Lyme Disease in Texas?
Enhancing Prevention Through the Identification of Areas of Risk

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ABSTRACT

Lyme disease, currently the most common vector-borne disease in the United States, is an infection caused by a spirochete bacterium known as *Borrelia burgdorferi*. The bacteria are transmitted to humans through the bite of an infected tick. Failure to diagnose and treat aggressively can lead to disability or death, thus early detection and treatment is critical. However, Texas and other areas in which Lyme disease is not considered endemic have been largely ignored by informative, preventative and diagnostic efforts. As a result, many patients are left with few resources for diagnosis and treatment and must travel out of the region at great personal time and expense to receive the necessary care. The purpose of this study is two-fold: (a) to improve understanding of the prevalence of Lyme disease in Texas and (b) to identify the potential risk areas through habitat mapping of the vector. Prevalence of Lyme disease in Texas will be visually demonstrated using incidence reports and voluntary surveys. Statistically significant areas of disease will be identified using Exploratory Spatial Data Analysis. Conditions necessary for preferred tick habitat are also examined and applied to construct suitability ranges within the state. Identifying potential risk levels and hotspots of Lyme and other vector-borne diseases in previously overlooked regions allows greater awareness, faster diagnostics, and improved prevention techniques, all of which contribute to better quality of life.

Keywords: Lyme, vector-borne disease, tick, Texas, risk, prevalence, habitat suitability

BACKGROUND

Lyme disease, an infection caused by a corkscrew-shaped spirochete bacterium, is the most common vector-borne disease in the United States (CDC, 2013a). Since, 1970, when the first case was reported, a steady rise in the number of cases has been reported. Between 17,000 and 29,000 cases are reported per annually (average = 23,000) in the USA (CDC, 2014).

The first known erythema chronicum migrans rash in the United States was recorded in 1970 on a patient bitten by a wood tick in Wisconsin (Scrimenti, 1970). In 1975, a cluster of erythema chronicum migrans cases occurred in Connecticut in conjunction with a mysterious outbreak of symptoms, initially thought to be arthritis and juvenile rheumatoid arthritis (State of Connecticut Department of Public Health, 2013; Steere et al., 1977). Investigators noticed that most of the ill children resided near wooded areas and began experiencing symptoms in the summer, suggesting an insect-related vector. Although the illness was linked to ticks as early as 1978, the specific causative agent remained unknown until 1982 when it was finally isolated and identified by Doctor W. Burgdorfer, a zoologist and microbiologist at National Institute of Allergy and Infectious Diseases' (NIAID) Rocky Mountain Laboratories (U.S. Department of Health and Human Services, 2008), hence the name *Borrelia burgdorferi* in his honor (U.S. Department of Health and Human Services, 2008). The disease was renamed from 'Lyme arthritis' to 'Lyme disease' after the town of Lyme, Connecticut, where the original cluster of diseases had occurred (State of Connecticut Department of Public Health, 2013). Reports have also been made in the California, where the *Ixodes pacificus* tick was incriminated as the responsible vector (Burgdorfer & Kierans, 1983) as well as in Arkansas, Georgia, and Texas (Burgdorfer & Kierans, 1983). Lyme disease has a much greater range of distribution in the United States than previously believed (Burgdorfer & Kierans, 1983).

The bacteria is transmitted to humans through the bite of an infected tick belonging to the genus *Ixodes*, also known as blacklegged ticks or deer ticks after the deer they commonly feed on. *Ixodes* ticks are quite small, no bigger than a pinhead in their larval and nymphal stages (less than 2 mm) as shown in Figure 1, often enabling them to feed unnoticed. Three elements are required for Lyme disease to exist in any given area: the Lyme bacteria, the ticks that can transmit the bacteria, and hosts that serve as a blood meal for the feeding ticks. The ticks become infected with the *Borrelia* bacteria when they feed on a variety of infected hosts, and in turn transmit the bacteria to other hosts, including dead-end hosts such as humans (Todar, 2012) (Figure 1). Ticks feed on a large range of hosts. For example, adult ticks typically feed on larger hosts (e.g. deer, dogs, cattle in fall and spring (Burgdorfer & Kierans, 1983), nymphs feed on medium-size hosts (e.g. squirrels in spring and summer) and larvae feed on small rodents (e.g. mice, chipmunks, voles, etc in late summer and fall) (Radolph, Caimano, Stevenson, & Hu, 2012; Werden et al., 2014), thus acting as both hosts and reservoirs for the *Borrelia* bacteria. Once infected, ticks can transmit the bacteria at any life-stage (Burgdorfer & Kierans, 1983).

Reported human cases are highest during the warmer summer months and lowest during cooler winter months (Figure 2), corresponding to both the life cycle of the tick and increased outdoor activity by humans. This may vary geographically due to seasonal variations in temperature and precipitation (Moore, Eisen, Monaghan, & Mead, 2014).

Lyme disease is reported throughout the USA (Figure 2). Maps that currently exist are either inaccurate or not very specific, and many states – such as Texas – have been grossly neglected in terms of Lyme information (Figure 2). For example, Figure 2A is an example of a commonly disseminated Lyme-disease map that mainly concentrates on the eastern US states and does not address the western half of the country (Diuk-Wasser et al., 2012). The map is also inaccurate since it does not correspond with actual reported cases of Lyme disease, causing researchers such as Herman-Giddens (2012) to criticize the methodology behind the creation of such maps as well as caution against the public health issues that could arise from depending on such a map. Therefore, developing accurate Lyme disease risk maps is important not only for monitoring the incidence of the disease throughout the USA, but also for identifying new problem areas.

In the USA, Lyme disease has mainly been reported in the Northeast, Upper Midwest, Northern California and Oregon (Figure 2). Lyme disease continues to spread due to migratory birds and deer, development encroaching on habitat ecosystems, and reforestation (Lyme Research Alliance, n.d.). Evidence is mounting that tick-borne illnesses are also increasing in northern Europe (Githeko, Lindsay, Confalonieri, & Patz, 2000). Recent studies have shown that climate change may also be contributing to the spread of Lyme and other vector-borne diseases (Ogden et al., 2014; Brownstein, Holford, & Fish, 2008), particularly as tick hosts such as mice and deer are able to expand their range of distribution (Roy-Dufresne, Logan, Simon, Chmura, & Millien, 2013).

Several tick species vector the disease. These include *Ixodes scapularis* which is predominately distributed in the south-central and eastern US states ranging from southern Texas to Maine, along the Canadian border to the central states of Wisconsin, Illinois and Michigan (Figure 3) and *Amyblomma americanum*, which is predominant in the southeast, including Texas.

Factors affecting the distribution of tick populations

The distribution of ticks is strongly associated with climatic factors such as temperature and rainfall (Estrada-Peña, 1999, 2008). Temperature affects the different life-stages of tick as well as the habitats that the ticks reside in (e.g. land cover (Githeko et al., 2000; Brownstein, Holford, & Fish, 2003); vegetation for shelter and protection from environmental extremes (Estrada-Peña, 2008). Therefore, identifying landscapes that capture the habitats that ticks are likely to reside in are useful for detecting the potential presence of the vector, pathogen and host (Brownstein et al., 2003).

In an effort to try to identify high risk Lyme disease areas, veterinary information from pet dogs has been used (Guerra, Walker, & Kitron, 2001). This is based on the theory that dogs can serve as “sentinels” for tracking Lyme disease, rather like the proverbial canary in the coal mine, due to their frequent outdoor exposure and production of antibodies which are detectable for up to two years (Lindenmayer, Marshall, & Onderdonk, 1991). Many of these canine-focused studies determined a positive correlation between canine seropositive rates and human incidence rates, and that dogs residing in forested areas were twice as likely to be seropositive as those in agricultural areas (Guerra, Walker, & Kitron, 2001). Interestingly, seropositive canines were also found in areas previously considered to be of low or no risk for Lyme disease, thus indicating that tick populations and Lyme disease may be expanding (Guerra, Walker, & Kitron, 2001).

