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THE EFFECT OF LAND-COVER/LAND-USE AND HABITAT FRAGMENTATION ON SPATIAL PATTERNS OF LYME DISEASE IN THE EASTERN UNITED STATES

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THE EFFECT OF LAND-COVER/LAND-USE AND HABITAT FRAGMENTATION ON SPATIAL PATTERNS OF LYME DISEASE IN THE EASTERN UNITED STATES

THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in Forest and Natural Resource Sciences in the
College of Agriculture, Food and the Environment
at the University of Kentucky

By

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2023

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ABSTRACT OF THESIS

THE EFFECT OF LAND-COVER/LAND-USE AND HABITAT FRAGMENTATION ON SPATIAL PATTERNS OF LYME DISEASE IN THE EASTERN UNITED STATES

Lyme disease has been of national concern for the past few decades. As our understanding of the role of landscape structure in epidemiology expands, it is essential to apply the principles of landscape ecology to the research of vector-borne and zoonotic disease. This study examined the strength of the relationship between land-cover class, degree of habitat fragmentation and county-level Lyme disease cases. Forest, agricultural, and urban land cover types were the categories of interest, while percent cover, edge density, and patch density were the landscape metric used to measure habitat amount and fragmentation. The general linear trends were modelled with the Quasi-Poisson family to quantify the relationship between land cover metrics and case numbers. Forest land had the greatest effect on case numbers, while urban and agriculture had either positive or negative relationships depending on the chosen metric. Fragmentation had a substantial effect on case number, regardless of cover type. The findings can be employed by policy makers and those who work in environments that foster high disease incidence, to keep workers and the local populations safe and healthy.

KEYWORDS: Landscape Ecology, Lyme disease, Land-cover/Land-use, Habitat Fragmentation

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7/20/2023
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DEDICATION

To the five members of the family-owned, family-run logging company in Clementsville, Kentucky that brought my research to life by sharing their personal experiences contracting tick-borne diseases and how that affected their health and livelihood. They provided a face to those who we strive to protect with our academic work.

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Thank you to my professors, especially my advisor Dr. Yang for guiding me every step of the way. I would also like to thank my other committee members: Dr. Crocker and Dr. Sanderson CIH. To CDC/NIOSH who so graciously provided the funding for my graduate study and opened up a whole new world of interdisciplinary research and connections I would never have made otherwise. Thank you to my parents Jenny and Paul, who have always cheered me on every step of the way, I hope I've made you proud. Also, to my family and friends. Josh, my best friend, and life partner was my greatest support and companion through all of this and still is. A special thanks to my classmates and now friends for understanding all the struggles of graduate life and providing much needed stress relief during these last two years, with a special shout-out to Amy, for always knowing what we needed to hear.

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CHAPTER 1. INTRODUCTION

1.1 Background

In the context of the recent pandemic and ongoing global change, human modification of the landscape has become more important than ever to understand as an ecological driver of the spread of infectious disease. As a cause of infectious disease, tick-borne pathogens are increasingly prevalent both in the United States and abroad, which highlights the need for a greater understanding of environmental factors contributing to the rising case numbers and the increasing geographic spread (Kuehn, 2019; Rochlin & Toledo, 2020; Rosenberg et al., 2018). This geographic expansion is shaped by the changing land cover and land use types, connectivity of host habitat, and proximity to human communities. Land-cover is primarily defined as the material that makes up an area, such as forest, grassland, or concrete, while land-use is defined by the human usage of said land, such as farmland or cities. These two terms are used in unison to describe land as simply what it is and what it is used for. As two major ecological drivers of biodiversity, land-cover/land-use change and habitat fragmentation have been widely used to measure anthropogenic impacts on the diverse ecosystems that are home to the vectors of zoonotic diseases (Haddad et al., 2015; Hooper et al., 2012; Newbold et al., 2015). Zoonotic diseases (also called zoonoses) are caused by pathogens that are transmitted between wildlife and humans. Well-known examples are the Ebola virus, COVID-19, and salmonellosis. The transmission of zoonoses is directly tied to the animal's environment and as such is affected by ecological processes, including those that alter biodiversity. These ecological drivers of land cover change and habitat fragmentation could exert far reaching yet variable influence on the spatial patterns of Lyme disease and other tick-borne infectious diseases.

Lyme disease is the most common vector-borne disease in the U.S. The first known case was described in Wisconsin in 1970, though it occurred in isolation. The first documented cases of what we now know as Lyme disease were from Old Lyme, Connecticut in 1977, where it got its namesake. It is transmitted by the genus *Ixodes*, which are hard ticks. Symptoms are similar to the common flu sometimes accompanied by a conspicuous bullseye shaped rash. Lyme disease is present in Europe as well, but has fewer cases on a yearly basis (Marques et al., 2021).

Infectious zoonotic diseases such as Lyme disease can cause significant strain on public healthcare systems (Dantas-Torres et al., 2012; Mac et al., 2019) with serious physiological and neurological impacts in infected people (Eremeeva & Dasch, 2015; Kaiser & Holzmann, 2000; Steere et al., 2016) and pose an increased risk of infection in pets and livestock (Parola et al., 2005; Wikel, 2018). Humans that were previously treated for Lyme disease are shown to have higher incidences of joint issues, memory impairment, and mental dysfunction (Shadick et al., 1999). Canines have a higher risk of developing chronic kidney disease if they are exposed to the pathogen that causes Lyme disease (Drake et al., 2021).

Due to the domestic and global implications of tick-borne disease, there has been some research on the patterns of potential ecological drivers of their transmission (Estrada-Peña & De La Fuente, 2015; Ogden, 2013; Rochlin & Toledo, 2020). Ecological drivers that have been previously studied are host species range, habitat, climate, and host competency (Alkishe et al., 2021; Singh & Girschick, 2003; Wang et al., 2015). Some landscape level processes such as habitat fragmentation and land-cover/land-use change have been studied in relation to tick-borne disease (Diuk-Wasser et al., 2021). However, the spatial extent examined in previous studies was limited to a few counties in New England or a single neighborhood. And a full geographic scope of the spatial trends of Lyme disease is lacking. It is understood that the disease is prominent in the Eastern United States, especially in the New England region. The disease has been endemic in this region for almost 50 years, but it has been expanding rapidly throughout the entire eastern US. Studying the full spatial extent of this disease is paramount for future management and is especially pertinent in the current epidemiological struggle we are facing.

The risk of Lyme disease can seem commonplace in much of the country, but the habitats that support the ticks and their hosts are incredibly localized. The geographic ranges of these medically important tick species have shifted over the years; this is particularly true for the species *Ixodes scapularis*, commonly referred to as the deer tick or black-legged tick, which is the main vector of the Lyme disease bacterium, a spirochete called *Borrelia burgdorferi* in the Eastern United States (Bacon et al.; Dennis et al., 1998; Eisen et al., 2016). The habitat ranges of the ticks could be expanding because of the cumulative effect of climate change and human modification of environment, which could help many *Ixodes* genus by facilitating the pathogen transmission cycle, reproduction, and dispersion (Azad, 1988; Ogden, 2013). The role of hosts in range expansion is also important. In a study conducted by Madhev. et al (2004), they summarized the impacts different host species can have on the range of ticks. Large mammal hosts with high tick burdens and a large geographic range of their own, i.e., white-tailed deer (*Odocoileus virginianus*), play the most crucial role in assisting the range expansion. In contrast, many small mammal hosts with limited home ranges could actually limit expansion, but avian hosts, with the ability to rapidly move long distances could have a positive impact on tick home range expansion, although this has yet to be supported. Birds, both migratory and ground species, can be considered either competent hosts (able to effectively transmit the pathogen of interest to other wildlife) or reservoir species (species that do not build up an immunity to the pathogen and will hold the infection for an extended period of time, even up to their lifetime) (Comstedt, 2006; Martin et al., 2016).

The host species of these important tick species play an integral role in the transmission of the infectious pathogen, *Borrelia burgdoferi*. Since wildlife are an essential linkage in the pathogen transmission cycle, those species pertinent to this infection cycle have been studied in relation to the increase in tick-borne diseases in North America and Lyme disease in Europe (Comstedt, 2006; Tsao et al., 2021). The infection cycle between ticks and wildlife hosts is a complicated physiological process that involves immune responses of both vector and host (Singh & Girschick, 2003). A decrease in host density would impact the transmission process and as a result, the rates of tick-borne disease. Whether tick species are considered host specialists or host generalists, they are limited by the biological and biogeographic constraints of their host species (Halsey et al., 2018; Mccoy et al., 2013). One reservoir host for *I. scapularis*, the white-footed mouse (*Peromyscus. leucpus*), is affected by changes in the structure of the forested lands the host species inhabit (Kaufman et al., 1983). Additionally, any climate change impacts on hosts such as the white-tailed deer and white-footed mouse could in-turn affect tick distribution (Dawe & Boutin, 2016; Roy-Dufresne et al., 2013). Some of these host species have been considered an "edge species" where they can live on the borders between land-cover classes, that typically occur because of habitat fragmentation and natural transitional zones (Peterson, 2018; Williamson & Hirth, 1985).

The ability of edge species to reside at interfaces between land-cover classes ties into other recent work on tick-borne disease ecology, which has discussed the impact of both land-use and habitat fragmentation on tick-borne disease (Diuk-Wasser et al., 2021). One study found that there was no difference in nymphal tick abundance between different land-use categories, but the density of nymphs was found to be dependent on land-use types (Rosà et al., 2018). This measure of the density of nymphs is often correlated with risk of disease, even though it doesn't directly measure case numbers. The intersection between different characteristics of land, such as land cover, land use, and land ownership, were important in predicting the spatial distribution of another tick-borne disease: Tick-borne encephalitis in Latvia (Vanwambeke, 2010). Forested land cover is clearly associated with the hosts species and tick populations, and people regularly encounter ticks in forested areas. In a 2018 study in Virginia, Ferrell & Brinkerhoff examined landscape drivers of *B. burgdorferi* infection prevalence and abundance of *I. scapularis* ticks (Ferrell & Brinkerhoff, 2018). Their conclusions were that the amount of forest cover is the most important indicator of increased tick density, seeming to support the general idea that more forest equals more ticks, which could increase disease risk. In an early study in 1998, nymphal density was found positively associated with the proportion, area and patch frequency of woodland cover within residential areas (Frank et al., 1998). Decreasing woodland patch size may also increase the density of infected nymphs, which is correlated with higher risk of Lyme disease (Allan et al., 2003). This seemingly contradicts what some studies previously discussed about large, intact forest patches having a higher risk of disease (Ferrell & Brinkerhoff, 2018). But whether large swaths of unbroken forest or the peri-urban forests that made up those residential patches have the same level of risk has been debated. In one study conducted in Poland, no informative differences in tick abundance were observed between the forest patches in the urban setting and so called "natural forests" (Kowalec et al., 2017), while another study found variation in tick abundance in different kinds of forested patches (Borşan et al., 2020). The latter study showed that the significant predictors of abundance in their study were climate conditions and the presence of host populations. Anthropogenically driven land-use changes continue to be explored as to their effect on the pathogen transmission cycle and which of those mechanisms increase or decrease risk of disease (Gottdenker et al., 2014). While the results of these paint a certain picture of how land-cover and land-use differences could affect Lyme disease transmission, through tick abundance and density, they do not directly address actual reported cases of any tick-borne disease, leading one to question how human behavior factors into the actual diagnosis of Lyme disease. The study presented in this thesis attempts to quantify the relation of these landscape factors and disease cases, adding a further dimension of understanding in this research field.

Many studies about the effect of habitat fragmentation on biodiversity and tick-borne disease have proposed a theory or hypothesis called the "dilution effect" (Brownstein et al., 2003; Rosà & Pugliese, 2007; Schmidt & Ostfeld, 2001). While the dilution effect is a debated topic in disease ecology, at the base it asserts that biodiversity, measured by the species richness and evenness of vertebrate hosts, could decrease the risk of disease (Ostfeld & Keesing, 2000). The theory is that if there are greater numbers of animal species in an area, they will range in competency as a host for carrying the pathogens transmitted by tick bites. Not all animals have equal competency and ticks can feed on non-reservoir hosts. Consequently the risk of infection is diffused over the landscape since there are pockets that are less able to sustain the transmission cycle. Some studies dispute this “dilution effect” hypothesis, citing the greater influence of other factors such as metapopulation characteristics and community composition (Zolnik et al., 2015).

While forests are considered the most prominent land-cover class tied to Lyme disease in the literature, other land cover classes deserve focused attention as well. In a study conducted in central Illinois, which included young and mature forest, prairie land, and flood plains, it was found that prairie land had the highest pathogen prevalence (Rydzewski et al., 2011). The authors also discussed how this could have been due to the general patchiness of the landscape. Agricultural land and urban areas bordered many of these land-cover classes and the patches had a high connectivity, allowing for movement of hosts species and points of contact with human populations. In general, the intensification of agricultural processes has been observed to increase zoonotic diseases, including Lyme disease (Jones et al., 2013). This is primarily linked to increasing the wildlife-urban-interface as agricultural and suburban areas encroach on natural areas. In France, it was found that living in a rural area and farming occupations are risk factors for contracting Lyme disease (Letrilliart et al., 2005). As agricultural development and land-use change persist, forest patches and total forest area will continue to shrink in size, increasing their proximity to human settlements and cases of tick-borne disease are likely to continue to rise (Jones, 2013).

Peri-urban areas, more commonly known as suburbs, often occur at the intersection of human populations and result in behaviors that can increase contact with suitable tick habitat. Finch et al (2014) found that in neighborhoods on an island off the coast of Rhode Island, the age of residents, the number hours spent in vegetation, and most notably the edge density of shrubs increased the risk of Lyme disease. While the study presented in this thesis will not directly measure human behaviors, certain human-landscape interactions will be inferred through the land-cover classes and fragmentation metrics chosen.

This thesis examines Lyme disease cases synthesized at a county scale across the eastern United States. The reported Lyme disease case numbers aggregated at the county level are associated with county's land-cover percentage and fragmentation metrics, which offers a perspective on disease cases that is different from previous studies that look at disease risk or tick density as the dependent variable.

1.2 Research Questions and Hypotheses

The overarching research questions of this thesis are: What are the spatial patterns of Lyme disease in the Eastern U.S. at the county level? And to what degree can such patterns be attributed to land-cover/land-use and habitat fragmentation?

Specific research questions**:**

1. Population size: How does a county's population size affect Lyme disease case numbers? Does the population effect differ in hotspot counties versus non-hotspot counties?
2. Land cover: What land cover classes are more strongly associated with the county-level Lyme disease case numbers? Does the amount of forest habitat affect the case numbers more than agricultural land or urban land?

3. Fragmentation: How do habitat fragmentation metrics such as edge and patch density affect Lyme disease case numbers? Which land cover's fragmentation metrics are more important in explaining the variation of county-level Lyme disease case numbers?

This study is interested in quantifying the spatial patterns and drivers of Lyme disease in the Eastern U.S. through testing the following hypotheses:

1. The spatial clusters of Lyme disease are predicted to be focused in the Northeast and the Lake States, where there is a historical presence of reported cases among the populations. Outside those regions, the disease will be prevalent in highly populated counties.
2. Counties dominated by forest land cover are predicted to have the highest instance of Lyme disease, followed by agriculture and urban land cover.
3. Counties with higher proportions of forest and agriculture edge habitat will have more Lyme disease cases.

CHAPTER 2. METHODS

2.1 Study Area

This study is focused on the eastern contiguous United States, which is covered by the Census designated regions of the Northeast, South, and Midwest (Figure 2.1) and includes 37 states with 2,374 counties. In 2019 the total population of these counties was 326,063,037. These counties contain a variety of land-cover types such as forest, both deciduous and coniferous, wetlands, grasslands, a large proportion of agricultural land, and pockets of intense urbanization and highly populated cities.

Over the study period (2000-2019) the eastern USA had a total of 435,983 cases of Lyme diseases reported to the Centers for Disease Control and Prevention (CDC). These cases were mainly concentrated in the New England region and the Lake States. Pennsylvania had the highest average number of cases over the study period. This study focuses on the eastern US because most of the reported Lyme disease cases are concentrated in the eastern. While there are Lyme disease cases found in almost every state, there are differing ecological conditions in many of the western states that could make comparison between the eastern US and the western US difficult. For example, in the eastern states the primary tick vector of Lyme disease is *Ixodes scapularis,* while the primary vector in the western states is *Ixodes pacificus.* These two species are similar, but have differences in life cycle, availability of hosts, and distance from the geographic origin of cases.

