Biodiversity and Disease Risk: the Case of Lyme Disease

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Abstract: *Utilitarian arguments concerning the value of biodiversity often include the benefits of animals, plants, and microbes as sources of medicines and as laboratory models of disease. The concept that species diversity per se may influence risk of exposure to disease has not been well developed, however. We present a conceptual model of how high species richness and evenness in communities of terrestrial vertebrates may reduce risk of exposure to Lyme disease, a spirochetal (*Borrelia burgdorferi*) disease transmitted by ixodid tick vectors. Many ticks never become infected because some hosts are highly inefficient at transmitting spirochete infections to feeding ticks. In North America, the most competent reservoir host for the Lyme disease agent is the white-footed mouse (*Peromyscus leucopus*), a species that is widespread and locally abundant. We suggest that increases in species diversity within host communities may dilute the power of white-footed mice to infect ticks by causing more ticks to feed on inefficient disease reservoirs. High species diversity therefore is expected to result in lower prevalence of infection in ticks and consequently in lower risk of human exposure to Lyme disease. Analyses of states and multistate regions along the east coast of the United States demonstrated significant negative correlations between species richness of terrestrial small mammals (orders Rodentia, Insectivora, and Lagomorpha), a key group of hosts for ticks, and per capita numbers of reported Lyme disease cases, which supports our "dilution effect" hypothesis. We contrasted these findings to what might be expected when vectors acquire disease agents efficiently from many hosts, in which case infection prevalence of ticks may increase with increasing diversity hosts. A positive correlation between per capita Lyme disease cases and species richness of ground-dwelling birds supported this hypothesis, which we call the "rescue effect." The reservoir competence of hosts within vertebrate communities and the degree of specialization by ticks on particular hosts will strongly influence the relationship between species diversity and the risk of exposure to the many vector-borne diseases that plague humans.*

Biodiversidad y Riesgo de Enfermedades: El Caso de la Enfermedad de Lyme

Resumen: *Argumentos utilitarios relacionados con el valor de la biodiversidad frecuentemente incluyen los beneficios de animales, plantas y microbios como recursos para medicinas y como modelos de enfermedades en laboratorio. Sin embargo, la idea de que la diversidad de especies* por sí misma *puede influenciar el riesgo de exposición a enfermedades no ha sido bien desarrollada. Presentamos un modelo conceptual de cómo la riqueza de especies y la uniformidad en comunidades de vertebrados terrestres puede reducir el riesgo de exposición a la enfermedad de Lyme, una enfermedad causada por una espiroqueta (*Borrelia burgdorferi*) y transmitida por una garrapata ixódida. Muchas garrapatas nunca son infectadas debido a que los huéspedes son altamente ineficientes en la transmisión de espiroquetas a las garrapatas que se alimentan de ellos. En Norte América, el huésped reservorio más competente del agente de la enfermedad de Lyme es el ratón de patas blancas (*Peromyscus leucopus*), una especie de amplia dispersión y localmente abundante. Sugerimos que los incrementos en la diversidad de especies dentro de las comunidades de huéspedes pueden diluir el potencial de infección de las garrapatas por el ratón de patas blancas al ocasionar que más garrapatas se alimenten de reservorios ineficientes en la transmisión de la enfermedad. Por lo tanto, se esperaría que una alta diversidad de especies resulte en una prevalencia de infección de garrapatas reducida y, por lo tanto, en una disminución del riesgo de exposición de humanos a la enfermedad de Lyme. Un análisis por estado y de*

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varios estados a lo largo de la costa este de los Estados Unidos demostró correlaciones significativamente negativas entre la riqueza de especies de mamíferos terrestres pequeños (órdenes Rodentia, Insectivora, y Lagomorfa), un grupo clave de huéspedes para garrapatas, y los números per capita de casos de la enfermedad de Lyme reportados, lo cual apoya nuestra hipótesis de efecto de dilución*. Contrastamos estos resultados con lo que se podría esperar cuando los vectores adquieren eficientemente agentes de la enfermedad de muchos huéspedes, caso en el cual, una alta diversidad causaría la prevalencia de infección de garrapatas permaneciendo alta aún cuando la diversidad de huéspedes disminuyera. Una correlación positiva entre los casos de la enfermedad de Lyme per capita y la riqueza de especies de aves residentes del suelo apoya esta hipótesis, que hemos llamado* efecto de rescate*. La capacidad de reservorio de huéspedes dentro de las comunidades de vertebrados y el grado de especialización de las garrapatas en huéspedes particulares, influenciaría fuertemente la relación entre la diversidad de especies y el riesgo de exposición a muchas de las enfermedades transmitidas por vectores que infectan a humanos.*

