rates (Altizer *et al.* 2003). By elevating overall disease prevalence, such hosts can amplify transmission throughout multiple species' communities.

In extreme cases, amplification hosts that make disproportionate contributions to community-wide disease transmission relative to their abundance may be considered "superspreading species". With a definition analogous to that of superspreading individuals (Lloyd-Smith *et al.* 2005), a superspreading species can be identified by determining the expected distribution of community-wide transmission events assuming homogeneous transmission potential across host species (Panel 1). A species responsible for more infections than the *n*th percentile of the expected distribution can be classified as a community superspreader (Panel 1; eg Kilpatrick *et al.* 2006). When identifying superspreading species, the transmission event of interest should be defined explicitly. This could include transmission that is either intra- or interspecific, or to a host species of particular interest (eg humans or domestic animals), depending on the research or management objective. For WNV, Kilpatrick *et al.* (2006) demonstrated that robins are an example of a superspreading species because the proportion of mosquitoes potentially infected by robins relative to the proportion of the host community that they represent is far greater than would be expected from chance alone if the host community were homogeneous (Panel 1).

Environmental transmission heterogeneity

Pathogens are also characterized by spatial heterogeneity in transmission, and regions with particularly high pathogen prevalence (percentage of infected hosts), intensity (pathogens per infected host), or transmission rates are frequently referred to as "hotspots" or transmission foci. Hotspots may also be "source areas", from which pathogens disperse to less infected areas across a landscape. Environmental hotspots are often characterized by conditions that facilitate either elevated pathogen survival or greater densities of amplification hosts (for diseases with density-dependent transmission; Figure 2). For instance, *Vibrio cholerae*, the bacteria that causes cholera, can become concentrated on water hyacinths (*Eichornia crassipes*), which enhance the pathogen's survival (Spira *et al.* 1981), potentially leading to transmission hotspots in areas that have been heavily invaded by water hyacinth. Similarly, Farnsworth *et al.* (2005) found that chronic wasting disease prevalence in Colorado mule deer (*Odocoileus hemionus*) populations was twice as high near human developments as compared with that in more remote areas. This may have been caused by elevated deer densities that can result from artificial feeding stations, small home ranges, and lack of predators in developed areas.

Changes in host susceptibility, community structure, and contact rates that generate disease hotspots in humans, plants, and wildlife are frequently associated with anthropogenic environmental changes, such as fragmentation and eutrophication, that alter habitat quality and territory size (Patz *et al.* 2004; Johnson *et al.* 2010). For instance, poor habitat quality and populations isolated in fragmented habitats can cause stress and reduced genetic diversity in host populations, thereby reducing host immunity and resulting in spatial variability in transmission potential across the landscape (Pearman and Garner 2005; Bradley and Altizer 2007). Nutrient enrichment can also elevate disease risk through changes to pathogen abundance and virulence, host and vector densities, or host susceptibility (Johnson *et al.* 2010). For example, a study in Belize showed that nutrient enrichment of water bodies associated with agricultural areas supports different aquatic plant communities that promote breeding by an efficient malaria vector, *Anopheles vestitipennis* (Grieco *et al.* 2006). Alternatively, fragmentation and nutrient enrichment can impede the spread of a disease by reducing host density and contact rates (Bradley and Altizer 2007; Johnson *et al.* 2010).

Regional variability in host contact rates in settings such as daycare facilities, hospitals, markets, and farms, as well as regional differences in behavior, can also create hotspots of disease. Marine salmon farms, in which high densities of captive salmon are maintained in coastal pens, are examples of transmission foci that can enhance sea lice infection pressure for nearby wild salmon by as much as four orders of magnitude (Krkošek *et al.* 2005). Similarly, aggregation of children in schools enhances transmission of childhood diseases, such as measles (eg Bjørnstad *et al.* 2002). Social animal behaviors that tend to aggregate and increase contacts between hosts, such as those that occur at collective mating grounds (eg leks), overwintering dens, watering holes, and feeding sites, can also elevate disease transmission at those sites (Altizer *et al.* 2003, 2006). Cultural differences in human behavior can also influence disease transmission by shifting

host–pathogen contact rates (Alexander and McNutt 2010). For instance, regional differences in caregiving and nursing techniques may have contributed in part to differences in the rates of human-to-human transmission and mortality from Nipah virus outbreaks in Bangladesh as compared with those in Malaysia (Chong *et al.* 2008), creating regional heterogeneity in disease transmission.