2.2 Data

All data used in analysis was secondarily sourced. Lyme disease case data was obtained from the CDC National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD) (Division of Vector Borne Disease, 2022). This data was a record of all reported cases of Lyme disease per county between the years 2000-2019. Since Lyme disease is a nationally notifiable disease, data is compiled by this federal organization to monitor the progression of the disease and can be accessed through the CDC website. The shapefile of all county boundaries in the United States was downloaded from the Census Bureau website (Cartographic Boundary Files - Shapefile, 2018) and then cropped in ArcGIS Pro (ArcGIS Pro 3.1) to the counties included in the study area. The data source that was used to obtain the population of each county was the decennial census collected by the U.S. Census Bureau and accessed through their website (PEPANNRES| Annual Estimates of the Resident Population: April 1, 2010 to July 1, 2019, 2010).

The National Land Cover Database (NLCD) was the source of the geospatial land cover data. The survey is done at least every 5 years and tracks 20 categories of land cover. This database is provided by the U.S. Geological Survey and is accessible through the Multi-Resolution Land Consortium website(Dewitz, 2021). This study accessed the NLCD data through the *FedData* package in R (Bocinsky, 2023) using the *get_nlcd* function to produce a raster of the land-cover of the Eastern US. The most recent (i.e., 2019) NLCD data was used in the subsequent analyses.

2.3 Spatial Analysis

ArcGIS Pro (ArcGIS Pro - Hotspot Analysis, 2023) was used to conduct the Hotspot Analysis. Hotspot analysis was completed through the Optimized Hot Spot Analysis tool. This tool uses the Getis-Ord G_i* statistic of each feature provided in a spatial dataset to find statistically significant "hot" and "cold" spots within the study area, given a set of weighted features. The formulas are given in Equations 1, 2, 3.

Equation 1

$$G_i^* = \frac{\sum_{j=1}^{n} w_{i,j}\, x_j - \bar{X} \sum_{j=1}^{n} w_{i,j}}{S \sqrt{\frac{\left[n \sum_{j=1}^{n} w_{i,j}^2 - \left(\sum_{j=1}^{n} w_{i,j} \right)^2 \right]}{n-1}}}$$

x_j is the attribute value for feature j, $w_{i,j}$ is the spatial weight between feature i and j, n is equal to the total number of features. $\bar{X}$ and S are calculated by

Equation 2

$$\bar{X} = \frac{\sum_{j=1}^{n} x_j}{n}$$

Equation 3

$$S = \sqrt{\frac{\sum_{j=1}^{n} x_j^2}{n} - (\bar{X})^2}$$

High attribute values must be surrounded by other high attribute values to be considered statistically significant. The G_i^* statistic value that results for each feature attribute is a G_i z-score, additionally this analysis tool produces p-values for each feature's attribute z-score. The p-value denotes the statistical significance of the case numbers of each county in relation to the surrounding counties. *G_i_Bin* is a categorical variable that represents the confidence interval determined by the Gi z-score and p-value. If the county had a positive (>=1) *G_i_Bin* score then it was identified as a hotspot county with a confidence interval greater than 90%. If the *G_i_Bin* was a negative score (<=-1) then it was identified as a cold spot with a confidence interval greater than 90%. This categorical determiner was transformed so that any county with a *G_i_Bin* score of greater than or equal to 1 is considered significant and was marked as hotspot status of 1. Any county with *G_i_Bin* score less than 1 was marked as hotspot status 0, so it was a binary variable. The hotspot status was included in the modelling as a predictor variable when quantifying the effect of population on case numbers and a confounding variable when examining the effect of land-cover and fragmentation on cases.

After obtaining the raster layer of land-cover data, the land-classes of interest were aggregated into three broad categories, forested land, agricultural land, and urban land. This was accomplished by reclassification from the original NLCD categories and grouped by the following: forest (classes 41-43), agriculture (classes 81-82), and urban (classes 21-24). The next package that was utilized was *landscapemetrics* (Hesselbarth, 2019), which is compatible with the larger R package ecosystem *tidyverse* (Wickham, 2019). It is a package that calculates a host of metrics for landscape patterns produced by categorical land-cover data. These metrics can be measured at the landscape, class, and patch level. The class-level metrics that were calculated for this study were Percentage of Landscape (PLAND), Area of Class (CA), Edge Density (ED), Total Edge (TE), Number of Patches

(NP) and Patch Density (PD). PLAND and CA are the measures of the amount of habitat on the landscape, while TE, NP, and PD are measures of the level of habitat fragmentation. The percentage of landscape (PLAND) is calculated by the summation of the area of all patches of one class, divided by the total area of the observational unit and multiplied by 100 to form the percent value. Class area (CA) is calculated by the summation of all patch areas of one class and its unit is hectares. Edge density (ED) is an edge metric, dividing the land-cover class total edge length by the total area of the observational unit. The unit for ED is meters per hectare. Total edge (TE) is a simple length metric, with meters as its unit. Number of patches (NP) is an aggregation metric that counts the number of non-connected patches of the land-cover class of interest. Finally patch density (PD) takes the number of patches within the observational unit divided by the total area of the observational unit.

2.4 Statistical Analysis

The descriptive statistics of both the response variable and predictor variables were calculated by using the base stats package in R. The basic statistics included mean, median, IQR, and range. Histograms were produced by the *geom_hist* function in the *ggplot2* package. Boxplots were also created in the *ggplot2* package, but by using the *geom_boxplot* function instead.

The specific research questions and subsequent hypotheses were analyzed with generalized linear models in the Quasi-Poisson family with a log link. This was chosen because Quasi-Poisson family models are appropriate for count data sets that are skewed and over-dispersed (Hoef, 2007). Additionally, the Quasi-Poisson family can be applied to data where the variance is greater than the mean, which was true of this data set. The models were run in R, with the *glm* function. The response variable was total number of

Lyme disease cases while population, hotspot status, percentage cover of landscape (PLAND), and class-level edge density (ED) were the response variables. Edge density was chosen for analysis instead of total edge length (TE) since it allows comparisons between counties of varying sizes. These generalized linear models only explored the first order effects present in the relationship between case numbers and the predictor variables. Higher orders of effects were not captured by these models. To assemble the model result into tables, the package *jtools* (Long, 2022) was used to compile all the model formulas for each hypothesis. The function that was utilized was the *export_summs* function. The *exp* argument was set true to exponentiate the coefficients and the scale argument was set true to scale the original values of the predictor continuous variables into mean centered. Mean-centering changes the way these coefficients are interpreted, so that all coefficients are on the same scale and represent the magnitude change based on distance of standard deviation from the mean. Any coefficient greater than 1 was interpreted as a positive effect and any coefficient value less than one was interpreted as a negative effect. Doing so allows for straightforward comparison and quantifies the ratio of the incidence rate or the magnitude change in the response variable.

2.5 Figures

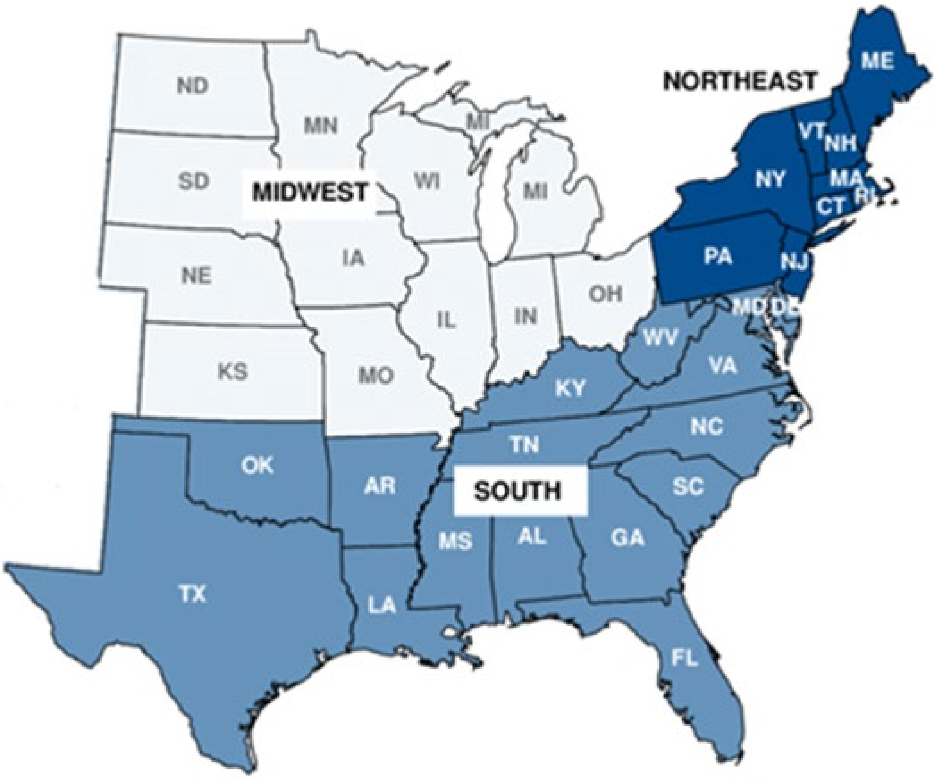


Figure 2.1: Map showing the study area and its Census designated regions

CHAPTER 3. RESULTS

3.1 Spatial Patterns of Lyme Disease in the Eastern U.S.

The reported Lyme disease cases for the study period were concentrated most heavily in the New England region and in a concerted part of the Lake States (Figure 3.1). The top five counties in terms of the Lyme disease case numbers reported from the year 2000 to 2019 are Dutchess County, NY (12 931 cases), Fairfield County, CT (10 293 cases), Morris County, NJ (9 326 cases), Middlesex, MA (8 471 cases), Columbia County, NY (8 080 cases) respectively. All these counties are in the New England region. Outside of these regions, the top five counties are Washington County, PA (4 153 cases), Hennepin County, MN (3 431 cases), Ramsey County, MN (2 117 cases), Dane County, WI (1 935 cases), and Crow Wing, MN (1 912 cases). Hennepin County, Minnesota had the highest case numbers of any county in the Lake States. Within this region, the states with the most cases were Minnesota and Wisconsin. Cases in this area are clustered north and east across the counties surrounding Hennepin, which is the seat of Minneapolis, the most populated county in Minnesota. One common geographic characteristic of the top five hotspot counties and non-hotspot counties was their placement between the 40th and 45th parallels. Over half of all counties in the study area (1829 out of 2694) had at least one reported Lyme disease case between 2000-2019. Counties with no reported cases are found mostly along the western portion of the study area and some scattered counties in the Southeastern states.

3.2 Population and Hotspot Analysis

The first research question was related to how the population size of each county is related to the total number of Lyme disease cases. This study question was a building block, so that additional variables of interest, specifically the percent land cover and the chosen fragmentation metrics, could be modelled in addition to the effect of population on the case numbers. Hotspot status was included in the models as a counfounding variable. Two variables of interest included in the hotspot analysis output were: the G_i*_Bin* score and the G_i z-score. The hotspot map is given in Figure 3.2, where the red color denotes the "hotspot" counties, which are counties with a G_i*_Bin* classification of +1,+2,+3. There were 223 counties considered hotspots and 2471 counties classified as non-hotspots. Among the 223 counties considered hotspots, the average population in 2019 was 170 156, which was substantially greater than the average population (74 680) for the 2471 counties classified as non-hotspots. Figures 3.3 and 3.4 indicate the effect of population on cases in hotspot counties and non-hotspot counties respectively. In hotspot counties, the general trend shows increasing case numbers with an increasing population (Figure 3.3). However, this trend does not hold for counties with over 1 million people. There are eleven counties in a hotspot region with over 1 million in population. One county is in Maryland, one in Massachusetts, six in New York, two in Pennsylvania, and one in Virginia. There is a less clear relationship with population after reaching 1 million, and it is a generally negative trend. In comparison, non-hotspot counties exhibited a less steep positive relationship between case numbers and population, and this relationship reached the "tipping point" sooner, which is approximately 2.5 million people (Figure 3.4) Within the hotspot counties, the simple uni-variable Model 1 including only population as a predictor (Table 3.1) shows that population accounts for about 12% variation in Lyme disease cases. In contrast, Model 2 with the identical formula but was specifically the non-hotspot counties, only explained about 5% variation (Table 3.1). The effect size of population on case numbers in hotspot counties was higher than that of non-hotspot counties. The effect of population in hotspot counties is 1.4 times higher, whereas non-hotspot counties only have 1.2 times higher cases than counties with the mean population. Model 3 accounted for all counties and its predictor variable was hotspot, whereas Model 4 instead had population as its predictor variable. Model 5 accounted for all counties where population and hotspot status were predictor variables, both had significant positive coefficients. This model explalined 60% variation of the county-level case numbers across the eastern US.

3.3 Land Use and Land Cover

Figure 3.5 is a boxplot that shows distribution of the percent cover of each land-cover type by county in 2019. Agriculture and forest land cover were the two classes with the highest average percentage at the county level. Agriculture had an average of 38% cover per county, while forest covered an average of 28% of the land. Urban land-cover had an average of 11%. The maps of these land-cover distributions are shown in Figures 3.6, 3.7, and 3.8. Agricultural and urban percentage cover were both skewed data sets, while forest percentage was distributed evenly. Urban land had the smallest interquartile range, but the largest number of outliers compared to the other land class types.

Counties with a high percent cover of forest land were largely concentrated along the Appalachian Mountain range, from the southern end of Maine trailing down into

Mississippi (Figure 3.6). The New England hotspot counties do not have a consistent forest cover percentage, while the Lake States hotspot is largely within the lower percentages (< 50%) of forest land cover. Figure 3.9 is the scatterplot showing the relationship between the percentage of forest land cover and case numbers. The general trend is positive, but it is not an entirely linear relationship. Case numbers increase until about 50% cover, then drop off. Counties with the highest case numbers (> 7500 cases) fall within the 25-60% range. These counties are also in the intermediate (> 100 000) or high (> 1000 000) end of population size.

Agricultural percentage cover was highest in the Midwest and Plains States (Figure 3.7). The New England hotspot was largely counties with less than 25% coverage. The Lake State hotspot showed a similar pattern but was bordered by a mass of counties that were dominated by agriculture land cover (Figure 3.7). In contrast, the New England hotspot did not share this characteristic. The scatterplot (Figure 3.10) shows that there was a great amount of variability in the case numbers for the counties with less than 25% coverage of agriculture land, and the relationship between agricultural land and Lyme disease cases is generally negative. The highest populated counties were expected have low percent cover (<25%) of agriculture land. Counties that were predominantly agricultural land (>50%) had low case numbers and lower populations, along with a majority classified as non-hotspots.

Urban percent cover had small pockets of high percentage cover (>50%) focused in large established cities like Atlanta (Georgia), Chicago (Illinois), Detroit (Michigan) and New York City (New York) (Figure 3.8). Cities such as New York City, NY and Minneapolis, MN are within hotspot clusters, but most hotspot counties had less than 25%

urban cover. In Figure 3.14, the percent cover of urban land shows a non-linear relationship, cases increase until urban percent reaches approximately 50%, then case numbers decreased. Most counties had less than or equal to 50% coverage of urban land. The counties with population of 1 million or higher have at least 40% or higher urban land coverage. In general, these counties are within the hotspot regions and have over 500 total cases.

Quasi-Poisson models that included of the percentage of each land cover type, population, and hotspot as the predictor variable showed that the percent forested cover had a positive effect (corresponding coefficient greater than 1) on Lyme disease case numbers, whereas agriculture and urban land percentage did not (Table 2). Urban land percentage was also not significantly related to cases ($p > 0.05$). Agricultural land percentage had an overall negative effect on cases, with the overall case numbers of Lyme disease 0.71 lower than the average if the urban land percentage is 1 standard variation greater than the average. The model including percentage of agricultural land as an explanatory variable was slightly higher than the models including forest or urban, at pseudo R2= 0.61, 0.60, and 0.60 respectively.

3.4 Habitat Fragmentation

3.4.1 Edge Density

The fragmentation metrics that were measured were edge density, total edge, number of patches and patch density, but only edge density and patch density were used in the analysis and model building. Since edge density and patch density are both density metrics, their values can be compared across counties of varying areas, which is useful with the large variation of county size in this study. The *landscapemetrics* package records the unit of edge-density as meters per hectare (m/ha) and patch density as number of patches per 100 hectares (#/100 ha). Edge density maps of each land-cover class can be seen in Figures 3.12, 3.13, and 3.14. Forest edge density had the highest mean value at 43 m/ha, followed by agriculture at 40 m/ha, and urban at 35 m/ha (Figure 3.15).

The map of forest land-cover edge density showed a clear gradient from east to west (Figure 3.12). The western most part of the study area had very low forest edge density, while forest land-cover edge density tended to increase further east, peaking on the New England coast and in the Carolinas. Comparatively the Lake States hotspot has counties with lower edge densities than the New England hotspot. The scatter plot (Figure 3.16) showed a positive relationship between forest edge density and case numbers, which steadily increased until approximately 90 m/ha and then trended negative. There were four counties with more than 100 m/ha of edge density, those included counties in Georgia, Maryland, Massachusetts, and Connecticut. Among these, Fayette County of Georgia was the only one that was not a hotspot county and had a very low number of cases, with only 8 recorded from 2000-2019. On the opposite end of the spectrum, Fairfield of CT had over 100 m/ha of forest edge and over 10,000 cases.

