SPATIAL PATTERNS OF LYME DISEASE RISK IN CALIFORNIA BASED ON DISEASE INCIDENCE DATA AND MODELING OF VECTOR-TICK EXPOSURE

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Abstract. Ixodes pacificus, particularly the nymphal life stage, is the primary vector to humans of the Lyme disease agent Borrelia burgdorferi in California. During 2004, we collected I. pacificus nymphs from 78 woodland sites in ecologically diverse Mendocino County, which has a moderately high incidence of Lyme disease. Within this county, nymphal density was elevated in forested areas with a growing degree day range of 2,600–3,000 (10°C base). Using a geographic information systems approach, we identified all areas in California sharing these environmental characteristics and thus projected to pose high acarologic risk of exposure to host-seeking nymphal ticks. Such areas were most commonly detected in the northwestern part of the state and along the Sierra Nevada foothills in the northeast, but the analysis also identified isolated areas with high acarologic risk in southern California. This mirrors the spatial distribution of endemic Lyme disease during 1993–2005; most cases occurred in counties to the northwest (58%) or northeast (26%), whereas fewer cases were reported from southern California (16%). Southern zip-codes from which Lyme disease cases had been reported were commonly located in close proximity to areas with high projected acarologic risk. Overall, Lyme disease incidence in zip code areas containing habitat with high projected acarologic risk was 10-fold higher than in zip code areas lacking such habitat and 27 times higher than for zip code areas without this habitat type within 50 km. A comparison of spatial Lyme disease incidence patterns based on county versus zip code units showed that calculating and displaying disease incidence at the zip code scale is a useful method to detect small, isolated areas with elevated disease risk that otherwise may go undetected.

INTRODUCTION

In California, Ixodes pacificus is the primary vector to humans of Borrelia burgdorferi, the causative agent of Lyme disease in North America. The nymphal tick stage is considered more important as a vector of this spirochete to humans than adult female ticks for several reasons. First, the proportion of nymphs infected with B. burgdorferi typically is manifold higher than for adults of the same generational cohort. Second, because of their smaller size, nymphs are more likely to avoid early detection and to remain attached to a human long enough for transmission of B. burgdorferi to occur. Finally, most incident Lyme disease cases in California report onset of symptoms from April to August, which coincides more closely with the April–August peak seasonal activity period of I. pacificus nymphs than the October–April peak period of adult tick activity.

Previous studies have demonstrated that humans are at risk for exposure to I. pacificus nymphs in dense woodlands with a ground cover dominated by leaf or fir needle litter, but that risk is minimal in grass-dominated habitats and chaparral. Furthermore, density of questing I. pacificus nymphs can be highly variable within a single county. These findings led us to speculate that both nymphal density and Lyme disease risk in California may be more spatially variable than previously thought.

We had three primary goals in this study. First, we wanted to determine if the result of a model for detection of areas with high projected acarologic risk of exposure to I. pacificus nymphs (i.e., areas characterized by high densities of host-seeking nymphs) developed within a single county in California was applicable to the entire state; this entailed evaluating the strength of the association between presence of areas with high projected acarologic risk and Lyme disease incidence at the spatial scale of the zip code. Our second goal was to examine how spatial Lyme disease incidence patterns in California differ when calculated and displayed based on county versus zip-code geographic units. Third, we wanted to produce a risk map for California combining information on spatial patterns of acarologic risk for exposure to I. pacificus nymphs and Lyme disease incidence.

MATERIALS AND METHODS

Development of a spatial dependence kriging model for density of I. pacificus nymphs in Mendocino County. Mendocino County was chosen as the basis for development of our acarologic risk model based on the considerable ecologic and climatic diversity occurring within the county and a moderately high incidence of Lyme disease. Peak densities of host-seeking I. pacificus nymphs were determined in spring 2004 in 78 dense woodland sites located throughout Mendocino County and representing all major woodland habitats present (Figure 1). The location of each site was determined using a Trimble Geo XT (Trimble Corp., Sunnyvale, CA) global positioning system with submeter accuracy. The woodland sub-types included, the tick sampling methodology used, and the resulting densities of I. pacificus nymphs have been previously described.