Land cover is a dominant factor associated with the presence of ticks (Guerra et al., 2002). In particular, *Ixodes scapularis* populations have been found to be positively associated with deciduous forests and negatively associated with grasslands and wetlands (Glass et al., 1994). These findings align with other studies that also correlated the presence of *Ixodes scapularis* with wooded vegetation (Kitron & Kazmierczak, 1997). Tick densities tend to be greatest in oak-dominated forests, followed by maple, and lowest in conifer woods that produce minimal leaf litter (Kitron & Kazmierczak, 1997). Indeed, leaf litter appears to be an important component of tick microclimate (Guerra, Walker, & Kitron, 2001). Similar findings were also identified for another tick species, *Ambylomma americanum* (Brown et al., 2011; Texas A&M Agrilife Extension, n.d.). In addition, proximity to forest edge was also a strong indicator of human risk (Yang, Wong, Miao, & Yang, 2010). Although urban environments generally have low tick densities (Glass, Amerasinghe, Morgan, & Scott, 1994), Lyme disease can still be contracted in these environments (Junttila, Peltomaa, Soini, Marjamäki, & Viljanen, 1999). In summary ticks are most likely to be found in wooded areas, near forest edges (i.e. where woods or fields meet lawns), in shady areas, in tall brush or grass, under leaf litter and ground cover, and near stone walls and wood piles (Lyme Disease Association, 2012).

Regardless of tick species, climate variables such as temperature and moisture were cited repeatedly, along with factors such as land use, land cover, and host availability (see Table 1 for summary by tick species). Although the list of key factors seems somewhat overwhelming, Cumming (2002) concluded that climatic variables tend to factor more heavily than vegetative variables, but that predictive ability increases substantially when these two components are considered together. Randolph (2000) determined that not only are climate and vegetation better predictors than host-related factors, but that the remotely-sensed Normalized Difference Vegetation Index (NDVI) is consistently the most significant variable for predicting tick distributions, likely due to its relation between vegetation and available moisture so critical to tick survival. Similar to Cumming’s later findings, Randolph concluded that the NDVI’s predictive power increases when combined with temperature indices (Randolph, 2000).

Table 1: Key factors important to tick survival and habitat suitability.

Tick Species	Geographic Location	Factors	Source
A. americanum	S Missouri, Texas	Forest, humidity, vegetation	Brown et al., 2011; Texas A&M Agrilife Extension, no date.
I. scapularis	N America	Negative association: urban, wetlands, saturated soils	Glass et al., 1994.
I. scapularis	N. Eastern USA Maryland, Wisconsin, Illinois, Michigan, Massachusetts, Connecticut; Canada	Temperature, precipitation, vapor pressure, land cover, deciduous forest, leaf litter, deer abundance, small mammal richness and abundance, canopy cover	Brownstein, Holford, & Fish, 2005; Brownstein, Holford, & Fish, 2003; Diuk-Wasser et al., 2012; Githeko et al., 2000; Glass et al., 1994; Guerra et al., 2002; Guerra, Walker, & Kitron, 2001; Kitron, Bouseman, & Jones, 1991; Kitron & Kazmierczak, 1997; Lindenmayer et al., 1991; Moore et al., 2014; Ogden et al., 2014;Roy-Dufresne et al., 2013; State of Connecticut Department of Public Health, 2013; Yang et al., 2010;Werden et al., 2014
Ixodes ricinus	Europe, Finland	Vegetation, host availability, urban, temperature	Junttila et al., 1999; Estrada-Peña, 2008
B. microplus (Ixodidae)	S. America	Temperature, humidity	Estrada-Peña, 1999.

A literature review yielded multiple studies of ticks and the key factors of their associated habitats, which was compiled into the extensive addendum found in Appendix A. The addendum has been consolidated according to tick species for Table 1, shown above. The table reveals the climatological and vegetation characteristics which affect the distribution and potential spread of the tick species.

Diagnosis and Quality of Life for Lyme Patients

Although approximately 30,000 Lyme disease cases are reported to the federal government annually, underreporting is a major issue. The estimated numbers of actual cases - derived from insurance claims, laboratories, and patient reports - may actually be ten times higher, or 300,000 cases annually (CDC, 2013b). Unfortunately, many patients are not diagnosed in a timely manner even in highly-endemic areas, possibly due to the very small poppy-seed size of the tick, the painless bite, lack of the characteristic bullseye rash, unfamiliarity with the complex and myriad symptoms or criteria for positivity, insensitivity of blood tests, and possible delayed symptomatology which may occur long after exposure (Aucott, Rebman, Crowder, & Kortte, 2013; Savely, 2008). A recent study found that 61.7% of study participants were not diagnosed for at least two years (Johnson, Wilcox, Mankoff & Stricker, 2014).

The effects of delayed diagnosis can result in poor health and debilitating symptoms (Aucott et al., 2013; Johnson et al., 2014) (Figure 4a,b). In particular, Chronic Lyme disease (CLD) is associated with a poorer quality of life than most other chronic illnesses, including congestive heart failure, diabetes, multiple sclerosis and arthritis. Specifically, patients with CLD reported significantly lower health quality, more bad mental and physical health days, a significant symptom disease burden, greater limitations on activity, impaired ability to work, increased utilization of healthcare services, and greater out of pocket medical costs (Johnson et al., 2014). Therefore greater awareness and earlier diagnosis, as well as better education, prevention, and treatment methods, are clearly needed and is the premise of this study.

Lyme disease in Texas

Current maps of Lyme disease show that Texas is a low risk area (Figure 2A). However, *Borrelia burgdorferi* spirochete cases have been recorded in the state of Texas as early as 1983 (Burgdorfer & Kierans, 1983) and a total of 1,490 cases of Lyme disease were reported to the CDC between 1992 and 2011 (Figure 5). At least two known tick vectors, *Ixodes scapularis* and *Amblyomma americanum*, are distributed throughout central and eastern Texas (Figure 3) and previous research indicated that 1 to 4% of ticks tested, in every public health region of the state, are infected with the *Borrelia burgdorferi* bacteria (Texas Lyme Disease Association, 2014). More recent research, however, found *Borrelia* infection in 45% of Ixodes ticks collected from 20 counties in Texas and regions of northeastern Mexico (Feria-Arroyo et al., 2014). The study by Feria-Arroyo et al. (2014) suggests that standard sampling methods for northeast and Midwestern U.S. sites may not be as well-suited to southern sites, and therefore further ecological studies are needed specifically for southern areas.

In addition to Lyme disease, the Ixodes genus is a known vector of other pathogens, including those responsible for Rocky Mountain spotted fever, anaplasmosis, babesiosis, bartonellosis, and ehrlichiosis (Texas Department of State Health Services, 2011; Swanson, Neitzel, Reed, & Belongia, 2006; Texas Senate, 2000). These co-infections complicate treatment and must be diagnosed and addressed in order to achieve a successful treatment outcome (TXLDA, 2014).

Though some researchers note low rates of human-biting by *I. scapularis* nymphs in the south (Stromdahl and Hickling, 2012), others argue that the more predominant southern tick species, *A. americanum*, are notoriously aggressive and may result in increased risk of acquiring exposure to *A. americanum*-transmitted pathogens (Herman-Giddens, 2014; Schulze et al., 2006) and the public health relevance of lone star ticks is no longer in question (Childs and Paddock, 2003). Furthermore, milder winters make Lyme disease a year-round risk in the southern U.S. (Stony Brook Medicine, 2014). Regardless of how much lower a southerner's chances of acquiring Lyme disease are compared to a northerner, or which tick species is most likely to bite a Texas resident, researchers generally agree that Lyme disease does exist in southern states and it is time for medical professionals and citizens to develop greater knowledge and awareness in order to minimize risk. Furthermore, with all the weaknesses and criticisms of the available Lyme tests on the market, some experts feel that there is greater risk in patients not being diagnosed and treated due to a false negative test, rather than being diagnosed and treated due to a false positive test (International Lyme and Associated Diseases Society, 2009; Grier, 2000) .