Introduction

Arguments concerning the value of biodiversity can be divided into those that are ethical or aesthetic and those that are utilitarian (Lovejoy 1997; Patrick 1997). Among the most powerful of the utilitarian arguments are those concerning the effects of eroding biodiversity on human health. Because humans rely so strongly on animals, plants, and microbes as sources of pharmaceutical agents, and because scientists continue to discover animal and microbial models of human disease, both scientists and public health advocates have asserted that the preservation of biodiversity is crucial for present and future human health (Chivian 1997; Grifo et al. 1997). This argument maintains that if biodiversity continues to decline, future biotic sources of drugs and laboratory models will disappear before they are discovered, inhibiting the ability of scientists to understand and treat diseases. Thus, the preservation of biodiversity will prevent the decline or extinction of particular species of high biomedical value. But because most species will have little or no biomedical value, this argument focuses more on preserving particular biomedically important organisms than on biodiversity per se.

Until recently, there has been little scientific evidence for the value of biodiversity per se for human health. Recent ecological research, however, suggests that biodiversity may be fundamentally important in reducing the risk of exposure to certain zoonotic diseases. Zoonotic diseases are those maintained within natural communities of animals but which are occasionally transmitted to humans. Diversity within these animal communities could play an important role in the maintenance of a disease and in the probability of its transmission to humans. Such a situation has recently been documented for Lyme disease, a widespread vector-borne disease (Van Buskirk & Ostfeld 1995, 1998). Understanding the role of biodiversity in reducing the risk of Lyme disease requires knowledge of ecological interactions, particularly interactions between the tick vector of the disease and its community of vertebrate hosts.

Ecology of Lyme Disease

Between 10,000 and 17,000 cases of Lyme disease are reported each year by state health departments to the U.S. Centers for Disease Control and Prevention (CDC), making Lyme disease the most common vector-borne disease in the United States (CDC 1998). Thousands of cases occur per annum in Europe and Asia (Lane et al. 1991; Barbour & Fish 1993). Lyme disease is caused by a spirochete bacterium (*Borrelia burgdorferi*) that is transmitted to humans via the bite of ticks of the genus *Ixodes* (*I. scapularis* and *I. pacificus* in North America; *I. ricinus* and *I. persulcatus* in Europe, Asia, and Africa).

Ixodes scapularis ticks complete their life cycle over 2 years and during that time pass through four developmental stages (Van Buskirk & Ostfeld 1995). Female adult ticks lay eggs in the spring. These eggs hatch into larvae, which seek a host, often a small mammal or a bird. Each larva takes a single blood meal from its host during the summer, then drops off and molts into the nymphal stage. This nymphal stage overwinters, then seeks a host the following late spring or early summer. After a single blood meal, the nymph drops off its host and molts into the final stage, an adult. In the fall of that year, the adult seeks a host, often a white-tailed deer (*Odocoileus virginianus*), for its final blood meal. The adults mate while on the deer, and then the female drops off to overwinter before laying her eggs the following spring. Other species of ixodid ticks have similar life cycles involving four developmental stages and three blood meals over about 2 years, although the timing of development and association with hosts varies (Piesman & Gray 1994).

Virtually all larval ticks hatch from eggs free of *B. burgdorferi* because mother ticks only rarely transmit the spirochete to their offspring (Piesman et al. 1986; Patrican 1997). Thus, larval ticks are incapable of infecting a host. Nevertheless, larval ticks that take their blood meal from an infected vertebrate host may acquire the spirochete and retain the infection throughout the remainder of their lives, transmitting it to their subsequent

hosts. From an epidemiological standpoint, the nymphal stage is the most dangerous to humans because nymphs are tiny (approximately 1 mm diameter) and hard to detect, and are most active in summer when human outdoor activity typically peaks (Barbour & Fish 1993). Larvae are also small and active in midsummer, but they are not infected with the Lyme disease spirochete, whereas nymphs may be. Adult ticks, on the other hand, may be infected, but they are larger and easier to detect. Adults also are active in the mid to late autumn, when human outdoor activity is relatively low. Infection prevalence (percentage of ticks infected with the pathogen) in nymphal *Ixodes* populations throughout the United States and Europe varies between 1–5% and 40% (Lane et al. 1991; Mather & Ginsberg 1994), resulting in high geographic variation in risk of exposure to Lyme disease. Variation in infection prevalence among regions and among habitat types appears considerably higher than variation over time at particular localities. What might be responsible for this spatial variation in disease risk?