Peak nymphal densities were significantly ($P < 0.05$) spatially autocorrelated up to a distance of 70 km (Moran’s $I$; Z-statistic > 2.5 for distances $\leq 70$ km and $< 1.8$ for distances $> 71$ km). This spatial dependence allowed for creation of an interpolation model for nymphal density. The model was created by anisotropic ordinary kriging based on a spherical semivariogram including untransformed data from all 78 sites sampled and using default parameters in the Geostatistical
Analyst of Arc9 (Environmental Systems Research Institute [ERSI], Redlands, CA). Cross validation results indicated a good model fit, with similar root mean square error and average standard error, standardized mean error close to zero, and standardized root mean square error close to 1. Among candidate model types available in the Geostatistical Analyst package, the spherical model yielded the best fit according to the cross-validation criteria. The resulting model is displayed in Figure 2.

Correlation of kriging model results and environmental factors. The kriging model was used to divide Mendocino County into nymphal density classification regions representing high (H, > 10.50 nymphs/100 m²), medium (M, 6.41–10.50), low (L, 2.51–6.40), and very low (VL, < 2.51) nymphal densities (Figure 2). Nymphal density cut-off points were chosen based on natural breaks in the data. The large and ecologically variable low and very low density class regions were further subdivided into low southeastern (LSE), low southwestern (LSW), low northeastern (LNE), low northwestern (LNW), very low southwestern (VLSW), very low northwestern (VLNW), and very low northeastern (VLNE) areas. To assess variation in environmental factors between the nine regions (H, M, LSE, LSW, LNW, LNE, VLSW, VLNW, and VLNE), we randomly selected 100 pixels (30 × 30 m cell size) per region classified as dense woodland pixels by a previously described habitat model. For each woodland pixel, we extracted, using ArcView 3 (ESRI), data on two environmental factors from geographic information systems (GIS)–based data covering the entire state of California. These included base 50°F (10°C) mean annual growing degree days (GDDs) from 1961 to 1990 (Spatial Climate Analysis Service, Oregon State University, Corvallis, OR) and mean annual precipitation (PRE) for the same period (Water and Climate Center of the Natural Resources Conservation Service, Portland, OR). We then calculated means and 95% confidence intervals for GDD and PRE for each of the nine model regions. Overall, GDD values were more clearly separated than PRE values among the nine nymphal density regions (data not shown for PRE; see Table 1 for GDD). Therefore, only GDD was used in further analyses.

Modeling areas with high projected acarologic risk of exposure to host-seeking I. pacificus nymphs in California. Areas with high projected acarologic risk of exposure to host-seeking I. pacificus nymphs in California were determined as follows. The data shown in Table 1 demonstrate an association between a specific GDD range (2,600–3,000) and medium-high nymphal density regions (Table 1). Previous studies have found that human exposure to I. pacificus nymphs occurs predominantly in woodland habitats. Based on these findings, we created a GIS-derived data surface representing areas in California with high projected acarologic risk of exposure to host-seeking I. pacificus nymphs. This statewide data surface combined GIS-based data representing...
habitat type (adapted from the University of California at Santa Barbara California Gap analysis project) and GDD; areas classified as having high acarologic risk are characterized by forested habitat with a GDD range of 2,600–3,000 (Figure 3). The created data surface has a spatial resolution of 2 × 2 km.

**Lyme disease incidence data for California.** Lyme disease case histories for 1,325 cases reported to the California Department of Health Services from 1993 to 2005 were reviewed to determine the probable county of exposure for each case. Cases for which the reported county of likely exposure was not the county of residence (N = 355) were excluded from the study. This included cases with a tick bite likely acquired outside the county of residence or with a history of travel outside the county of residence in the 30 days prior to onset of symptoms. Residential zip-code information was missing for an additional 59 cases. The remaining 911 cases were designated by county and five-digit zip code corresponding to their reported residence. These cases and population data from 2001 were used to calculate a mean annual incidence of endemic Lyme disease for the period 1993–2005 by county and zip code within the state of California. Geographic units with estimated Lyme disease incidence of > 5 cases/100,000 person-years were considered areas of elevated risk. The GIS-based data for county and zip-code boundaries were obtained from ESRI and population data were obtained from the U.S. Census Bureau (county) or ESRI (zip code).

