



Tick-Borne Infections Council
of North Carolina, Inc.



NEWSLETTER 2024, Volume 3

Quotes: “The rapid evolution of Lyme disease risk in North Carolina over the past decade poses a substantial threat to public health, especially as many of the most highly impacted areas also experience limited access to health services. Urgent efforts are needed to raise public awareness and educate medical providers in order to prevent excess morbidity.” Neha V. Mokashi, et al., Spatiotemporal patterns of Lyme disease in North Carolina: 2010-2020, *The Lancet Regional*.

Highlights:

- **Spatiotemporal patterns of Lyme disease in North Carolina: 2010-2020**
- **Rickettsiosis in Kidney Transplant Recipient, North Carolina, USA, 2023**
- **Microbiome of *Haemaphysalis longicornis* in North Carolina, USA, 2024**
- **Incomplete Feeding Behaviors among South Carolina Ticks, USA, 2022**
- **Mapping Lyme Disease Distribution in the Mid-Atlantic United States using HER, 2008-2016**
- ***Borrelia burgdorferi* 0755, a Novel Cytotoxin with Unknown Function in Lyme Disease**
- **Evidence of Incomplete Feeding Behaviors among South Carolina Tick Populations**
- **Asian longhorned tick now in Mecklenburg County, VA**
- **Time Magazine report on chronic Lyme disease, May 16, 2024**
- **CDC recognizes a new Rickettsia**
- **Unknown genetic variant, rs1061632 associated with enhanced LB susceptibility**
- **Lyme induced pancreatitis**
- **Completion of primary vaccine series in Lyme disease vaccine Phase 3 Trial**

Vectorborne Disease Working Group (VBWG) meeting dates for 2024:

A zoom meeting was held on July 24, 2024. No further information from the meeting has been posted for those who could not attend.

Information sent to the Working Group prior to the July Zoom meeting. Hello Vector Borne and Zoonotic Working Group

We are working to organize our first (virtual) VBWG meeting since the onset of the COVID-19 pandemic, potentially in July; stay tuned for details.

In the meantime, there are a number of updates here at DHHS and happening across the US with respect to vector-borne diseases. Here are a few:

- **Tick Distribution and Tick-borne Disease Dashboard:** In September, we released our Tick Distribution and Tick-borne Disease dashboard. The dashboard illustrates the distribution of disease-causing ticks, by county, as submitted through the NC Tick Identification Program; it is updated quarterly. You can see the distribution of ticks in North Carolina along with the distribution of human vector-borne disease events here: <https://epi.dph.ncdhhs.gov/cd/ticks/figures.html>
- **Vector-Borne Disease Surveillance Summaries:** Each year, we release our vector-borne disease surveillance summaries, which highlight changes in both state and national trends in vector-borne disease. You can find the 2023 surveillance summaries for [ehrlichiosis](#), [spotted fever group rickettsiosis](#), [Lyme disease](#), and the 2012-2023 report for [West Nile virus](#) here: <https://epi.dph.ncdhhs.gov/cd/ticks/figures.html> and here: <https://epi.dph.ncdhhs.gov/cd/figures.html>
- **VectorSurv Mosquito Surveillance:** The public can now see North Carolina county-based mosquito arbovirus testing results (West Nile virus (WNV), La Crosse (LAC), and eastern equine encephalitis (EEE)), invasive species ranges, and dengue risk. NC-Surv users can also access mosquito abundance, WNV risk, Insecticide resistance results on the new VectorServ platform. Data are updated by each individual county and the State Laboratory of Public Health (SLPH) as they become available: <https://maps.vectorserv.org/arbo>.
- **New Publications:** We continue to leverage collaborations with our university partners to further vector-borne disease surveillance throughout North Carolina. Here are a few recent publications we have co-authored with university partners:
 - [Persistent spatial clustering and predictors of pediatric La Crosse virus neuroinvasive disease risk in eastern Tennessee and western North Carolina, 2003–2020](#). June 2024
 - [Spatiotemporal evolution of Lyme disease in North Carolina: 2010 to 2020](#). May 2024
 - [Don't Go Chasing Waterfalls: Increased Collection of Medically Relevant Ticks Further Away from Hiking Trails in the Piedmont of North Carolina](#). May 2024

