Integrated Assessment of Behavioral and Environmental Risk Factors for Lyme Disease Infection on Block Island, Rhode Island

Casey Finch1, Mohammed Salim Al-Damluji1,2,∗, Peter J. Krause1, Linda Niccolai1, Tanner Steeves1, Corrine Folsom O’Keefe1,3, Maria A. Diuk-Wasser1∗

1 Department of Epidemiology of Microbial Diseases at Yale School of Public Health, New Haven, Connecticut, United States of America, 2 Department of Internal Medicine at Yale School of Medicine, New Haven, Connecticut, United States of America, 3 Audubon Connecticut, Southbury, Connecticut, United States of America

Abstract

Peridomestic exposure to Borrelia burgdorferi-infected Ixodes scapularis nymphs is considered the dominant means of infection with black-legged tick-borne pathogens in the eastern United States. Population level studies have detected a positive association between the density of infected nymphs and Lyme disease incidence. At a finer spatial scale within endemic communities, studies have focused on individual level risk behaviors, without accounting for differences in peridomestic nymphaal density. This study simultaneously assessed the influence of peridomestic tick exposure risk and human behavior risk factors for Lyme disease infection on Block Island, Rhode Island. Tick exposure risk on Block Island properties was estimated using remotely sensed landscape metrics that strongly correlated with tick density at the individual property level. Behavioral risk factors and Lyme disease serology were assessed using a longitudinal serosurvey study. Significant factors associated with Lyme disease positive serology included one or more self-reported previous Lyme disease episodes, wearing protective clothing during outdoor activities, the average number of hours spent daily in tick habitat, the subject’s age and the density of shrub edges on the subject’s property. The best fit multivariate model included previous Lyme diagnoses and age. The strength of this association with previous Lyme disease suggests that the same sector of the population tends to be repeatedly infected. The second best multivariate model included a combination of environmental and behavioral factors, namely hours spent in vegetation, subject’s age, shrub edge density (increase risk) and wearing protective clothing (decrease risk). Our findings highlight the importance of concurrent evaluation of both environmental and behavioral factors to design interventions to reduce the risk of tick-borne infections.

Introduction

Lyme disease, caused by the spirochete Borrelia burgdorferi, is the most commonly reported vector-borne disease in the US, with greater than 20,000 cases reported annually [1]. The black-legged tick (Ixodes scapularis) serves as the principal vector for transmission to humans and is responsible for maintenance of the spirochete in natural reservoirs. Since the Lyme disease vaccine was removed from the market in 2002 [2], strategies to reduce the number of human cases of Lyme disease have focused on ways to control ticks and pathogens in zoonotic hosts through host-targeted acaricides [3,4] and host vaccination [5,6], or to help decrease contact between humans and infected ticks. The latter approach has consisted of either reducing the density of I. scapularis nymphs infected with B. burgdorferi (acarological risk) through area-wide acaricides [7–9], reducing human-tick contact through environmental management [10], or the use of personal protective measures [11–13]. These methods that modify behavior or the environment vary in their effectiveness in reducing human disease and there is no consensus on which ones should be emphasized [14–16].

Attempts to identify the best targets for intervention have been hindered by the disparity in approaches, in spatiotemporal scales and in the level of analysis of studies focusing on acarological, landscape or behavioral risk factors. A link between Lyme disease incidence and acarological risk was found at the aggregate town or county level [17–23]. At a neighborhood scale, landscape features have been linked to increased acarological risk [24–27], but the direct link between acarological risk and Lyme disease was found to be weak [27]. The latter study did not assess human behaviors, which can modify the association between acarological risk and human infection. On the other hand, studies of the effectiveness of human protective behaviors were conducted by telephone interviews and did not directly measure landscape patterns or acarological risk [28,29]. These studies may underestimate the
effectiveness of these protective behaviors if residents of high acarological risk properties are more likely to perform them.

Logistical challenges are likely responsible for the lack of integrated acarological, landscape, and behavioral studies. Measuring acarological risk in a large number of properties is difficult because of the short window of *I. scapularis* nymphal activity between late May and early July [30]. Another limitation of previous studies is the reliance on human clinical cases as the health outcome. Reports of clinical cases only identify symptomatic infections that are diagnosed and reported, which are only a portion of the actual number of infections [31–33].