The juvenile stages (larvae and nymphs) of *I. scapularis, I. pacificus, I. ricinus*, and *I. persulcatus* are highly nonspecific in their distribution on vertebrate hosts, having been reported on >100 species of mammals, birds, and reptiles (Lane et al. 1991; Matuschka et al. 1991; Tälleklint 1996). These vertebrate hosts differ dramatically in the probability that they will infect a feeding tick with the Lyme-disease spirochete. In the eastern and central United States, the white-footed mouse (*Peromyscus leucopus*) is the principal natural reservoir for the Lyme disease spirochete because 40–80% of larval ticks feeding on an infected white-footed mouse acquire the spirochete (Mather 1993). These ticks then become capable of infecting subsequent hosts during their nymphal and adult stages. A few other mammalian and avian hosts such as eastern chipmunks (*Tamias striatus*) and American Robins (*Turdus migratorius*), are moderately effective reservoirs, but most others are incompetent reservoirs of Lyme disease (Mather 1993). The physiological basis of reservoir competence is poorly understood, although the immune response by the host to the pathogen appears to be important. One host species, the western fence lizard (*Sceloporus occidentalis*), produces a circulating protein that kills Lyme disease spirochetes within the gut tissues of feeding ticks (Lane & Quistad 1998). Low infection prevalence of *Ixodes* ticks in areas within the geographic range of the western fence lizard has been attributed to the abundance of this incompetent reservoir (Lane & Quistad 1998).

Biodiversity and the Dilution Effect

Recently, Van Buskirk and Ostfeld (1995, 1998) developed an empirically based computer simulation model to explore how changes in the community of hosts for juvenile ticks would influence the abundance and infection prevalence of nymphs. The model was parameterized for *I. scapularis* and its host communities in the eastern and central United States, with one competent reservoir (the white-footed mouse) and one to several alternative hosts whose transmission efficiency is low or nonexistent. Because *I. scapularis* ticks feed successfully from a wide variety of vertebrate hosts, the simulation model found that tick density was relatively insensitive to changes in the relative abundance of competent versus incompetent reservoirs. The infection prevalence of nymphal ticks, however, was dramatically reduced when the relative abundance of nonmouse hosts was increased. The model varied the species diversity (species richness plus evenness) within the host community and showed that increasing the diversity of hosts reduced disease risk as measured by the infection prevalence of nymphal ticks.

Intuitively, this result can be understood as a "dilution effect." Any factor that decreases the representation by white-footed mice relative to other hosts in the vertebrate community would reduce the proportion of ticks infected with the Lyme disease spirochete. One mechanism of reducing the infection prevalence of ticks is therefore to reduce the abundance of white-footed mice while maintaining the presence of alternative host species. Another mechanism is to increase the number of alternative hosts, which typically are incompetent reservoirs (Matuschka et al. 1991, 1993).

White-footed mice are extreme habitat and dietary generalists and typically are among the most abundant vertebrates within forested landscapes of the eastern and central United States (Kaufman & Kaufman 1989). In the eastern states, white-footed mice occur in both species-poor and species-rich communities. As a result, a host community that is species poor tends to have a disproportionately high representation of white-footed mice, resulting in a high percentage of tick meals taken from this competent reservoir and, consequently, a high infection prevalence in the tick population. As species are added to the host community, these alternative hosts dilute the effect of white-footed mice by increasing the proportion of blood meals that are taken from incompetent hosts. The expected result is a lower infection prevalence in the tick population and hence a lower per capita risk of exposure to Lyme disease in humans. A similar result occurs if the population density of white-footed mice declines while the densities of other hosts remain constant or increases.