- Endemic La Crosse Virus Neuroinvasive Disease in North Carolina Residents: 2000–2020. May 2024
- Delayed diagnosis of locally acquired Lyme disease, central North Carolina, USA. March 2024
- Development of novel compact wind tunnel for testing efficacy of insecticide formulated products in mosquitoes. February 2024
- **Longicornis Tick Blitz:** From this past summer: The University of Tennessee in collaboration with the USDA is conducting a two-week tick blitz across the nation. Participants are asked to drag/flag/collect ticks and send them to approved laboratories for identification. All ticks will eventually be identified, but the main goal is the identify the presence and distribution of the longhorned tick *Haemaphysalis longicornis*.

Link to Notice to Medical Providers from the State Department of Public Health on Lyme Disease and Rickettsial Diseases: “Annual Update on Diagnosis and Surveillance for Tickborne Diseases”

The state has started issuing only one memo titled “Clinician Memo.” Please see the right side of the homepage on our website (www.tic-nc.org) to access.
 To look at the (state) NCDHHS’s tick data, go to epi.dph.ncdhhs.gov/cd/diseases/ticks.html.

Case data for Lyme disease from the CDC for North Carolina

Year	Cases
2019	334
2020	264
2021	338
2022	279

<https://www.cdc.gov/lyme/datasurveillance/surveillance-data.html>

Links to access Lyme and other tick-borne infections data from the CDC.

<https://www.cdc.gov/lyme/datasurveillance/surveillance-data.html>

Annual incidence. <https://www.cdc.gov/lyme/datasurveillance/surveillance-data.html>

https://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp

<https://www.cdc.gov/lyme/datasurveillance/maps-recent.html>



Where To Find CDC Case Definitions and their Statement that the Surveillance Case Definitions Are “not to be used as the sole criteria for establishing critical diagnosis”

Case Definition and Report Forms

The surveillance definition of Lyme disease was revised in January 2022.

See https://www.cste.org/resource/resmgr/ps/ps2021/21-ID-05_Lyme_Disease.pdf for the rationale behind the changes.

- ndc.services.cdc.gov/case-definitions/lyme-disease-2022/
- www.cdc.gov/lyme/resources/lymediseasereportform.pdf (for public health officials' use)
- **Note from the CDC:** *The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.* Accessed and copied Nov16, 2022 at <https://ndc.services.cdc.gov/case-definitions/lyme-disease-2022/>.

The surveillance definition of Rocky Mountain spotted fever/spotted fever rickettsiosis was revised in 2020.

- ndc.services.cdc.gov/case-definitions/spotted-fever-rickettsiosis-2020/

The Southeast Regional Center of Excellence in Vector-Borne Disease (SECVBD) will continue its vital work for another five years, thanks to renewed funding from the Centers for Disease Control and Prevention (CDC). See TIC-NC Newsletter Vol 2, 2023 for more details.

<https://physician-news.umiamihealth.org/cdc-renews-funding-for-study-of-vector-borne-diseases/>