Tick-borne illnesses "have become a growing concern and source of controversy" (Texas Senate, 2000). Eleven years later, the 2011 Texas Legislature enacted a law designed to encourage Texas physicians to become better educated on tick-borne diseases as a result of increased prevalence of this disease in Texas, but also because residents struggle to receive proper diagnosis and treatment from local doctors requiring them to seek medical help out of state (TXLDA, 2014). Thus, the purpose of this study is two-fold: First, to improve our understanding of the prevalence of Lyme disease in Texas by (a) analyzing known distribution of reported human cases in Texas and (b) through a survey of Texas residents with Lyme disease to establish human incidence within the state; Second, to identify the potential risk areas through habitat mapping of the vector.

By mapping incidence reports and voluntary surveys of disease cases, statistically significant areas can be identified along with potential risk levels in order to provide better education and knowledge for improved prevention strategies.

Methodology

To improve understanding of the prevalence of Lyme disease in Texas, we conducted a study that collected data through a survey, analyzed the spatial distribution of Lyme disease and identified key tick habitats throughout Texas based on a variety of environmental factors.

Survey Data. Self-report is a commonly-used method for collecting information regarding individuals' health and utilization of healthcare services (Bhandari and Wagner, 2006). Research suggests that patients' self-reports on many diseases are fairly accurate (Kriegsman, Penninx, Van Eijk, Boeke, & Deeg, 1996; Martin, Leff, Calonge, Garrett, & Nelson, 2000) and, in some cases, may be even more accurate than provider-reported data (Justice at al., 1999). Even so, accuracy can be improved with thoughtful questionnaire design, data collection methods, and pretesting (Bhandari and Wagner, 2006). Thus for the purpose of this study, a voluntary on-line survey was conducted from July 16 to September 8, 2014 to gain a better understanding of the prevalence of Lyme disease in Texas. Questions included: illness length, co-infections, where bitten (if known), diagnosis procedures and testing, whether the diagnosis was received in-state, and other relevant data that are HIPAA-compliant. The survey was administered through Survey Monkey on a HIPAA-complaint server to protect patient anonymity. The survey was publicized and disseminated through the Texas Lyme Disease Association and related support groups. A total of 608 people responded to the on-line survey.

Lyme disease cases are reported to the CDC at the county level for the entire USA. The total number of reported Lyme Disease cases for Texas were obtained from http://www.cdc.gov/lyme/stats/ for 1992-2011.

Identify risk areas by mapping tick habitats. Potential risk areas were determined by identifying habitats conducive for the vector. To do so, a site suitability analysis was performed using five variables that capture moisture, vegetation and temperature; factors considered to be important in the distribution of ticks (see Table 1, Supplementary Table S1 for details). Each of the five variables was reclassified on a scale from 0 (representing low risk) to 5 (representing high risk) based on their importance to tick activity and survival (see Table 2). The breakdown of each risk group is highlighted in more detail next.

Temperature. While it is difficult to find an exact and agreed-upon preferred temperature range for each tick species, the general requirements for *Ixodes* ticks ranges between -10°C and +35°C with tolerance to the extremes for only brief periods (Bueno-Mari, 2013; Ogden et al., 2004; Schulze, Jordan & Hung, 2001; Githeko, Lindsay, Confalonieri, & Patz, 2000). Although temperature ranges for *Amblyomma americanum* ticks are similar, their southern nature seems to cause a preference for slightly warmer temperatures, generally above 4.4°C (Schulze, Jordan & Hung, 2001). The ticks' ability to tolerate higher temperatures (e.g. > 40°C) appears to be more dependent on microclimate and the availability of water which prevents their desiccation (Tinsley & Chappell, 1999; Obenchain & Galun, 1982). The 4.4°C to 35°C range received a higher risk ranking due to the overlap of two tick species which are endemic to Texas, *Ixodes scapularis* and *Amblyomma americanum*,

Rainfall. Although precipitation can vary from year to year for the purpose of identifying key areas in Texas a 30-year average rainfall dataset was used to determine areas of high and low moisture. This was obtained from the United States Department of Agriculture Natural Resources Conservation Service at http://datagateway.nrcs.usda.gov. These raster layers contain average monthly and yearly precipitation in inches for the climatological period of 1981-2010 and were created from the Parameter-elevation Regressions on Independent Slopes Model (PRISM). The PRISM model uses point data and a digital elevation model (DEM) to generate gridded estimates of climatic parameters, incorporating a conceptual framework that addresses the spatial scale and pattern of orographic processes to account for complex variations.

Land cover type. Land cover type is a dominant factor influencing tick habitats. *Ixodes scapularis* populations have been found to be positively associated with wooded vegetation, particularly deciduous forests that produce leaf litter (Kitron & Kazmierczak, 1997; Glass et al., 1994). Similar findings have also been identified for *Ambylomma americanum* (Brown et al., 2011; Texas A&M Agrilife Extension, n.d.), though this species seems somewhat more adapted to drier and sunnier conditions (Schulze, Jordan & Hung, 2002). The National Land Cover Database (NLCD) was obtained from the United States Geologic Survey (USGS) (Fry et al., 2011). Texas contains sixteen different land cover types. Each of these were assigned a value from 0 to 5 as summarized in Table 2.

Soil. Soils data was downloaded from the U.S. Department of Agriculture's (USDA) State Soil Geographic Database, better known as STATSGO (Soil Survey Staff, n,d.) at http://sdmdataaccess.nrcs.usda.gov. Texas contains nine soil orders, of which seven are extensive across the state: alfisols (deciduous forests), aridisols (dry deserts), entisols and inceptisols (both of which are associated with poorly developed soils), mollisols (present under grasslands), ultisols (acidic red clay), and vertisols (unstable clay). The other two soil orders, Histosols (peat and organic matter) and Spodosols (develop beneath coniferous forests), cover relatively small areas in the southeastern portion of the state (USDA, n.d.). Tick presence has been positively correlated with alfisol-type soils of sandy or loam-sand textures, and negatively correlated with acidic soils of low fertility such as spodosols and poorly-drained soils, such as those with high clay content (Guerra et al., 2002; Glass et al., 1994; Kitron, Bouseman, & Jones, 1991). However, it should be noted that these studies were conducted on *Ixodes scapularis* ticks in more northern climates, so the behavior of ticks in Texas may not correlate in the same manner, particularly where the *Amblyomma americanum* tick species is concerned. Indeed, *Amblyomma americanum* ticks seem to be more tolerant of desiccating conditions and therefore less selective in their habitats (Schulze, Jordan & Hung, 2002). A summary of risk classifications associated with each soil type is summarized in Table 2.

NDVI. The final variable considered to be important for delineating tick habits was the Normalized Difference Vegetation Index (NDVI) (Cumming, 2002; Randolph, 2000). Since moisture and vegetation are especially important to ticks in the heat of summer, a 14-day summer NDVI dataset derived from NOAA's Advanced Very High Resolution Radiometer (AVHRR) satellite was used to calculate NDVI values across the state (NASA, 2013). Data was obtained from NASA Land Processes Distributed Active Archive Center (LP DAAC) at http://lpdaac.usgs.gov. The NDVI values were reclassified between 0 and 5 based on their importance to tick habitats (see Table 2). Some studies have found that ticks can survive quite well in areas with NDVI values as low as 0.3, though the mid-summer conditions are most critical (Estrada-Peña, 2001). These classifications can easily be considered conservative, as ticks are extremely hardy and can survive long periods of environmental stress. Not only have ticks developed a number of adaptations to limit water loss and tolerance to long periods of submersion in water, some species have been known to survive unfed for many years (F.D.F.G. Annex, 2012).

Once the individual layers were reclassified between 0 and 5, the surfaces were combined to create a single risk map. Surfaces were combined by adding together in ArcMap v 10.2.

Table 2: Risk values assigned to each value variable used to identify tick habitats in Texas.