If higher diversity in the community of tick hosts results in lower infection prevalence in the population of nymphal ticks, one would expect a negative correlation between species richness in the vertebrate community and the number of Lyme disease cases per capita. To test this expectation at a large spatial scale, we tallied the

species richness of terrestrial small mammals (orders Rodentia, Insectivora, and Lagomorpha; Hamilton & Whitaker 1998), ground-nesting, shrub-nesting, and ground-foraging birds (Ehrlich et al. 1988), and lizards (Conant & Collins 1998) in each state along the eastern seaboard of the United States from Maine to Florida. *Ixodes scapularis* occurs in all these states (Dennis et al. 1998), and these three groups of hosts represent the majority of hosts regularly available to this tick species, which seeks a host at or near ground level in forests, fields, and thickets. We aggregated small states into regions to avoid the potential for variation in state area to bias measurements of species richness, which increases with area (Preston 1960). Accordingly, Vermont, New Hampshire, Massachusetts, Connecticut, and Rhode Island were lumped into "New England," and New Jersey, Delaware, and Maryland were lumped into "Mid Atlantic." Neither species richness nor per capita numbers of Lyme disease cases were significantly correlated with area of the states and regions (for all regressions, $r^2 < 0.11$, df = 10, $p > 0.33$).

We regressed the number of cases of Lyme disease reported to the CDC in 1996 and 1997 (cases per 100,000 population; CDC 1997, 1998) against species richness of the three vertebrate classes by means of stepwise multiple regression analyses (with $\alpha = 0.15$ for inclusion), considering each year separately. We used states and the two multistate regions as the geographic units of measurement because the occurrence of host species in a state or region can be detected with standard range maps for each vertebrate taxon (National Geographic Society 1983; Conant & Collins 1998; Hamilton & Whitaker 1998) and because reported cases of Lyme disease from each state are highly likely to have been contracted within that state.

The stepwise multiple regressions showed a significant effect of species richness in components of the host community on per capita number of Lyme disease cases in the eastern United States. In 1996 both ground-dwelling birds and small mammals entered the multiple regression model, which explained 61.2% of the variation in per capita cases of Lyme disease. Numbers of Lyme disease cases per state or region were positively associated with the species richness of birds (partial r = 0.67, df = 1, $p = 0.02$) and negatively associated with the species richness of small mammals (partial r = -0.40, df = 1, $p = 0.10$). In 1997 only ground-dwelling birds entered the regression model (partial r = 0.69, df = 1, $p = 0.04$), which explained 39.4% of the variation in per capita cases of Lyme disease. Species richness of lizards did not enter the model for either year.

In the regression analyses Florida was consistently a statistical outlier (leverage > 0.8) because of its particularly high species richness of lizards and low richness of small mammals and ground-dwelling birds. Removing Florida from the analyses gave generally significant ef-

fects of all three vertebrate groups on per capita cases of Lyme disease (1996: birds, $r^2 = 0.54$, $p = 0.02$; small mammals, $r^2 = 0.47$, $p = 0.03$; lizards, $r^2 = 0.40$, $p = 0.05$ [Fig. 1]; 1997: birds, $r^2 = 0.46$, $p = 0.03$; small
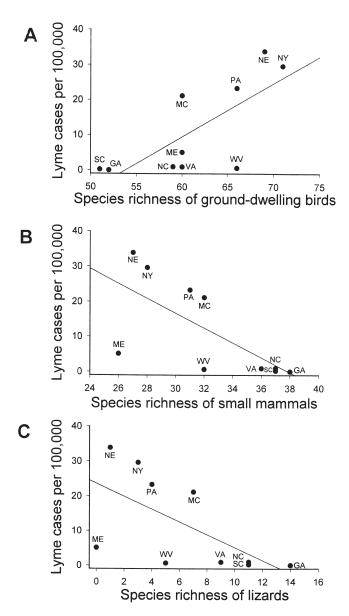

Figure 1. Relationship between cases of Lyme disease reported to the U.S. Centers for Disease Control and Prevention in 1996 and species richness in the community of (a) ground-dwelling birds, (b) small mammals, and (c) lizards (GA, Georgia, MC, Mid-Atlantic states; ME, Maine; NC, North Carolina; NE, New England states; NY, New York; PA, Pennsylvania; SC, South Carolina; VA, Virginia; WV, West Virginia). Regression lines represent simple linear regressions performed separately for each host component after removal of Florida as a statistically significant outlier. Regression statistics for both multiple and simple linear regressions for 1996 and 1997 are described in the text.

mammals: $r^2 = 0.40$, $p = 0.05$; lizards: $r^2 = 0.34$, $p = 0.08$).