The mean density of agricultural land edges was lower than forested areas and there were a few pockets of high edge density counties, particularly in the southeast region of Texas, the eastern half of Missouri along the western half of Illinois, and a group of counties stretching from the northernmost counties in Ohio down into Tennessee (Figure 3.13). The New England area had a wide range of agriculture edge density at the county level, while the high case number pockets in the Lake States had a bullseye pattern. The central counties in the Lake State hotspot had less than 50 m/ha while the counties surrounding those had edge densities greater than 50 up to 75 m/ha. Much like agricultural PLAND, the edge density of agricultural cover had a negative relationship with the reported case numbers. The highly populus counties had a lower edge density of agriculture land, while the county with the highest case number (Dutchess County, NY) sat near the mean edge density value of 43 m/ha.

The urban edge density map shows that there were two main pockets of high edge density (>75 m/ha), Atlanta,GA and Philadelphia, PA (Figure 3.14). Philadelphia and its neighboring counties were hotspot counties. Urban edge density had a generally positive trend (Figure 3.17). Most counties fell within the 25-75 m/ha range and the county with the highest case numbers (Dutchess County, NY) had approximately 55 m/ha edge density.

The modelling results indicated that forest land edge density had the highest effect size, followed by urban land-cover, and finally agricultural (Table 3). When controlling for population and hotspot status, forest edge density multiplied cases 1.9 times the expected value at the mean. In comparison, urban edge density multiplied case by 1.4 times and agriculture edge density slightly reduced the cases with a multiplication factor of 0.93. Agricultural edge density had a non-significant effect size ($p > 0.05$), while both forest and urban were significant ($p < 0.001$). Forest ED also explained more variations than the other two ED metrics.

3.4.2 Patch Density

The mean patch density was approximately the same between the three land-cover classes (Figure 3.19). Urban patch density was the highest at 2.7 patches/100 ha, forest was next at 2.09 patches/100 ha, followed by agricultural at 1.90 patches/100 ha. Forest land-cover had an outlier county that had over 20 patches/100 ha, which was substantially higher than any other county. This was Falls Church County, Virginia, which had 8 cases over the study period, but was one of the few counties that was considered a hotspot having less than 500 cases. This indicates that there were enough high case counties surrounding it to be considered statistically significant, even if the case number is low.

The forest patch density map indicates that coastal regions have the highest density, this includes both coasts bordering oceans and freshwater (Figure 3.20). As counties become more landlocked, the forest patch density decreased. Case hotspots had counties with 5-10 patches/100 ha, but there were other clusters of high values in the Southeast, especially in Georgia, North Carolina, and Florida. Counties in these states were not determined to be Lyme disease hotspots. The forest patch density scatterplot (Figure 3.21) shows a positive relationship up until 5 patches/100 ha and then drops off. Higher forest PD counties (>3 patches/100 ha) tend to be within the hotspots. The county with the highest number of cases sits around the mean PD value for forest land-cover.

Agricultural patch density was highest in the western half of North Carolina, South Carolina, and the northern part of Georgia. It was over 5 patches/100 ha in these areas (Figure 3.22). Hotspot counties fell in the 2.5-5 patches/100 ha range. The scatterplot (Figure 3.23) shows that almost all counties had less than or equal to 5 patches/100 ha and the highly populated counties had 2.5 or less. There is no obvious linear trend in this scatter plot.

Urban patch density, as seen in the map in Figure 3.24, was more dispersed across the study area. The highest urban PD (>10 patches/100 ha) was in Hunterdon County, NJ, which reported 7034 cases from 2000-2019 and was included in the New England hotspot cluster. The northwest portion of the study area had more contiguous urban areas since there was a lower number of patches. Regions that had variable ranges of PD are also where the highest case numbers were found. Like agriculture, there was a positive relationship between urban patch density and case numbers that peaked around 3 patches/100 ha which then dropped off. Highly populated counties had less than 5 patches/100 ha. The scatterplot (Figure 3.25) had a linear relationship, similar to the one between urban edge density and case numbers. The peak of cases was at approximately 5 patches/100 ha.

As shown in Table 4 urban patch density had the largest effect size and explained the most variation of cases. Compared to the mean, urban PD multiplied cases by 1.35 times (Model 3), agriculture multiplied them by 1.20 times (Model 1), and forest patch density came in with the smallest effect size at 1.16 times (Model 2). While urban patch density had the highest weight amongst the models, it was not substantially higher than either forest or agriculture, coming in at 0.63, 0.61 and 0.60 pseudo R^2 respectively.

3.5 Tables and Figures

Table 3.1: Results from quasi-Poisson family modelling of the effect of hotspot status and population on case numbers. Model 1 calculated the effect of population in hotspot counties, Model 2 calculated the effect of population on non-hotspot counties, while Models 3,4,5 grouped all the counties regardless of hotspot status.

	Model 1	Model 2	Model 3	Model 4	Model 5
(Intercept)	1436.62 ***	38.04 ***	151.51 ***	39.74 ***	38.19 ***
	[1431.57, 1441.69]	[37.80, 38.28]	[151.05, 151.98]	[39.50, 39.99]	[37.95, 38.43]
Hotspot				38.96 ***	32.57 ***
				[38.68, 39.24]	[32.33, 32.80]
Population	1.39 ***	1.19 ***	1.25 ***		1.23 ***
	[1.39, 1.39]	[1.19, 1.19]	[1.25, 1.25]		[1.22, 1.23]
N	223	2471	2694	2694	2694
Pseudo R2	0.12	0.05	0.09	0.56	0.60

All continuous predictors are mean-centered and scaled by 1 standard deviation. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

Table 3.2: Modelling results from a quasi-Poisson family generalized linear model (glm). Model 1 included forest PLAND (percentage of landscape), Model 2 included agricultural land, and Model 3 included urban land-cover.

	Model 1	Model 2	Model 3
(Intercept)	37.77 ***	36.97 ***	37.87 ***
	[31.48, 45.30]	[30.81, 44.36]	[31.47, 45.56]
PLAND_F	1.15 **		
	[1.04, 1.26]		
PLAND_A		0.71 ***	
		[0.62, 0.82]	
PLAND_U			0.97
			[0.91, 1.03]
Hotspot	30.25 ***	26.85 ***	33.71 ***
	[24.56, 37.25]	[21.70, 33.22]	[27.12, 41.90]
Population	1.25 ***	1.19 ***	1.25 ***
	[1.21, 1.29]	[1.16, 1.23]	[1.19, 1.30]
N	2688	2692	2694
Pseudo R2	0.60	0.61	0.60

Table 3.3: Modelling results of a generalized linear model in the quasi-Poisson family. Models 1,2,3 examined the effect of edge density of forest, urban, and agriculture on Lyme disease cases.

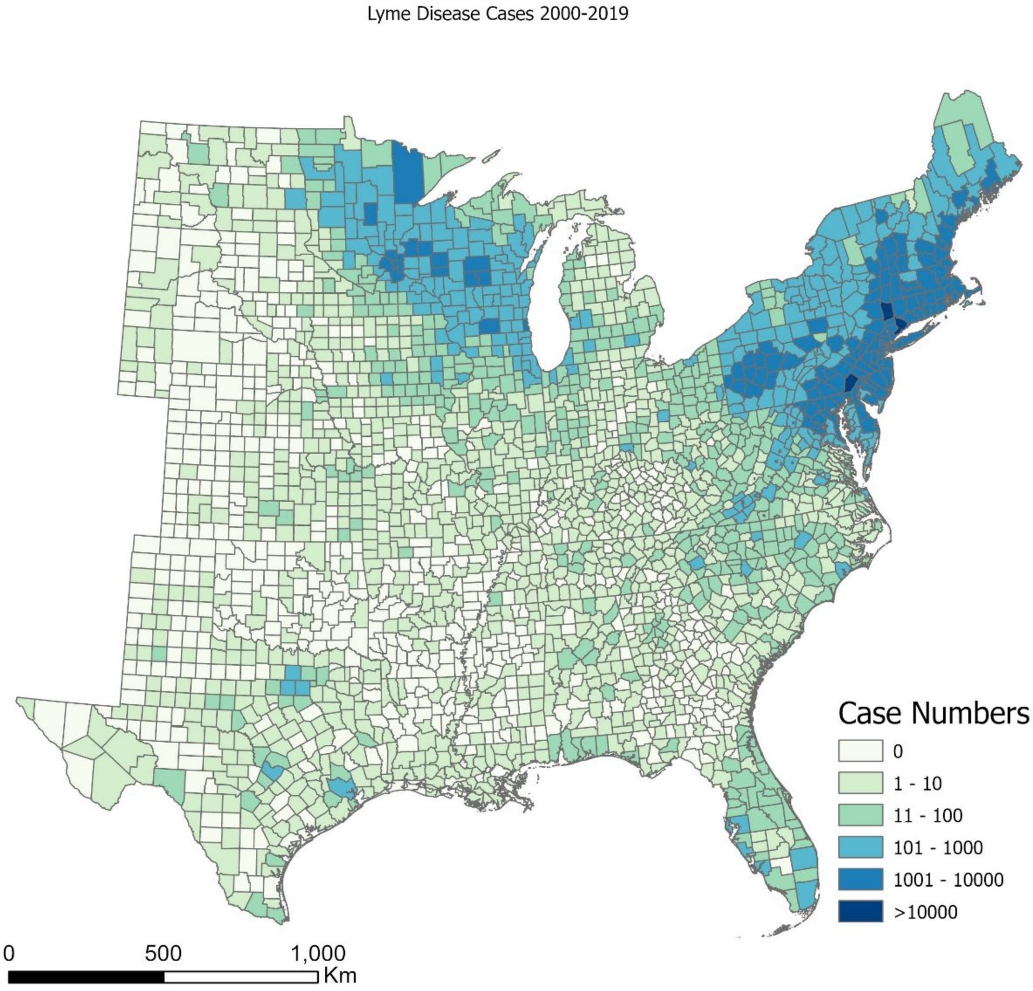
	Model 1	Model 2	Model 3
(Intercept)	32.22 ***	38.38 ***	36.67 ***
	[26.99, 38.46]	[31.92, 46.14]	[30.75, 43.73]
ED_U			1.38 ***
			[1.30, 1.47]
ED_F	1.89 ***		
	[1.71, 2.09]		
ED_A		0.93	
		[0.85, 1.02]	
Hotspot	21.94 ***	31.87 ***	22.07 ***
	[18.02, 26.70]	[25.83, 39.31]	[17.84, 27.30]
Population	1.30 ***	1.21 ***	1.25 ***
	[1.26, 1.34]	[1.17, 1.25]	[1.21, 1.29]
N	2688	2692	2694
Pseudo R2	0.65	0.60	0.63

All continuous predictors are mean-centered and scaled by 1 standard deviation. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

Table 3.4: Table 5: Modelling results of a generalized linear model in the quasi-Poisson family. Models 1,2,3 examined the effect of patch density of urban, forest, and agriculture on Lyme disease cases.

	Model 1	Model 2	Model 3
(Intercept)	37.07 ***	37.94 ***	35.97 ***
	[30.96, 44.38]	[31.75, 45.33]	[30.02, 43.09]
PD_U			1.35 ***
			[1.27, 1.44]
PD_F		1.16 ***	
		[1.12, 1.21]	
PD_A	1.20 ***		
	[1.09, 1.31]		
Hotspot	30.59 ***	28.45 ***	26.35 ***
	[25.04, 37.38]	[23.20, 34.90]	[21.47, 32.34]
Population	1.25 ***	1.23 ***	1.27 ***
	[1.21, 1.29]	[1.20, 1.27]	[1.23, 1.31]
N	2692	2688	2694
Pseudo R2	0.60	0.61	0.63

All continuous predictors are mean-centered and scaled by 1 standard deviation. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.



Lyme Disease Cases 2000-2019

Figure 3.1: Map of cumulative Lyme disease cases from 2000-2019 in the Eastern U.S.

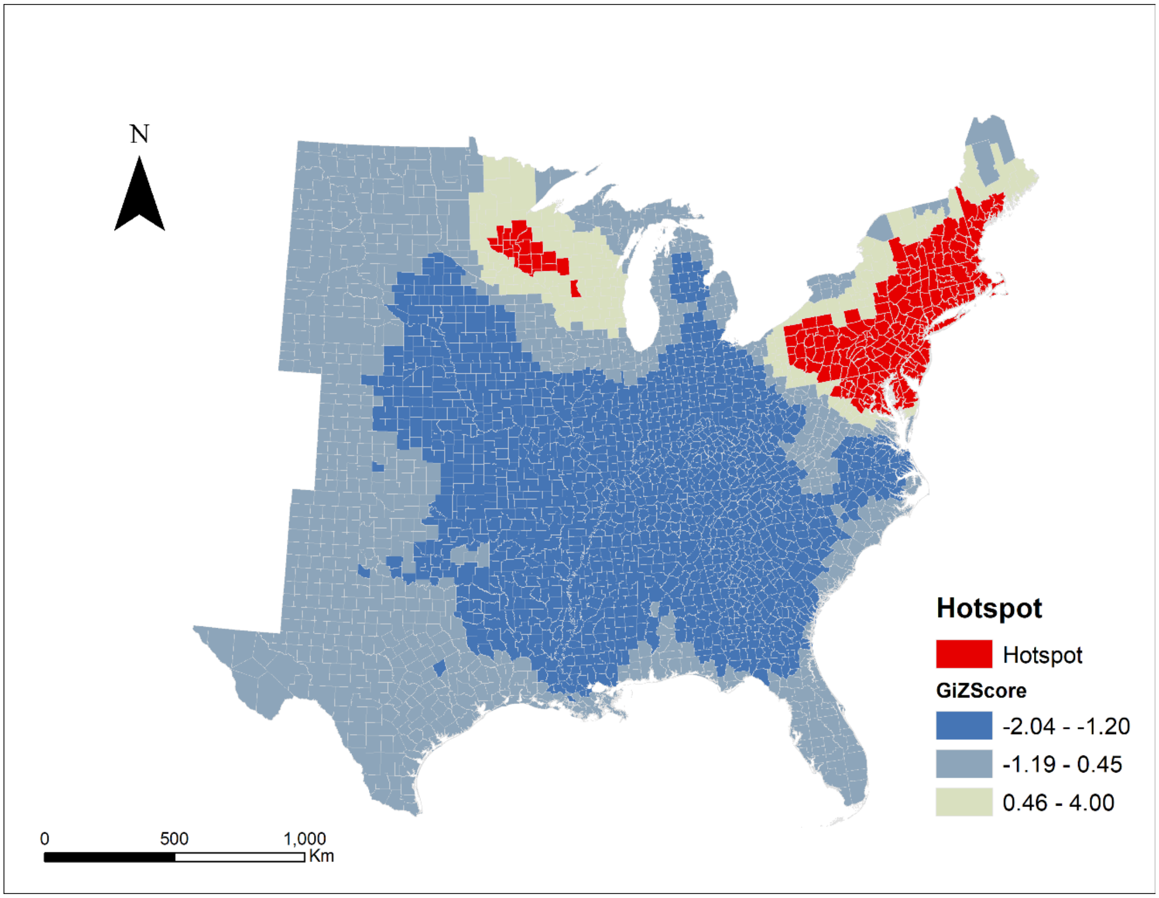


Figure 3.2: Hotspot map for Lyme disease cases from 2000-2019

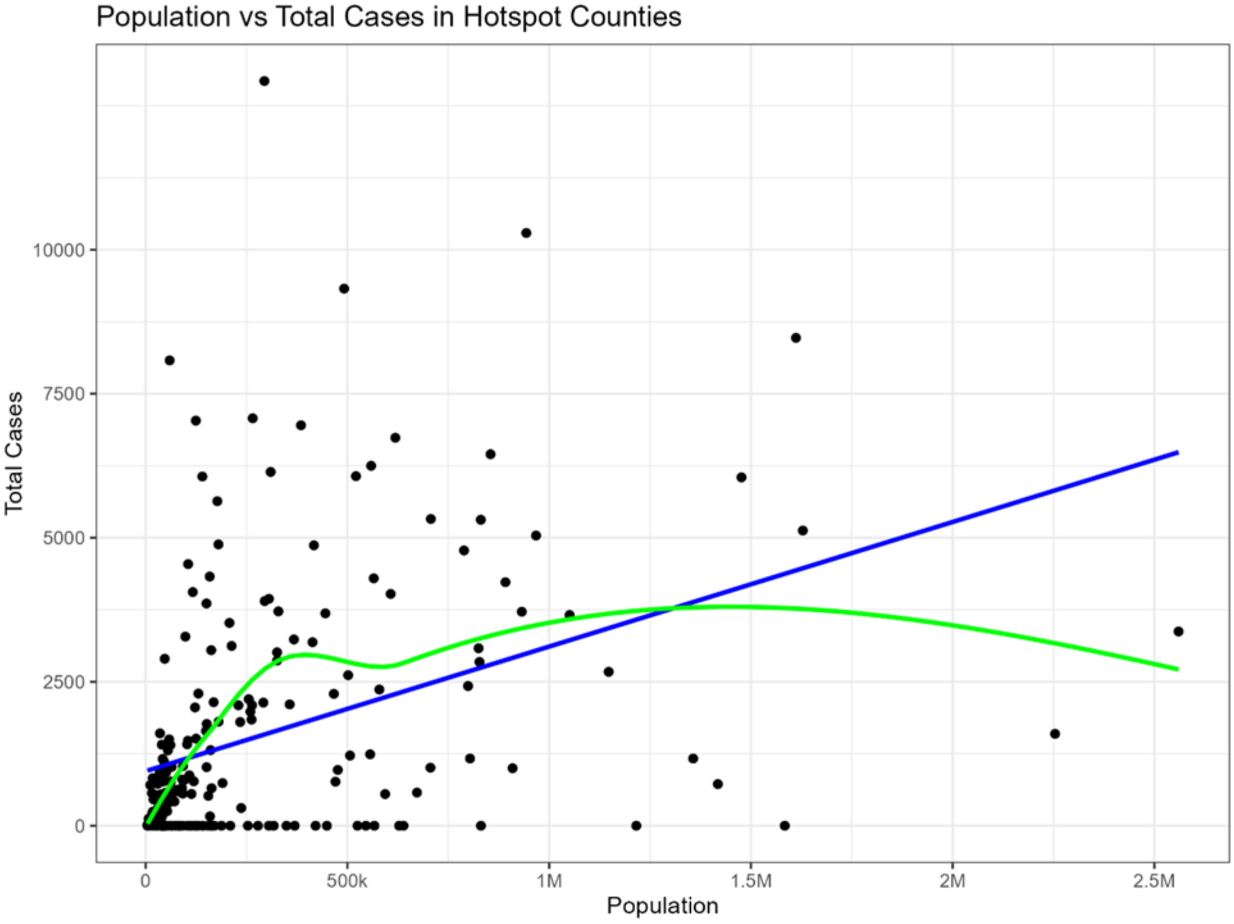


Figure 3.3: Population versus total Lyme disease Cases in hotspot counties. The blue line used the formula “glm” in the ggplot function geom_smooth while the green line uses “loess” or local regression.

