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Forest fragmentation predicts local scale heterogeneity of Lyme disease risk

Abstract Fragmentation of the landscape has been proposed to play an important role in defining local scale heterogeneity in Lyme disease risk through influence on mammalian host density and species composition. We tested this observed relationship in a suburban region around Lyme, Connecticut, where we collected data on the density of the tick vector, *Ixodes scapularis* and prevalence of the Lyme bacterium, *Borrelia burgdorferi* at 30 sites. Analysis of the landscape pattern of forest patches was performed using satellite imagery. The calculated landscape indices, which included patch size and isolation, revealed a positive link between fragmentation and both tick density and infection prevalence in ticks. In spite of higher entomologic risk, human incidence of Lyme disease is lower in fragmented contexts suggesting that entomologic risk is not the critical driver of human infections. These results represent a departure from the prior claims that fragmentation and human Lyme disease risk are positively linked. A complete understanding of the influence of landscape fragmentation will allow for improved risk mapping and potential environmental management of Lyme disease.

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Introduction

Landscape structure, the spatial arrangement of land-cover types, has had an historical impact on transmission risk of Lyme disease, the most common vector-borne disease in the United States (Orloski et al. 2000; Spielman et al. 1985; Turner 1989). The initial emergence of Lyme disease throughout the northeastern and mid-Atlantic states has been linked to reforestation over the past century, as a result of the repopulation of the white-tailed deer (*Odocoileus virginianus*), the primary host for the adult stage of the tick vector *Ixodes scapularis* (Barbour and Fish 1993; Piesman et al. 1979; Spielman et al. 1985). The subsequent rise in human incidence of Lyme disease over the last 2 decades in the Northeast is related to landscape modification through suburbanization (Barbour and Fish 1993; Frank et al. 1998; Maupin et al. 1991). Although the net amount of forest has not changed significantly, human development has created a higher numbers of forest patches interspersed with residential development. These changes in landscape structure have been linked to both increased human exposure to infected ticks and entomologic risk of Lyme disease, defined as the product of tick density and prevalence of the Lyme bacterium, *Borrelia burgdorferi* in ticks (Burgdorfer et al. 1982; Falco and Fish 1988; Frank et al. 1998; Maupin et al. 1991; Ostfeld and Keesing 2000; Steere et al. 1978). Landscape modification potentially impacts Lyme disease risk in a number of ways.

First, the fragmented suburban landscape can support high densities of the white-tailed deer as they benefit from the presence of edge habitat (Leopold 1933). Edge habitat is ideal as it provides preferred forage in abundant ecotonal vegetation. Suburban habitats further promote high deer densities through reduced hunting pressure, the absence of predators, and the presence of

ornamental vegetation providing winter forage (Barbour and Fish 1993; Frank et al. 1998). This type of landscape mosaic should experience higher tick densities than homogeneous forested landscapes because of the extremely high host numbers for adult tick-feeding and reproduction (Wilson et al. 1985).

Second, landscape structure will have an influence on the abundance and composition of small- and medium-sized mammals, which serve as hosts for the immature ticks as well as maintain the enzootic cycle of *B. burgdorferi* (Battaly and Fish 1993; Fish and Daniels 1990). Thus, fragmentation resulting from suburbanization may alter host diversity and abundance (Ostfeld and Keesing 2000). The reduction in forest patch size has been proposed to be positively correlated with disease risk by increasing the densities of the white-footed mouse (*Peromyscus leucopus*), considered the primary reservoir for *B. burgdorferi* and the main host for immature *I. scapularis*, and decreasing the numbers of less-competent hosts (Ostfeld and Keesing 2000; Schmidt and Ostfeld 2001). A subsequent study found that small forest fragments were found to have both increased tick density and tick infection prevalence (Allan et al. 2003).

Finally, landscape fragmentation may also influence human exposure to infected ticks. Residential suburban development in the Northeast has placed an increased number of people in close contact with the tick vector. Landscape structure plays an important role in defining the level of exposure as the density of infected ticks on a residential property is positively correlated with the proportion of vegetation cover on the property (Dister et al. 1997; Frank et al. 1998). Thus, the majority of the human infections have been shown to be contracted peridomestically (Falco and Fish 1988).