From the CDC: Announcements

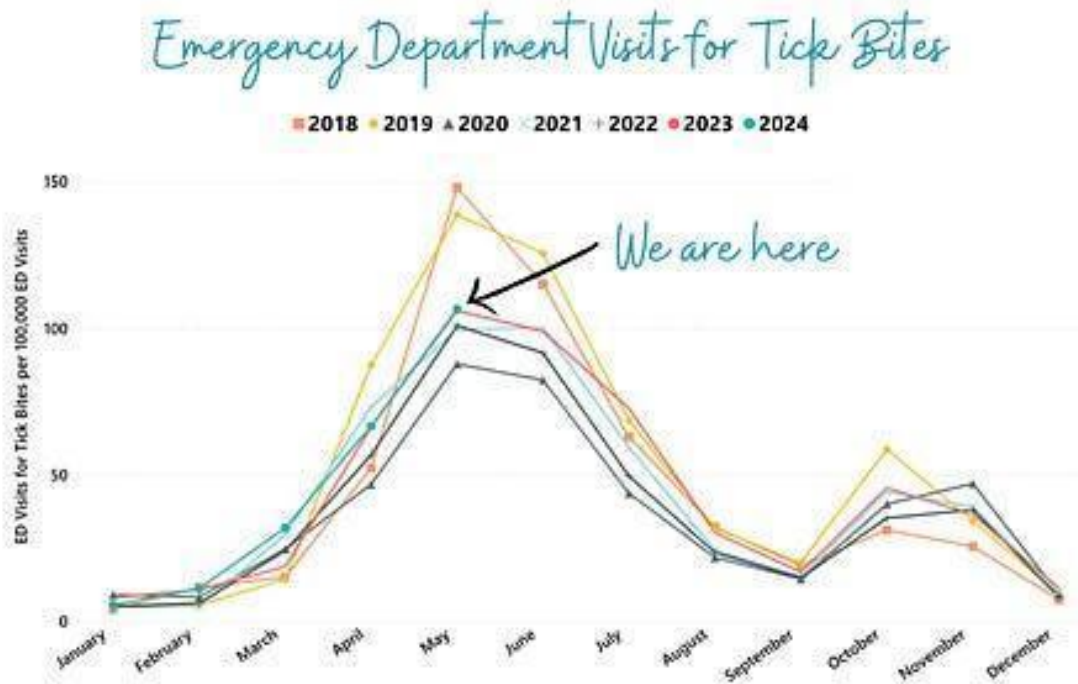
VBD National Strategy to Protect People

- **The Problem:**

Vector-borne diseases (VBDs) increasingly threaten the health and well-being of people in the United States, with reported cases doubling over the last two decades. Yet the United States is not adequately prepared to respond to these threats.

Vectors—biting insects and arachnids like mosquitoes, ticks, fleas, and lice—can spread germs that make people sick. These diseases are major causes of death and illness worldwide. More action is needed to protect people from VBDs.

- **A Coordinated Approach:** for entire report see: <https://www.cdc.gov/nceid/dvbd/framework.html>



CDC recognizes a new *Rickettsia*

Newly Recognized Spotted Fever Group *Rickettsia* as Cause of Severe Rocky Mountain Spotted Fever–Like Illness, Northern California, USA

The incidence of spotted fever group (SFG) rickettsioses in the United States has tripled since 2010. Rocky Mountain spotted fever, the most severe SFG rickettsiosis, is caused by *Rickettsia rickettsii*. The lack of species-specific confirmatory testing obfuscates the relative contribution of *R. rickettsii* and other SFG *Rickettsia* to this increase. We report a newly recognized rickettsial pathogen, *Rickettsia* sp. CA6269, as the cause of severe Rocky Mountain spotted fever–like illness in 2 case-patients residing in northern California. Multilocus sequence typing supported the recognition of this pathogen as a novel *Rickettsia* genotype most closely related to *R. rickettsii*. Cross-reactivity observed for an established molecular diagnostic test indicated that *Rickettsia* sp. CA6269 might be misidentified as *R. rickettsii*. We developed a *Rickettsia* sp. CA6269–specific real-time PCR to help resolve this diagnostic challenge and better characterize the spectrum of clinical disease and ecologic epidemiology of this pathogen. Probert WS, et al. Emerg Infect Dis. 2024 Jul doi.org/10.3201/eid3007.231771.