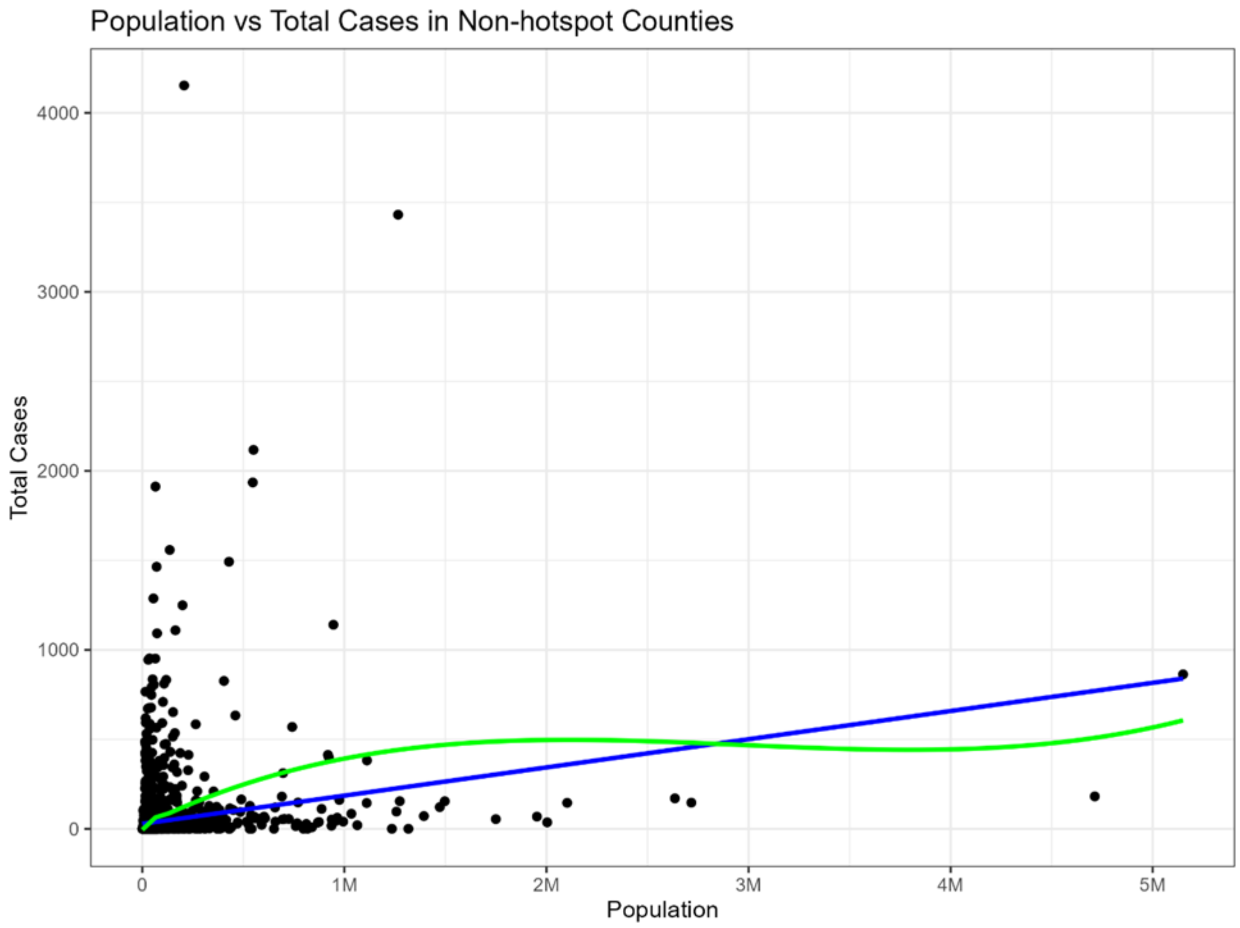


Figure 3.4: Population versus total Lyme disease Cases in Non-hotspot counties. The blue line used the formula “glm” in the ggplot function *geom_smooth* while the green line uses “loess” or local regression

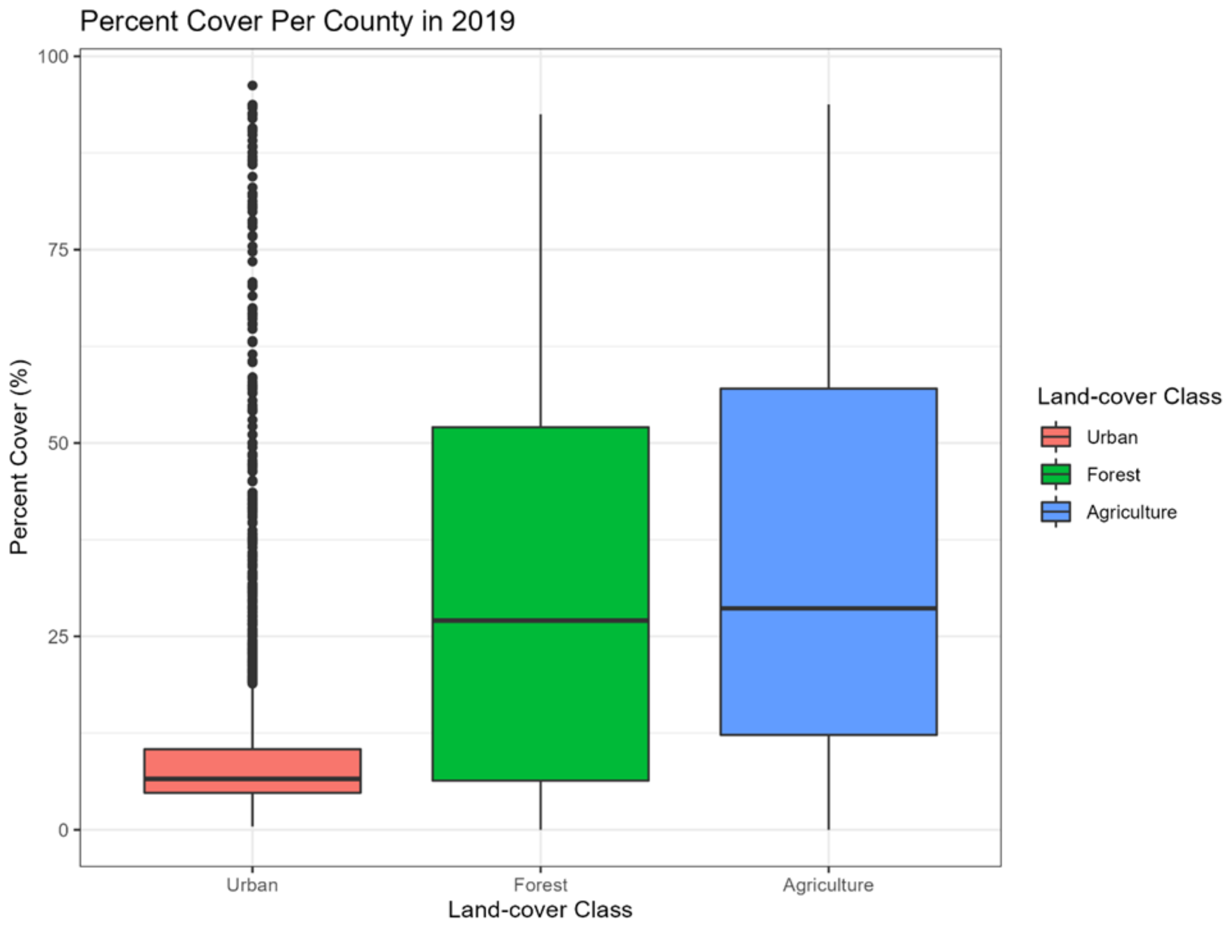


Figure 3.5: Boxplot of percent cover of each of the three land cover classes: urban, forest, and agricultural