We performed a field study in a 12-town area around Lyme, Connecticut, to quantify the relationship between landscape pattern and entomologic risk (tick density and tick infection prevalence). Furthermore, we were interested in determining how this relationship translates to human incidence rates, which represents the combination of entomologic risk and human exposure. Resolving the impact of landscape fragmentation could play an important role in understanding how environmental change drives local scale heterogeneity in risk for Lyme disease, and help guide the development of environmental management strategies for disease prevention.

Materials and methods

Sampling strategy

We constructed a multistage sampling strategy to estimate relative *I. scapularis* nymphal abundance and *B. burgdorferi* infection prevalence in adult stage ticks within a 12-town area around Lyme, Connecticut (Fig. 1). In order to ensure that samples were taken from a variety of landscapes, the first sampling stage was used

to select thirty 1-km^2 sampling sites using a stratified random design. In stratified sampling, the study population is divided into non-overlapping strata, and samples are selected independently from each stratum (Thompson 1992). The abundance of deciduous vegetation as determined by the normalized difference vegetation index (NDVI) and measured by the advanced very high resolution radiometer (AVHRR) satellite sensor was used to stratify the 12-town landscape. We relied on an image taken on 29 June 1995 with 1-km resolution. In order to derive NDVI thresholds by which to stratify the landscape, we overlayed the AVHRR image on the distribution of deciduous forest for Connecticut extracted from the 30-m resolution 1995 Connecticut land use land cover (LULC) data layer (Hurd and Civco 1996). The LULC is a mosaic of multi-date 30-m landsat thematic mapper (TM) and 10-m panchromatic imagery that have been classified into 28 categories by an unsupervised clustering algorithm. We used linear discriminant analysis to identify the NDVI value that best distinguishes between deciduous and non-deciduous areas. A threshold AVHRR NDVI of 1.63 correctly identified deciduous areas with a sensitivity of 72%.

Using Census 2000 town boundaries, we extracted the AVHRR grid cells that comprised the 12-town area ($N = 787$) (US Census Bureau 2000). Because the cells above threshold ($N = 655$) greatly outnumbered the cells below threshold ($N = 133$), we selected a second NDVI threshold of 1.68 creating a total of three strata ($N1 = 133$, $N2 = 322$ and $N3 = 333$). The 30 sample sites were distributed to each of the strata proportionally to strata area in order to maintain the sampling intensity in each group ($n1 = 5$, $n2 = 12$ and $n3 = 13$). The sample sites designated for each stratum were selected randomly. Overall sampling intensity was 4% (30/787).

The second stage of sampling comprised of selecting areas for tick collection within the chosen 1-km^2 sampling site. We determined the exact location for sampling within the grid cell by a global positioning system unit. If one of the randomly selected grid cells did not contain deciduous forest, sampling for this site was moved to the closest forest patch. Transects for sampling were selected randomly within the deciduous forest habitat closest to the center of 1-km^2 area.

Estimation of tick density and tick infection prevalence

Each sample site was found using Census 2000 road GIS data (US Census Bureau 2000). Ticks were collected by dragging a 1-m^2 flannel cloth, fixed to a wooden handle, through vegetation (Daniels et al. 2000; Milne 1943). To obtain tick infection prevalence, transects of variable length were taken in order to attempt to obtain a minimum of 20 adult ticks for adequate estimation of infection prevalence. To obtain relative tick density, two transects of 250 m^2 were selected for the collection of nymphal ticks, inspecting the cloth at 10-m intervals.

