Journal of Medical Entomology, 59(4), 2022, 1328–1335
https://doi.org/10.1093/jme/tjac049
Advance Access Publication Date: 18 May 2022
Research

Sampling, Distribution, Dispersal

Reported County-Level Distribution of Seven Human Pathogens Detected in Host-Seeking *Ixodes scapularis* and *Ixodes pacificus* (Acari: Ixodidae) in the Contiguous United States

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Subject Editor: Sarah Hamer

Received 1 February 2022; Editorial decision 2 April 2022.

Abstract

Tickborne disease cases account for over 75% of reported vector-borne disease cases in the United States each year. In addition to transmitting the agents of Lyme disease (*Borrelia burgdorferi* sensu strict [Spirochaetales: Spirochaetaceae] and *Borrelia mayonii* [Spirochaetales: Spirochaetaceae]), the blacklegged tick, *Ixodes scapularis*, and the western blacklegged tick, *Ixodes pacificus* collectively transmit five additional human pathogens. By mapping the distributions of tickborne pathogens in host-seeking ticks, we can understand where humans are at risk of contracting tickborne diseases and devise targeted strategies to prevent them. Using publicly available tickborne pathogen surveillance databases, internal CDC pathogen testing databases, and SCOPUS search records published since 2000, we mapped the county-level distribution of *Borrelia miyamotoi* (Spirochaetales: Spirochaetaceae), *Anaplasma phagocytophilum* (Rickettsiales: Anaplasmataceae), *Ehrlichia muris eauclairensis* (Rickettsiales: Ehrlichiaceae), *Babesia microti* (Piroplasmida: Babesiidae), and Powassan virus (Flaviviridae) reported in host-seeking *I. scapularis* or *I. pacificus* in the contiguous United States. We also updated recently published maps of the distributions of *Borrelia burgdorferi* sensu stricto and *Borrelia mayonii*. All seven pathogen distributions were more limited than the distributions of vector ticks, with at least one of the seven pathogens detected in 30 states out of 41 total states (73.2% of states) where vector ticks are considered to be established. Prevention and diagnosis of tickborne diseases rely on an accurate understanding by the public and health care providers of where people are at risk for exposure to infected ticks. Our county-level pathogen distribution maps expand on previous efforts showing the distribution of Lyme disease spirochetes and highlight counties where further investigation may be warranted.

Key words: tick surveillance, surveillance, pathogen distribution

Tickborne diseases are an increasing public health burden in the United States, accounting for over 75% of reported vector-borne infections in the United States each year (Rosenberg et al. 2018). A majority of reported tickborne infections are associated with the blacklegged tick (*Ixodes scapularis*) and the western blacklegged tick (*Ixodes pacificus*) (Eisen and Eisen 2018, Rosenberg et al. 2018). Over the past two decades, the number of counties in the eastern U.S. where *I. scapularis* is considered established based on published criteria has more than doubled (Eisen et al. 2016). In the western U.S., counties with established populations of *I. pacificus* are widespread, particularly in Pacific coastal states, but the reported distribution of the tick has remained relatively stable (Eisen et al. 2016, CDC 2021a). In addition to transmitting *Borrelia burgdorferi* sensu stricto, the primary causative agent of Lyme disease, which is the most commonly reported vector-borne disease in the United States, both *I. scapularis* and *I. pacificus* also transmit the bacterial agents

Published by Oxford University Press on behalf of Entomological Society of America 2022.

of hard tick relapsing fever (*Borrelia miyamotoi*) and anaplasmosis (*Anaplasma phagocytophilum*). Additionally, in the eastern and midwestern U.S., *I. scapularis* transmits a less common bacterial agent of Lyme disease (*Borrelia mayonii*), the bacterium causing a form of ehrlichiosis (*Ehrlichia muris eauclairensis*), a protozoan that causes babesiosis (*Babesia microti*), and Powassan virus (POWV), which causes a neuroinvasive disease (Eisen and Eisen 2018).

Of the seven *Ixodes*-borne human pathogens, six cause nationally notifiable conditions in the U.S.: Lyme disease (notifiable since 1991), anaplasmosis (2000), ehrlichiosis (1999), babesiosis (2011), and Powassan virus disease (2002) (Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System, 2021). However, case reporting does not differentiate between Lyme disease caused by *B. burgdorferi* s.s. or *B. mayonii*, nor between ehrlichiosis caused by *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, or *E. muris eauclairensis*, despite geographic differences in exposure risks. Tick surveillance is intended to provide current and accurate data on the distribution and abundance of medically important ticks and the presence and prevalence of their associated human pathogens to identify when and where persons are at risk for exposure to ticks and tickborne pathogens (Eisen and Paddock 2021). Recent national tick surveillance efforts have increased our understanding of the county scale distribution of *I. scapularis* and *I. pacificus* (Dennis et al. 1998, Eisen et al. 2016), and of *B. burgdorferi* s.s. and *B. mayonii* (Fleshman et al. 2021; Fig. 1, Supp. Table 1A–B). Similar distribution maps for other pathogens spread by *Ixodes* spp. are lacking. Through literature review and collating records submitted to CDC and other public tick surveillance databases, we present county-level distribution maps for the remaining human pathogens spread by *Ixodes* spp., including *B. miyamotoi*, *A. phagocytophilum*, *E. muris eauclairensis*, *Ba. microti*, and POWV.