Cases of Lyme disease are concentrated in more northerly states and regions (Fig.1), suggesting a latitudinal gradient in both Lyme disease incidence and species richness within all three vertebrate orders. We cannot rule out the possibility that the association between species richness and Lyme-disease incidence is spurious, being caused by some unmeasured factor that varies with latitude. We suggest, however, that the latitudinal gradient in species diversity causes the apparent latitudinal gradient in Lyme disease incidence, consistent with the dilution effect. Similarly, we cannot rule out the possibility that Lyme disease incidence has equilibrated in northern states but not in more southerly states due to its slow spread from Connecticut, where it was first discovered in the 1970s (Barbour & Fish 1993; Ostfeld 1997). But the relatively stable number of Lyme cases within the eastern states over the past 10 years (CDC 1998) does not support this contention. We are not aware of any evidence that more southerly areas are showing faster rates of increase in tick infection prevalence than are more northerly areas.

Similar geographic analyses at finer spatial scales of resolution (e.g., county level) are warranted, although they may be complicated by inaccuracies in species lists for smaller spatial units and by cases of Lyme disease acquired in one county but reported in another. Determination of local-scale relationships between species diversity and infection prevalence of ticks, followed by comparisons across large geographic areas, would provide a robust test of the power of the dilution effect to influence geographic patterns of disease risk. In the absence of data on the more appropriate, finer spatial scales, the large-scale patterns assessed here should be treated with caution.

Species Richness versus Evenness

Species diversity consists of two elements: richness (number of species) and evenness (proportional representation by each species). Ideally, the most appropriate independent variable in our state and regional analysis would be species evenness, because evenness represents the total distribution of opportunities for ticks to feed from each host species. Because evenness data are not available for entire host communities, however, we used species richness as a surrogate measure of species diversity. Recent studies of the effects of the changing abundance of white-footed mice and eastern chipmunks support the conclusions arising from large-scale analyses. Schmidt et al. (1999) analyzed the effects of population density of these two primary hosts for juvenile ticks for 3 years during which both species fluctuated. They found that a high density of chipmunks reduces burdens

of larval ticks on mice, supporting the existence of a dilution effect of chipmunks on mice. Thus, holding species richness constant at two species, the greater the species evenness, the lower the proportion of larval ticks feeding on mice. No comparable data are available for whole vertebrate communities.

Recently, Schmidt and Ostfeld (unpublished data) analyzed the dilution effect in local assemblages of vertebrate hosts for *I. scapularis.* They calculated that if larval ticks fed exclusively on the two most competent reservoirs (white-footed mice and eastern chipmunks), 86% of nymphal ticks should carry the Lyme disease bacterium. In actuality, only 36% of nymphal ticks were infected with *B. burgdorferi* at their sites. In general, Schmidt and Ostfeld found that the infection prevalence of ticks was only 44% as high as would be expected if ticks fed only on the two most competent reservoirs. Using a simple model, Schmidt and Ostfeld (unpublished data) determined that nonmouse, nonchipmunk hosts must provide approximately 61% of larval tick meals, indicating that the dilution effect is strong at the local scale.

Vector-Host Interactions in Ecological Communities

Three further considerations enrich the relationship between species diversity and disease risk. The first is the degree to which vector ticks are generalists that are unselective of hosts (Sonenshine 1994). The simulation model of Van Buskirk and Ostfeld (1995) assumed that the probability that a tick will take its blood meal from a particular species of host resulted from the density of the host relative to all possible hosts, combined with the specific host-finding efficiency. Because no data are available concerning the host-finding efficiency of *I. scapularis* for various hosts, Van Buskirk and Ostfeld (1995) used a constant value for all hosts. If juvenile ticks tend to select or feed more successfully on some hosts than on others, however, then the addition of host species to a vertebrate community will not result in a simple linear decrease in infection prevalence. For example, if larval ticks prefer to feed on a white-footed mouse over rarer host species, then incremental increases in the number of species will not result in incremental decreases in the infection prevalence of nymphs. Further studies of the distribution of juvenile ticks among hosts within vertebrate communities and of the mechanisms behind any biases shown are crucial to our ability to predict and mitigate the risk of Lyme disease.