Fig. 1 Study area in southern Connecticut, USA. A total of 30 sampling sites were selected by stratified random sampling based on the density of deciduous forest from satellite imagery. The three strata (high-, medium-, and low-density deciduous forest) are shown
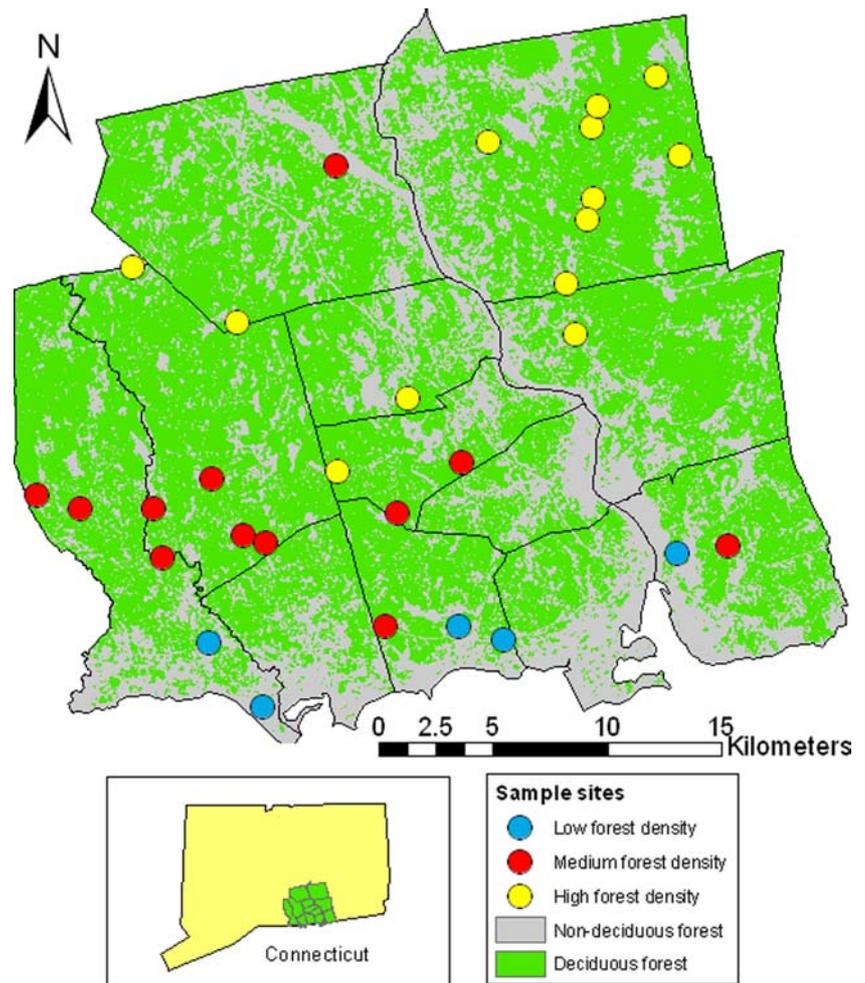
We performed sampling daily between 0900 and 1800 hours from 2 June to 16 June 2003 for nymphs and from 11 November to 21 November 2000 for adults, during their respective periods of greatest host-seeking activity (Daniels et al. 2000). All ticks were removed with forceps and preserved in 70% ethanol.

Tick infection with *B. burgdorferi* was assessed by nested polymerase chain reaction (PCR) assay targeting the 16S–23S rDNA spacer region. DNA from each of the sampled adult ticks was extracted using the Dneasy Kit for animal tissues (Qiagen, Chatsworth, CA, USA). Prior to extraction, ticks were placed in individual vials, sealed with parafilm and vacuum-dried for 30 min. Each tick was cut with a disposable sterile scalpel, and proteins were degraded overnight at 56°C in 180 μl of ATL buffer (Quiagen) and 20 μl of a proteinase K solution (14 mg/ml; Boehringer Mannheim, Indianapolis, IN, USA). The kit manufacturer's procedure was then followed with one exception. The elution step was carried out by the addition of two subsequent 25 μl of 72°C deionized water on the spin columns. The elutes were stored at −4°C until the PCR analysis was carried out.