Quantitative methods for estimating the net contribution of hotspots to landscape-level transmission may facilitate control measures. Extreme levels of spatial transmission heterogeneity might lead to environmental hotspots that are analogous to superspreaders (Lloyd-Smith *et al.* 2005), in that such patches are responsible for greater than the *n*th percentile of the expected fraction of regional transmission events (Panel 1). It is particularly important with spatial transmission heterogeneity to explicitly identify the transmission measure of interest before assessing the importance of transmission heterogeneity to disease dynamics. The relevant measure of transmission for habitat patches will depend on the management scenario and could include, for example, the number of farms infected by a single farm (Keeling *et al.* 2001) or the number of host infections that occur in spatially defined areas.

Integrating management of host and spatial transmission heterogeneity

Treating, vaccinating, or altering the contact patterns of potential individual superspreaders before an outbreak begins could reduce the chances of a major outbreak and slow initial epidemic growth rates, thereby increasing the effectiveness of applied control measures (Lloyd-Smith *et al.* 2005). Nonetheless, several issues surrounding the consequences of interspecific and spatial transmission heterogeneity for outbreak probabilities and epidemic trajectories are important avenues for future research (Panel 2). In addition, new theory for understanding when to expect transmission heterogeneity will improve disease mitigation strategies. Management could also be enhanced by identifying and addressing connections between host and spatial heterogeneity. Finally, it will be important to develop new strategies for identifying the most infectious hosts and landscapes, and new management tools to reduce their contribution to transmission.

Integration of previous research suggests several hypotheses regarding the causes of heterogeneous transmission patterns and the pathogen transmission modes most likely involved. For instance, we hypothesize that heterogeneity in contact rates is more important than heterogeneity in infectiousness for creating superspreaders, because in an age of globalized travel and practices that increase host density, such as industrialized farming and habitat fragmentation, contact rates may vary more than infectivity. Another testable hypothesis is that specific pathogen transmission modes are more commonly associated with certain types of transmission heterogeneity. For instance, transmission variability across hosts may be more common among infections transmitted through vectors or direct host-to-host contact; this is because there are no intermediate transmission steps (eg to other obligate host species) that would dilute the influence of variable contact rates, competence, or infectivity on overall transmission. Environmental transmission heterogeneity may be more prevalent among pathogens with density-dependent transmission or environmentally transmitted stages, because transmission foci are often characterized by high host or pathogen densities. Empirical testing of these hypotheses will require quantitative approaches for identifying transmission heterogeneity (Panel 1) in addition to meta-analyses that integrate the results from multiple studies.

Connections between host and spatial transmission heterogeneity are likely common and could have implications for disease management. Logically, superspreaders create hotspots of transmission around them, and hosts in a disease hotspot, by definition, experience increased infection pressure as compared with others in the population. For example, interspecific transmission heterogeneities in Lyme disease can theoretically lead to environmental hotspots because fragmented habitats often support a higher fraction of competent amplification hosts, which could increase disease risk (eg measured as nymph infection prevalence) in disturbed landscapes (LoGiudice *et al.* 2003). Environmental hotspots that occur as a result of temporary aggregation of hosts – for example, at a watering hole – could also facilitate individual superspreading by serving as a source location for infection among highly social individuals that disperse from the location and subsequently infect many others. Finally, heterogeneity occurs both among and within species, and amplification species may contain one or more superspreading individuals. For example, domestic dogs account for the majority of rabies cases in parts of rural Tanzania; infected dogs vary substantially in their biting rates, such that in addition to being the dominant amplification host in the system, some domestic dogs account for a disproportionate number of canine rabies transmission events (Hampson *et al.* 2009). These patterns suggest that a priority for future research in disease ecology should be the development of a framework integrating transmission heterogeneity across hosts and space (Panel 2).