In the present study, we simultaneously assessed the association between Lyme disease and both individual and environmental risks on Block Island, RI, between 2005 and 2011. High resolution imagery was used to measure the amount and configuration of lawn-shrub edges in all residential properties, where most human-tick contact is expected to occur. This measure of environmental risk was validated by collecting ticks along those edges on a subset of properties. A sensitive measure of human infection was obtained through serosurveys conducted twice a year, where personal protective behaviors and *B. burgdorferi* seroprevalence was assessed. The integration of behavioral and environmental risk assessments allows more accurate identification of intervention targets by controlling for modifying factors and minimizing confounding.

**Methods**

**Study Site**

Block Island is a 25.2 km² landmass located in Washington County, Rhode Island, 23 km south of mainland Rhode Island [34]. The population of permanent residents is around 1,000, which increases during the summer months to approximately 12,000 with the influx of summer residents [31]. Deciduous forest, which increases during the summer months to approximately 25% of the island, and then calculated the composition and configuration (landscape metrics) of shrub and lawn cover characteristics for each individual property. Finally, we assessed the association between the landscape metrics and the density of *I. scapularis* nymphs in a representative subset of properties, as described below.

**Study Population**

A longitudinal study was established in 1991 on Block Island, RI, by inviting all island residents to take part in serological surveys conducted every year in the spring and fall. The study population was restricted to residents who spent more than one month on the island during the May through September Lyme disease transmission period. The serosurvey was announced in the local newspaper, on television, and via flyers at local businesses and the Block Island Medical Center [31,36]. All subjects were asked to provide blood samples for *B. burgdorferi* and *B. microti* serological analyses and to complete a questionnaire. Written informed consent was obtained from all study participants in accordance with the human investigation committees at the University of Connecticut School of Medicine and the Yale School of Public Health. They each provide ethical review and oversight of human research endeavors and approved this study.

We restricted our analysis to subjects who participated in serosurveys from 2005 to 2011 because environmental exposure data acquired on September 10, 2010. WorldView2 has a spatial resolution of 1.82 m that allows detection of fine scale peridomestic landscape patterns. It also has high spectral resolution (8 bands), resulting in greater ability to discriminate among land cover types than the four bands typically available for other high spatial resolution sensors. We converted the data to top of the atmosphere radiance [39]. We performed a maximum likelihood land cover classification using ENVI (Environment for Visualizing Images) software (ITT 2011) [40]. To improve the accuracy of the classification, the image was stratified into vegetated and non-vegetated areas based on a threshold of the normalized difference vegetation index = 0 [40] and the classification was performed independently for each stratum. Training and testing pixels were obtained by collecting ground information for all vegetation classes and by visual inspection of a 2010 orthophoto for the water and urban-associated classes, which easily could be distinguished. A randomly selected subset of 80% of the pixels was used to train the classification and 500 pixels were randomly selected from the remaining 20% for each of the classes for testing. After the classification, the two strata were combined in one raster layer and a 3×3 pixel median filter was applied to remove the salt and pepper effect (Figure 1).

**Landscape metric calculation.** Spatial analysis was performed utilizing geo-spatial modeling environment (GME) software version 0.5.8 beta [41] and Fragsstats software version 3.3 [42]. We used a municipal parcel layer (Town of New Shoreham) to calculate the following landscape metrics for shrubs and lawns...
in each property parcel: area of the landscape class, largest patch index, total edge, edge density and landscape shape index (calculations described in Table S1). Landscape metrics were normalized using the Z-scale ([X-mean]/standard deviation) prior to use in statistical analyses.

**Association between landscape metrics and the density of *I. scapularis* nymphs.** During 2012, *I. scapularis* nymphs were collected from 105 properties of serosurvey participants from May 15th to August 23rd. The property surveys consisted of dragging 1 m² corduroy cloths along the edge of the lawn and shrub vegetation as outlined in previous studies [43–45]. Between 2 and 5 transects of approximately 100 meters in length were completed at each property, proportionally to the size of the property. Most properties were repeatedly sampled during the season, resulting in a total of 258 samples. Attached *I. scapularis* nymphs were counted, placed in 70% ethanol, and species confirmed using taxonomic keys [46]. We based our measure of risk only on the density of host-seeking *I. scapularis* nymphs (hereafter density of nymphs) without calculating the proportion infected with *Borrelia burgdorferi* because the small number of nymphs collected on most properties prevented an accurate estimate of infection prevalence.

**Statistical Analyses**

**Identification of environmental risk factors.** Negative binomial regression was used to assess the association between landscape metrics and the density of nymphs. Only those landscape metrics found to be significantly associated with the density of nymphs on a property were considered biologically relevant and thus included as potential risk factors in further analyses.