State tick research and/or reports

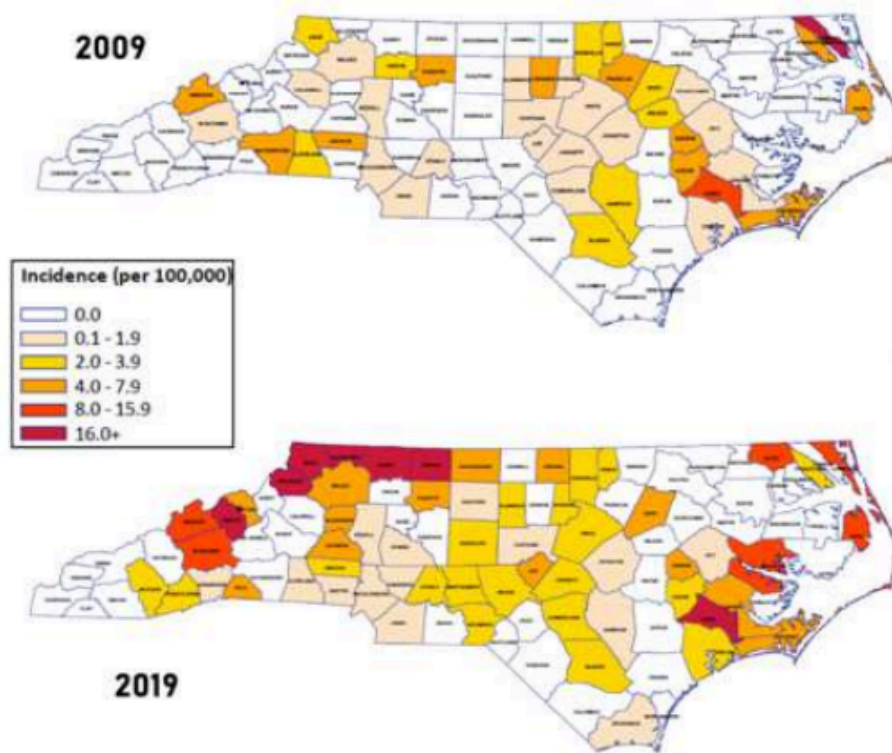
Vectorborne and Zoonotic Working Group

The 2023 tick borne disease surveillance summaries are now complete. You can view them at the bottom of the NC DHHS Epi Section Facts & Figures page, under **Vector**.

<https://epi.dph.ncdhhs.gov/cd/lyme/LymeSurveillanceSummary2023.pdf>

<https://epi.dph.ncdhhs.gov/cd/rmsf/RMSFSurveillanceSummary2023.pdf>

Figure 6. Maps of 2009 and 2019 of LD cases in North Carolina showing a shift in the geographical distribution of confirmed and probable LD cases from a more eastern-central distribution to a clear cluster in northwestern counties of North Carolina (NC Division of Public Health, 2019).



Report from the State or Vectorborne Disease Work Group meeting

A Zoom meeting was held on July 24, 2024, the first since the beginning of the pandemic.

TIC-NC Activities

Screening of *The Quiet Epidemic* in Durham, NC
November 14, 2023



TIC-NC Talks and Materials Distributed

Link to the panel discussion following the showing of *The Quiet Epidemic* in Durham, NC last year.

<https://youtu.be/yx36rguaAYA>

TIC-NC and Denise Spector co-sponsored the screening of *The Quiet Epidemic* at the Carolina Theatre, Durham, NC on November 14, 2023. The film is an award-winning documentary on Lyme disease. The panel following the meeting featured David Alcorta, PhD, Ed Breitschwerdt, DMV, Marcia Herman-Giddens, DrPH, and Bill Rawls, MD. The film's co-directors are Lindsay Keys and Winslow Crane-Murdoch. See TIC-NC's newsletter, Vol 4, p9 for more description.



TICKS! Speaker Event at Durham County Library, July 16, 2024

TIC-NC and the Durham County Library held a presentation on ticks and tick-borne diseases as part of the Durham County Library's "Who, What, Where, When, and Why?" speaker series on July 16th, 2024. The speaker series aims to educate the public on misunderstood or notorious animals native to North Carolina, and this event saw over 40 people in attendance. Dr. Marcia Herman-Giddens, the Scientific Advisor for TIC-NC, presented and led a discussion on the ubiquity of ticks in the environment, the extent of tick-borne diseases in North Carolina, and the challenges to tick-borne infection diagnosis.



From the Center for Lyme Action lymedisease.org

House Appropriations Committee approves Lyme-related funding increases By Bonnie Crater, Center for Lyme Action

...Last week [early July], the House Appropriations Committee approved the Fiscal Year 2025 Department of Labor, Health and Human Services Appropriations (L-HHS) bill and provided descriptions of programs with significant new report language.

While the overall FY25 bill is \$8.6B lower than FY24, our Lyme and tick-borne disease (TBD) funding levels continue to grow. In a year of overall lower funding, this is a big win.

...p.62 **Southern Tick Associated Rash Illness** — The Committee directs CDC to publicly release a report on Southern Tick Associated Rash Illness (STARI) including its prevalence, the tick-vector or vectors causing STARI, and the progress in identifying the causative pathogen of STARI or any suspected non-infectious disease-causing mechanism. The Committee directs CDC to provide a briefing to the Committee on this topic within 180 days of the enactment of this Act.