Methods

Methods followed Fleshman et al. (2021). Briefly, county records from host-seeking *B. miyamotoi*, *A. phagocytophilum*, *E. muris eauclairensis*, *Ba. microti*, or POWV-infected *I. scapularis* or *I. pacificus* collected from 2004 to 2021 were obtained from ArboNET, a Centers for Disease Control and Prevention (CDC) database containing tick surveillance and testing results from CDC field studies, and ticks collected by public health and university partners for public health surveillance. Additionally, we updated previously published county-level distributions of *B. burgdorferi* s.s. and *B. mayonii* (Fleshman et al. 2021) with ArboNET records reported through December 31, 2021. Ticks submitted to CDC were tested using real-time polymerase chain reaction (PCR) assays as described previously (Graham et al. 2018), which had high sensitivity and were species-specific. Public health and academic partners conducting tick testing used various molecular testing methods but confirmed that testing assays met minimum sensitivity and specificity criteria according to CDC *Ixodes* spp. surveillance guidance (CDC 2018). Notably, because a majority of studies reporting *A. phagocytophilum* presence did not differentiate between the human-active variant and other strains that have not been demonstrated to be pathogenic in humans, *A. phagocytophilum* was not segregated into human and nonhuman pathogenic strains in this review.

We also conducted independent literature searches using the Scopus database and combinations of the search terms "*Borrelia miyamotoi*," "hard tick relapsing fever," "*Anaplasma phagocytophilum*", "*Anaplasma phagocytophila*," "*Ehrlichia phagocytophila*" "*Babesia microti*," "babesiosis," "Powassan virus disease," "Powassan virus encephalitis," "POWV," "Deer Tick virus," "DTV," "*Ehrlichia muris eauclairensis*," "*Ehrlichia muris*-like," "EME," "EML," "EMLA," "*Ixodes scapularis*," "*Ixodes pacificus*," "host-seeking," "questing," and "tick." Based on the records produced with these search terms, references were included if 1) pathogens were detected in host-seeking *I. scapularis* or *I. pacificus* ticks collected in the United States, 2) the county of tick collection was included, 3) pathogen detection methods were adequately specific to correctly identify the pathogens listed above, and 4) publications provided pathogen testing data for counties not already included in ArboNET records. To obtain additional data meeting our criteria, we searched publicly available tickborne pathogen surveillance archives located on health department websites for states with established populations of *I. scapularis* or *I. pacificus*.

We focused our study on host-seeking ticks, including only tick records collected via flagging, dragging, or CO_2 traps, due to the difficulties associated with confirming county of tick exposure for ticks collected from humans, wildlife, livestock, or pets (CDC 2021a, Eisen and Paddock 2021). For comparability to national human tickborne disease case reporting and to previous efforts reporting the distributions of medically important ticks in the U.S., we reported data at the county spatial scale. For publications where county of collection was not reported but that otherwise met our inclusion criteria, we contacted authors and included any county-level pathogen infection data, when provided. If a tickborne pathogen was present in a host-seeking *I. scapularis* or *I. pacificus* in a county according to any source meeting our inclusion criteria, we considered the pathogen to be present in that county. We used ArcMap 10.7 (ESRI, Redlands, CA) to map pathogen presence data, and pathogen-positive ticks were joined on five-digit Federal Information Processing Standard (FIPS) codes, along with a county-level map of the contiguous U.S.

Results

Of the 956 records identified by our Scopus searches, 67 records met our inclusion criteria (Supp. Table). Combining all data sources, we show that the reported distributions of each of the pathogens were more limited than the previously reported distributions of their vectors, *I. scapularis* and *I. pacificus*, in the contiguous U.S. (Figs. 1 and 2).

B. miyamotoi was detected in *I. scapularis* in 242 counties spanning 21 eastern states and the District of Columbia, and in *I. pacificus* in 29 counties spanning 3 western states: California, Oregon, and Washington. A majority of counties where *B. miyamotoi* was present were located in the North Central, Northeastern, and Mid-Atlantic regions (Supp. Table 1C, Fig. 1B), and all counties where *B. miyamotoi* was present also reported presence of *B. burgdorferi* s.s. (Fig. 1A). The distribution of *B. miyamotoi* was also similar to the distribution of *A. phagocytophilum*, though *B. miyamotoi* was reported in ticks in a few additional counties in California and Minnesota. *B. miyamotoi* was not reported in ticks from West Virginia or New Hampshire, where *A. phagocytophilum* was reported in several counties. In Delaware, Iowa, and Tennessee, *B. miyamotoi* was reported in ticks in only one county each and was reported in ticks in only two counties in Oregon, Ohio, Massachusetts, and Maine.