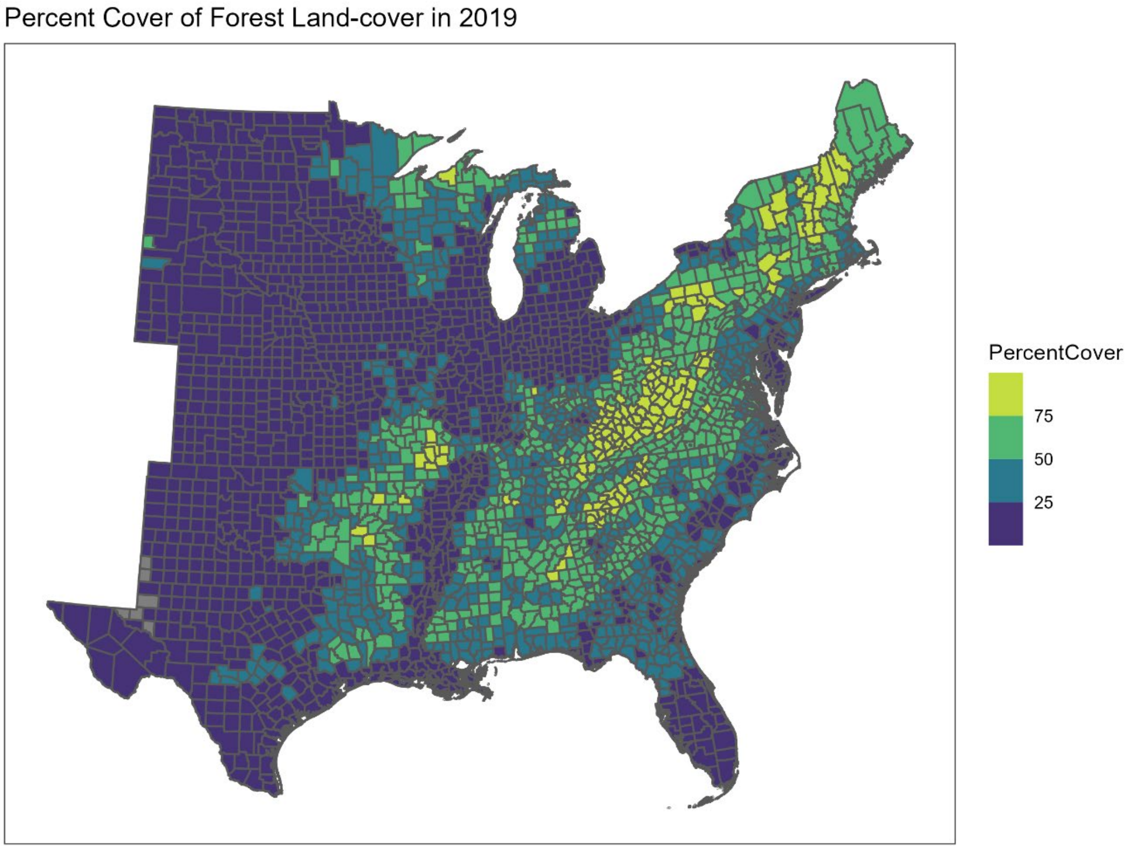


Figure 3.6: Map of forest land-cover percentage by county

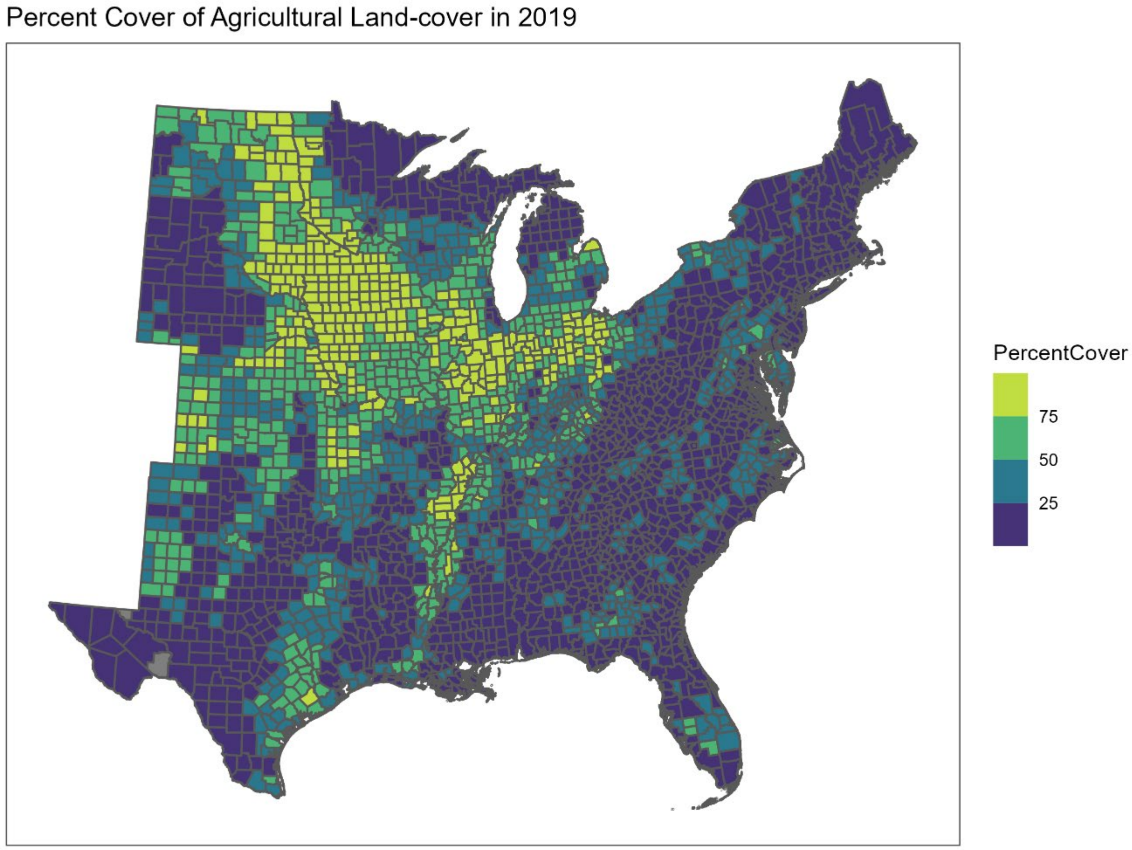


Figure 3.7: Map of agricultural land percent cover by county

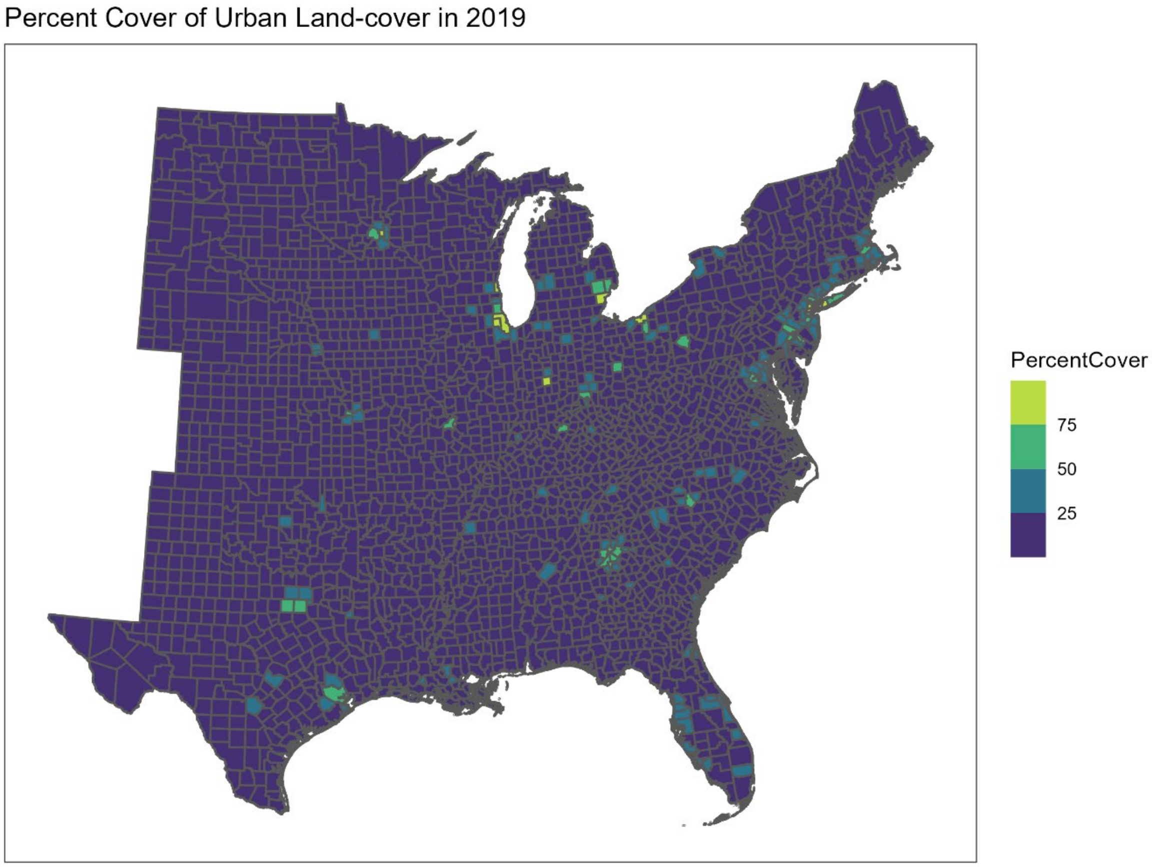


Figure 3.8: Map of urban land-cover percentage per county

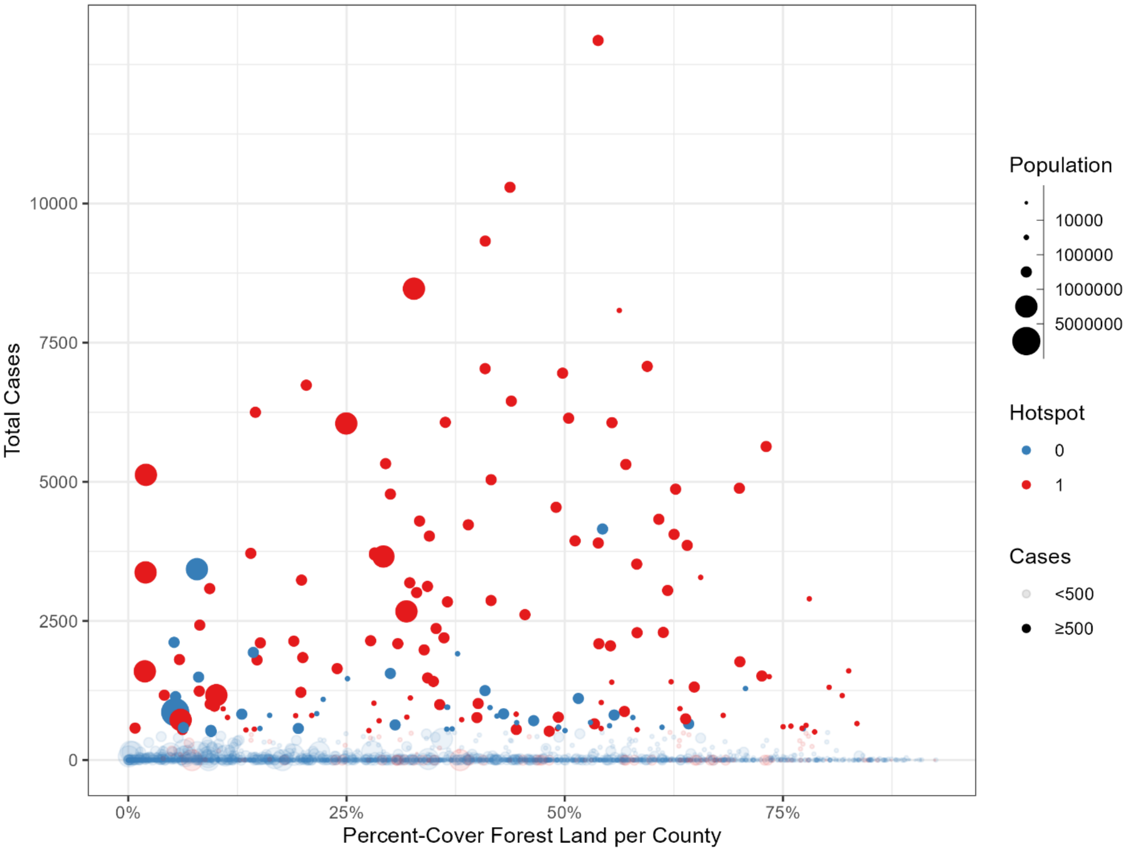


Figure 3.9: Scatterplot of forest land cover percentage per county versus total Lyme disease cases

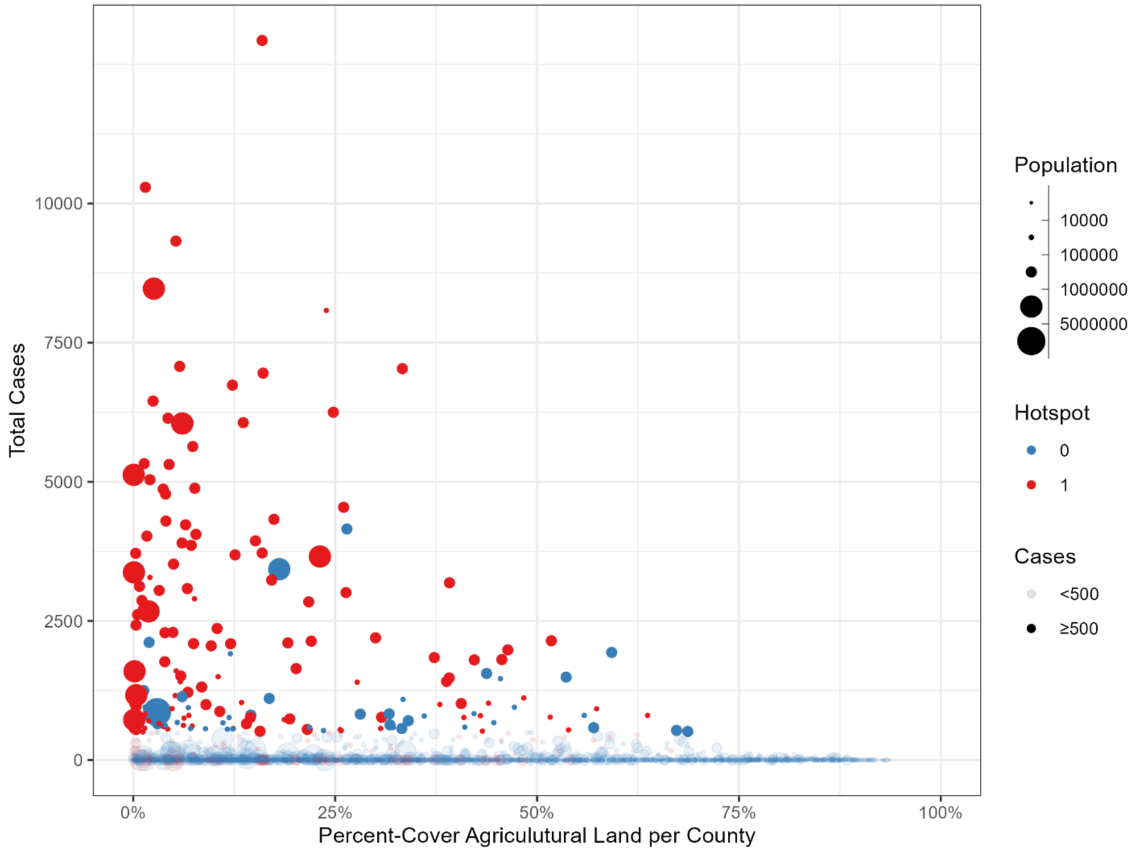


Figure 3.10: Scatterplot showing relationship between percentage cover of agricultural land and Lyme disease case totals.

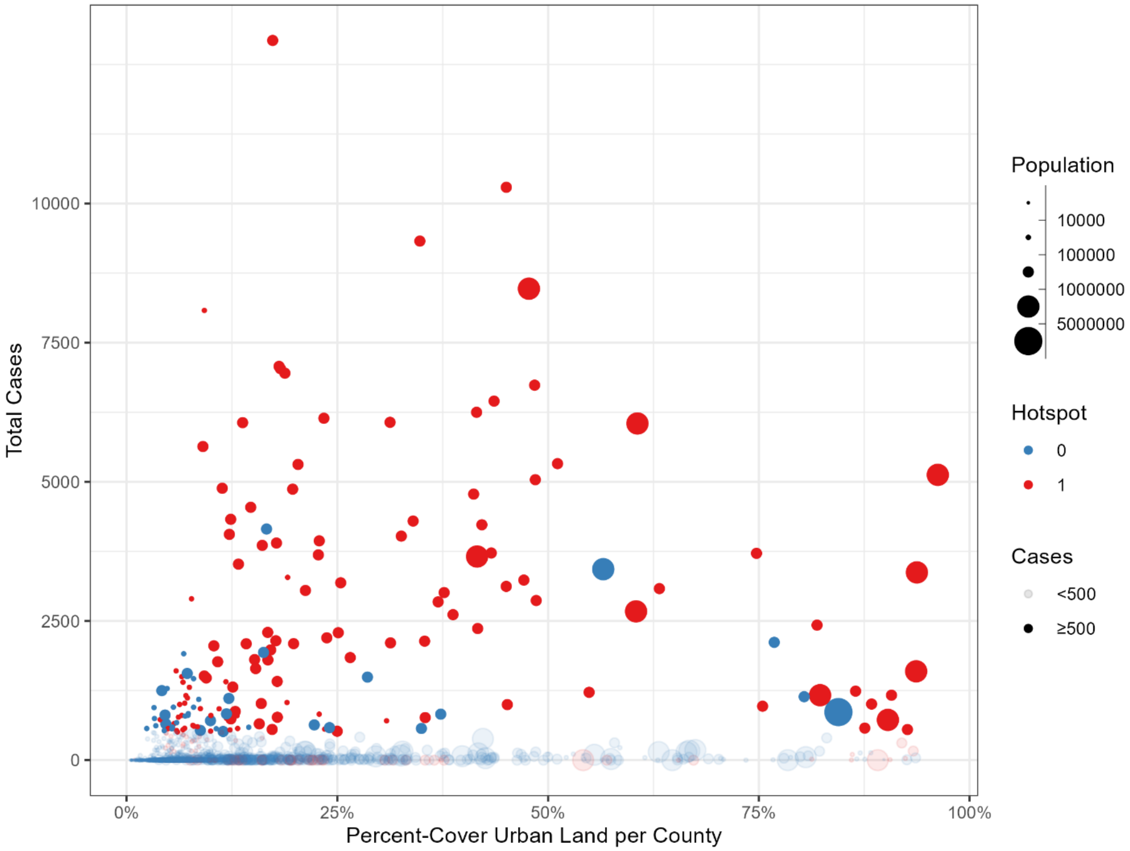


Figure 3.11: Scatterplot of the relationship between percent cover of urban land and total Lyme disease cases.