Reclassification	Average Annual Precipitation	Average Temperatures	NDVI Values	NLCD 2006 Class / Value	Soils
0: No Potential Risk	< 10 inches	< -10°C and >40.5°C	Negative values (typically	11: Open Water	All dunes, bare rock outcroppings, badlands, and open

			open water)		water
1: Very Low Potential Risk	10 to 20 inches	-10°C to 0°C	Very Low NDVI values (0.1 or less)	31: Barren Land (rock/sand/clay); 24: Developed High Intensity; 90: Woody Wetlands 95: Emergent Herb. Wetlands	acidic soils such as spodosols and clay-rich soils such as ultisols and vertisols; Aridisols
2: Low Potential Risk	20 to 30 inches	1°C to 4°C	Low NDVI Values (0.2 to 0.3)	23: Developed Medium Intensity; 81: Pasture/Hay ;82: Cultivated Crops	Histosols, entisols
3: Medium Potential Risk	30 to 40 inches	35.5°C to 40°C	Moderate NDVI Values (0.4 to 0.5)	21: Developed, Open Space; 22: Developed, Low Intensity; 52: Shrub/Scrub; 71: Grassland/Herbaceous	Inceptisols
4: High Potential Risk	> 50 inches	4.4°C to 35°C	High NDVI Values (0.6 to 0.8)	42: Evergreen Forest ; 43: Mixed Forest	Mollisols
5: Very High Potential Risk	40 to 50 inches		Very High NDVI Values (0.9 to 1.0)	41: Deciduous Forest	Alfisols

Analysis

Kernel Density Estimates (KDE). KDE creates a continuous, smooth surface layer that represents the density of points across space, in this instance, Lyme cases in the state of Texas. KDE was used to detect local density "hot spots" (O'Sullivan and Unwin, 2010). A potential challenge with the Kernel Density Estimate method is selecting an appropriate radius (also known as bandwidth) to be used in the calculations. If the chosen radius is too large, more points may fall within the area causing an oversmoothing which obscures most of the structure of the data and allowing less risky areas to be skewed by more risky areas. Likewise, if the chosen radius is too small, it will be undersmoothed and fewer points will fall within the area, causing some regions to appear less risky than they may really be. Rather than arbitrarily choosing a radius, the freeware package Geospatial Modeling Environment (GME) (Beyer, 2014) in tandem with statistical freeware R (R Core Team, 2013) were utilized with ArcGIS (ESRI, 2013) to logically calculate an optimal bandwidth number on a Gaussian (bivariate normal) kernel density. For this study a bandwidth of X was used.

Out of curiosity would the results from GeoDa be quite different if you used incidence rates (e.g. total counts/population)?

Spatial Autocorrelation. Statistically significant areas of Lyme disease were identified using Exploratory Spatial Data Analysis. The survey data included zipcodes. These were matched to known geographic location of zipcodes and analyzed in GeoDa v. (website). Two analyses were conducted that include the Global Moran's *I* and a Local Indicators of Spatial Association (LISA).

Moran's *I* values may range from -1 to +1, with values closer to -1 indicating strong negative spatial autocorrelation, values closer to +1 indicating strong positive autocorrelation, and values close to 0 indicating no spatial autocorrelation. However, since most maps will not ever be perfectly autocorrelated, a Moran's value of -1 or +1 are hard to come by. A more reasonable real-world guideline is that a Moran's *I* score above 0.3 or below -0.3 is generally a good indicator of relatively strong autocorrelation (O'Sullivan & Unwin, 2010). Although the Moran's *I* provides a good measure of spatial autocorrelation for an entire dataset, it does not specify regions in which autocorrelation is strongest or weakest. Therefore, LISA, which compares values of areas against each other rather than the average of their neighbors was used for detecting localized clusters. The statistical significance is calculated by comparing each area's actual LISA value to a great many possible LISA values as determined by a complex Monte Carlo randomization procedure (O'Sullivan, 2014). The higher the actual LISA score ranks against the possible scores, the more statistically significant the actual score really is. For example, if an actual score is in the top 1 % of theoretical LISA scores, it is significant to the 0.01 level (ibid).

Tobler's 'first law' of geography broadly asserts that "Everything is related to everything else, but near things are more related than distant things" (O'Sullivan and Unwin, 2010). When defined in a more precise way, this premise is also known as spatial autocorrelation – specifically, that spatial data nearer to one another will be more alike than spatial data located farther apart. Based on this premise, it is more likely that people in close proximity to high risk tick habitats will be at higher risk than those further away. To investigate this relationship we analyzed the proximity of survey respondents who had not left Texas to risk areas.

Correlation between Lyme disease habitats and reported cases of the disease.

<u>Results</u>

<u>Survey Findings</u>

Only 35% (n=209) of survey respondents had any kind of rash they were aware of and, of those, 39% (n=82) experienced something other than the classic bullseye erythema migrans rash while another 6% (n=13) were unsure or did not know. Only 35% (n=211) of respondents were aware of a tick bite. Although many doctors state that there is no Lyme disease in Texas, only 27% (n=57) of respondents who were aware of a tick bite reported being bitten outside of the state.

45% (n=271) were refused testing by a doctor in Texas. When testing was refused, almost three-fourths of patients were told the reason for the refusal was because there is no Lyme disease in Texas. Other common reasons given for testing refusal included stating that there was no rash or that the rash was not “the right kind”, that it had to be some other medical issue, or a flat-out refusal to treat Lyme disease at all.

Once symptoms developed, a mere 11% (n=66) of respondents received a diagnosis within 4 months. 26% (n=159) were not diagnosed for more than ten years.

Not only did it take a great deal of time to receive a proper diagnosis, it also required multiple physicians. 34% (n=202) of respondents consulted ten or more physicians after symptoms had developed before receiving a Lyme diagnosis.

75% (n=448) were given another diagnosis altogether for their symptoms by a Texas healthcare provider. Many were misdiagnosed with Fibromyalgia or Chronic Fatigue Syndrome, but an even larger percentage (53%, n=205) were misdiagnosed with depression. Some of the ‘other’ diagnoses ranged from allergies and mononucleosis to anxiety, stress, or the rather condescending assessment of hypochondria. More than 21% of the ‘other’ diagnoses listed by respondents were related to mental health issues.

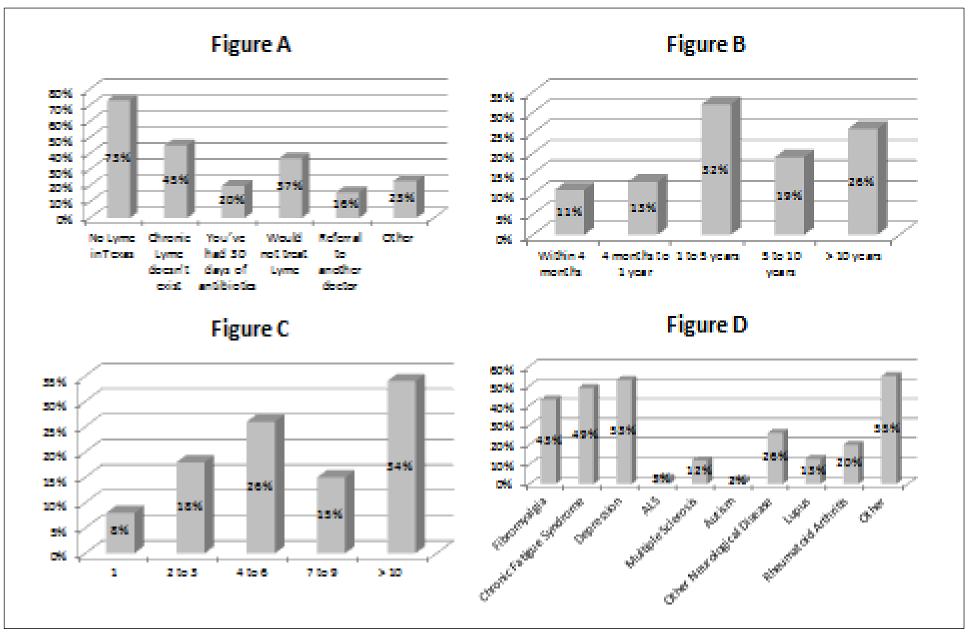

Figure 1: Results from the ‘2014 Lyme disease in Texas’ survey. Figure A: Reasons given for refusal of testing; Figure B: Length of time from onset of symptoms until Lyme disease diagnosis; Figure C: Number of physicians consulted between symptom onset diagnosis; Figure D: Other diagnoses given for symptoms

Another accusation many patients hear often is that Lyme is ‘overdiagnosed’, so respondents were asked how their diagnoses were ultimately received and validated. It turns out that the vast majority, 77% (n=464), were diagnosed through some type of blood testing or lab workup, and another 7% (n=40) were diagnosed from a classic Erythema Migrans bullseye rash (see Figure

10). Some respondents who reported ‘other’ methods of diagnosis mentioned spinal taps. This effectively shatters many of the myths surrounding Lyme disease in Texas, namely that it does not exist here or that it is all in patients’ heads. Furthermore, the large percentage whose labs were positive even according to controversial CDC standards proves that the CDC’s argument that Lyme does not exist in Texas, or that it is merely a “Lyme-like” illness, is obviously and demonstrably false.