A. phagocytophilum was identified in 291 counties in 23 states and the District of Columbia; it was reported most commonly in *I. scapularis* in counties in the northeastern and upper midwestern U.S. but was found also in *I. pacificus* in the western U.S. in northern California and southern and northwestern Washington (Supp. Table 1D, Fig. 1C). Similar to the distribution of Lyme disease spirochetes (*B. burgdorferi* s.s.) in *I. scapularis* (Fig. 1A), *A. phagocytophilum*

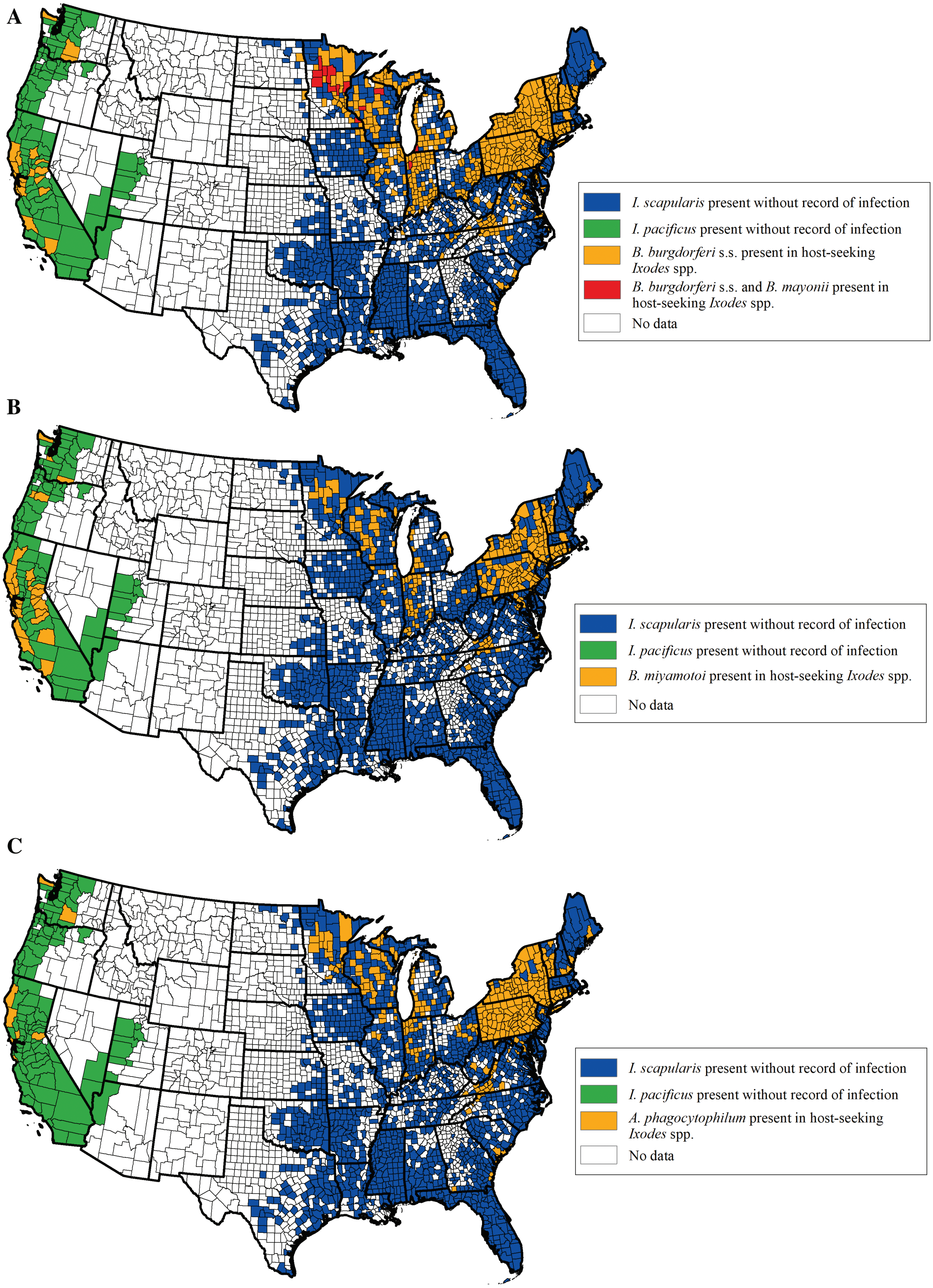

Fig. 1. Reported county-level distribution of bacterial pathogens (A) *B. burgdorferi* s.s. and *B. mayonii*, (B) *B. miyamotoi*, and (C) *A. phagocytophilum* (strain not differentiated), in host-seeking *I. scapularis* (eastern United States) or *I. pacificus* (western United States), relative to the previously reported distribution of these vector species. Ticks were considered present in a county if at least one tick was recorded (Eisen et al. [2016] or CDC [2021]). Counties where ticks have been reported without records of infection may be reported as such either if ticks were not tested or if the pathogen was not detected in tested samples.

was reported in all Connecticut and Pennsylvania counties, nearly all New York counties, and many counties in Indiana, Michigan, Minnesota, Wisconsin, and Vermont. *Anaplasma phagocytophilum* was reported also, albeit in fewer counties, in northern Illinois, southern New Hampshire, eastern Ohio, southern West Virginia, and southern Virginia. In several states where *B. burgdorferi* s.s.