**Examination of association between presence of areas with high projected acarologic risk of exposure to host-seeking *I. pacificus* nymphs and Lyme disease incidence.** The strength of the association between presence of areas with high projected acarological risk of exposure to *I. pacificus* nymphs (forested habitat with a 2,600–3,000 annual GDD range) and elevated Lyme disease incidence was tested at the spatial scale of the five-digit zip-code area. This divided California into 1,661 separate data units, ranging in size from 17 to 985,536 hectares (ha) (median = 4,472 ha). Zip codes lacking human population (N = 21) were excluded from further analyses. Using the spatial analyst in Arc9, we calculated the percentage of each zip code covered by areas with habitat representing high projected acarologic risk. Furthermore, we created a 100 × 100 m grid for the state of California to calculate the straight line (Euclidean) distance from each zip code to the nearest area with high projected acarologic risk (distance = 0 m if such areas were contained within the zip code). Thereafter, we evaluated the associations between Lyme disease incidence by zip code and 1) the percentage of the zip code classified as area with high projected acarologic risk (chi-square test) and 2) the distance to the nearest area with high projected acarologic risk (Wilcoxon rank sum test with normal approximation). Nonparametric statistics were used in the latter case because data were not normally distributed and transformation could not make them so. All statistical analyses described below were carried out using ver-

<table>
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<th>Nymphal density region</th>
<th>Mean GDD*</th>
<th>95% confidence interval</th>
<th>200 GDD increment</th>
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<td>3,357</td>
<td>3,292–3,423</td>
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* Based on 100 observations per nymphal density region.

Figure 3. A, Classification of California counties by percentage coverage of areas with high projected acarologic risk of exposure to *Ixodes pacificus* nymphs (i.e., forested areas with a 10°C-base annual growing degree day range of 2,600–3,000): <1.00% coverage, white; 1.00–4.99% coverage, light gray; 5.00–9.99% coverage, medium gray; >10.00% coverage, dark gray. B, Actual distribution of areas with high projected acarologic risk (shaded black).
sion 5.1 of the JMP® statistical package and the results were considered significant when $P < 0.05$.

RESULTS

**Determination of areas in California with high projected acarologic risk of exposure to host-seeking *I. pacificus* nymphs.** In the first modeling step, we created a kriging model for peak density of *I. pacificus* nymphs in Mendocino County woodlands based on data from 78 sampling sites (Figures 1 and 2). The model fit was good (model errors for 78 of 78 samples; root mean square error = 3.715, average standard error = 3.886, standardized mean error = 0.005, standardized root mean square error = 1.069) and peak nymphal densities predicted from the model corresponded well to observed values (linear regression of model-predicted density on actual density; $r^2 = 0.91$, $F_{1,76} = 770.30$, $P < 0.001$). This kriging model was used to separate Mendocino County into regions representing different nymphal density classes (Figure 2 and Table 1). Medium to high nymphal density regions were associated with a data range of 2,600 to 3,000 mean annual base 50°F (10°C) GDDs, whereas lower or higher GDD values were associated with low or very low nymphal density regions (Table 1).

Thereafter, we created a data surface for areas with high projected acarologic risk of exposure to *I. pacificus* nymphs in California (i.e., forested areas with a 2,600–3,000 annual GDD range predicted to have densities of host-seeking nymphs exceeding 6.4/100 m²) (Figure 3). The overall coverage by areas with high projected acarologic risk was 5.4% for California ($≈ 22,000$ km²), with > 10% coverage recorded for four northwestern counties (Humboldt, Lake, Mendocino, and Trinity), Santa Cruz County on the central coast, and Nevada County in the northeastern part of the state (Figure 3A). Areas with high projected acarologic risk most commonly occurred to the northwest and along the Sierra Nevada foothills (Figure 3B). However, the model also indicated presence of small, isolated areas with high projected acarologic risk in numerous counties in southern California (Figure 3B).