Tick Borne Diseases External Engagement — The Committee strongly encourages CDC to establish a panel of expert outside stakeholders to evaluate and review the Lyme disease information on its website for its inclusion of a balance of scientifically valid perspectives, primarily regarding the state of the science for diagnostics and treatments. The stated goals and purposes of the review and the identity of review participants, including the balanced panel of experts, including experienced TBD clinicians, researchers, and educators, should be fully transparent.

TIC-NC ed note: There are no data on the prevalence of STARI as without a test for it and the symptoms sometimes or often being misdiagnosed as Lyme disease, along with victims often not finding or keeping the tick that caused their symptoms, and other factors. We do not think there is a specific ICD code for STARI. An online search found : SNOMEDCT: 444100007 – Southern tick-associated rash illness. “SNOMED CT, or Systematized Nomenclature of Medicine Clinical Terms, is a multilingual clinical terminology system that helps with the electronic exchange of health information.” We have no information on exactly how this is used or if it is ever used.

For further details see: <https://www.lymedisease.org/lyme-funding-update-fy25/>

North Carolina and the South

Spatiotemporal patterns of Lyme disease in North Carolina: 2010-2020

Lyme disease is the most common vector-borne disease in the United States with the majority of cases occurring in the Northeast, upper Midwest, and mid-Atlantic regions. While historically considered a low incidence state, North Carolina (NC) has reported an increasing number of cases over the past decade. Therefore, the aim of this study was to characterize the spatiotemporal evolution of Lyme disease in NC from 2010 to 2020.

Confirmed and probable cases reported to the NC Division of Public Health without associated travel to high-transmission state were included in the analysis. The study period was divided into four sub-periods and data were aggregated by zip code of residence. The absolute change in incidence was mapped and spatial autocorrelation analyses were performed within each sub-period.

We identified the largest absolute changes in incidence in zip codes located in northwestern NC along the Appalachian Mountains. The spatial distribution of cases became increasingly clustered over the study period (Moran's I of 0.012, $p = 0.127$ in 2010–2012 vs. 0.403, $p < 0.0001$ in 2019–2020). Identified clusters included 22 high-incidence zip codes in the 2019–2020 sub-period, largely overlapping with the same areas experiencing the greatest absolute changes in disease incidence.

Lyme disease has rapidly emerged in northwestern NC with some zip codes reporting incidence rates similar to historically high incidence regions across the US Northeast, mid-Atlantic, and upper Midwest. Efforts are urgently needed to raise awareness among medical providers to prevent excess morbidity. Mokashi NV, et al. *The Lancet*,

[www.thelancet.com/journals/lanam/article/PIIS2667-193X\(24\)00119-4/fulltext](http://www.thelancet.com/journals/lanam/article/PIIS2667-193X(24)00119-4/fulltext).

Funding was provided by a “Creativity Hub” award from the UNC Office of the Vice Chancellor for Research. Additional support was provided by Southeastern Center of Excellence in Vector Borne Diseases (U01CK000662).