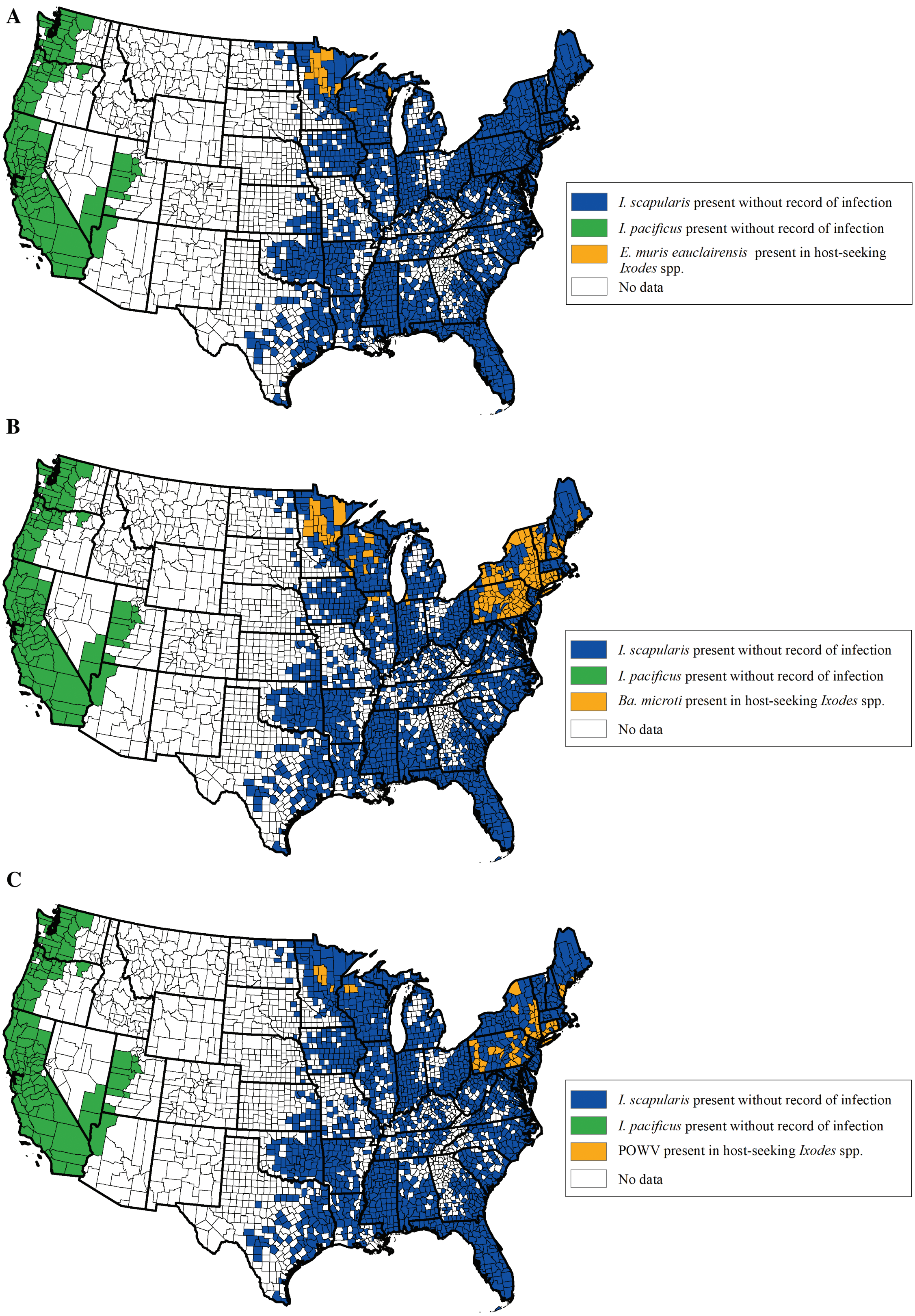

Fig. 2. Reported county-level distribution of (A) *Ehrlichia muris eauclairensis*, (B) *Babesia microti,* and (C) Powassan virus in host-seeking *Ixodes scapularis* (eastern United States) or *Ixodes pacificus* (western United States), relative to the previously reported distribution of these vector species. Ticks were considered present in a county if at least one tick was recorded (Eisen et al. [2016] or CDC [2021d]). Counties where ticks have been reported without records of infection may be reported as such either if ticks were not tested or if the pathogen was not detected in tested samples.

has been reported in *I. scapularis*, such as Louisiana, Massachusetts, North Dakota, South Dakota, and Tennessee, *A. phagocytophilum* was not found to be reported.