Additionally, 78% (n=464) had also been diagnosed with at least one co-infection, such as Babesia, Bartonella, mycoplasma, Ehrlichia, Tularemia, Brucella, Morgellons, or Rocky Mountain spotted fever.

Unfortunately, the challenge does not end once a Texas patient finally receives proper testing and diagnosis. Even with positive labwork, most patients (59%, n=351) were refused treatment from Texas healthcare providers. 17% (n=99) did not request treatment from a Texas doctor, often opting to travel outside of the state to find a higher standard of knowledge and care.

Why are Texas doctors refusing to treat patients even after diagnosis? 59% (n=208) of patients were told that there is no Lyme disease in Texas, even though many of them had positive labwork showing otherwise. An alarming 39% (n=137) were told that the doctors were unwilling to accept Lyme patients for one reason or another, usually because the case was considered too complex or there was fear of disciplinary action from the Texas Medical Board. Many respondents also commented that their doctors insisted that there must be another medical problem behind it and, when confronted with positive labwork, attempted to discount it by saying the labs were “unreliable” or “false positives”.

In fact, of the patients who were refused testing, diagnosis, or treatment by a doctor in Texas, 63% (n=248) stated that the refusal reason given or implied related specifically to concerns about potential repercussions by the Texas Medical Board, and 51% (n=296) reported that the doctor who did treat them also expressed concerns about Texas Medical Board actions against doctors who treat Lyme disease.

Needless to say, this creates a substantial difficulty in finding a knowledgeable doctor who is willing to treat Lyme disease in Texas. Only 4% (n=25) reported that it was either “easy” or “no more difficult than finding any other physician”, whereas an overwhelming 96% (n=574) reporting some degree of difficulty, 70% (n=416) of which categorized the difficulty level as “extremely difficult”.

Finding a knowledgeable physician to treat seems to require leaving the state. 42% (n=247) of respondents had traveled outside of the state of Texas for treatment. 21% (n=121) of those who sought treatment in Texas had traveled between 101 and 500 miles to do so.

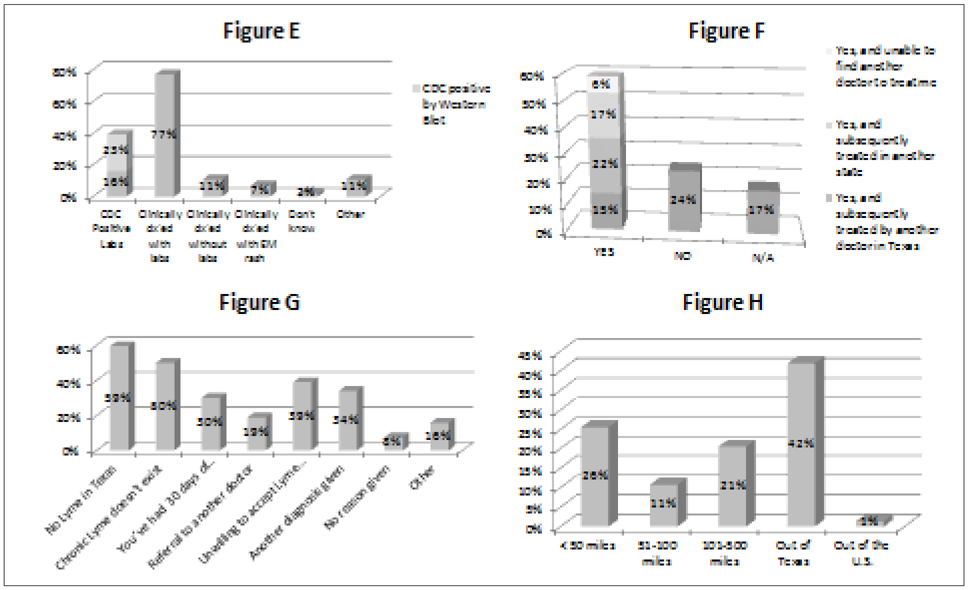

Figure 2: Results from the '2014 Lyme disease in Texas' survey. Figure E: How patients were diagnosed; Figure F: Even refused Lyme disease treatment by a Texas doctor; Figure G: Reasons given for refusal of treatment; Figure H: Greatest distance traveled for Lyme disease treatment.

When asked if they would ever consider seeing a physician who follows IDSA guidelines for treating Lyme disease, 13% (n=75) said yes, but generally indicated (in the open-ended text box provided) that it was only because some treatment is better than none at all. 19% (n=108) didn't know if they would or not, for generally the same reason, and 64% (n=371) said NO, with some interesting language accompanying that vote, usually along the lines of "not even when pigs fly".

Of the 246 respondents (43%) who had ever seen an Infectious Diseases specialist, 44% (n=108) were given no treatment at all and 20% (n=50) were offered only IDSA guidelines treatment recommendations of less than 30 days of antibiotic treatment. Only 16% (n=38) received long-term antibiotics according to their symptomatology.

A staggering 95% (n=201) of the 212 respondents who were initially treated under the IDSA guidelines protocol (less than 30 days of antibiotic therapy), reported that this protocol did not restore their health, and an additional 3% were unsure. Only 2% (n=4) of those treated according to IDSA guidelines reported a return to health.

85% of respondents (n=514) reported continuing to have symptoms after receiving at least 21 days of treatment, which is clearly indicative of the failure in adhering to the flawed IDSA guidelines and the burden that falls on patients with inadequate treatment.

52% (n=108) reported some degree of improvement after additional treatment, which strongly validates the argument for treatment beyond the general IDSA guidelines. Unfortunately, only 44% said their insurance policy covers antibiotic treatment for Lyme disease beyond the 30-day treatment recommended by IDSA protocol, which is particularly troublesome as many insurance companies base their policies on the IDSA guidelines. This is a substantial obstacle towards health, since 49% (n=280) of respondents reported that treatment costs even AFTER insurance payments were a “great problem”. An additional 35% (n=204) said it was a “moderate problem”, and only 16% (n=92) said it was “not really a problem”.

Furthermore, of the 15% (n=89) of respondents who applied for medical insurance (before passage of the Affordable Care Act), 28% (n=25) were turned down specifically due to the Lyme disease diagnosis and another 9% (n=8) said they had kept the diagnosis a secret from their insurance company. Of the 20% of respondents (n=114) who applied for disability benefits due to Lyme disease, 60% (n=68) were denied benefits based on the guidelines of the Infectious Diseases Society of America.

So, why can’t patients simply take whatever treatment they can get and be content with that? Is Lyme really that much of a problem? 94% (n=537) of respondents had to cut down or limit their usual activities, including work, housework and school-related activities, as a result of Lyme disease. 49% (n=263) and 21% (n=110) were unable to work or attend school at all, respectively, while 21% (n=111) had to scale back to part-time work or school. 69% (n=367) were unable to keep up with housework or other family-related duties. The 39% (n=209) who reported some other type of limitation described situations such as continuing to work in order to maintain insurance, but using all their leave and struggling to keep their job, an inability to participate in sports and activities that they had previously excelled in, or being unable to continue attending church and other social functions. These cutbacks are a pronounced decline in quality of life, as well as a burden to society, and therefore strongly support the argument that finding better approaches to Lyme disease in Texas should be made a high priority.