Quantification of landscape structure

The level of deciduous forest fragmentation was estimated by describing forest patch configuration on the landscape through the use landscape metrics. Patches of deciduous forest were isolated using the extracted deciduous forest cover from the Connecticut 1995 LULC (Hurd and Civco 1996). The spatial pattern analysis on the raster data of deciduous forest cover was performed using FRAGSTATS, a program that computes several landscape metrics (McGarigal and Marks 1995). Patches, which are continuous areas of the same cover type, were defined from the raster data based on 8-neighbor pixel connectivity. A moving window analysis program was necessary to assess landscape structure at each of the sites. We used the Focal Patch extension within the Arcview 3.X GIS software environment, which runs FRAGSTATS at each location with a user-defined radius around the sampling point. We selected 500 m as the default radius given that this was the resolution of sample grid cells. The analysis was also performed using buffer sizes of 250, 750 m, 1 and 5 km.
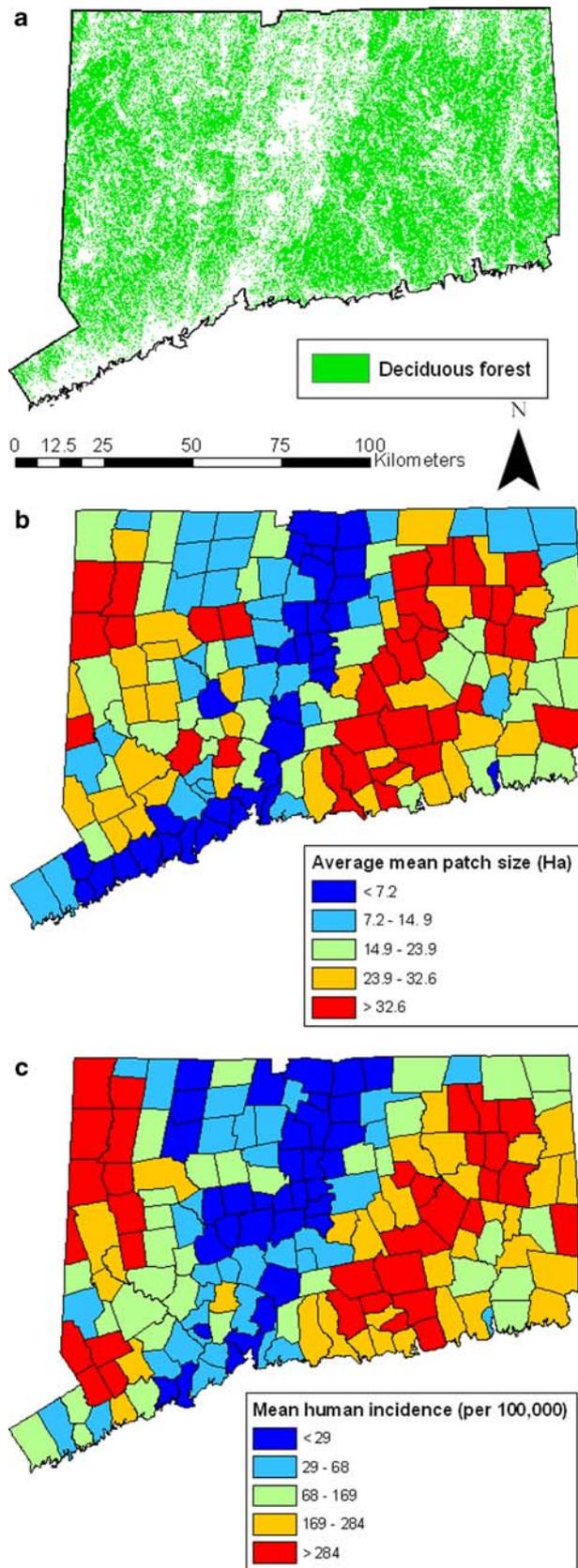
a

Deciduous forest

0 12.5 25   50   75   100
Kilometers

N

b

Average mean patch size (Ha)
- < 7.2
- 7.2 - 14.9
- 14.9 - 23.9
- 23.9 - 32.6
- > 32.6

c

Mean human incidence (per 100,000)
- < 29
- 29 - 68
- 68 - 169
- 169 - 284
- > 284

◄

Fig. 2 a Deciduous forest cover for the state of Connecticut in 1995, extracted from the Connecticut land use land cover (LULC). **b** Level of fragmentation for each Connecticut town is shown. Moving window analysis was performed to calculate landscape indices on 1-km grid of Connecticut using a 500-m buffer for analysis at each point (mean patch size index shown). Average fragmentation is based on averaging the landscape indices for all grid cells within each town. **c** Average human Lyme disease incidence (1991–2002) for each Connecticut town collected by the Connecticut Department of Public Health

necticut. We repeated the calculation of mean forest patch size and isolation based on the forest cover image of the state of Connecticut at each centroid of the 1-km pixels (Fig. 2a). Zonal analysis was then performed to obtain average indices for each Connecticut town.