**Individual and environmental risk factors for Lyme disease.** We used general estimating equation models (XTGEE) in STATA/SE, version 12.0 (STATA Corporation, College Station, TX) to assess the association between personal protective behaviors, age, landscape metrics and individual serological status. These models fit generalized linear models that yield logistic regression models via a Bernoulli distribution of the dependent variable and a logit link function. The models accounted for potential autocorrelation among observations in a time series - in this case serological tests at different time periods on the same subject.

We performed univariate analyses for all variables and then examined multivariate models including all possible combinations of variables found to be significant in univariate analyses. We assessed two groups of models: one including self-reported Lyme disease diagnosis and one excluding this variable. Including self-reported Lyme disease is informative in terms of the consistency between previous and current risk; excluding this variable allowed for identification of current risk factors for Lyme disease infection.

The maximum model size was reached when larger models reported Lyme disease is informative in terms of the consistency between previous and current risk; excluding this variable allowed for identification of current risk factors for Lyme disease infection. The maximum model size was reached when larger models resulted in all non-significant variables. We included age in all models to control for confounding. No more than one landscape metric was included in a model because these variables were highly collinear. Pairwise correlation among all variables was assessed and only variables with Pearson correlation coefficient lower than 0.2 were included in the same model. Models were compared by the QIC criterion, which an extension of the Akaike information criterion (AIC) [47–48] used for generalized estimating equation models [49]. The QIC is a measure of the relative quality of a statistical model for a given set of data. Similar to AIC, QIC not only rewards goodness of fit, but also includes a penalty that is an increasing function of the number of estimated parameters, resulting in the most parsimonious model [50]. We additionally assessed whether inclusion of variable interactions improved model fit and assessed the goodness-of-fit of the final model using the Hosmer-Lemeshow test [51,52]. Finally, to
Figure 1. Land cover classification of Block Island, Rhode Island. Examples of properties with a) low shrub edge density and b) high shrub edge density. Map shows a Worldview2 image acquired on Sept. 4, 2010 from Digital Globe, Inc. doi:10.1371/journal.pone.0084758.g001
determine whether there were spatial relationships among the properties not captured by the measured variables, we evaluated whether the residuals of the model were significantly autocorrelated using the Moran’s I test included in the ArcGIS Spatial Statistics toolbox [53,54].

Results

Study Subjects
Of 611 subjects participating in at least one serosurvey between 2005 and 2011, blood samples and completed questionnaires were available from 520 (1132 records). In order to obtain data from subjects whose behavior was not potentially altered by knowledge of recent Lyme disease, 34 participants (86 records) were excluded because of a self-reported Lyme diagnosis in the two years prior to their enrollment in the study, resulting in a dataset of 486 participants (1046 records). Additionally, 136 subsequent records were excluded after subject’s developed positive B. burgdorferi serology, resulting in a final set of 486 participants (910 records).

The B. burgdorferi seropositivity rate from all blood samples was 9.5% (86/910). The average age of the participants at the testing date was 61.5 (SD 16.5) years. The use of any form of tick protection was reported by 72.9% of the study participants. Routine tick checks were the most commonly used protective measures (53.3%), while use of repellent was practiced the least (16.6%). A summary of behaviors reported by seronegative and seropositive participants is provided in Table 1.

Identification of Environmental Risk Factors
Land cover classification accuracy was 83.6% and the Kappa coefficient was 0.82. The class-specific accuracy metrics are reported in Table S2. Two lawn-associated metrics evaluated were significantly and negatively associated with the density of nymphs, while all shrub-associated metrics were positively associated with the density of nymphs (Table 2). A total of 373 nymphs were collected in 166 transects, with an average collection of 4.9 (SD 23.5) nymphs per 100 m transect.

Individual and Environmental Risk Factors for Lyme Disease
Factors significantly associated with positive Lyme disease serology in univariate models included the average number of hours spent outdoors near vegetation, age at the time of testing, a self-reported previous Lyme disease diagnosis three or more years before testing and shrub edge density (Figure 2). Wearing protective clothing was significantly associated with negative Lyme serology (Table 3).

A multivariate model that included a previous Lyme disease diagnosis three or more years prior to recruitment and the subject’s age had the lowest QIC (423.38). When we excluded previous Lyme disease diagnosis from the analyses, the best fit multivariate model (QIC = 481.64) included hours spent outdoors near vegetation, shrub edge density and age (increased risk) and wearing protective clothing (decreased risk) (Table 4). Excluding either the landscape or behavioral factors from this model resulted in increases of QIC of more than two units, which indicate a significantly worse fit to the data [51]. There were no significant models including any combination of five or more variables. Inclusion of variable interactions did not improve model fit. The Hosmer-Lemeshow test indicated a good model fit (p = 0.17) and the Moran’s I test on the logistic regression residuals showed no significant autocorrelation (p = 0.38).