E. muris eauclairensis was the least commonly reported pathogen in this study. It was identified in *I. scapularis* in 11 counties in only two states: Minnesota (ten counties) and Michigan (one county) (Supp. Table 1E, Fig. 2A).

B. microti was present in *I. scapularis* in 154 counties in 17 states. The distribution of *Ba. microti*-infected ticks in our study mirrored that of *A. phagocytophilum*, except for in the western U.S., where *Ba. microti* was absent (Supp. Table 1F, Fig. 2B). States where *Ba. microti* was reported most commonly included Connecticut, Minnesota, New Hampshire, New York, Pennsylvania, and Vermont. Though the pathogen was reported in fewer counties per state, *Ba. microti* was also found in *I. scapularis* in Illinois, Maine, New Jersey, Virginia, and Wisconsin. Additionally, *Ba. microti* was found to be present in one county in each of the following states: Indiana, Massachusetts, Michigan, and Rhode Island. *Ba. microti* was not found in any states south of Virginia.

POWV was found in only 55 counties, primarily in the Northeast and Upper Midwest US. Specifically, POWV was reported in Connecticut, Maine, New York, and Pennsylvania in the Northeast, and Minnesota and Wisconsin in the Midwest (Supp. Table 1G, Fig. 2C).

Based on additional ArboNET submissions representing public health tick surveillance, we added 72 and two county records for *B. burgdorferi* s.s. and *B. mayonii* to recently published maps (Fleshman et al. 2021), bringing the totals to 476 and 12 counties, respectively. Additional *B. burgdorferi* s.s. records were primarily from the Midwest, including Illinois, Indiana, Michigan, and Ohio. *Borrelia burgdorferi* s.s. has now been detected in 30 of 41 (73.2%) states where vector ticks are known to be present. *Borrelia mayonii* was detected in host-seeking *I. scapularis* in one county each in Indiana and Michigan, bringing the total number of states where the pathogen has been identified to four (Indiana, Michigan, Minnesota, Wisconsin).

Discussion

Here, we present the first county-level maps of the reported distributions of *B. miyamotoi*, *A. phagocytophilum*, *E. muris eauclairensis*, *Ba. microti*, and POWV in host-seeking *I. scapularis* or *I. pacificus* ticks in the contiguous U.S. We found reported distributions of each of these pathogens to be more limited than the distributions of vector ticks or the distribution of the Lyme disease spirochete, *B. burgdorferi* s. s. (Eisen et al. 2016, Fleshman et al. 2021). While the data reported here are an important first step in defining the geographic distribution of *Ixodes* spp.-associated human pathogens, we recognize the reported distributions are incomplete. Each of the pathogens were detected within the same geographic foci as *B. burgdorferi* s. s., and some appear to be more widespread (e.g., *A. phagocytophilum*, *B. miyamotoi*, *Ba. microti*) than others (*E. muris eauclairensis*, POWV). All seven pathogen distributions were more limited than the distributions of vector ticks, with at least one of the seven pathogens detected in 30 of 41 states (73.2%) where vector ticks are considered to be established. While some pathogens may indeed be more geographically limited than others, the reported distributions may differ, in part, because testing efforts were not uniform across counties or years. Pathogens that occur at lower prevalence in ticks or that were discovered more recently are more likely to be under-represented due to detection bias. Additionally, biological and ecological differences in transmission efficiency may limit pathogen distribution and prevalence in ticks.

The geographic range of counties where *B. miyamotoi* was reported was concordant with the distribution of Lyme spirochetes reported in host-seeking ticks, with the majority of reported counties clustered in northeastern and upper midwestern states in *I. scapularis*, and northern and coastal California in *I. pacificus* (Fleshman et al. 2021). Overall, the reported range of *B. miyamotoi* is more limited than the reported distribution of *B. burgdorferi* s.s., which may be due to relatively limited *B. miyamotoi* testing or detection in host-seeking *I. scapularis* and *I. pacificus* ticks. *B. miyamotoi* infection prevalence estimates in host-seeking *I. scapularis* or *I. pacificus* nymphs and adults are consistently low across areas surveyed, with infection prevalence generally ranging from 1 to 2% (Lehane et al. 2021). By contrast, prevalence of *B. burgdorferi* s.s. in nymphs and adults is more geographically variable, but in Lyme disease-endemic areas, is commonly in the 10–15% and 20–60% range, respectively (Lehane et al. 2021). As a result, testing of larger numbers of ticks to detect *B. miyamotoi* is needed compared with *B. burgdorferi* s.s. The reported low prevalence of *B. miyamotoi* infection in host-seeking ticks may be due to biological factors such as transmission efficiency from hosts to feeding ticks and maintenance of spirochete infection in ticks. While *B. miyamotoi* spirochetes have been shown to be transovarially transmitted from adult *I. scapularis* females to their offspring (which might lead to the expectation of higher prevalence of infection in tick populations) (Scoles et al. 2001, Breuner et al. 2018), recent studies suggest that natural infection in immune-competent reservoir hosts may be transient, and that *B. miyamotoi* is not efficiently maintained transstadially (Lynn et al. 2019). Nonetheless, transovarial transmission and limited reliance on amplifying hosts might suggest the pathogen should have a wide geographic distribution within vector ticks.