In host communities with a single, highly competent reservoir that is also a community dominant, exemplified by *P. leucopus* in eastern North America, the diversity of the host community will be reduced when the population density of the principal reservoir declines.

Disease risk thus may be closely tied to population fluctuations of a single host. But not all host communities are that simple. The second consideration concerns host communities in which several species are similar in their reservoir competence, as may be the case with Lyme disease in parts of Europe (Tälleklint & Jaenson 1994; Craine et al. 1995; Randolph & Craine 1995). Where multiple competent reservoirs exist, each reservoir species may contribute to a "rescue effect," whereby the disease agent is maintained at a relatively constant prevalence even when host populations fluctuate. For instance, in European regions where several species of rodents, including voles (*Clethrionomys* spp.), mice (*Apodemus* spp.), and grey squirrels (*Sciurus carolinensis*), are all competent reservoirs, reduction in the density of one of these hosts may have little or no effect on disease risk because the enzootic cycle is maintained through the remaining hosts. In cases such as this, high diversity in the host community is likely to maintain the constancy of disease risk because the infection prevalence of vectors will not be closely tied to fluctuations of a single host (Sonenshine 1994; Randolph & Craine 1995). The positive association between the species richness of birds and per capita cases of Lyme disease (Fig. 1) suggests that ground-dwelling birds may promote a rescue effect in the eastern United States. These results also suggest that some species of birds may be highly competent reservoirs for Lyme bacteria and that comprehensive studies of avian reservoir competence are warranted.

The third consideration arises from the realization that species within host communities interact, for instance through competitive or predator-prey relationships. Models that simply vary the species richness of a community of vertebrate hosts for ticks may fail to capture the effects of interactions on the relative abundance of each host. When species richness in a host community increases via the addition of species that compete with or prey upon the principal reservoir, then the dilution effect is compounded by reductions in the absolute density of the reservoir beyond the reduction in relative density expected when no interactions occur.

Effects of Habitat Fragmentation

Recent studies of white-footed mice in eastern and central North America show that population densities often are considerably higher in small, isolated woodlots embedded in agricultural or urbanized landscapes than they are in continuous forest (Nupp & Swihart 1996, 1998; Lewellen & Vessey 1998). Moreover, these populations within habitat fragments appear to fluctuate unregulated by biotic interactions (e.g., food supply, predation) and are regulated only by certain extreme weather conditions. The same studies show that predators tend to be absent from these small woodlots and that probable competitors, such as eastern chipmunks and fox squirrels (*Sciurus niger*), occur at lower densities in these areas than in more continuous habitat. Therefore, because the fragmentation of habitat causes a reduction in biodiversity within host communities, even within remnant patches, such landscape disturbance may increase the local risk of exposure to Lyme disease by increasing both the absolute and the relative density of the primary reservoir, the white-footed mouse.

Implications

Our arguments derive from the Lyme-disease system, in which a generalized vector parasitizes numerous host species, of which one or a few are competent reservoirs. The basic conclusions of the conceptual model may apply to other vector-borne diseases that have similar elements, including cutaneous leishmaniasis, Chagas' disease, human granulocytic ehrlichiosis, babesiosis, plague, louping ill, tularemia, relapsing fever, Crimean Congo hemorrhagic fever, and LaCrosse virus. Diseases in this diverse group vary in the degree to which vertebrate reservoirs are important, in the generalization by the vector on diverse hosts, and other features. Nevertheless, the role of biodiversity in the community of vertebrate hosts for these diseases is worthy of close attention. Within the range of a given vector-borne disease, we expect higher incidence where there are fewer host species, but why there are apparently more diseases in the species-rich tropics is an entirely separate matter (Mayer & Pimm 1997).

Comparative, experimental, and modeling approaches to understanding the effects of biodiversity on disease risk are warranted. Comparative studies should be undertaken to determine the degree to which diversity and the incidence of disease covary across different geographic regions or habitat types. Experimental studies should be conducted in which the diversity of the host community is directly manipulated to test a priori predictions regarding effects on disease risk. Modeling efforts tailored for individual disease systems could clarify the nature of expectations for comparative and experimental studies. If the relationship between biodiversity and disease risk is strong and general, then societal debates about the value of biodiversity to human welfare will become better informed and more urgent.

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