Discussion

Our study emphasizes the need for integrated studies of both environmental and behavioral risk factors to identify Lyme disease intervention targets. The best fit model for Lyme disease included two behaviors that consisted of hours spent in vegetation (increased risk) and wearing protective clothing (decreased risk), and an environmental factor that consisted of a landscape metric quantifying the density of edge between shrubs and other land use classes, particularly lawn, where human exposure to ticks is more likely to occur (increased risk). Higher density of shrub edge was positively associated with the density of nymphs, supporting this habitat as a source for human infection. Although human risk of infection with Lyme disease was best predicted by a self-reported previous Lyme disease diagnosis, we excluded this variable from further analyses to gain insights into specific behavioral and

Table 2. Landscape predictors of the density of host-seeking I. scapularis nymphs.

| Landscape Metric          | Coefficient | P-value |
|---------------------------|-------------|---------|
| Lawn Class Area           | -0.383      | 0.572   |
| Lawn Largest Patch Index  | -0.357      | 0.005   |
| Lawn Total Edge           | 0.113       | 0.715   |
| Lawn Edge Density         | -0.347      | 0.022   |
| Lawn Landscape Shape Index| 0.285       | 0.143   |
| Shrub Class Area          | 1.348       | 0.021   |
| Shrub Largest Patch Index | 0.422       | 0.018   |
| Shrub Total Edge          | 0.857       | 0.012   |
| Shrub Edge Density        | 0.486       | 0.002   |
| Shrub Landscape Shape Index| 0.485      | 0.002   |

Negative binomial regression univariate models of the association between lawn and shrub landscape metrics and the density of host-seeking Ixodes scapularis nymphs (statistically significant results at p < 0.05 are indicated in bold).

Figure 2. Proportion of seropositive subjects living in properties with increasing shrub edge density. Residences are classified into quartiles based on increasing shrub edge density. doi:10.1371/journal.pone.0084758.g002
environmental risk factors. The strength of the previous Lyme disease association suggests that the same sector of the population tends to be repeatedly infected, either because of their behavior or their environmental exposure or both. These data also suggest that people at high risk of Lyme disease remain at high risk over time.

The first line of defense in the effort to prevent Lyme disease is personal protective behavior [14]. Consistent with previous studies [29], wearing protective clothing was a significantly protective behavior against Lyme disease. We did not identify a significant effect of tick checks, which was found to be effective in one previous study [28] but not in another [29]. Notably, despite the potential protective value of these methods and the high prevalence of Lyme disease on Block Island reported in this study and in previous studies [31], Block Island residents were less likely to use protective measures than residents of Connecticut [12,28,29]. The most common protective measure was tick checks (53%), followed by wearing protective clothing (44% overall; 46% of seronegative subjects and 28% of seropositive subjects). Only a quarter of the population used any landscape-related control measure, 17% reported using repellents, and 1.5% reported using acaricides. The modest use of protective measures may partially explain the high incidence of Lyme disease on Block Island.

Table 3. Univariate models.

| Variable                             | OR (95% CI) | QIC  |
|--------------------------------------|-------------|------|
| Age at the test                      | 1.024 (1.002–1.046) | 562.28 |
| Previous Lyme diagnosis              | 7.437 (4.419–12.515) | 426.69 |

### BEHAVIOR

|                | OR (95% CI) | QIC  |
|----------------|-------------|------|
| Hours in vegetation | 1.469 (1.081–1.996) | 562.22 |
| Owning a dog     | 1.149 (0.719–1.835) |      |
| Owning a cat     | 1.294 (0.788–2.125) |      |
| Owning a different pet | 1.960 (0.826–4.649) |      |
| Frequency of deer seen on property   | 0.976 (0.727–1.310) |      |
| Tick bite within the past year        | 1.111 (0.737–1.674) |      |
| Tick bite within the past year on Block Island | 1.136 (0.659–1.960) |      |
| Use of any protective measure         | 0.726 (0.454–1.161) |      |
| Repellant                           | 0.683 (0.337–1.386) |      |
| Protective clothing                  | 0.456 (0.273–0.761) | 505.14 |
| Avoiding brush                       | 0.801 (0.490–1.309) |      |
| Tick checking                        | 0.786 (0.495–1.247) |      |
| Landscape-related tick control measures | 1.001 (0.605–1.654) |      |
| Occupational exposure to tick habitat | 0.639 (0.263–1.556) |      |