Perhaps the most practical information about transmission heterogeneity from a management perspective is determining what measures may be useful for identifying the most infectious individuals, species, and locations so that they can be targeted before infecting others. If, as hypothesized, contact rates play the greatest role in transmission heterogeneity, then quantifying contact networks representing the set of interactions between nodes (eg individuals, species, or environments) could provide a surrogate measure for identifying potential superspreaders (Figure 3; eg Keeling and Eames 2005), particularly if traits characteristic of the highest contact nodes can be identified. Importantly, specific characteristics, such as the duration of infectiousness and contact, must be considered

to determine the role of high contact nodes (eg Craft *et al.* 2011). Additionally, because infectiousness frequently co-varies with susceptibility (Hudson *et al.* 2008; Lloyd-Smith *et al.* 2008), another potential indicator for identifying possible superspreaders and amplification hosts could involve measures of susceptibility such as body condition, testosterone level, or immunocompetence (Beldomenico and Begon 2010). Identifying the most infectious hosts before they infect others offers a superior management strategy to post hoc analyses that detect such hosts from infection levels or transmission studies; however, recognizing these individuals and determining the probability that they will become infected can be challenging. Intriguingly, advanced tools, such as therapeutic interfering particles (particles engineered to replicate along with the pathogen, but that inhibit pathogen growth), can eliminate the challenges of identifying superspreaders a priori because they are transmitted among hosts along with the pathogen, naturally making their way to the most high-risk populations (Metzger *et al.* 2011). Further research that identifies the conditions under which easily observable host or landscape traits are associated with high transmission rates will aid targeted disease control efforts.

Conclusions

Transmission heterogeneity occurs among hosts and across space (Figure 1); more formal quantification of these heterogeneities, along with the costs associated with their identification and targeted control, could help to make targeted management more cost-effective (Panel 1). Importantly, such heterogeneities in transmission are intimately linked (Figure 2), so that a better understanding of these linkages will lead to important advances. Addressing critical questions about when host and spatial transmission heterogeneities are stochastically generated or temporally variable and what the implications are for disease dynamics and host–pathogen evolution will require the integration of modeling and empirical approaches (Panel 2). Given the growing influence of anthropogenic environmental change on disease risk for humans, plants, and animals, focusing research efforts toward developing an integrative theory for understanding transmission heterogeneity across scales will be useful for ecologists, public health officials, and wildlife managers.

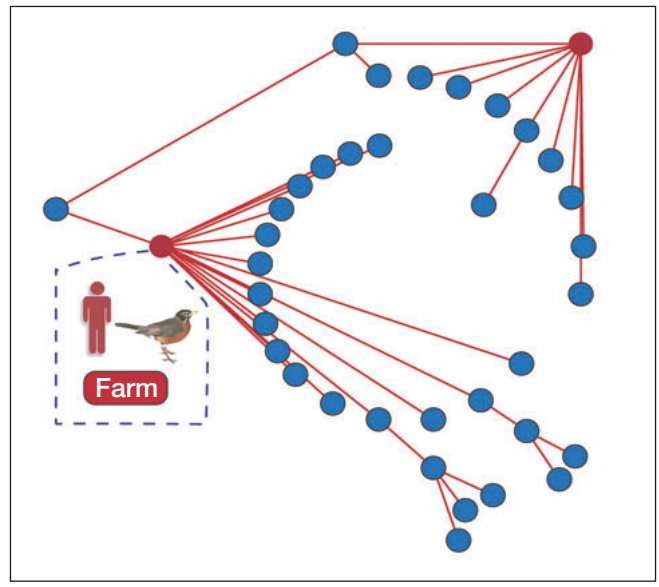

Figure 3. *Hypothetical contact network showing potential superspreaders (red circles) with higher than average connections to the rest of the network. The human, robin, and farm icons represent some of the possible identities of these potential superspreaders. Blue circles represent nodes (eg individuals, species, or locations) with lower than average connections (red lines) to the rest of the network.*

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