A number of patch-based metrics have been proposed to describe the level of forest fragmentation (McGarigal and Marks 1995; O'Neill et al. 1988; O'Neill et al. 1999). We chose two simple indices: (1) Mean patch size, which measures the average area of forest patches within the buffer, (2) Mean patch isolation, which measures patch isolation by the average minimum distance between patch edges. With increasing fragmentation, we expect a reduction in patch size and increase in patch isolation.

Relationship between fragmentation
and epidemiological data

Because samples in one location may not be independent of occurrence in neighboring locations, the number of degrees of freedom reduces and the chance of a type I error increases (Legendre 1993). This phenomenon of spatial autocorrelation which may preclude the use of parametric statistics was evaluated by Moran's I using Crimestat (Levine 2000). Evaluation of spatial auto-correlation by Moran's I showed no significant tendency for sampled tick density and tick infection prevalence to be more similar in closer sample sites.

We fit generalized linear models to both sampled tick density and tick-infection prevalence using the two landscape indices as predictor variables in separate models. Poisson distribution was assumed as it is appropriate for modeling counts and proportions. To account for the overdispersion in the count data, extra-Poisson variability was modeled and incorporated into estimates of standard errors (Brillinger 1986). Specifically, standard errors were multiplied by a dispersion (scale) parameter, a ratio of the deviance to its associated degrees of freedom.

Overall model fit for each of the Poisson regression model was calculated by comparing deviance statistics with their asymptotic chi-squared distribution. A significant contribution of each effect to model fit was assessed by using two-tailed chi-squared tests and $\alpha \leq 0.05$ for rejecting the null hypothesis of no effect. The value of each landscape index in predicting entomological risk was determined by calculating the proportion of the deviance explained, similar to the R^2. Maximum like-

For comparison of landscape structure with human incidence data, the moving window analysis was also performed on a 1-km grid of the entire state of Con-

Table 1 Results from Poisson regression models for prediction of Lyme disease risk based on indices of habitat fragmentation

Risk index[a]	Landscape index[b]	Estimate (β)	95% Confidence limits	P value	% Deviance explained
Tick density	Patch size (ha)	−0.0076	−0.0156, 0.0004	0.0636	10.7
	Patch isolation (m)	0.0070	0.0021, 0.0118	0.0046	20.8
Infection prevalence	Patch size (ha)	−0.0049	−0.0091, 0.0006	0.0248	15.6
	Patch isolation (m)	0.0024	−0.0007, 0.0054	0.1295	8.8
Human incidence	Patch size (ha)	0.0628	0.0542, 0.0714	< 0.0001	51.8
	Patch isolation (m)	−0.0291	−0.0339, −0.0244	< 0.0001	52.1

[a]Tick density is nymphal density of *Ixodes scapularis* and infection prevalence is percent infection of *Borrelia burgdorferi* in adult *Ixodes scapularis* for 30 sample sites within a 12-town area around Lyme—Connecticut—2000 and 2003. Human incidence is the rate of human cases of Lyme disease from 1991 to 2002 in Connecticut
[b]Patch size, the average size of forest patches; patch isolation, the average minimum distance between forest patches

lihood estimation of model parameters was performed by GENMOD in SAS v. 8.2 for Windows (The SAS Institute Inc., Cary, NC, USA).

We also assessed the ability of the landscape variables to predict human incidence rates of Lyme disease. Human incidence rates were calculated from the reported human case data for Connecticut towns collected by the Connecticut Department of Public Health. The average incidence rate for each town from 1991 to 2002 was used to investigate the relationship between disease rate and landscape pattern. Regression models were once again fit using Poisson regression models as described above. Analyses were performed for the entire state as well as for subsets of the state, including all suburban areas, eastern suburban areas, western suburban areas, and the 12-town area around Lyme, Connecticut.