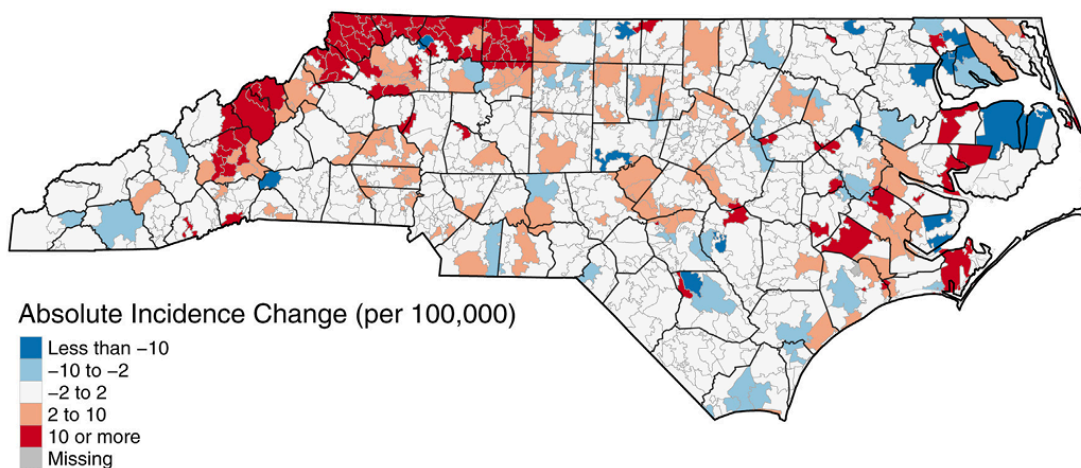


Fig. 4: Absolute change in the incidence of reported confirmed and probable cases of Lyme disease between the first (2010–2012) and most recent (2019–2020) sub-periods.

[https://www.thelancet.com/journals/lanam/article/PIIS2667-193X\(24\)00119-4/fulltext](https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(24)00119-4/fulltext)

***Rickettsia parkeri* Rickettsiosis in Kidney Transplant Recipient, North Carolina, USA, 2023**

Spotted fever rickettsiosis in solid organ transplant recipients is rarely described, and all reports document disease acquired months to years after the transplant, after recognized tick bites or exposures to tick-infested habitats (1–4). In the United States, *Rickettsia parkeri* rickettsiosis is a tickborne infection transmitted by the Gulf Coast tick (*Amblyomma maculatum*) that results in a disease similar to but milder than Rocky Mountain spotted fever. Human infection with *R. parkeri* was first described in 2004 (5). We report a case of *R. parkeri* rickettsiosis in a kidney transplant recipient in North Carolina, USA, during the immediate posttransplant period. Phadke GM, et al. *Emerging Infectious Diseases*. 2024;30(7):1459-1462. doi:10.3201/eid3007.240217.

Microbiome of Invasive Tick Species *Haemaphysalis longicornis* in North Carolina, USA

The Asian longhorned tick (ALHT), *Haemaphysalis longicornis*, is an invasive pest that threatens domestic livestock. Normally found in Asia and the Pacific islands, where it is a vector of human disease, this tick was reported for the first time in the United States in 2017. In this study, we collected *H. longicornis* ticks of different developmental stages and used bacterial 16S rDNA amplicon sequencing to examine their microbiome.

We identified numerous bacterial taxa, with *Coxiella*, *Sphingomonas*, *Staphylococcus*, *Acinetobacter*, *Pseudomonas*, *Sphingomonadaceae*, *Actinomycetales*, and *Sphingobium* as the most prevalent in the bacterial community. We documented a remarkable turnover in bacterial assemblage between life stages. These findings reveal important associations between life stages and their bacterial community and provide important insights to guide future research. Ponnusamy L, et al. *Insects* 2024, doi.org/10.3390/insects15030153.

Evidence of Incomplete Feeding Behaviors among South Carolina Tick Populations

Dynamic environmental conditions, such as climate change and host availability, have greatly influenced the expansion of medically relevant tick vectors into new regions throughout the southeastern United States of America. As tick populations migrate into new areas, it has been suggested they can exhibit a phenomenon known as incomplete feeding. With this phenomenon, tick vectors feed on more than one host at each life stage, thus increasing the likelihood of pathogen transmission. Although this behavior is not well understood, it presents an important threat to human health.

Here we present evidence of incomplete feeding behaviors in multiple tick species in South Carolina. Engorged, blood-fed female ticks were collected from feral dogs at animal shelters across South Carolina in 2022. All ticks were tested for human blood meals using rapid stain identification blood tests.

Approximately one third (33.78%) of all ticks tested positive for a human blood meal, with various patterns seen across species, geographic location, and collection month. The results of this pilot study follow the current national trend of increasing rates of tick-borne disease incidence in the southeastern United States of America and warrant further investigation into the relationship between seasonality, geographic distribution, species, and incomplete feeding among tick populations in South Carolina. Bramlett KE et al. *Insects* 2024, doi.org/10.3390/insects15060385.

Mapping the distribution of Lyme disease at a mid-Atlantic site in the United States using electronic health data

Lyme disease is a spatially heterogeneous tick-borne infection, with approximately 85% of US cases concentrated in the mid-Atlantic and northeastern states. Surveillance for Lyme disease and its causative agent, including public health case reporting and entomologic surveillance, is necessary to understand its endemic range, but currently used case detection methods have limitations. To evaluate an alternative approach to Lyme disease surveillance, we have performed a geospatial analysis of Lyme disease cases from the Johns Hopkins Health System in Maryland.