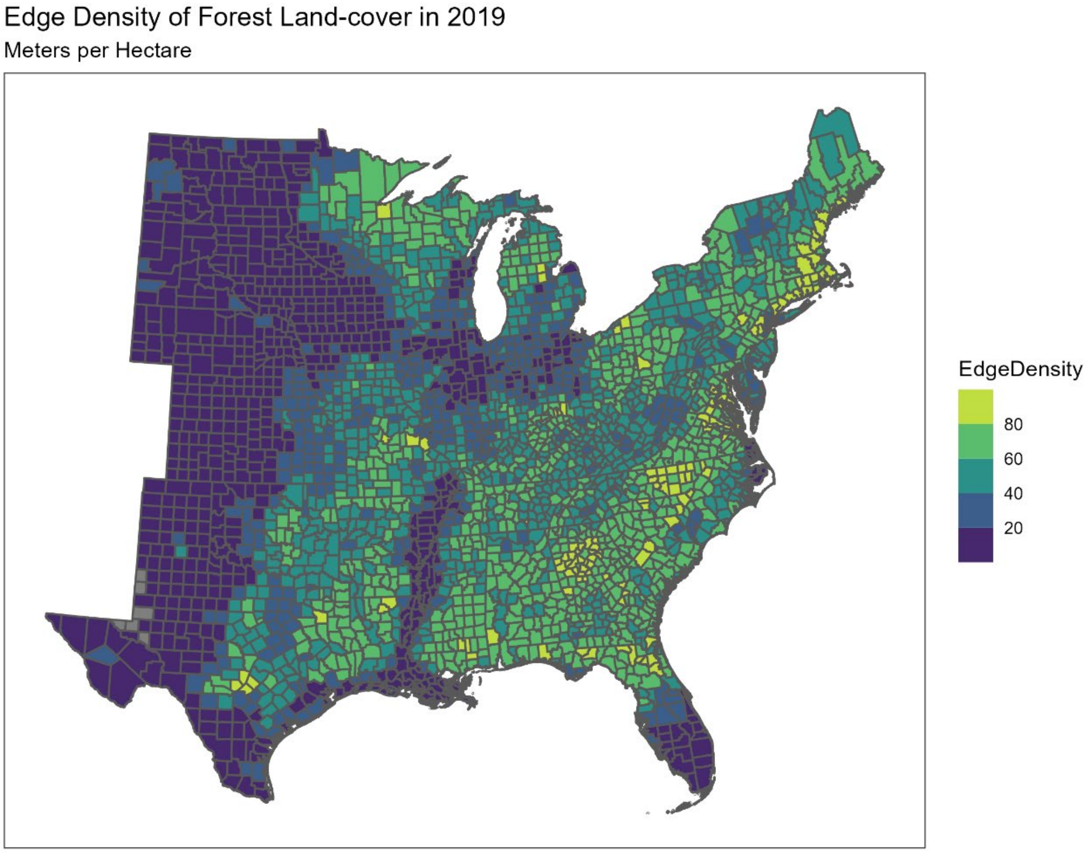


Figure 3.12: Map of forest land-cover edge density

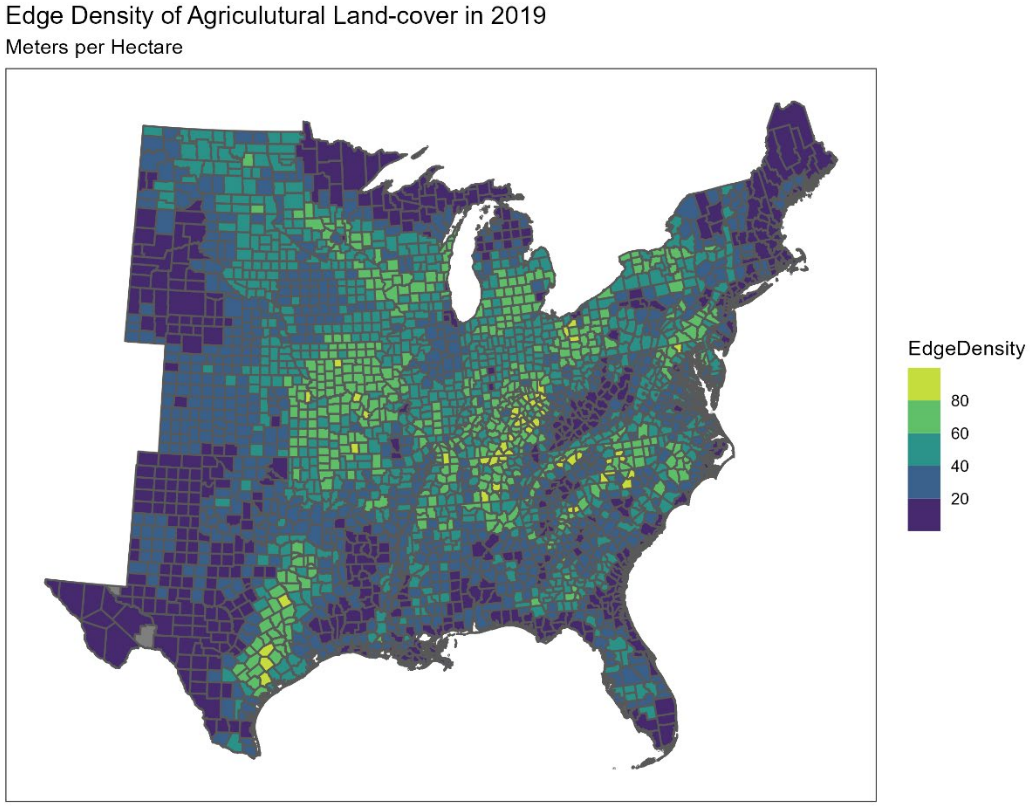


Figure 3.13: Map of agricultural land-cover edge density

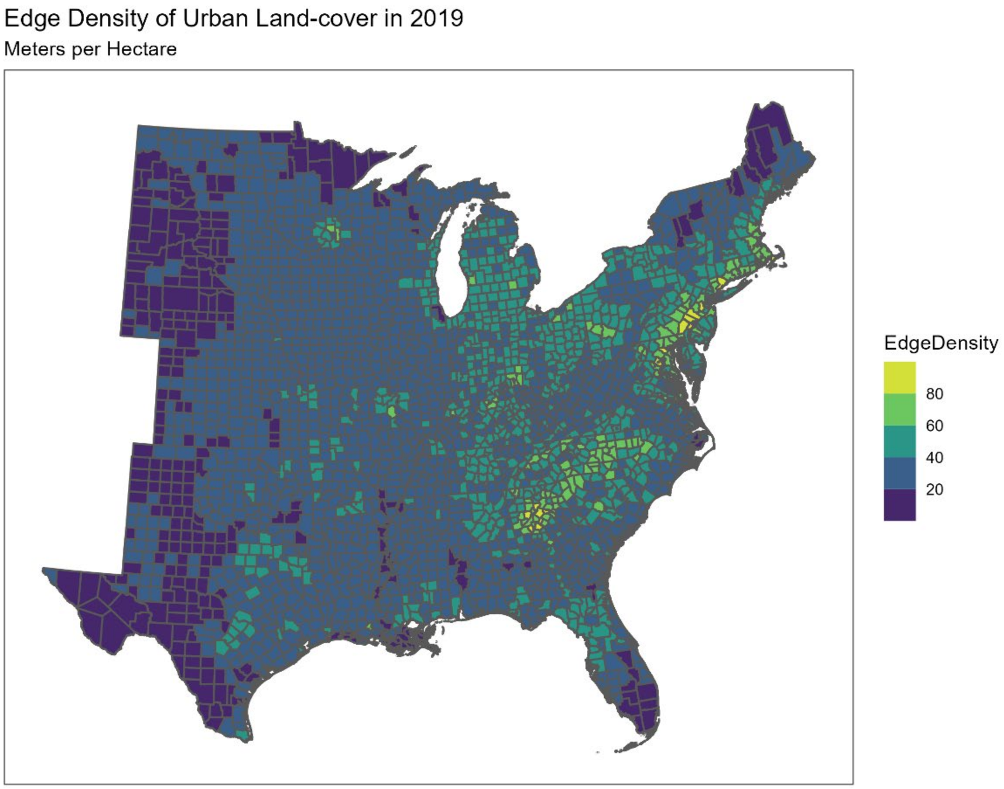


Figure 3.14: Map of urban edge density values distribution

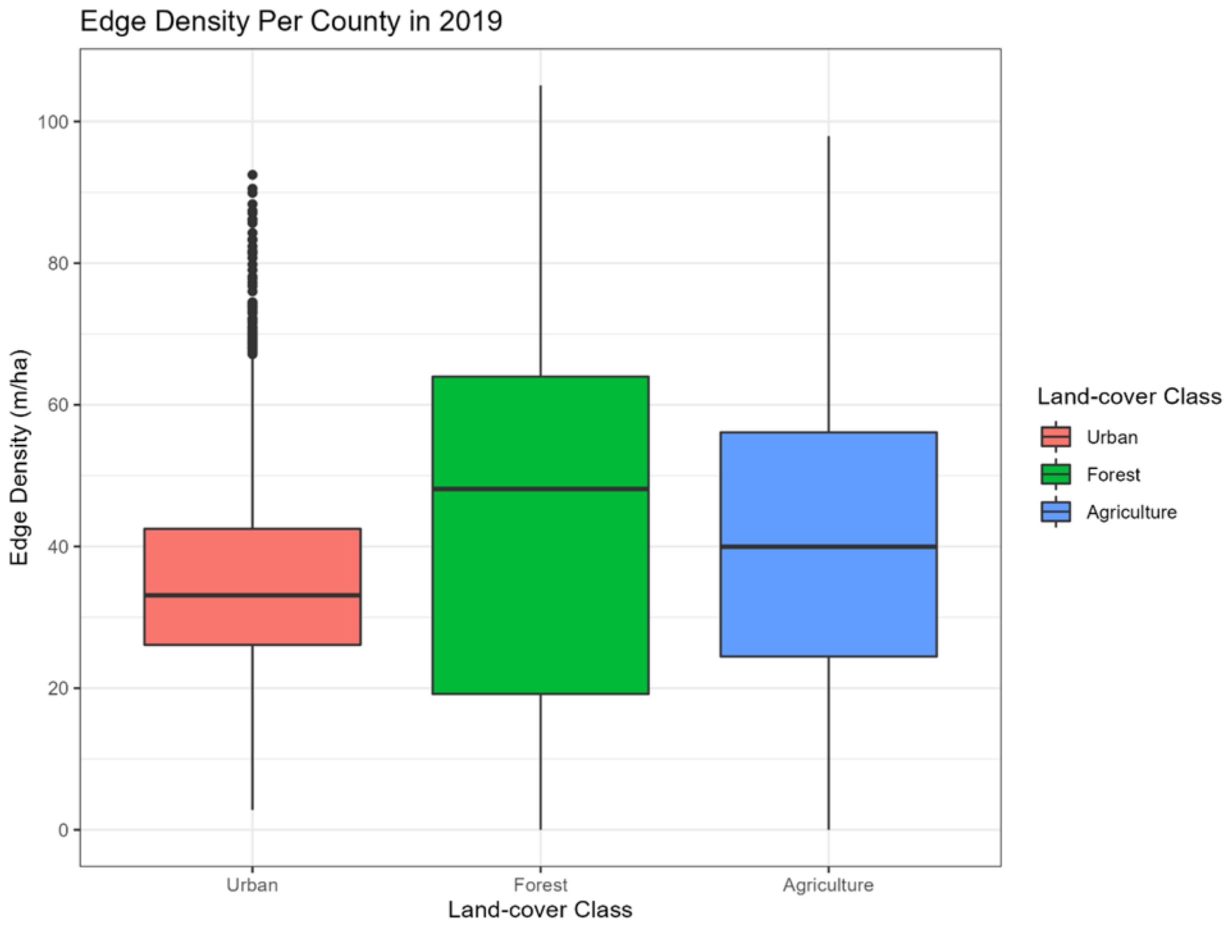


Figure 3.15: Boxplot showing the statistical distribution of edge density of the three land-cover classes.

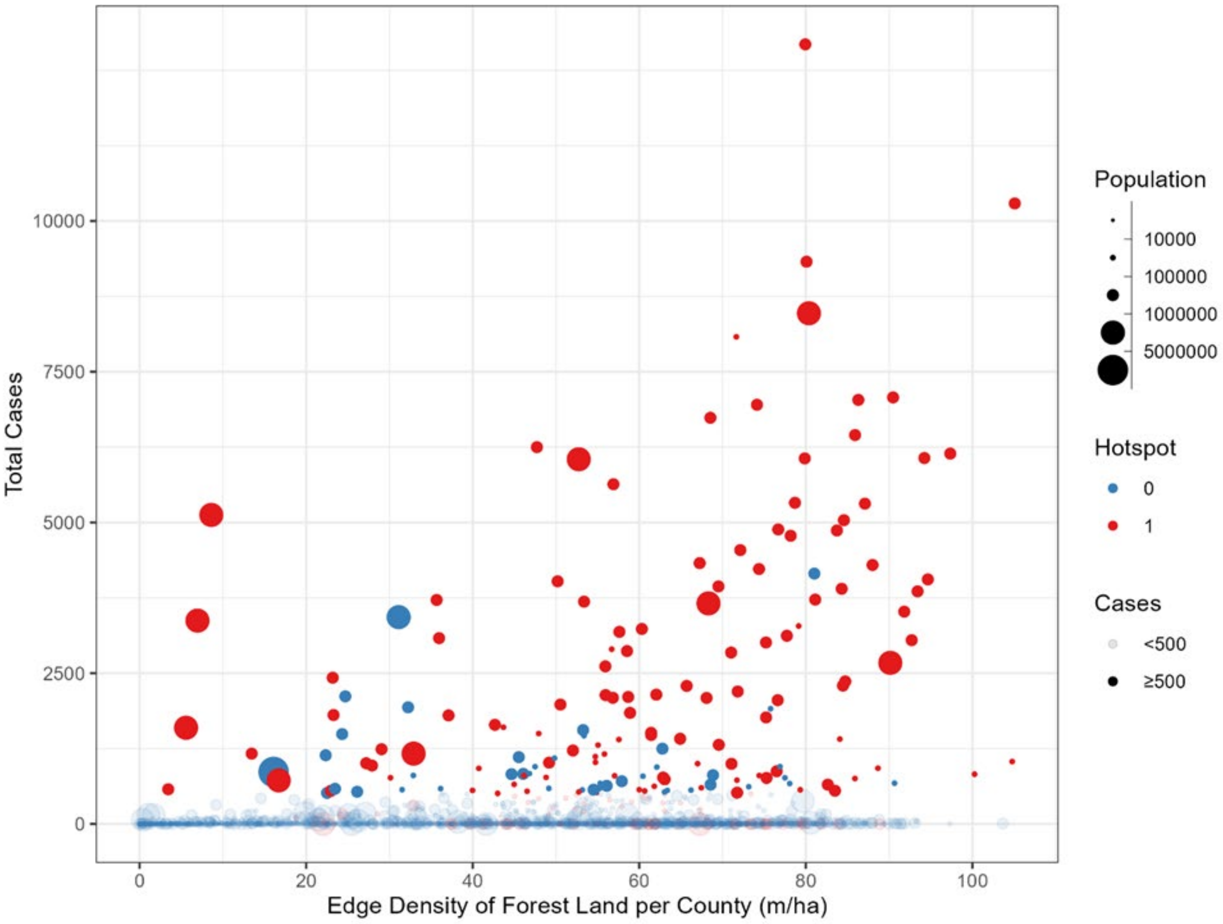


Figure 3.16: Scatterplot of forest edge density versus total cases of Lyme disease

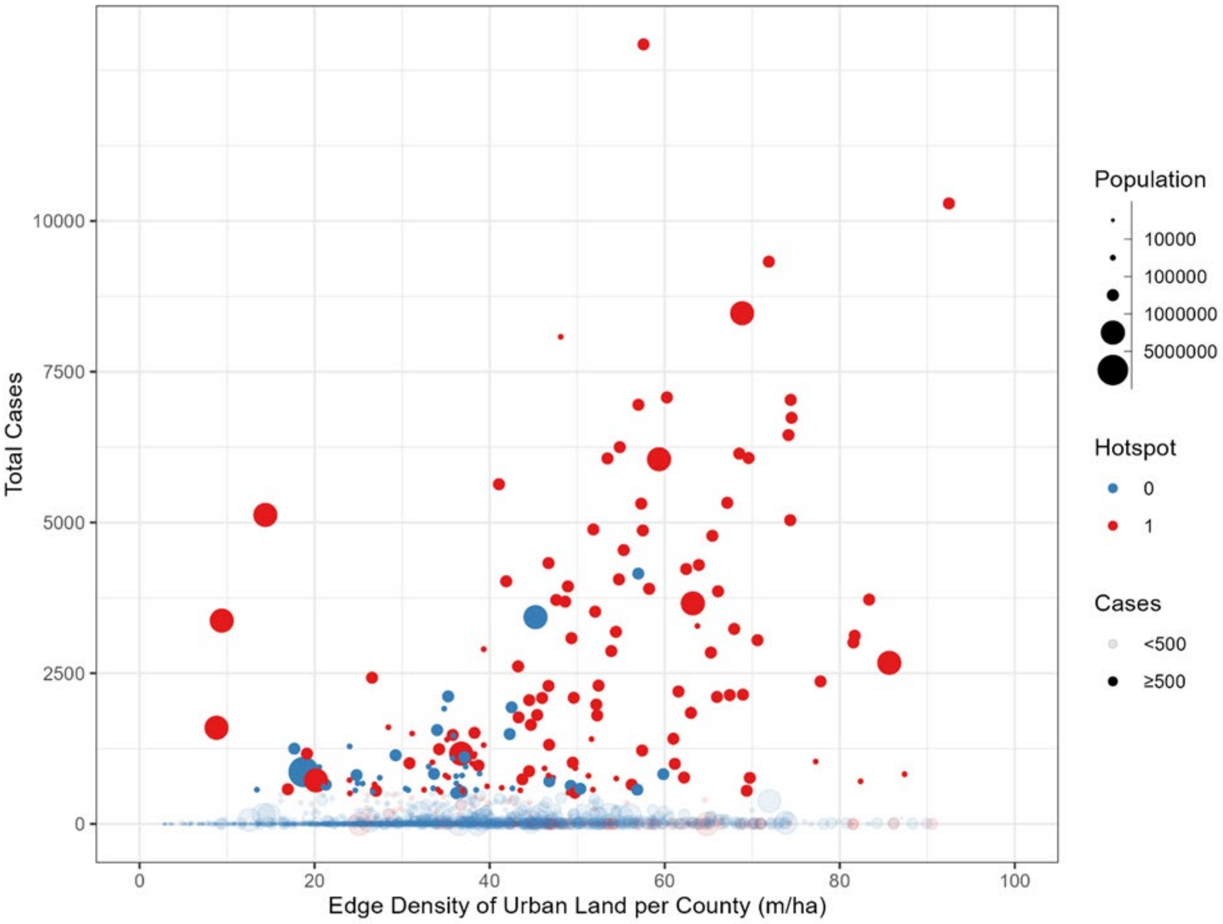


Figure 3.17: Scatterplot showing relationship between urban land edge density and total Lyme disease cases.