Results

The map in Fig. 1 shows the spatial distribution of the 30 sites selected in the 12-town area according to the sampling scheme, where samples were stratified by deciduous forest density. One site, which was randomly selected on the coast, was moved inland to the closest deciduous forest area. We found an average nymphal tick density of 0.042 ± 0.027 (SD) per m^2. For infection prevalence determination, an average of 26.1 ± 12.7 (SD) adult ticks was found per site. The average infection prevalence obtained from these ticks was 35.3 ± 13.1(SD)%.

The distribution of deciduous forest in the 12-town area obtained from the Connecticut landcover dataset is also shown in Fig. 1. Based on the landscape pattern analysis using a 500-m buffer size, the mean forest patch size for the sites ranged from 3.1 to 76.1 ha and had an overall mean of 46.5 ± 27.6 (SD) ha. This translates to percent forest cover ranging from 3.9 to 97.0% and a mean of 59.2 ± 35.2 (SD)%. The mean patch isolation ranged from 0 to 134.2 m and had a mean of 26.9 ± 38.8 (SD) m. Landscape analysis on a 1 km grid of the 12-town area ($n = 3,359$) produced an average mean forest patch size of 36.7 ± 27.6 (SD) ha and had an average mean patch isolation of 36.9 ± 51.2 (SD) m.

Generalized linear modeling was then carried out to assess the relationship between tick density and tick-infection prevalence and landscape indices, assuming a Poisson distribution for the count data (Table 1). For tick density, a significant positive relationship was found with mean patch isolation ($P = 0.0046$). By contrast, regression analyses of sampled tick-infection prevalence showed a significant negative relationship with mean patch size ($P = 0.025$). The same relationships resulted when implementing the landscape analysis using differ-
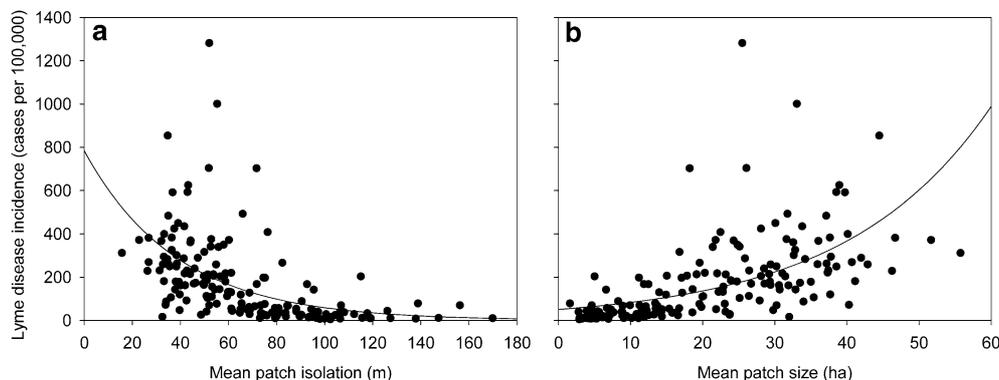
Fig. 3 Relationship between human Lyme disease incidence and indices of habitat fragmentation in a 12-town area around Lyme—Connecticut, USA. **a** A significant negative relationship was found with mean patch isolation, the average minimum distance between forest patches ($P < 0.0001$). **b** A significant positive relationship was found with mean patch size, the average size of forest patches ($P < 0.0001$)

ent buffer sizes. Overall, by different landscape measures, our results reveal a positive relationship between forest fragmentation and entomologic risk.