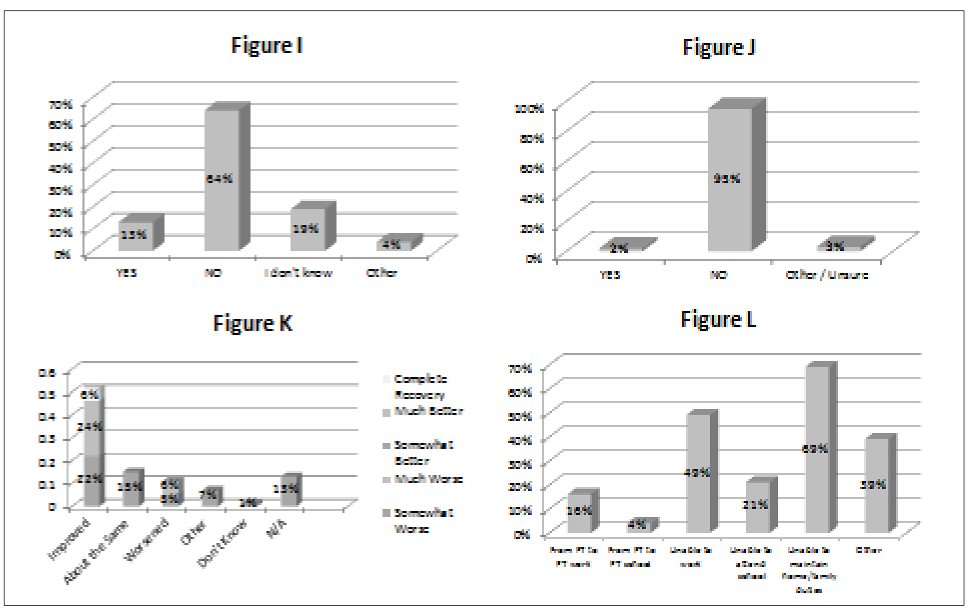

Figure 3: Results from the ‘2014 Lyme disease in Texas’ survey. Figure I: Would consider seeing a physician who follows IDSA guidelines for treatment; Figure J: If treated by IDSA guidelines initially (<30 days abx), was health restored; Figure K: How did additional antibiotic treatment (>30 days) affect your health; Figure L: How have you had to limit activities as a result of Lyme disease.

Spatial distribution of Lyme disease

KDE, CDC map (slide 11)

Exploratory Spatial Data Analysis of Lyme disease cases

The Moran's *I* score of 0.299 indicated strong positive autocorrelation with the majority of prevalence clusters occurring in the upper right ("high-high") quadrant (Figure 4 scatterplot). The vast majority of Texas is not statistically significant (N=1,529 zip codes). Areas that have both high number of reported Lyme disease cases as well as neighboring areas with high counts (high-high) are shown in red (N = 89) (Figure 4). Areas in blue represent areas of low reported Lyme disease cases surrounded by neighboring areas, also with low cases ("low-low"). Eighty-one "low-high" and fifty-nine "high-low" areas are also shown.

Results from the LISA analysis highlighted 95 zip code areas that are significant at the 0.05 level (colored bright green) and another 135 zip codes that are significant to the 0.01 level (colored a slightly darker green). These areas indicate which specific locations are contributing the most strongly to the whole outcome.

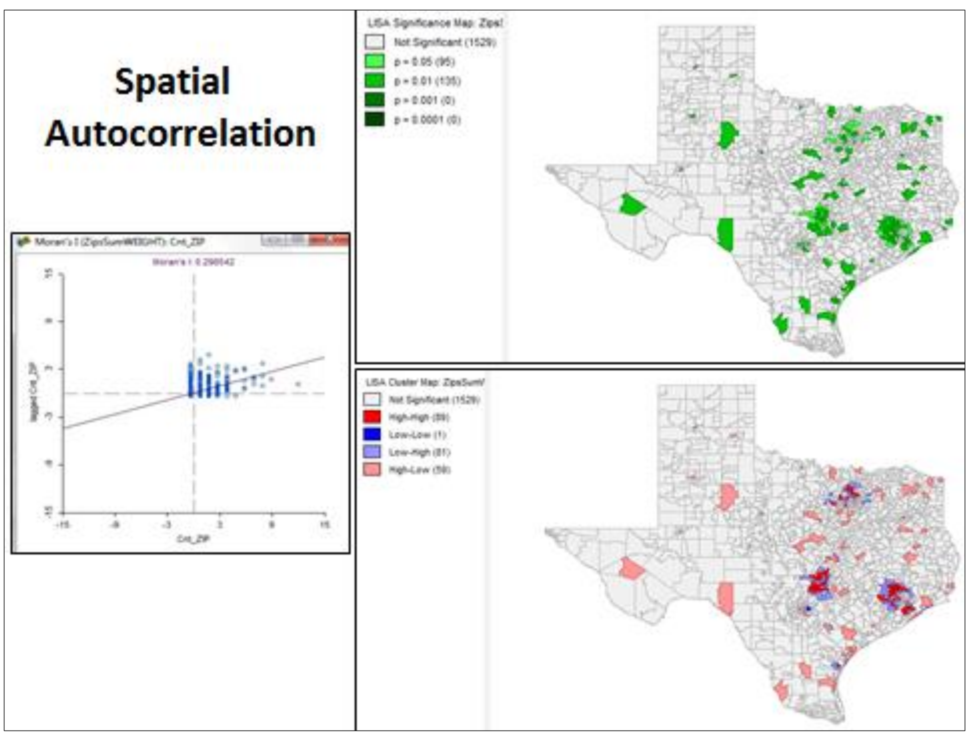

Figure 4: Moran's I and Local Indicators of Spatial Association (LISA) scores to determine spatial autocorrelation of the survey results.

Habitat Mapping of the Vector

Texas's climate varies widely as the eastern portion of the state typically has the heaviest precipitation, particularly along the coast which can received upwards of 61 inches annually, while the western region is a desert climate with only nine inches of rain per year on average. Western Texas is predominantly shrub/scrub land with some grasslands, the northern panhandle area is mainly cropland while the eastern portion of the state is a mix (e.g. conifer forests, wetlands, blackland prairie).

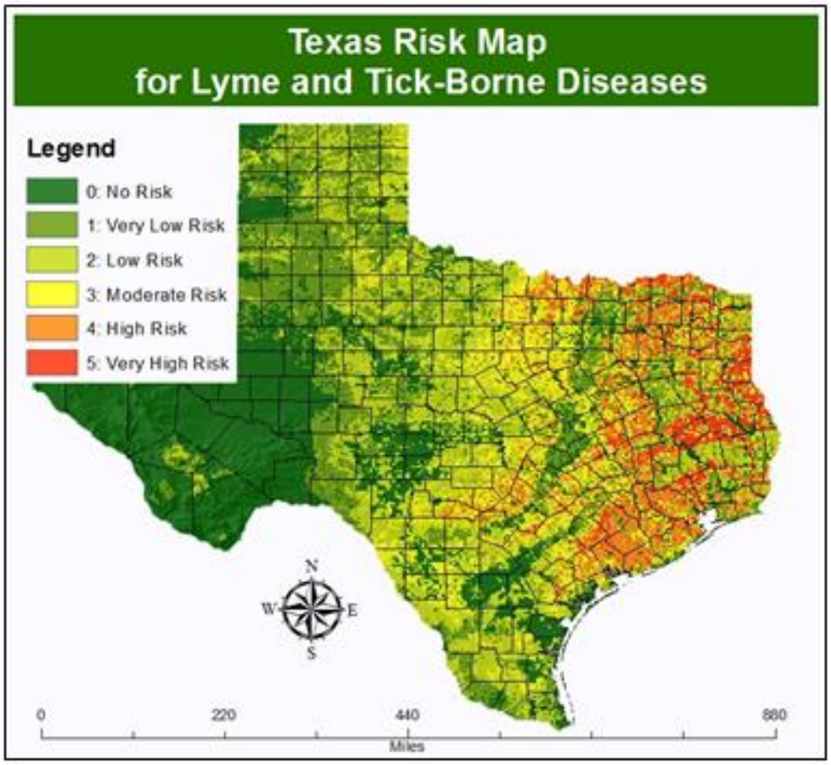

Figure 5: Potential Risk Map of Lyme disease in the state of Texas based on habitat.