We used two sources of cases: a) individuals with both a positive test for Lyme disease and a contemporaneous diagnostic code consistent with a Lyme disease-related syndrome; and b) individuals referred for a Lyme disease evaluation who were adjudicated to have Lyme disease. Controls were individuals from the referral cohort judged not to have Lyme disease. Residential address data were available for all cases and controls. We used a hierarchical Bayesian model with a smoothing function for a coordinate location to evaluate the probability of Lyme disease within 100 km of Johns Hopkins Hospital.

We found that the probability of Lyme disease was greatest in the north and west of Baltimore, and the local probability that a subject would have Lyme disease varied by as much as 30-fold. Adjustment for demographic and ecological variables partially attenuated the spatial gradient. Our study supports the suitability of electronic medical record data for the retrospective surveillance of Lyme disease. Lantos PM, et al. PLoS ONE 19(5): e0301530.

<https://doi.org/10.1371/journal.pone.0301530>.

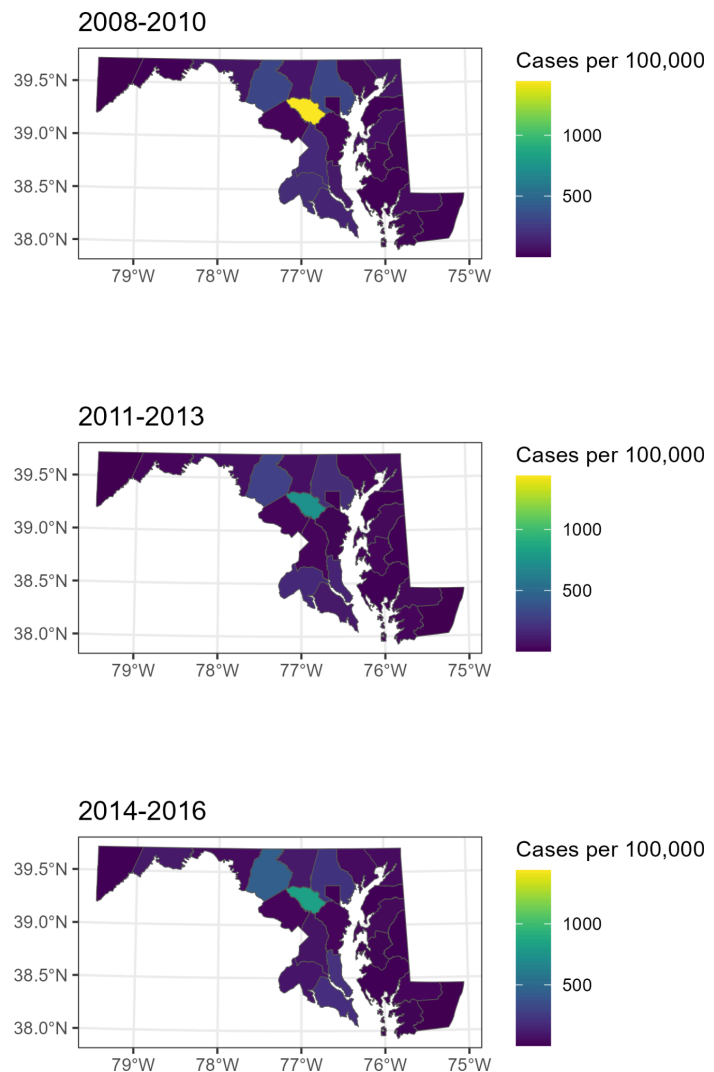


Fig 5. Maryland county-based Lyme disease incidence data from 2008–2016, divided into 3 year intervals.

Lyme disease case data comes from public health surveillance data from the Maryland Department of Health, and population data from the United States Census. The geographic distribution of Lyme disease remained relatively constant over the study period.