### LANDSCAPE

|                | OR (95% CI) | QIC  |
|----------------|-------------|------|
| Lawn largest patch index | 0.899 (0.699–1.156) |      |
| Lawn edge density     | 1.009 (0.809–1.258) |      |
| Shrub class area      | 1.152 (0.941–1.410) |      |
| Shrub largest patch index | 1.204 (0.965–1.503) |      |
| Shrub total edge      | 1.109 (0.938–1.310) |      |
| Shrub edge density    | 1.283 (1.015–1.621) | 566.68 |
| Shrub landscape shape index | 1.158 (0.944–1.419) |      |

Univariate logistic regression models of the association between human behaviors and landscape metrics and positive Lyme disease serology. Statistically significant results at p < 0.05 are indicated in bold.

doi:10.1371/journal.pone.0084758.t003

Table 4. Multivariate model.

|                | Odds Ratio | SE | Z-score | P-value | 95% CI (Lower) | 95% CI (Upper) |
|----------------|------------|----|---------|---------|----------------|----------------|
| Hours in vegetation | 1.735     | 0.308 | 3.10 | 0.002 | 1.224 | 2.460 |
| Protective clothing | 0.413     | 0.108 | –3.38 | 0.001 | 0.247 | 0.689 |
| Shrub edge density | 1.315     | 0.182 | 1.98 | 0.048 | 1.002 | 1.725 |
| Age at test       | 1.033     | 0.013 | 2.48 | 0.013 | 1.006 | 1.060 |
| Constant          | 0.005     | 0.006 | –4.78 | 0.000 | 0.001 | 0.047 |

Best fit (lowest QIC score) multivariate logistic regression model of the association between human behaviors and landscape metrics and positive Lyme disease serology.

doi:10.1371/journal.pone.0084758.t004

Our study is the first to describe the direct association between landscape structure of individual properties and Lyme disease infection. The landscape metric included in the final model - shrub edge density, was associated with both higher density of nymphs and higher human seropositive rates for Block Island residents. At larger spatial scales, forest fragmentation has been associated with increased tick density and infection prevalence of ticks. Forest fragmentation increases the amount of forest edge and may increase densities of the white-footed mouse (*Peromyscus leucopus*), the most competent host for immature ticks and *B. burgdorferi* [55,56]. Increased forest edge also has been linked to increased [22] and decreased [21] Lyme disease incidence. Although all shrub-associated landscape metrics were associated with higher density of nymphs, we found that only higher shrub edge density was associated with positive Lyme serology. This metric measures the length of edge per total property area, and may result in more frequent residents’ contact with shrub edges – and ticks, compared with properties with more edge but distributed over a larger area.

Further research is needed to better understand people’s interaction with their environment to help refine general recommendations [57] that may not be applicable to a specific lifestyle or may be undesirable for environmental or recreational reasons [15].

We used serology as a marker of *B. burgdorferi* exposure because it captures subjects with asymptomatic and symptomatic infection and minimizes inclusion of patients misdiagnosed as having had Lyme disease. While *B. burgdorferi* antibody clears in most people who experience Lyme disease within two years, it may persist for many years in some individuals [59,60], which motivated our exclusion of subsequent visits after a positive Lyme serology test. Although the use of antibody is an excellent method to assess *B. burgdorferi* exposure status, some cases of Lyme disease may have been missed. The two-tiered assay has low sensitivity (about 50%) in acute sera obtained from patients with early Lyme disease [58]. On the other hand, there is higher sensitivity in convalescent sera of such patients and especially in patients with late Lyme disease infection. We maximized the sensitivity by obtaining sera in mid to late Fall and early Spring, weeks to months following the preceding Lyme disease transmission season.

One of the limitations of our study was our inability to determine the site where exposure occurred. Even though the study was restricted to people who lived on Block Island more than three months during the peak transmission period, island residents might have acquired the infection on the mainland or away from their residence, reducing the expected association between peridomestic risk and infection. Peridomestic exposure has been found to be the main site of acquisition of *B. burgdorferi* infection in the Northeast [24], while recreational exposure has been proposed to mainly
account for infection patterns in the Midwest [18]. However, recreational exposure may also occur in the Northeast [61], including Block Island. Further research is needed to quantify the relative roles of these different exposures. An additional limitation was our inability to investigate the variability in the way protective behaviors are used. For example, we did not enquire about the frequency of protective measure use, so we were not able to assess the protective effect that might occur with increasing use.