Although *B. miyamotoi* disease is not a nationally notifiable condition and human disease frequency is unknown, previous studies have demonstrated that the risk of human exposure to *B. miyamotoi*-infected ticks is geographically widespread (Crowder et al. 2014, Wagemakers et al. 2015, Lehane et al. 2021, Porter et al. 2021). Utilizing tick surveillance as a risk metric is especially important in the absence of human case-based surveillance data. Similar rates of *B. miyamotoi* infection reported by both passive and active tick surveillance methods (Lehane et al. 2021, Porter et al. 2021, Xu et al. 2021) suggest that infection prevalence in ticks collected from people may be a comparable metric to estimate regional prevalence rates of *B. miyamotoi* in host-seeking ticks. While passive surveillance data do not provide the geographic specificity or granularity of active surveillance data, they may offer useful estimates of pathogen infection prevalence in ticks at the regional level, which is helpful to direct public health action. In addition, passive tick surveillance data may be useful in guiding site selection for active tick surveillance activities.

While counties, where *A. phagocytophilum* was reported, were more limited in the western U.S., in the eastern U.S., its distribution was concordant with that of *B. burgdorferi* s.s. in *I. scapularis* (Fleshman et al. 2021). Both *B. burgdorferi* s. s. and *A. phagocytophilum* are reported from the northeastern, mid-Atlantic, and upper-midwestern U.S., but the distribution of *A. phagocytophilum* is more limited in the southern extent of those regions compared with *B. burgdorferi* s.s., particularly in southern Illinois, Indiana, and Ohio in the Midwest, and Virginia and West Virginia in the mid-Atlantic. Though human anaplasmosis is reported in 37 states, consistent with the reported distribution of *A. phagocytophilum* in *I. scapularis*, most cases are reported from eight northeastern and upper midwestern states where *I. scapularis* is endemic: Connecticut, Massachusetts, Maine, Minnesota, New Hampshire, New York, Vermont, and

Wisconsin. Anaplasmosis cases have been reported in other parts of the U.S., such as southeastern and south-central states, where the pathogen has not been reported in host-seeking ticks (CDC 2021b). Many areas where *A. phagocytophilum* has not been reported are along the leading edge of the geographic ranges of *I. scapularis* and *I. pacificus*, suggesting a potential time lag between establishment of *B. burgdorferi* s.s.-infected tick populations and the establishment of *A. phagocytophilum* (Hamer et al. 2014). However, absence of *A. phagocytophilum* in ticks may also be a result of limited surveillance in those areas, rather than a true absence of the pathogen. Additionally, some reported anaplasmosis cases in southeastern and south-central U.S. may be due to patient travel to states with documented endemic *A. phagocytophilum* transmission or misdiagnosis of anaplasmosis due to serologic test cross-reactivity (Comer et al. 1999, Walls et al. 1999) in patients infected with other rickettsial pathogens, such as *Ehrlichia chaffeensis*, or *Ehrlichia ewingii*, transmitted by ticks common in the region such as the lone star tick, *Amblyomma americanum*.

While the distribution of the pathogen in host-seeking ticks and the distribution of human disease cases are expansive, the prevalence of *A. phagocytophilum*, as reported in other studies (Prusinski et al. 2014, Diuk-Wasser et al. 2016, Johnson et al. 2018, Lehane et al. 2021), seems to be low in *I. scapularis* and *I. pacificus* ticks compared to the prevalence of *B. burgdorferi* s.s. in ticks. Lehane et al. (2021) found the highest prevalence of *A. phagocytophilum* infection in *I. scapularis* ticks in the northeastern U.S., at 5.76% for nymphs and 8.07% for adults, whereas the prevalence of *B. burgdorferi* s.s. in that region was 21.26% in nymphs and 58.04% in adults. Interestingly, when infection rates were summarized on a global scale, Karshima et al. (2022) found the global prevalence of *A. phagocytophilum* in questing and host-attached ticks to be 4.76%, remarkably similar to prevalence rates reported in the US. Low prevalence of *A. phagocytophilum* in ticks may be a result of the relatively short-lived infection of *A. phagocytophilum* maintained in reservoir hosts, such as the common reservoir, the white-footed mouse (*Peromyscus leucopus*) (Telford et al. 1996, Stafford et al. 1999, Levin and Ross 2004). Additionally, most pathogen assays reported here did not distinguish between the rodent-associated, human disease-causing variant of *A. phagocytophilum* (ha-variant), and the deer-associated variant, *A. phagocytophilum* (v1), that is not known to be pathogenic to humans. Although the strains generally co-occur geographically (Massung et al. 2002, Courtney et al. 2003), the distribution of human pathogenic *A. phagocytophilum* reported in this study may be inflated.