Discussion

Due to regional variations based on multiple ecological processes, it is important that spatial analysis of risk is calculated for particular geographic areas rather than a generic one-size-fits-all model (Ostfeld, Glass, and Keesing, 2005). This is the first detailed map showing potential risk areas to Lyme disease in Texas based on tick habitats, and was created based on habit requirements found for the same tick species in other regions. As mentioned previously, the bulk of studies are done on northeastern sites, so we may find some differences once studies are done specifically on behaviors of ticks in Texas (Feria-Arroyo, 2014). However, until further studies are done, this is the most accurate map we currently have based on what is known about tick habitats, and can help guide future studies.

A limitation of this study is that the cases used for this analysis are where patients reside rather than where they were infected. However, this is the same surveillance methodology used by the CDC (CDC, 2013d).

All of these analyses can be taken together to confidently conclude that the spatial pattern of the Lyme disease cases are likely due to some underlying process and not due to random chance. Determining what that underlying process (or multiple processes) may be is another matter entirely! This cannot be emphasized enough in a health-related analysis. For example, a visual inspection of these maps seems to show prevalence rates are highest, in general, in areas with larger cities. This could perhaps indicate a reporting bias – that residents in these regions are more likely to go to a doctor or that doctors in these regions have a greater awareness of Lyme disease.

The main issue here is that the CDC continues to assert that Lyme disease does not exist nationwide (CDC, 2013a), even though their own reporting shows that it actually does (CDC, 2013e). Furthermore, the CDC and IDSA insist that fewer than 30 days of antibiotics will cure Lyme disease (CDC, 2014), which would result in a very low prevalence rate. Clearly, that is not the case. While it would be irresponsible to compare prevalence to incidence rates, it should be noted that only 17% (n=99) of the survey respondents reported a complete recovery or remission of symptoms, leaving *at least* 488 current cases (point prevalence) of Lyme disease. At the CDC's calculated incidence rate of 0.2 per capita for the state of Texas (CDC, 2013e), this would have taken many years to achieve the current point prevalence of 488 cases. So either the CDC is incorrect in its incidence rate for Texas, incorrect in that Lyme is easily and quickly cured and therefore has low prevalence in Texas, or both.

It should be noted that freezing temperatures do not necessarily kill ticks. Rather, ticks can retreat into leaf litter or other sheltering microclimates for a type of semi-dormant period, then emerge again any time temperatures are above freezing (Tick Encounter Resource Center, 2013). So although temperatures are a good general indicator of overall habitat suitability, they will not take into account the many variations that exist within microclimates where ticks may seek off-host shelter.

Texas is not the only region that has been overlooked in terms of Lyme disease risk (Figure 2). Other states have been similarly discounted, such as Florida (South Florida Lyme Disease Support Group, n.d.), Virginia (Ross, 2011), Louisiana (Leydet & Liang, 2014), Georgia and other southeastern states (Orent, 2013), and other countries such as Canada (Vancouver Sun, 2010), Mexico (Feria-Arroyo et al., 2014) and Australia (O'Toole, 2014). These are all regions like Texas in which Lyme has been reported but is currently being generally ignored.

Similar mapping techniques can also address other vector-borne diseases besides Lyme, such as West Nile, Dengue, Malaria, and Yellow Fever, to name a few.

Countries not previously considered suitable for tick survival are becoming potential habitats due to climate change (Ogden et al., 2014), and multiple vector-borne diseases are spreading in a similar manner (Bezirtzoglou, Dekas, & Charvalos, 2011). In fact, an overall resurgence of vector-borne diseases is occurring due to multiple factors such as demographic and societal changes and genetic changes in pathogens (Gubler, 1998). West Nile Virus, for example, has become a growing problem, having spread across the United States in only ten years, and Dengue Fever has resurfaced in Florida (CDC, 2011b). Although the Caribbean region battles Dengue, Yellow Fever, and Malaria, tick-borne illnesses were not thought to be a risk. However, a "Lyme-like" illness was reported in the Caribbean as early as 1989 (Winward & Smith, 1989), and recent studies are referring to the disease as a "Caribbean erythema migrans–like illness", likely spread by ticks of the *Amblyomma* species which are found in the region (Sharma, Jaimungal, Basdeo-Maharaj, Rao, & Teelucksingh, 2010).

The World Health Organization's 2014 theme is focused on vector-borne diseases in an attempt to draw global awareness to these threats, as every year more than one million people die from vector-borne diseases and many more are left with chronic illness and disabilities (WHO, 2014). More than half the world's population is at risk of these diseases, and that percentage is increasing with our society's increased mobility. Not only do these diseases have a profound effect on people's health but they are a serious impediment to poverty reduction and socioeconomic development (WHO, 2014).

Although vector-borne diseases are among the most complicated to prevent and control (CDC, 2011b), effective prevention strategies can help reverse their spread and resurgence (Gubler, 1998). Potential risk mapping of any region is therefore a key component, enabling greater awareness, faster diagnostics, and improved prevention techniques, all of which result in a better quality of life for humans.

RECOMMENDATIONS: Effective prevention of Lyme disease is through integrated tick management that includes awareness and education, personal protection, landscape management, and vector reduction.

<u>Awareness and Education</u>

1. Increase education and awareness among both the public and healthcare providers. This can be accomplished in any number of ways, including but not limited to:
    - media campaigns and public service announcements
    - adding a unit on tick-borne diseases to school health curriculums, so students will learn the importance of using insect repellents, to report a tick-bite instantly to their school nurse and parents, how to remove ticks safely, and symptoms to be aware of
    - School nurses and camp counselors should receive information on Lyme.

- Various jurisdictions (federal, state, county, or local, as appropriate) should post signage in known tick-dense areas to warn people to take personal precautions

2. Better training on tick-borne diseases for healthcare providers. Healthcare providers should also recognize that there are multiple protocols for treatment, and the protocol selected should be tailored to the individual patient (Johnson & Stricker, 2010). IDSA treatment guidelines, which were investigated by the Connecticut Attorney General and found to be flawed due to exclusionary practices, commercial conflicts of interest, and suppression of scientific evidence that supported rival viewpoints (Connecticut Attorney General's Office, 2008), severely limit treatment options yet are viewed as 'mandatory' by medical societies, government agencies and insurance companies (Johnson & Stricker, 2010). Most Lyme disease physicians, patients, advocacy groups, and nonprofit organizations agree that IDSA guidelines are ill-equipped to treat the complexity of Lyme disease and instead recommend ILADS treatment guidelines because they are evidence-based and patient-centered (Cameron, Johnson, & Maloney, 2014).

3. Legal protection for healthcare providers who treat tick-borne diseases. Due to fear of disciplinary action from many state medical boards, many healthcare providers are unable to treat Lyme disease patients with anything other than the flawed IDSA treatment guidelines (Johnson & Stricker, 2010). In order to increase effective treatment and the number of treating physicians, legal protection should be put in place for those healthcare providers who select alternative protocols for their patients' needs.

4. Actions against insurance companies who deny doctor-recommended treatment for tick-borne diseases. Similar to number three, above, many insurance companies are denying coverage based on the same flawed IDSA guidelines (Johnson & Stricker, 2010).

5. Greater research into tick-borne diseases and their associated treatments by those with non-competing interests.

6. Greater research on ticks specifically in southern habitats and climates, which may behave differently than those studied in northern regions (Feria-Arroyo et al., 2014).

<u>Personal Protection</u>

7. Encourage minimal exposure to ticks by reducing time spent in tick-infested habitats (Fish, 1995; Stafford, 2007; Center for Disease Control, 2011a).

8. If reducing time in infested habitats is unavoidable, wear light-colored clothing to spot ticks easily, minimize exposure of skin, use insect repellents (e.g. DEET or permethrin (TXLDA, 2014; Stafford, 2007; Fish, 1995; Center for Disease Control, 2011a)) applied

to clothing (Center for Disease Control, 2011a) and perform tick checks on both humans and pets, removing ticks promptly (TXLDA, 2014; Stafford, 2007; Fish, 1995; Center for Disease Control, 2011a). Transmission can take as little as 30 minutes (TXLDA, 2014).