In conclusion, our results suggest that both environmental and behavioral factors are associated with positive Lyme disease serology. Wearing protective clothing when exposed to tick habitat appears to be the most effective method to reduce exposure to Lyme disease. Employing landscaping strategies which reduce the amount of peridomestic shrub edge density may reduce exposure. Future prospective cohort studies should be conducted to ascertain the interactions between acarological risk, landscape design, and personal protective behaviors in reducing Lyme disease in a community.

Supporting Information

**Figure S1** Questionnaire for the biannual Block Island serosurveys.

(DOCX)

**Table S1** Landscape metric description.

(DOCX)

**References**

1. Bacon RM, Kugler KJ, Mead PS (2008) Surveillance for Lyme disease—United States, 1992-2006, MMWR Surveill Summ 57: 1–9.
2. Nigrinc LE, Thompson KM (2007) The Lyme vaccine: a cautionary tale. Epidemiol Infect 135: 1–8.
3. Daniels TJ, Fish D, Falco RC (1991) Evaluation of host-targeted acaricide for reducing risk of Lyme disease in southern New York state. J Med Entomol 28: 537–543.
4. Brei B, Brownstein JS, George JF, Pound JM, Miller JA, et al. (2009) Evaluation of the United States Department Of Agriculture Northeast Area-wide Tick Control Program by meta-analysis. Vector Borne Zoonotic Dis 9: 425–430.
5. Tsao JJ, Wootten JT, Buniku J, Luna MG, Fish D, et al. (2004) An ecological approach to preventing human infection: vaccinating wild mouse reservoirs intervenes in the Lyme disease cycle. Proc Natl Acad Sci U S A 101: 18159–18164.
6. Voordouw MJ, Tupper H, Onder O, Deverry G, Graves CJ, et al. (2013) Reductions in human Lyme disease risk due to the effects of oral vaccination on tick-to-mouse and mouse-to-tick transmission. Vector Borne Zoonotic Dis 13: 203–214.
7. Schulze TL, Jordan RA, Hung RW, Taylor RC, Markowski D, et al. (2001) Efficacy of granular deltamethrin against Ixodes scapularis and Amblyomma americanum (Acari: Ixodidae) nymphs. J Med Entomol 38: 344–346.
8. Curran KL, Fish D, Piesman J (1995) Reduction of nymphal Ixodes dammini (Acari: Ixodidae) in a residential suburban landscape by area application of insecticides. J Med Entomol 30: 107–113.
9. Stafford KC, 3rd (1991) Effectiveness of cararyl preparations for the control of Ixodes dammini (Acari: Ixodidae) nymphs in an endemic residential area. J Med Entomol 28: 32–36.
10. Schulze TL, Jordan RA, Hung RW (1995) Suppression of subadult Ixodes scapularis (Acari: Ixodidae) following removal of leaf litter. J Med Entomol 32: 730–733.
11. Hayes EB, Piesman J (2005) Current concepts - How can we prevent Lyme disease? N Engl J Med 354: 2424–2430.
12. Gould LH, Nelson RS, Griffith KS, Hayes EB, Piesman J, et al. (2008) Knowledge, attitudes, and behaviors regarding Lyme disease prevention among Connecticut residents, 1999-2004. Vector Borne Zoonotic Dis 8: 769–776.
13. Dalmatory LH, Phillips C, Lew R, Wright E, Shadick NA, et al. (2007) A controlled trial of a novel primary prevention program for Lyme disease and other tick-borne illnesses. Health Educ Behav 34: 531–542.
14. Piesman J, Beard GB (2012) Prevention of tick-borne diseases. J Environ Health 74: 30–32.
15. Piesman J, Eisen L (2008) Prevention of tick-borne diseases. Annu Rev Entomol 53: 323–343.
16. Hayes EB, Piesman J (2003) How can we prevent Lyme disease? N Engl J Med 348: 2424–2430.
17. Falco RC, McKenna DF, Daniels TJ, Nadelman RB, Nowakowski J, et al. (1999) Temporal relation between Ixodes scapularis abundance and risk for Lyme disease associated with erythema migrans. Am J Epidemiol 149: 771–776.
18. Kiron U, Kazmierczak JJ (1997) Spatial analysis of the distribution of Lyme disease in Wisconsin. Am J Epidemiol 145: 558–566.
19. Stafford KC, III, Carter ML, Magarelli LA, Ertel SH, Mshar PA (1998) Temporal correlations between tick abundance and prevalence of ticks infected with Borrelia burgdorferi and increasing incidence of Lyme disease. J Clin Microbiol 36: 1240–1244.
20. Diuk-Wasser MA, Hoern AG, Caido P, Brinkerhoff R, Hamer SA, et al. (2012) Human risk of infection with Borrelia burgdorferi, the Lyme disease agent, in eastern United States. Am J Trop Med Hyg 86: 320–327.
21. Brownstein JS, Skelly DK, Hololfos TR, Fish D (2005) Forest fragmentation predicts local scale heterogeneity of Lyme disease risk. Oecologia 146: 469–475.
22. Jackson LE, Levine JF, Hillborn EJ (2006) A comparison of analysis units for associating Lyme disease with forest-edge habitat. Community Ecology 7: 109–139.
23. Eisen RJ, Lane RS, Fritz CL, Eisen L (2006) Spatial patterns of Lyme disease risk in California based on disease incidence data and modeling of vector-tick exposure. Am J Trop Med Hyg 75: 669–676.
24. Falco RC, Fish D (1988) Prevalence of Ixodes dammini near the homes of Lyme disease patients in Westchester County, New York. Am J Epidemiol 127: 826–830.
25. Dieter SW, Fish D, Bros SM, Frank DH, Wood BL (1997) Landscape characterization of peridomestic risk for Lyme disease using satellite imagery. Am J Trop Med Hyg 57: 671–672.
26. Klein JD, Epper SC, Hunt P (1996) Environmental and life-style risk factors for Lyme disease in children. Clin Pediatr (Phila) 35: 359–363.
27. Connolly NP, Ginsberg HS, Mathier TN (2006) Assessing peridomestic entomological factors as predictors for Lyme disease. J Vector Ecol 31: 364–370.
28. Connolly NP, Duarte AJ, Youssef-Hinds KM, Meek JI, Nelson RS, et al. (2009) Peridomestic Lyme disease prevention: results of a population-based case-control study. Am J Prev Med 37: 201–206.
29. Vazquez M, Muehlenbein C, Carter M, Hayes EB, Ertel S, et al. (2008) Effectiveness of personal protective measures to prevent Lyme disease. Emerg Infect Dis 14: 210–216.
30. Gateswood AG, Liebman KA, Vourch G, Buniku J, Hamer SA, et al. (2009) Climate and tick seasonality are predictors of Borrelia burgdorferi genotype distribution. Appl Environ Microbiol 75: 2476–2483.
31. Krase PJ, McKay K, Goddaw J, Christianson D, Closter L, et al. (2009) Increasing health burden of human babesiosis in endemic sites. Am J Trop Med Hyg 60: 431–436.
32. Meek JI, Roberts CL, Smith EV Jr, Carter ML (1996) Underreporting of Lyme disease by Connecticut physicians, 1992. J Public Health Manag Pract 2: 61–65.
33. Young JD (1996) Underreporting of Lyme disease. N Engl J Med 338: 1629.
34. Rosenzweig C, Duhaime R, Mandeville A, August P (2000) Ecological geography of Block Island. In: Paton P, Gould L, August P, Frost AO, editors. The ecology of Block Island. Kingston, RI: Rhode Island Natural History Survey. 163–196.