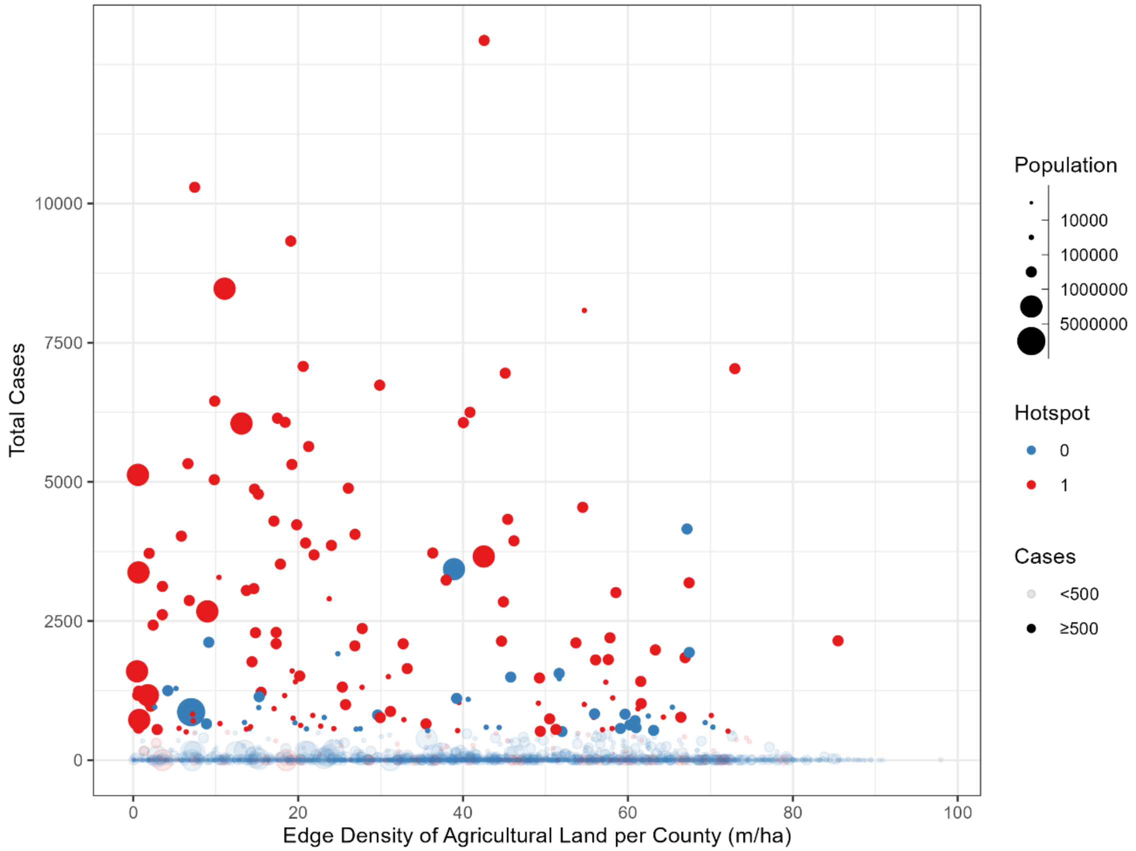


Figure 3.18: Scatterplot of agricultural edge density versus case numbers

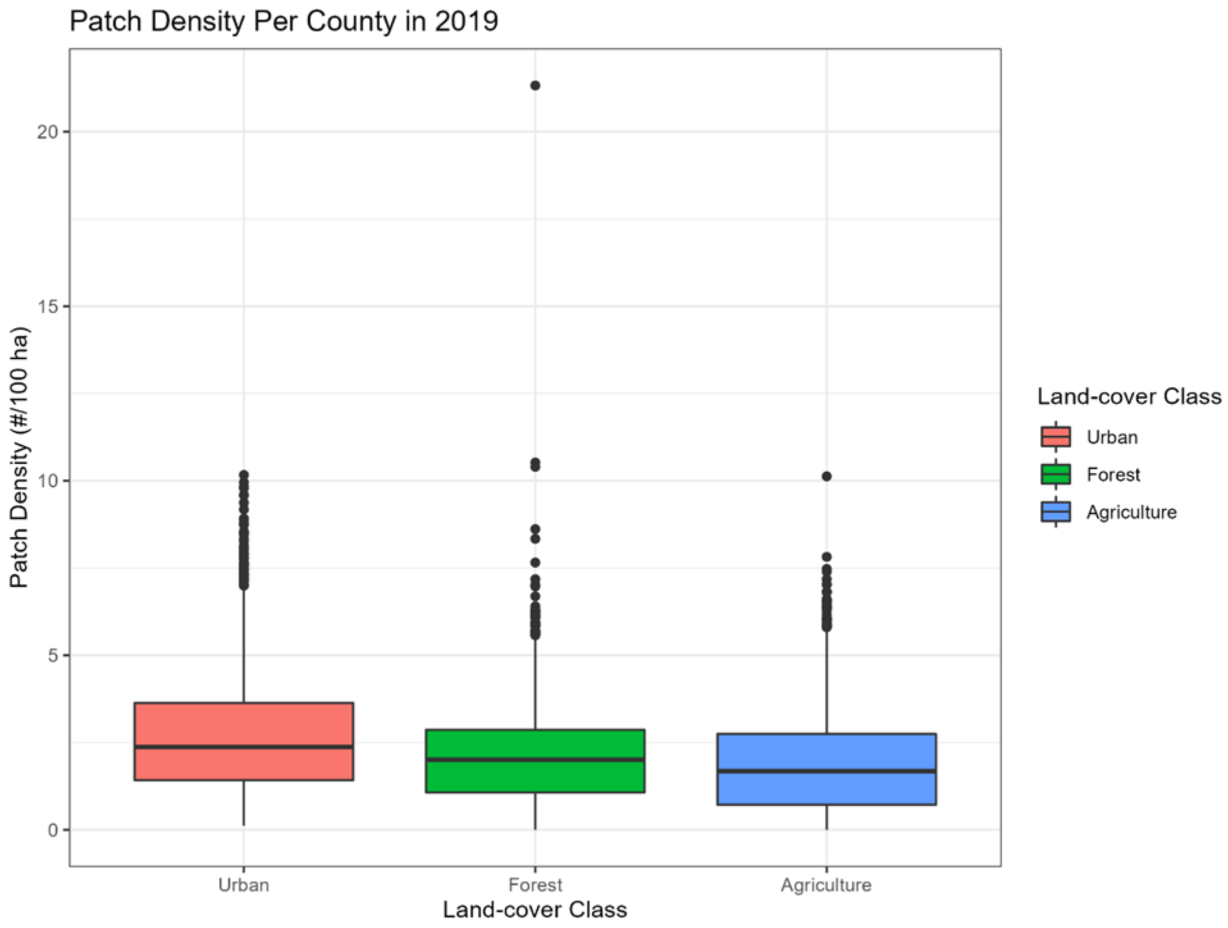


Figure 3.19: boxplot showing statistical distribution of patch density among three land-cover classes.

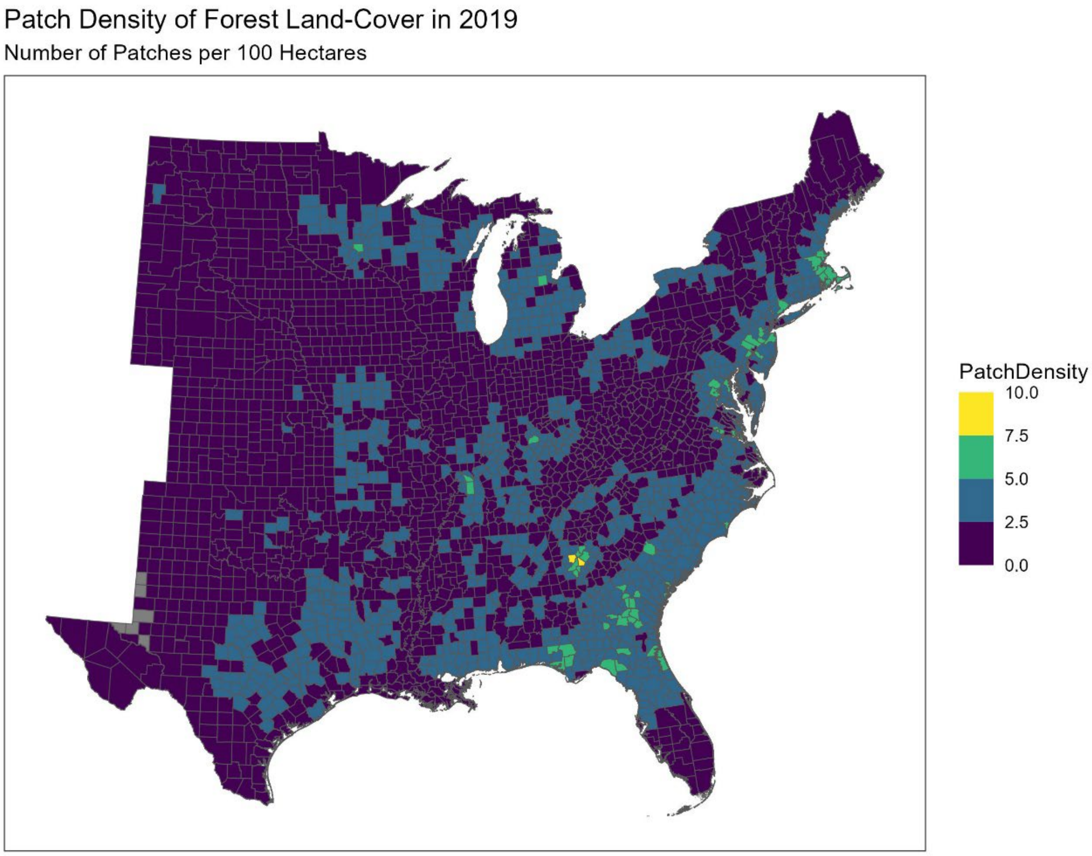


Figure 3.20: Map of patch density of forest in 2019

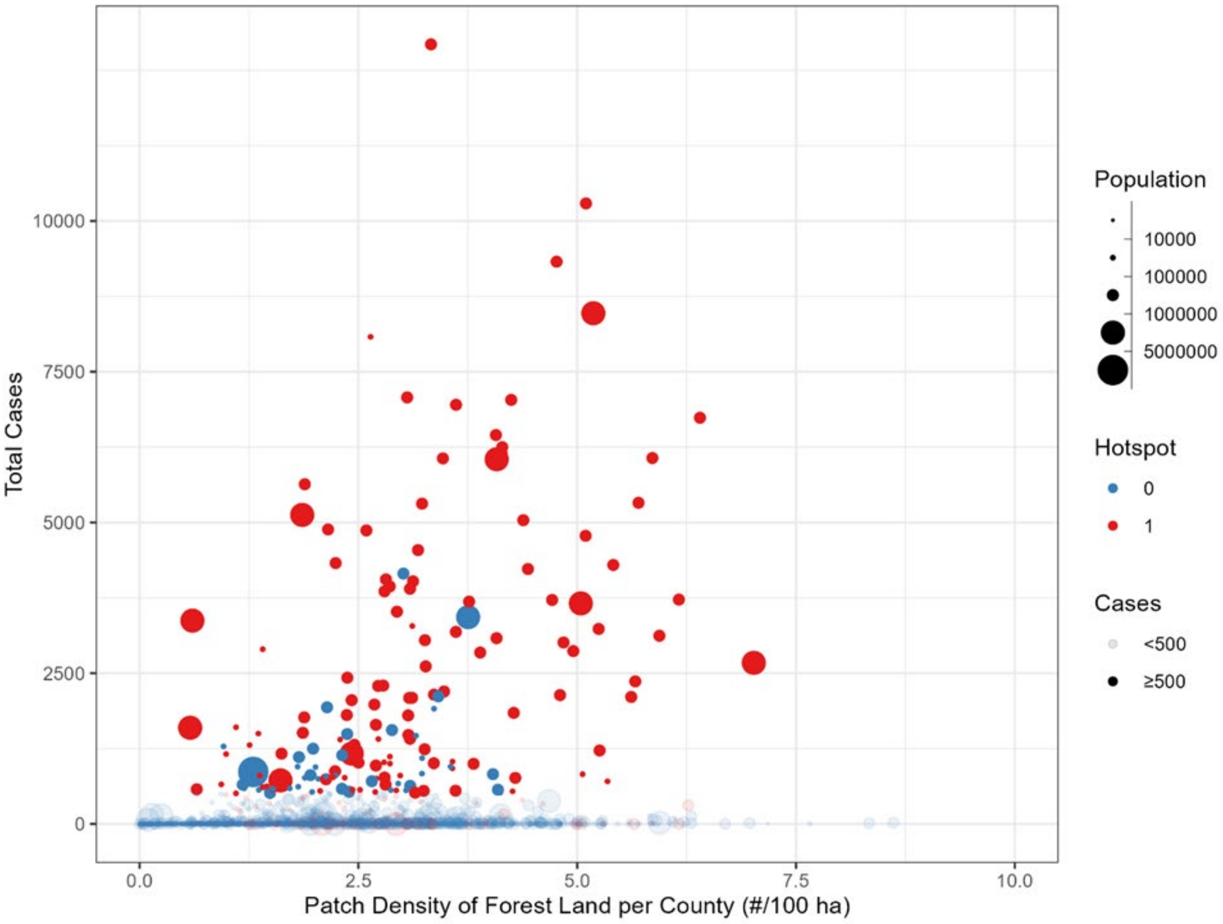


Figure 3.21: Scatterplot showing patch density of forest land versus total Lyme disease cases