The reported distribution of *E. muris eauclairensis*, the most recently identified and geographically focal human pathogen in *I. scapularis*, was limited to 10 counties in Minnesota and one county in Michigan. Since the discovery of the pathogen in 2009 (Pritt et al. 2011), *E. muris eauclairensis* has been detected only in *I. scapularis* in the upper midwestern U.S. (Johnson et al., 2018). However, given the limited duration of surveillance for this pathogen, the number of counties reporting its prevalence is quite likely an underestimate. *E. muris eauclairensis* is nationally notifiable as "undetermined human ehrlichiosis" (Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System, 2021), and thus, information on the distribution of human cases attributable to *E. muris eauclairensis*, versus *E. chaffeensis* or *E. ewingii* (spread by different vectors), is also limited. However, a blood sample analysis of 75,007 patients collected from 2004 to 2013 from 50 states found that samples from only 69 patients (0.1%) were positive for *E. muris eauclairensis* by real-time PCR. All positive samples were from patients from five states (Indiana, Michigan, Minnesota, North Dakota, Wisconsin) and a majority (93%) were from Minnesota and Wisconsin (Dahlgren et al. 2016). These data indicate that the current distribution of *E. muris eauclairensis* is localized in the upper Midwest, suggesting the pathogen possibly evolved in midwestern *I. scapularis* populations that were geographically isolated from populations in the northeastern and southeastern U.S. during the Pleistocene glacial period (Spielman 1988). The tick populations were geographically isolated until very recently (Eisen et al. 2016). Given the low prevalence of *E. muris eauclairensis* in ticks, suggesting a low force of infection, the rate of spread beyond the upper Midwest is expected to be slow. While the risk of encountering *E. muris eauclairensis* appears limited to areas in the upper midwestern U.S., additional research is needed to better define the ecological niche of *E. muris eauclairensis* and predict the extent of potential range expansion.

We found that the distribution of counties where *Ba. microti* has been reported in *I. scapularis* (no reports of *Ba. microti* were found in *I. pacificus*) was more limited than the distribution of *B. burgdorferi* s.s. (Fleshman et al. 2021), with fewer counties reporting its presence in several upper midwestern states along the leading edge of *I. scapularis* expansion (Illinois, Indiana, Michigan, and Ohio), despite substantial pathogen testing efforts in the region (Lehane et al. 2021). Counties where *Ba. microti* was reported largely mirrored the distribution of reported human cases of babesiosis, except for several counties in the southeastern U.S., where babesiosis cases have been reported with no supportive data showing *Ba. microti* infection in ticks (CDC 2021d). Again, reported cases of babesiosis in the southeastern U.S. may be attributable to travel exposures, but enhanced tick surveillance may be justified in counties where babesiosis cases without plausible travel exposures are reported but where infection records in ticks are lacking. In 2019, babesiosis was a reportable disease in 40 states with at least one case of babesiosis reported in 25 states (215 counties), but most cases were reported in seven states in the Northeast and Upper Midwest US (Connecticut, Massachusetts, Minnesota, New Jersey, New York, Rhode Island, and Wisconsin). All 36 counties with the highest numbers of reported cases of babesiosis were in the Northeast where reports of *Ba. microti* in *I. scapularis* were common (CDC 2021d). From 2011 to 2019, there has been an increasing trend in reported cases of babesiosis, accounting for a >2-fold rise (1,126 cases in 2011, to 2,418 cases in 2019) in the U.S. However, in states where babesiosis cases were reported, case incidence remains low, ranging from less than 0.1 per 100,000 persons to 14.9 per 100,000 in Rhode Island in 2019 (CDC 2021d). In *I. scapularis* ticks, Lehane et al. (2021) noted comparably low infection rates of *Ba. microti*, at 5.69% in nymphs and 3.53% in adults in the Northeast, and 2.46% in nymphs and 0.29% in adults in the Midwest.