**Spatial patterns of Lyme disease incidence in California.** Most Lyme disease cases in California with a probable exposure within the county of residence occurred in counties to the northwest (58%; counties ranging from Santa Cruz and Santa Clara to Del Norte and Siskiyou) or northeast (26%; counties ranging from Madera to Modoc), whereas fewer cases were recorded from the southern part of the state (16%; counties ranging from San Diego and Imperial to Monterey, Fresno, and Inyo). Individual zip codes with elevated Lyme disease incidence ($> 5$ cases/100,000 person-years) most frequently occurred in the northern Coast Ranges and Sierra Nevada foothills (Figures 4 and 5). However, our data indicate that small, isolated areas characterized by elevated Lyme disease incidence occur also in southern California (Figures 4 and 5). This finding was corroborated by our model for areas with high projected acarologic risk; southern zip codes with elevated Lyme disease incidence typically occurred in close proximity to areas with high projected acarologic risk of exposure to host-seeking nymphs (Figure 4B).

A comparison of spatial Lyme disease incidence patterns based on county versus zip-code units indicate that calculating and displaying disease incidence at the zip-code scale is a useful method to detect small, isolated areas with elevated disease risk that otherwise may go undetected (Figure 4). As a case in point, zip codes with Lyme disease incidence exceeding 5 cases/100,000 person-years were detected within several southern counties with overall incidence of less than 0.25 cases/100,000 person-years (Imperial, Kern, Monterey, San Diego, and Tulare; Figure 5). Conversely, zip codes with low Lyme disease incidence (< 1 case/100,000 person-years) occurred within counties on the north coast with an overall incidence exceeding 5 cases/100,000 person-years and including multiple zip codes with incidences > 20 cases/100,000 person-years (Humboldt and Mendocino; Figure 5).

![Figure 4. Distribution of California counties (A) and zip code areas (B) with Lyme disease incidence exceeding one case (light gray) or five cases (gray) per 100,000 person-years, 1993–2005. B. Distribution of areas with high projected acarologic risk of exposure to *Ixodes pacificus* nymphs (is shown in red). This figure appears in color at www.ajtmh.org.](image-url)
Association between presence of areas with high projected acarologic risk of exposure to host-seeking I. pacificus nymphs and Lyme disease incidence. We found strong associations between presence of areas with high projected acarologic risk of exposure to host-seeking I. pacificus nymphs and Lyme disease incidence at the zip-code scale. Lyme disease incidence was positively associated with percentage coverage by areas with high projected acarologic risk (Figure 6). Zip codes containing at least some areas with high projected acarologic risk had a 10-fold higher Lyme disease incidence (1.35 cases/100,000 person-years) than zip codes lacking such areas (0.13 cases/100,000 person-years) ($\chi^2 = 66.52$, degrees of freedom [df] = 1, $P < 0.0001$). Furthermore, Lyme disease incidence was 53-fold higher for zip codes with more than 50% of their area representing high projected acarologic risk (6.94 cases/100,000 person-years; $n = 9$ zip codes) than for zip codes entirely lacking such areas (0.13 cases/100,000 person-years; $n = 1,398$ zip codes) (Figure 6).

We also found that Lyme disease incidence was negatively associated with distance to nearest area with high projected acarologic risk (Figure 7). For example, Lyme disease incidence for zip codes containing areas with high projected acarologic risk ($n = 261$ zip codes; 1.35 cases/100,000 person-years) was 27 times higher than for zip codes located more than 50 km from the nearest area with high projected acarologic risk ($n = 269$ zip codes; 0.05 cases/100,000 person-years). Finally, the minimum distance to areas with high projected acarologic risk was lower for zip codes where Lyme disease cases occurred compared with zip codes without reported cases; the mean (SD) distance to areas with high projected acarologic risk was 18.85 km (21.05) for 382 zip codes with Lyme disease cases and 29.57 km (24.37) for 1,258 zip codes without cases ($z = -8.47$; df = 1, 1,638, $P < 0.001$). Finally, our statewide model for areas with high projected acarologic risk accurately predicted the presence of areas with high incidence of Lyme disease.
elevated Lyme disease risk not only in northwestern California, but in the northeastern and southern parts of the state as well (Figure 4B).