**Table S2 Land cover classification accuracy assessment.**

Producer and user accuracy reflecting omission and commission, respectively, are shown as percent and number of correct classifications.

| Land Cover Class | Producer Accuracy | User Accuracy | Omission | Commission |
|------------------|-------------------|--------------|----------|------------|
| Forest           | 85.2%             | 83.4%        | 14.8%    | 16.6%      |
| Agriculture      | 90.6%             | 88.9%        | 9.4%     | 11.1%      |
| Urban            | 75.0%             | 72.7%        | 25.0%    | 27.3%      |

**Acknowledgments**

We would like to acknowledge Laura Cronin, Keith Ellis, Elsa Cardenas, Nicholas Presley and Patrick Shea for conducting the field work and tick identification; statistical assistance was provided by Paul Gaido and remote sensing assistance by Dr. Pawan Joshi. We thank Scott Comings at the Block Island office of The Nature Conservancy for housing and logistical support and the Town of New Shoreham GIS office (Martha Rolan) for providing us with the municipal parcel layer. We particularly want to thank the Block Island Medical Center staff (Linda Closter, R.N., Janice Miller, M.D., Monty Stover) for their support in conducting the serosurveys. We thank Lindsay Rollend, Molly Rosenberg and Durland Fish for logistical support and useful discussions.