Previous studies have reported that *I. scapularis* are frequently coinfected with *Ba. microti* and *B. burgdorferi* s. s. and have suggested that tick infection with *B. burgdorferi* s. s. may contribute to the emergence and establishment of *Ba. microti* (Dunn et al. 2014). Thus, it is perhaps not surprising that in every county where *Ba. microti* was reported, *B. burgdorferi* s. s. has also been reported (Fleshman et al. 2021). However, the low prevalence of *Ba. microti* in *I. scapularis* ticks (Lehane et al. 2021) and more limited reported geographic distribution of host-seeking ticks and human cases may be partially due to *Ba. microti* being less efficiently maintained in nature compared with *B. burgdorferi* s. s.. Studies have documented that, although the common reservoir, *Peromyscus leucopus*, can maintain *Ba. microti* infections for long periods of time (Spielman et al. 1981, Mather et al. 1990, Telford et al. 1997), reservoir competence is less efficient than it is for *B. burgdorferi* s.s., and transstadial survival of *Ba. microti* in *I. scapularis* is lower (Mather et al. 1990, Hersh et al. 2012, Dunn et al. 2014). Additionally, reservoir competence (as measured by the number of feeding ticks infected by a *Ba. microti*-infected host) of several common *I. scapularis* hosts including, but not limited to white-footed mice, eastern chipmunks, and short-tailed shrews, is lower for *Ba. microti* than for *B. burgdorferi* s.s. (Hersh et al. 2012).

We found that the reported distribution of POWV in *I. scapularis*, though limited, largely overlapped the geographically focal and restricted range where human POWV disease cases have been reported. Whereas human POWV cases have now been reported in 14 total states (Connecticut, Indiana, Massachusetts, Maine, Minnesota, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Pennsylvania, Rhode Island, Virginia, and Wisconsin) (CDC 2017, 2021c, Hassett et al. 2021), we found reports of POWV in *I. scapularis* in only six states across two regions- Minnesota and Wisconsin in the midwestern U.S., and Connecticut, Maine, New York, and Pennsylvania in the northeastern U.S. Although the number of human neuroinvasive POWV cases has increased from eight cases in 2010 to 39 cases in 2019, the average annual incidence of POWV by county remains low (CDC 2017). Similarly, the prevalence of POWV reported in host-seeking *I. scapularis* is also low. Aliota et al. (2014) found POWV in less than 4% of host-seeking *I. scapularis* adults in New York, and Johnson et al. (2018) found POWV in less than 1% of host-seeking *I. scapularis* nymphs in Minnesota. Despite a seemingly geographically focal range, our understanding of the geographic distribution of POWV in ticks is limited by various factors, including the small number of jurisdictions and agencies actively testing for the virus (within CDC databases, we identified only 53 counties in three states reporting any testing data) and the few published county-level records of POWV in *I. scapularis* or *I. pacificus* ticks (only seven total articles identified in our SCOPUS review). Powassan virus is transmitted transovarially and transstadially in nature (Costero and Grayson 1996), suggesting that the low reported prevalence in field-collected ticks and geographic focality may be influenced by factors such as transmission dynamics and vector-host relationships. The influence of cofeeding transmission (where aggregated infected ticks transmit the virus to closely feeding uninfected ticks) in the focality of POWV is yet to be determined but is a hallmark of tick-borne encephalitis virus (TBEV), a flavivirus closely related to POWV, transmission in Europe (Labuda et al. 1993). Additionally, more study is needed to elucidate the ecology of POWV in the US. In Europe, TBEV vectored by *Ixodes ricinus*-complex ticks, is associated with burrowing rodents such as voles. In the U.S., common hosts for *I. scapularis*, such as the white-footed mouse (*P. leucopus*) and the eastern chipmunk (*Tamias striatus*), have yet to be definitively implicated as reservoirs for the virus, suggesting that shrews, such as the Northern short-tailed shrew (*Blarina brevicauda*) (Goethert et al. 2021) and/or other burrowing rodent species (Hassett et al. 2021), may be alternative reservoirs.

While the tickborne pathogen distribution maps presented here likely under-represent the true distributions of these pathogens, they provide initial assessments of known county pathogen distributions at a national scale and serve as an important starting point to identify counties where enhanced surveillance may be justified. It is important to note from our review that in counties where tickborne pathogen data are lacking we cannot assume that the seven pathogens addressed are not present in host-seeking *Ixodes* ticks, but rather, additional substantive efforts are required to collect and test ticks to confirm presence or absence. The summary data presented here may also be limited due to our strict inclusion criteria, requiring all pathogens to be tested and verified using species-specific methods and pathogen testing results to be reported by county of tick collection. Additionally, because we did not evaluate pathogen prevalence and considered counties where at least one tick was reported to be positive for a pathogen as "present," it should be noted that acarological risk for a pathogen varies and is dependent upon infection prevalence and host-seeking tick densities (Mather et al. 1996, Pepin et al. 2012, Hahn et al. 2018). As tickborne diseases continue to emerge in the U.S., prevention and diagnosis rely on an accurate understanding by the public and health care providers of when and where people are at risk for exposure to infected ticks (Eisen and Paddock 2021). Our county-level pathogen summary maps display the known distribution of human pathogens spread by *Ixodes* spp. ticks and complement previous maps showing the distribution of Lyme disease spirochetes (Fleshman et al. 2021). However, we recognize these maps represent incomplete distributions of the pathogens and highlight counties where further investigation may be warranted.

Supplementary Data

Supplementary data are available at *Journal of Medical Entomology* online.

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