**DISCUSSION**

Within Mendocino County in north coastal California, density of *I. pacificus* nymphs, which are the primary vectors to humans of the Lyme disease spirochete in the far western United States, was elevated in forested areas with a base 50°F (10°C) annual GDD range of 2,600–3,000. Previous GIS- or remote sensing–based studies from the eastern United States have also found associations between forested habitat and climate factors and presence or density of the *B. burgdorferi* vector *I. scapularis* or occurrence or incidence of Lyme disease in humans or domestic animals. Using a GIS approach, we showed that a Mendocino County–derived combination of environmental factors representing high projected acarologic risk of exposure to host-seeking nymphal ticks accurately predicted the presence of areas with elevated Lyme disease incidence (>5 cases/100,000 person-years) throughout the state of California (Figure 4B).

The usage of both Lyme disease incidence and acarologic risk of tick exposure in overall Lyme disease risk assessments is important because, unless case investigations determine the actual spatial location of tick exposure, disease incidence data will tend to be based on residential address and, therefore, primarily reflect peri-domestic exposure. Conversely, modeling of acarologic risk provides information on risk areas irrespective of presence of a human population. This approach is especially appropriate for geographic areas such as California, where the human population is clustered and public lands are used heavily for recreational activities placing people at risk for exposure to vector ticks.

Both our model for areas with high projected acarologic risk of exposure to *I. pacificus* nymphs and the zip code–based Lyme disease incidence data show patchy spatial risk patterns in California (Figures 3–5). This applies not only to southern California, where small, isolated high risk “islands” occur within “oceans” of low risk, but also to areas in the northern part of the state typically considered high risk areas for Lyme disease. Using Mendocino County on the north coast as an example of the latter, high-risk areas clustered in the eastern, inland part of the county both for Lyme disease incidence and acarologic risk of exposure to host-seeking nymphs (Figures 3–5). A recent field study similarly found higher densities of *I. pacificus* nymphs in the eastern part of the county.

There are some early records of *B. burgdorferi*-infected *I. pacificus* ticks from the border of Orange and San Diego counties and from Fresno, Kern, San Benito, San Bernardino, and Tulare counties in southern California. However, these studies preceded the delineation of North American *B. burgdorferi* into the Lyme disease agent *B. burgdorferi* and *B. bisetii*, which is commonly found in Californian rodents but yet to be implicated as a cause of human disease in North America. There also is evidence of currently uncharacterized *B. burgdorferi* sensu lato spirochetes, with unknown pathogenicity to humans, from *I. pacificus* ticks in California. Regardless of whether the older reports from southern California detected *B. burgdorferi*, *B. bisetii*, or currently uncharacterized *B. burgdorferi* sensu lato spirochetes, we predict that examination of *I. pacificus* from areas with high projected risk in our acarologic model will conclusively demonstrate the presence of *B. burgdorferi* in southern California.

Although Lyme disease risk overall is very low for southern California, our fine-scale assessments of disease risk and acarologic risk will be useful to inform the medical community that small, isolated areas of elevated risk do occur in this region and that people living in close proximity to or commonly engaging in recreational activities in these areas may be at increased risk for exposure to the Lyme disease spirochete. This is especially relevant in southern California, where most areas with high projected acarologic risk are located on public lands and zip codes with elevated Lyme disease incidence tend to be located adjacent to these public lands (data not shown).