**Author Contributions**

Conceived and designed the experiments: CF MSAD PK MDW. Performed the experiments: CF MSAD PK TS CFOK MDW. Analyzed the data: CF MSAD PK LN MDW. Wrote the paper: CF MSAD PK LN MDW.

(EOX)

**Table S2 Land cover classification accuracy assessment.**

Producer and user accuracy reflecting errors of omission and commission, respectively, are shown as percent and number of pixels.

(EOX)
35. Enser R (2000) The vascular flora of Block Island, Rhode Island. In: Paton P, Gould L, August P, Frost AO, editors. The ecology of Block Island. Kingston, RI: Rhode Island Natural History Survey. 183–196.
36. Krause FJ, Foley DT, Burke GS, Christianson D, Closter L, et al. (2006) Reinforcement and relapse in early Lyme disease. Am J Trop Med Hyg 75: 1090–1094.
37. Skogman BH, Ekerfelt C, Ludvigsson J, Forsberg P (2010) Seroprevalence of Borrelia IgG antibodies among young Swedish children in relation to reported tick bites, symptoms and previous treatment for Lyme borreliosis: a population-based survey. Arch Dis Child 95: 1013–1016.
38. Center for Disease Control and Prevention (1995) Recommendations for test performance and interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. MMWR Morb Mortal Wkly Rep 44: 590–591.
39. Updike T, Comp C (2010) Radiometric Use of Worldview-2 Imagery. Digital Gobe, Colorado, USA.
40. Lillesand TM, Kiefer RW (2008) Remote sensing and image interpretation. New Jersey: John Wiley & Sons. 756 p.
41. Beyer H (2011) Geospatial Modelling Environment, Spatial Ecology LLC. www.spatialecology.com. Accessed December 4, 2103.
42. McGarigal K, Cushman SA, Neel MC, Ene E (2002) FRAGSTATS: Spatial Pattern Analysis Program for Categorical Maps. http://www.umass.edu/landeco/research/fragstats/fragstats.html. Accessed December 4, 2013.
43. Daniels TJ, Falco RC, Fish D (2000) Estimating population size and drag sampling efficiency for the blacklegged tick (Acari: Ixodidae). J Med Entomol 37: 357–363.
44. Schulze TL, Jordan RA, Hung RW (1997) Biases associated with several sampling methods used to estimate abundance of Ixodes scapularis and Amblyomma americanum (Acari: Ixodidae). J Med Entomol 34: 615–623.
45. Durden LA, Keirans JE (1996) Nymphs of the genus Ixodes (Acari: Ixodidae) of the United States: taxonomy, identification key, distribution, hosts and medical/veterinary importance. Lanham, MD: Entomological Society of America.
47. Akaike H (1974) New Look at Statistical-Model Identification. IEEE Trans Automat Contr AC19: 716–723.
48. Hurvich CM, Tsai CL (1989) Regression and Time-Series Model Selection in Small Samples. Biometrika 76: 297–307.
49. Pan W (2001) Akaike’s information criterion in generalized estimating equations. Biometrics 57: 120–125.
50. Johnson JB, Omland KS (2004) Model selection in ecology and evolution. Trends Ecol Evol 19: 101–108.
51. Hosmer DW, Lemeshow S (1989) Applied logistic regression. New York, NY: Wiley.
52. Hosmer DW, Jhot NL (2002) Goodness-of-fit processes for logistic regression: simulation results. Stat Med 21: 2723–2738.
53. Cliff AD, Ord JK (1973) Spatial autocorrelation. London: Pion Press.
54. Cliff AD, Ord JK (1981) Spatial processes: Models and applications. London: Pion Press.
55. Allan BF, Keesing F, Ostfeld RS (2003) Effect of forest fragmentation on Lyme disease risk. Conserv Biol 17: 267–272.
56. Ostfeld R, Keesing F (2000) The function of biodiversity in the ecology of vector-borne zoonotic diseases. Can J Zool 78: 2061–2078.
57. Stafford KC 3rd (2007) Tick Management Handbook: An Integrated Guide for Homeowners, Pest Control Operators, and Public Health Officials for the Prevention of Tick-Associated Disease. 78 p.
58. Aguero-Rosenfeld ME, Nowakowski J, Bittker S, Cooper D, Nadelman RB, et al. (1996) Evolution of the serologic response to Borrelia burgdorferi in treated patients with erythema migrans and neuroborreliosis. J Clin Microbiol 32(6): 1519–1525.
59. Falco RC, Fish D (1989) Potential for exposure to tick bites in recreational parks in a Lyme disease endemic area. Am J Public Health 79(1): 12–15.