Figure 2b shows the output of the moving window analysis on a 1-km grid of Connecticut to quantify habitat fragmentation at each grid cell. Northwestern and southeastern Connecticut were found to be the most highly fragmented regions of the state. This spatial pattern of fragmentation is closely related to that of Lyme disease incidence (Fig. 2c). We once again used Poisson regression models to resolve the relationship between human incidence rates and landscape indices (Table 1). A significant positive relationship was found with mean patch size ($P < 0.0001$), and a significant negative relationship was found with mean patch isolation ($P < 0.0001$) (Fig. 3). Unlike the field-collected tick data, human cases are more common in larger and less-isolated patches. The analysis using subsets of towns that included only non-urban portions of the state produced the same significant results.

Discussion

Landscape analysis of a suburban environment revealed a significant relationship between landscape structure and the density of *I. scapularis* as well as infection prevalence with *B. burgdorferi*. Increasing fragmentation in the landscape through decreasing patch size served to increase tick-infection prevalence, while increasing inter-patch distance served to increase tick density. Previous studies of the influence of habitat structure on Lyme disease risk in the Northeast United States have focused attention on habitat types as indicators of risk (Dister et al. 1997; Frank et al. 1998; Ginsberg and Ewing 1989; Maupin et al. 1991; Stafford and Magnarelli 1993). Here, we report that landscape pattern in addition to composition is a strong determinant of entomologic risk for Lyme disease.

The relationship between inter-patch distance and tick density suggests the effect of landscape pattern on white-tailed deer distribution and density. Increasing patch distance is indicative of suburban development, ideal habitat for deer populations. In turn, deer population densities have been shown to be positively associated with tick density (Stafford et al. 2003; Wilson et al. 1985). On the other hand, white-tailed deer are not competent reservoirs for *B. burgdorferi* (Telford et al. 1988). Although we might expect the presence of high deer numbers to therefore reduce tick infection prevalence, their ability to dilute the effects of the more competent reservoirs such as the white-footed mouse is minimal (LoGiudice et al. 2003).

The effect of landscape on tick infection prevalence is more likely to be mediated through the composition of small mammals and birds, many of which are reservoir-competent (Fish and Daniels 1990). Particularly, the white-footed mouse, *P. leucopus*, considered to be a major reservoir for *B. burgdorferi*, has been shown to have a positive relationship with fragmentation by reducing patch size (Nupp and Swihart 1996; Robinson et al. 1992). A study in Dutchess County, New York, also revealed patch size to have a positive influence on tick infection prevalence (Allan et al. 2003).

The relationship between fragmentation and entomologic risk for transmission to humans does not necessarily translate to a higher number of human cases. Our study clearly shows a negative relationship with human disease incidence. While tick density and tick infection prevalence define the entomologic risk for Lyme disease, cases are also dependent on human contact with infected ticks. In our study, we find that suburban residential development is negatively linked to peridomestic risk. This phenomenon can be explained by the fact that increased fragmentation due to residential property development means a reduction in forest patch size and an increase in isolation. Thus, fewer properties will contain or adjoin woodlots that support tick populations (Maupin et al. 1991), resulting in an overall reduction in peridomestic exposure. Our study points to the fact that human disease incidence in the southern region of Connecticut is driven more by human exposure than by entomologic risk. This result reveals the potential for the misinterpretation of tick-collection data, which has become a keystone of Lyme disease surveillance for human risk.

Limitations of satellite imagery for the delineation of patches could affect the interpretation of our results. The resolution of the satellite imagery (30 m) may make the precise description of patches impossible by imposing a minimum patch size that can be discerned. Patches may also be lumped together when inter-patch distance is small (Turner et al. 2001). Digitized maps of forest cover by aerial photography and ground-truthing could provide more detailed information on the patch matrix landscape.

Previous studies have indicated that countering fragmentation would reduce Lyme disease risk through influence on entomologic risk (Allan et al. 2003; Ostfeld and Keesing 2000). In spite of higher entomologic risk, our study found that human incidence of Lyme disease is lower in fragmented contexts. With the current rate landscape fragmentation (Griffith et al. 2003; Vogelmann 1995), exposure to Lyme disease may decrease without need for intervention. Still, as a significant predictor of human risk, the relationship between landscape structure and disease risk could be used to inform residential planning and development. Residential configurations that preserve remnant forests in such a way that reduces adjacency of households to forest fragments would also serve to reduce human exposure to infected ticks.

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