Both the spatial Lyme disease incidence data and the modeling of areas with high projected acarologic risk of exposure to *I. pacificus* nymphs must be viewed as rough estimates of true spatial geographic patterns. Areas that the acarologic model identified as having elevated risk of nymphal exposure remain presumptive pending field validation. It also needs to be established that *I. pacificus* nymphs are infected with *B. burgdorferi* in areas of eastern and southern California where such information is currently lacking. However, the high degree of concordance between the spatial patterns of our two independently derived risk estimates (acarologic risk and human disease incidence) indicate that considered jointly they provide a reliable approximation of actual spatial risk patterns.

Some aspects of our zip code–based Lyme disease incidence map deserve special mention. First, inflated disease incidence in zip codes with a low population base is a potential problem associated with the use of this small geographic unit. This was, to some extent, counteracted by the use of disease data collected over a long time period (>10 years). Second, our acarologic risk model failed to detect some areas with elevated Lyme disease incidence in four sparsely populated Sierra Nevada counties (Lassen, Modoc, Mono, and Plumas) (Figure 4B). Based on the assumption that the few cases reported from these counties were acquired locally, we modified the GDD range of the acarologic risk model in an attempt to incorporate these areas in a secondary version of
the model. Expansion of the GDD range from 2,600–3,000 to 2,300–3,300, which would have included Mendocino County areas characterized as having “low” nymphal densities in Table 1, indicated presence of areas with low-medium projected acarologic risk of exposure to nymphal ticks in Lassen and Mono counties (data not shown). Future models of acarologic risk in California would benefit from including field-derived data from the Sierra Nevada region because populations of \textit{I. pacificus} occurring in this area may be adapted to different local climates than the northwestern tick populations used in our model development.

Third, the identification of a zip code with very high Lyme disease incidence (>50 cases/100,000 person-years) in northwestern San Diego County (Figure 5) likely resulted from an artificially inflated disease incidence. This particular zip code represents the Marine Corps Base of Camp Pendleton. Our GIS-derived data-base used a permanent population of 80 for this zip code, whereas the single Lyme disease case reported from Camp Pendleton very likely also drew from the larger population of temporary Marine Corps personnel stationed at the base, thus probably artificially inflating disease incidence.

Our comparison of spatial Lyme disease incidence patterns based on county versus zip-code units (Figure 4) showed that calculating and displaying disease incidence at the zip-code scale is a useful method to detect small, isolated areas with elevated disease risk that otherwise would go undetected. Although this may not be epidemiologically important at a statewide scale, an individual residing within such an area may be at increased risk for Lyme disease without the benefit of residents or the medical community being aware of the possibility of local exposure. Furthermore, calculating and displaying both county- and zip code–scale disease risk assessments is easily done using existing GIS technology.

Visualization of spatial risk of vector-borne disease at the zip-code scale is especially appropriate for the western United States. Counties in western states are typically larger and ecologically more variable than counties in the east. For example, although California contains 58 counties to Connecticut’s 8, the average size of a county in California (mean = 7,000 km², range = 122–51,960 km²) is more than four-fold greater than for a county in Connecticut (mean = 1,600 km², range = 956–2,383 km²) (data from the National Association of Counties, available from http://www.naco.org). Furthermore, counties in Connecticut tend to be ecologically homogenous; most counties are dominated by deciduous forest interspersed with coniferous forest or agricultural land (data from the University of Connecticut, available from http://nemo.uconn.edu). In contrast, many counties in California encompass considerable habitat variability. For example, 9,000-km² Mendocino County in north coastal California includes habitats ranging from moist and cool redwood forests in the west to hot and dry oak woodlands and chaparral in the southeast and montane coniferous forest in the far northeast (data from the University of California at Santa Barbara California Gap analysis project, available from www.biogeog.ucsb.edu). Similarly, habitat types in San Bernardino County in the south range from large eastern tracts of desert interspersed with grassland to chaparral and juniper or pinyon-juniper areas, montane hardwood-conifer, and Sierran mixed conifer forest in the far southwestern part of the county. We conclude that determination and visualization of vector-borne disease (e.g., Lyme disease, West Nile virus disease) incidence at a zip code scale in the western United States provides a cost-effective method for detection of isolated areas of elevated disease risk that might otherwise be overlooked.

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