9. People should be made aware of and reminded that insect repellents and “bug sprays” are generally eligible expenses claimed against Medical Flexible Spending Account (FSAs), Dependent Care Accounts (DCAs) and Health Savings Accounts (HSAs), though this can vary according to plan provider (Discovery Benefits, 2014)**.**

Landscape Management

10. Reduction of tick habitats and disease reservoirs (e.g. elimination or reduction of hosts such as rodents, chipmunks, deer that are a major food source for adult ticks and integral to the reproductive cycle of infected ticks (Stafford, 2007; Oliver, 1996)). Landscape designs should favor limited contact with vegetation (locate seating away from dense brush, wooded areas, overhanging vegetation), create barriers between wooded areas and field areas (e.g. three-foot wood chip barrier) (Lyme Disease Association, 2012; Stafford, 2007; Ward & Brown, 2004), increase direct solar exposure (Stafford, 2007; Ward & Brown, 2004; Fish, 1995) and reduce leaf litter.

11. Possible incentives could be introduced to generate more participation, such as rebates or tax breaks for both businesses and landowners who meet certain criteria. In much the same way that car owners can receive discounts on car insurance for taking a defensive driving course, people could perhaps receive discounts on medical insurance for taking a tick-borne disease awareness course.

12. The reduction of invasive plant species which serve as a ‘pathogenic landscape’ by providing preferred habitats for ticks (Esteve-Gasent et al., 2014; Allan et al., 2010; Lambin et al., 2010). Transitioning back to native vegetation helps restore ecology and create a better tick barrier (Goolsby, 2014).

Vector Reduction

13. The use of pesticides, such as acaricides (Fish, 1995, Stafford, 2007) and fungal pathogens such as *Beauveria bassiana* and *Metarhizium anisopliae* have been shown to be pathogenic to *Ixodes scapularis* in the laboratory and field (Stafford, 2007). Acaricides in particular have been shown to reduce tick abundance by 81-99% (Stafford, 2007).

FUTURE STUDY RECOMMENDATIONS

In order to strengthen future studies on this topic, the following recommendations are offered:

1. Perform a more extensive soils analysis using the detailed SSURGO database rather than STATSGO, and also taking into account the drainage characteristics of each soil type.

2. Using the Enhanced Vegetation Index (EVI) in addition to or perhaps even in place of the NDVI. The EVI minimizes canopy background variations even in dense vegetation conditions and uses the blue band to remove residual atmosphere contamination caused by clouds or smoke (NASA, 2013).

3. Utilizing data generated from Texas-specific studies to better account for tick behavior in the state (related to number 6 in the Lyme Prevention Recommendations section).

Conclusion

Within the past decade, the USA has seen the spread or overall resurgence of many new vector-borne diseases including West Nile Virus, Dengue, Chikungunya, and Lyme disease, due to multiple factors such as climate change, demographic and societal changes, and genetic changes in pathogens. Recognizing that these diseases have become established or expanded their range is important for minimizing public health risks.

A lack of awareness and knowledge regarding Lyme disease among both patients and healthcare providers is leaving many Texas patients undiagnosed or misdiagnosed, resulting in health, financial, and quality-of-life issues. Regardless of where a person is infected with Lyme disease, Texans need access to appropriate testing and treatments options within the state where they reside, rather than being forced to travel out of the state at great personal time and expense. Risk mapping using GIS can aid in developing more effective prevention measures, enabling more precise targeting of educational programs and diagnostic or treatment methodologies.

CONFLICT OF INTEREST STATEMENT

The author declares that this research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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APPENDIX A: Key factors important to tick survival and habitat suitability

Tick Species	Geographic Area	KEY FACTORS	HOW DATA USED	Source
A. americanum	Southern Missouri	Significant predictors: Forest habitat and average June relative humidity	Map of potential Tularemia risk in Missouri to facilitate disease prevention initiatives	Brown et al., 2011.
I.scapularis	North America	Temperature, Landcover	To forecast tick-borne disease emergence and outline where control strategies and prevention efforts are needed	Brownstein, Holford, & Fish, 2005.
I.scapularis	United States	Temperature and vapor pressure	To reveal essential environmental determinants of habitat suitability and predict emerging areas of risk	Brownstein, Holford, & Fish, 2003.
multiple	Africa	Covariance of temperature and rainfall.	Long-term control and eradication efforts.	Cumming, 2002.
I.scapularis	Eastern United States	Closed-canopy deciduous forest, elevation < 510m, low vapor pressure deficit, low temperature extremes	To guide surveillance, control, and prevention efforts and act as a baseline for studies tracking the spread of infection	Diuk-Wasser et al., 2012.
B. microplus (Ixodidae)	South America	Temperature and humidity	Predictive tool for tick distribution and habitat suitability estimations	Estrada-Peña, 1999.
Ixodes ricinus	Europe	Vegetation (shelter and protection from environmental extremes), host availability, landscape configuration	Review of modeling trends to assess adequacy for extrapolating habitat suitability.	Estrada-Peña, 2008.
I.scapularis	North America	Land cover, soil, elevation, temperature, moisture	To determine climate change effects on vector-borne epidemiology	Githeko et al., 2000.
I.scapularis	Kent County, Maryland	Negative association to urban land use, wetlands, and soils saturated with water or poorly drained.	To assess the use of environmental data to anticipate risk of exposure to vectors over large areas.	Glass et al., 1994.
I.scapularis	Wisconsin, Illinois, and Michigan	Soil order (sandy or loam-sand) and land cover (deciduous) were key.	To determine risk by predicting currently infested areas and if nonendemic areas may allow new populations to establish.	Guerra et al., 2002.
I.scapularis	Wisconsin and northern Illinois	Wooded habitats and leaf litter. Seropositive dogs found in areas where Lyme is considered low / no risk.	Rates of Lyme in dogs used to determine distribution and environmental risk factors to assess endemecity	Guerra, Walker, & Kitron, 2001.
Ixodes ricinus	Helsinki, Finland	Lyme can be contracted in urban environments	Increased awareness of risk for health care officials	Junttila et al., 1999.
I.scapularis	Rock Island County, Illinois	Wooded vegetation, sandy soil, and proximity to rivers	To assess the suitability of using GIS to study spatial patterns of disease	Kitron, Bouseman, & Jones, 1991.
I.scapularis	Wisconsin	High NDVI values in spring (late April) and fall (September) which indicate forest coverage	Improved mapping of risk to enhance surveillance measures	Kitron & Kazmierczak, 1997.
I.scapularis	Massachusetts	Dogs residing at < 200 ft altitude were more likely to be infected	To determine whether dogs might serve as sentinels for risk.	Lindenmayer et al.,
I.scapularis	northeastern U.S.A.	Temperature, precipitation.	Identifying factors associated with timing of Lyme season in order to improve control and prevention efforts	Moore et al., 2014.
I.scapularis	Canada and northeastern U.S.A.	Temperature.	To highlight the need to focus on risks of climate change and the effect on vector-borne diseases	Ogden et al., 2014.
Ixodidae family	various	Normalized Difference Vegetation Index and temperature	Predict renewed appearances and spread of existing pathogens.	Randolph, 2000.
I.scapularis	Canada, northern USA	average winter length, maximum temperature	Assessment of climate change impact in northern regions that have yet to be exposed to Lyme disease	Roy-Dufresne et al., 2013.
I.scapularis	Connecticut	Changes in land use, specifically reforested land developed for suburban residential use.	To maintain surveillance for Lyme disease	State of Connecticut Department of Public
A. americanum	Texas	Wooded areas with underbrush, along creeks/rivers by animal paths	Public education	Texas A&M Agrilife Extension, no date.
I.scapularis	eastern Ontario, Canada	Deer abundance, canopy cover, temperature, small mammal species richness and relative abundance of mice	Devising management strategies as this vector-borne disease expands its range.	Werden et al., 2014.
I.scapularis	Maryland	Land use, forest edge, availability of competent hosts.	Determine suitability of remotely-sensed data to assess risk	Yang et al., 2010.