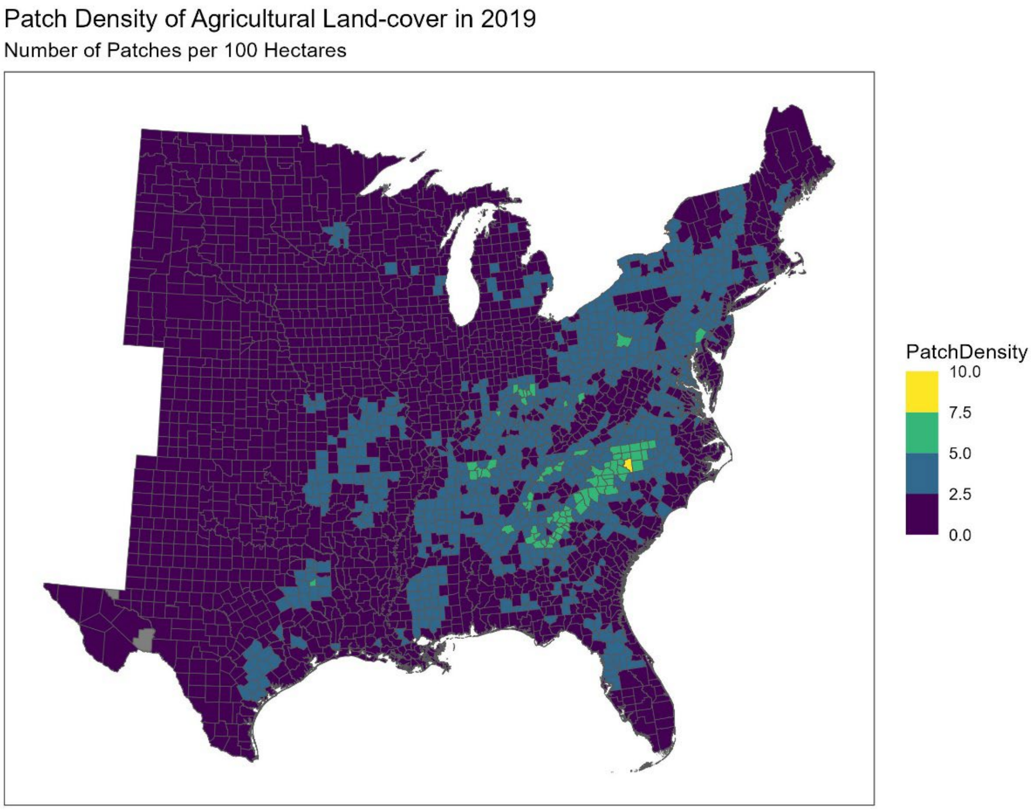


Figure 3.22: Map of patch density of agricultural land in 2019

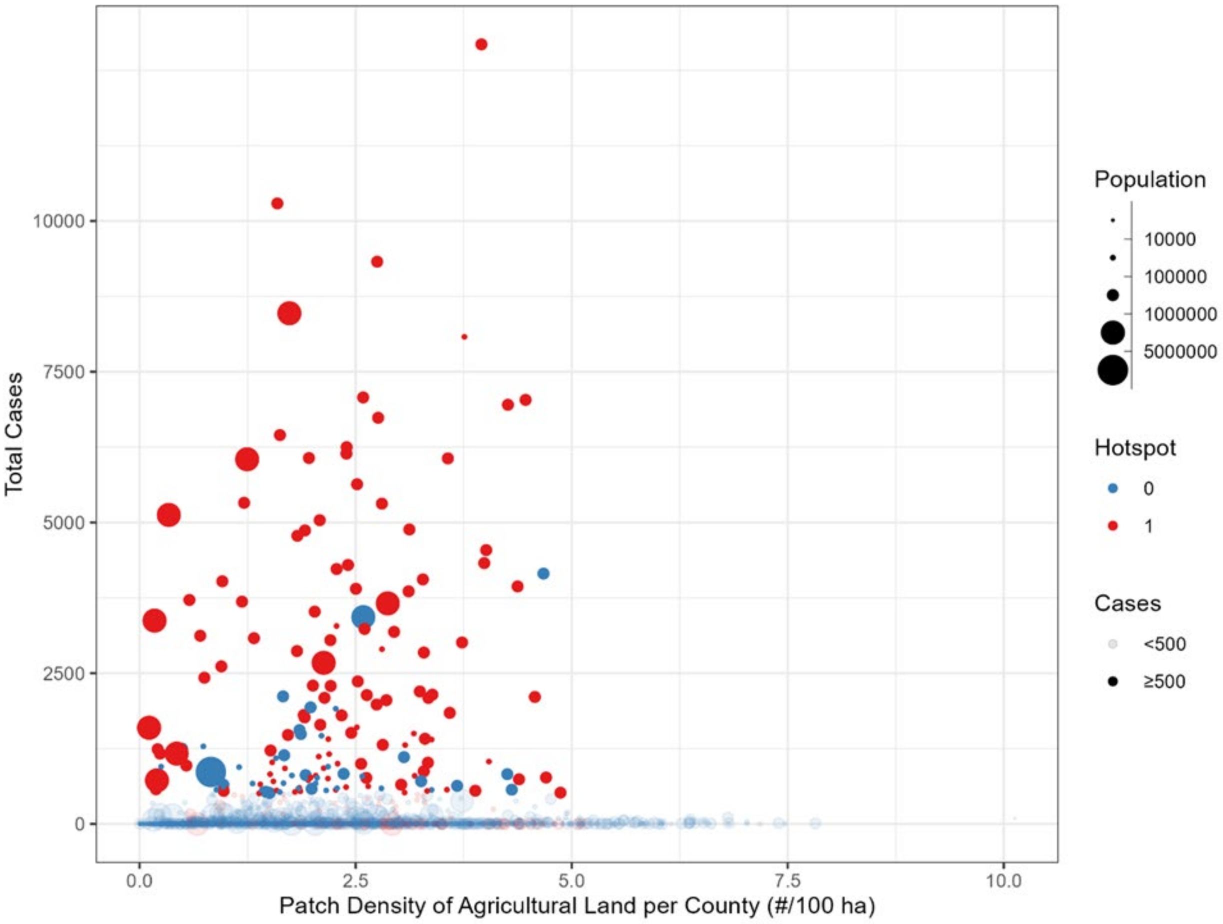


Figure 3.23: Scatterplot of agricultural land patch density per county

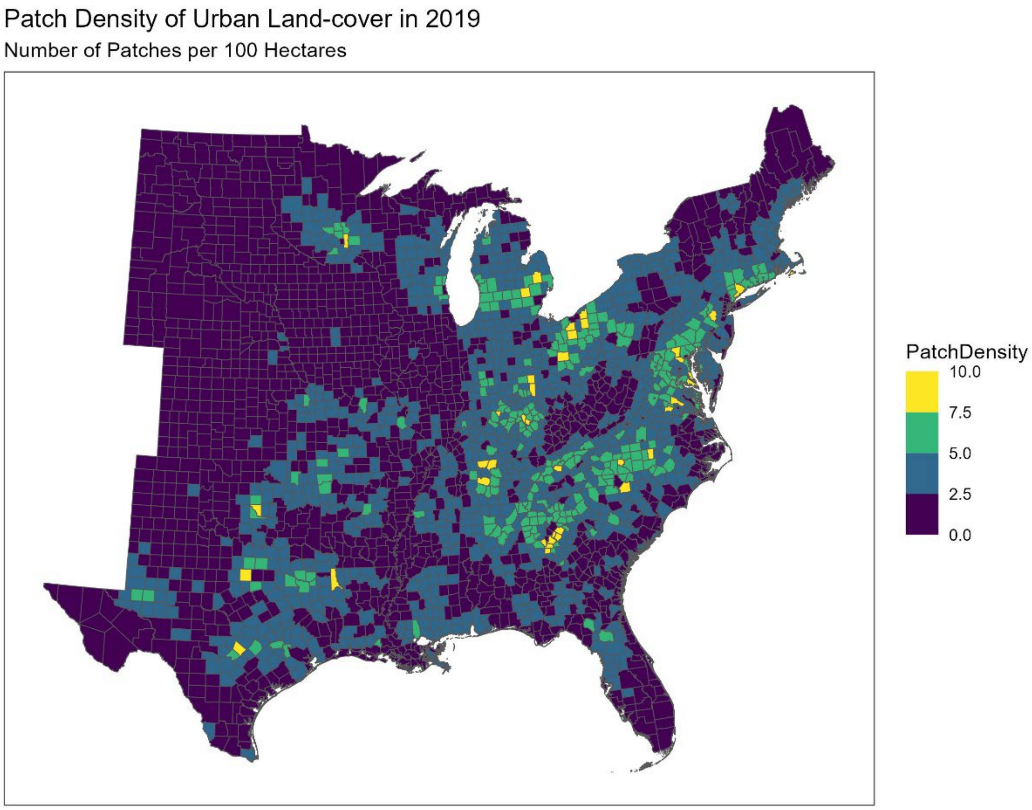


Figure 3.24: Map of urban land patch density by county

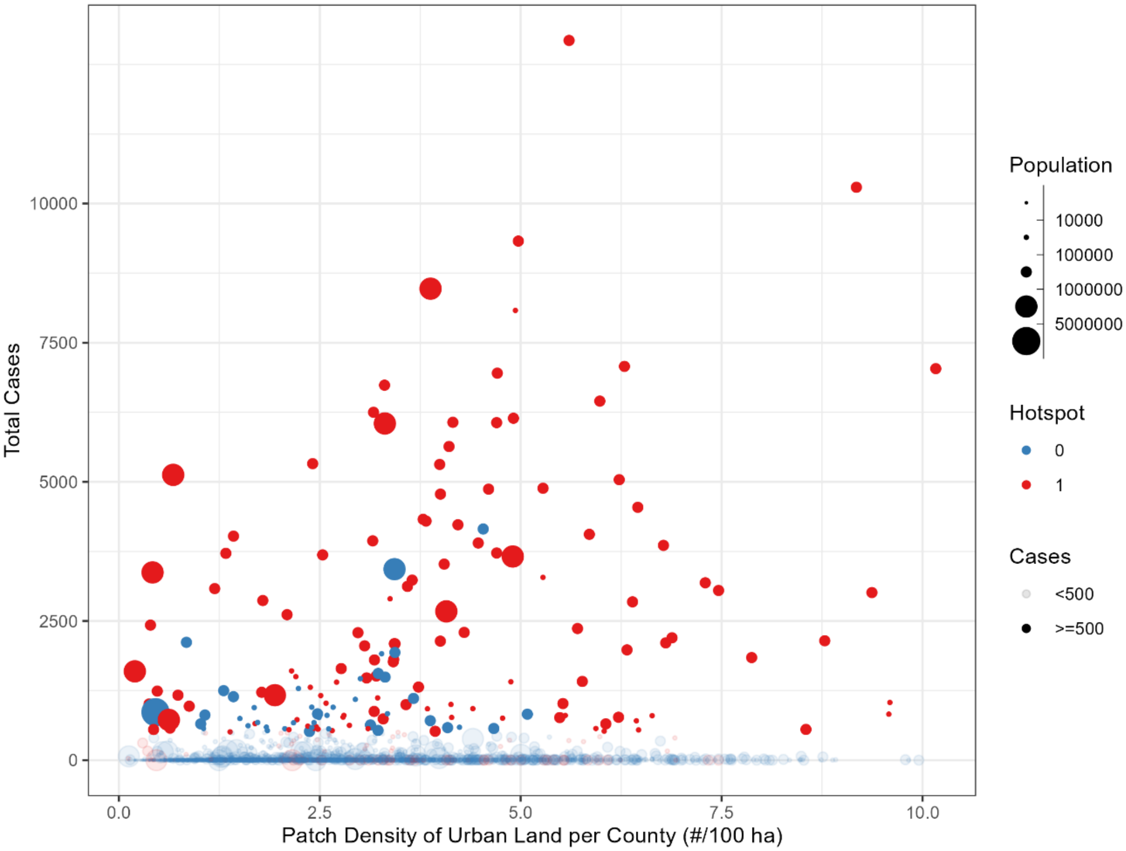


Figure 3.25: Scatterplot of urban land patch density by county

CHAPTER 4. DISCUSSION

4.1 Hotspot and Population Analysis

Both population and hotspot showed a significant positive relationship with case numbers. While our first hypothesis predicted that population would play a more significant role in non-hotspot counties, we found that it was actually the hotspot counties that had more variation in case numbers explained by population. The models including both population and hotspot status as explanatory variables explained about 60% of the variation in cases.

The impact of hotspot status was consistently observed through the models constructed for the second and third hypotheses, in short, the addition of hotspot status in multivariate models increased explanatory power significantly. In the second hypothesis we predicted that percentage of forest cover would be indicative of the largest case load per county and the third predicted that forest and agricultural edge density would have a greater impact on case numbers. Hotspot status was theorized to represent many different aspects of tick-borne disease spread. Since Lyme disease was first recorded in Connecticut, epidemiologic principles state that disease incidence will spread radially from the first known point of contact. So, it is no surprise that New England predictably saw the greatest number of counties within the hotspot. The other was in the Lake States region, seeming to start in a singular county in Wisconsin and expanding to neighboring counties from there. Hotspot status encompasses the geographic relation to the first point-event, along with potentially other factors. If an area has a high number of cases and there is public awareness of that, then those areas could see an inflated number of cases since people are aware of the symptoms and there are medical professionals that are testing for it. For Lyme disease and other tick-borne diseases, the symptoms can be very generic, so many people may not be thinking it could be anything more than the common cold. Additionally in areas that do not have that extended history of having reported cases, when people seek medical care, doctors may not know to test for it. Even further, many states and counties have very limited ability to test for these diseases. Many require serological analysis in a lab. Rural residents may not have access to healthcare facilities with those capabilities. As a personal antidote, we met with a small family run logging company in south-east Kentucky. Three of the five employees had had one or more tick-borne diseases, even though Kentucky was only reported to have an average of 2 confirmed cases per year in the CDC dataset. They expressed the fact that they had to travel to one of major cities almost 3 hours away to be assessed and diagnosed with these diseases. Overall, it was surmised that hotspot status could represent distance from the origin of cases, healthcare access, public awareness of the symptoms, medical professionals knowing how to administer the diagnostic tests.

4.2 Land-cover Effects

The land-cover classes of interest were forest, agriculture, and urban land. As described in the methods, these were inclusive groupings and as such, the analysis could be lacking some finer details. This does not detract from the findings and offers an approximate picture of the overarching spatial patterns determined by land-cover classes in the eastern half of the country. Future work can further elucidate the patterns seen with the more limited classes measured by the NLCD. One previous study that compared land-cover classes between the Northeast and Upper Midwest are congruent with the results of this study (Dong et al., 2020). They kept the land-cover classes as their original categories as defined by the land-cover database, rather than grouping them together.

While deciduous forest has been previously correlated with higher disease risk in the Northeast (Dong et al., 2020), both deciduous and coniferous can provide ample habitat, microclimate conditions, and host habitat.

The agricultural land percentage per county was consistently negatively related to case numbers. Population and hotspot status decreased the negative impact when included in the model as confounding variables. Population has such a significant impact on case numbers and since population declines as agricultural land increases, this could explain some of why agricultural land has lower case numbers.

Urban land-cover, like agricultural land, had a negative influence, but was not statistically significant, unlike the fragmentation metrics. Since there is such a range in urban land-cover per county, this could explain the lack of significance of the relationship. It was expected that urban would follow a similar pattern to forest land-cover, where there is a tipping point when urban land would have a negative impact on the number of disease cases. In those counties with close to median value of urban land percentage, it is expected that it would maximize number of people that can be exposed, and enough “natural” ecosystems that would house the ticks and their hosts. Urban land itself isn’t necessarily conducive to supporting all the stages in the Lyme disease pathogen transmission cycle, but plays a key role in containing the dead-end hosts, humans. Future studies may keep the different levels of urbanization classified by the NLCD in their original categories and re-run the model analysis including population and hotspot status.

4.3 Habitat Fragmentation

The effects of habitat fragmentation on tick-borne disease have been of interest in landscape epidemiology. Since habitat fragmentation is somewhat of a vague term and has varied attributes, this study focused its analysis on two fragmentation metrics. Edge density and patch density were chosen since they could easily be compared between counties of varying sizes. Total edge and number of patches were also measured but are harder to accurately compare between counties. The multivariate analysis included population and hotspot status as confounding variables.

4.3.1 Forest Fragmentation

The relationship between edge density of forest peaks at around 80 m/ha, so the number of cases is generally increasing in a linear manner with higher density of edge habitat. A higher density of forest edges can provide suitable habitat for both ticks and their hosts. White-tailed deer have been shown to use forest edge for browsing (Williamson & Hirth, 1985). The density of white-footed mice (*Peromyscus leucopus*) has been found to be higher on forest edges (Anderson et al., 2003).

4.3.2 Agricultural Fragmentation

The edge density of agricultural patches has a negative linear relationship with Lyme disease cases. The counties with the highest number of cases tended to have less than 20 m/ha density of agricultural edges. These agricultural edges may present a higher entomological risk, especially if they are adjacent to forest land, but this may not be enough to outweigh human behavioral risk and/or population factors. Agricultural communities tend to have lower, more sparse populations and a unique relationship with healthcare access. The edges may provide suitable habitat for ticks and hosts (vertical vegetation structure, appropriate humidity, browsing, protection etc.) so future work could draw attention to the specific edge effects between agricultural and forested patches. Since agricultural edge density and forest edge density are two opposing land-cover classes, there may be unique factors about the contrast of those edge types that were not able to be deduced from this study. Additionally, the edge density metric measurement in this case was a static, cumulative mean measure. It was the average edge density of the years between 2001-2019. The rate of change in agricultural edge density could be studied as well to see if the changing metric values have a different effect on cases than found here.

Patch density of agricultural land was the only agricultural variable that had a positive linear relationship with number of cases. This relationship was a surprising find considering all other agricultural metrics were consistently negatively related to case numbers. One explanation could be that the relationship between agricultural patch density and population was higher than edge density or percentage of landscape. Since population had a positive effect on case numbers as well, counties with a high density of agricultural patches are most likely to have higher populations. The farms and livestock pastures in these counties are probably smaller family-owned operations, thus allowing people to live closer together.

4.3.3 Urban Fragmentation

Urban land-cover class edges are edges touching either forested or agricultural land and was demonstrated to have a significant positive relationship with case numbers. Urban edges are most likely the locations of where people are encountering ticks and the hosts they feed on. The entomological risk isn't necessarily higher on urban edges, so the density of ticks may not be any more substantial, but the human behavioral risk is higher (Bron et al., 2020). When examining the relationship between the level of urban fragmentation and Lyme Disease cases, it was expected that there would be certain threshold value where the factors (i.e., population) that lead to the increase of cases then "work against" case numbers and no longer provide suitable conditions for more contact between humans and vectors. Since the relationship between urban fragmentation metrics and case numbers was not precisely linear a generalized linear model with a quadratic term was run, but it did not describe the relationship more completely than the linear models already had. Urban edge density had a smaller effect size with the quadratic term, as well as the same factor size. This pattern was the same as urban patch density, the effect size was lower, as was the factor.

By using the patch density metric as a measure of the level of fragmentation of urban land, it indicates that the relationship is not purely linear. The so-called "ideal" patch density of urban land, where the highest number of cases would be expected would be in the mid-range values. Counties that have moderate levels of fragmentation have the highest risk. This would be especially pertinent in counties that are in the early stages of urbanization, land developers and residents should be made aware of the increased possibility of contracting Lyme disease, especially in counties that surround counties with known cases. This land conversion could be from forest-to-suburbs, forest-to-farm, or farm-to-suburbs, so it will be important for future studies to focus on the specific edges between land-cover classes, to fully examine the difference in disease risk and case outcomes.

4.4 Policy Implications

With the focus on land-development, we do not believe that the results of this study should recommend sweeping policy changes, but rather encourage ongoing public health initiatives and occupational regulations. With regard to occupational health, having more comprehensive education on the efficacy of those policies already in place. This includes protective clothing, use of insect repellants, and behavioral modifications. The demonstrated effects of land cover can be used to target these educational reinforcements.

4.5 Drawbacks and Limitations

While the findings of this study will complement and add onto the existing body of knowledge, there are limitations to this study that should be addressed. Firstly, this study was focused on elucidating broad spatial patterns of disease and the landscape factors that could impact case numbers, but this study did not assess the temporal aspect of disease. The cases were accumulated over the entire study period 2000-2019 and only the area and edge metrics from the most recent NLCD were used. In using the most recent landcover data, we did not measure the change in metrics, but rather postulated that 2019 represented the aggregate of all land-cover changes throughout the study period. The understanding of these patterns could be furthered by studying the temporal trends. Averaging the case numbers over 5-year periods and running the models with 5-year average landscape metrics could be useful in contrasting the patterns found here with different time periods. Additionally, examining the change in case number over time and conducting a time series analysis of the effect of the changing landscape metrics would help provide a more complete picture.

CHAPTER 5. CONCLUSIONS

The broad scale spatial patterns of Lyme disease in the eastern United States are affected by land-cover and habitat fragmentation. With human environmental modification and climate change intensifying, teasing out these patterns is more imperative than ever. Forest and urban land-cover demonstrated a positive relationship with Lyme disease cases initially but reached threshold values where the trend reversed at higher levels. This pattern followed with fragmentation metrics of the other land-cover classes as well. Agricultural land-cover percentage and edge density were correlated with a decrease of cases, but patch density showed the opposite effect. Highly fragmented counties, regardless of the land-cover class of the patches, exhibited higher incidence rate ratios than more contiguous counties. The moderate values of all the forest and urban metrics showed the highest proportion of cases, so those counties undergoing development or land-use changes are at the highest risk of disease. These spatial patterns can be utilized in both public health education and occupational health regulations to improve the safety of all citizens, whether at work or at home.

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