Asian longhorned tick now in Mecklenburg County, VA (on the NC border)

New report of *Haemaphysalis longicornis* (Ixodida: Ixodidae) in Mecklenburg County, Virginia from field collections

Haemaphysalis longicornis (Neumann) was first established in New Jersey and has rapidly spread across most of the eastern United States. This tick has the potential to infest a wide variety of hosts and can reproduce quickly via parthenogenesis, presenting a new threat to animal health.

Here we report the first record of a single *H. longicornis* tick in Mecklenburg County, Virginia, from incidental field collections of ticks. In addition to *H. longicornis*, we collected 787 *Amblyomma americanum*, 25 *Dermacentor variabilis*, 6 *Ixodes affinis*, 1 *Haemaphysalis leporispalustris*, and 1 *Amblyomma maculatum* using standard dragging and flagging techniques. The expansion of *H. longicornis* will have economic consequences for livestock producers in south-central Virginia, who must now manage this species. Enhanced surveillance is needed to fully understand its growing geographic distribution in the United States and the subsequent consequences of its spread. Adams, et al. *Journal of Medical Entomology*, <https://doi.org/10.1093/jme/tjae090>.

National Section

Time Magazine, May 16, 2024, report: <https://time.com/6974403/chronic-lyme-disease-research/>

Long Dismissed, Chronic Lyme Disease Is Finally Getting Its Moment
By Jamie Ducharme | Photographs by Jiatong Lu

***Borrelia burgdorferi* 0755, a Novel Cytotoxin with Unknown Function in Lyme Disease**

The pathophysiology of Lyme disease, especially in its persistent form, remains to be determined. As many of the neurologic symptoms are similar to those seen in other toxin-associated disorders, a hypothesis was generated that *B. burgdorferi*, the causative agent of Lyme disease, may produce a neurotoxin to account for some of the symptoms.

Using primers against known conserved bacterial toxin groups, and PCR technology, a candidate neurotoxin was discovered. The purified protein was temporarily named BbTox, and was subsequently found to be identical to BB0755, a protein deduced from the genome sequence of *B. burgdorferi* that has been annotated as a Z ribonuclease. BbTox has cytotoxic activity against cells of neural origin in tissue culture. Its toxic activity appears to be directed against cytoskeletal elements, similar to that seen with toxins of *Clostridioides*

difficile and *Clostridioides botulinum*, but differing from that of cholera and *E. coli* toxins, and other toxins.

It remains to be determined whether BbTox has direct cytotoxic effects on neural or glial cells in vivo, or its activity is primarily that of a ribonuclease analogous to other bacterial ribonucleases that are involved in antibiotic tolerance remains to be determined. Donta ST. *Toxins* 2024, 16(6), 233; <https://doi.org/10.3390/toxins16060233>.

The global distribution and the risk of prediction of relapsing fever group *Borrelia*: a data review with modeling analysis

The recent discovery of emerging relapsing fever group *Borrelia* (RFGB) species, such as *Borrelia miyamotoi*, poses a growing threat to public health. However, the global distribution and associated risk burden of these species remain uncertain. We aimed to map the diversity, distribution, and potential infection risk of RFGB.

We searched PubMed, Web of Science, GenBank, CNKI, and eLibrary from Jan 1, 1874, to Dec 31, 2022, ... to assess the environmental, ecoclimatic, biological, and socioeconomic factors associated with the occurrence of four major RFGB species: *Borrelia miyamotoi*, *Borrelia lonestari*, *Borrelia crocidurae*, and *Borrelia hermsii*; and mapped their worldwide risk level.

We retrieved 13 959 unique studies, among which 697 met the selection criteria and were used for data extraction. 29 RFGB species have been recorded worldwide, of which 27 have been identified from 63 tick species, 12 from 61 wild animals, and ten from domestic animals. 16 RFGB species caused human infection, with a cumulative count of 26 583 cases reported from Jan 1, 1874, to Dec 31, 2022. *Borrelia recurrentis* (17 084 cases) and *Borrelia persica* (2045 cases) accounted for the highest proportion of human infection. *B. miyamotoi* showed the widest distribution among all RFGB, with a predicted environmentally suitable area of 6.92 million km², followed by *B. lonestari* (1.69 million km²), *B. crocidurae* (1.67 million km²), and *B. hermsii* (1.48 million km²). The habitat suitability index of vector ticks and climatic factors, such as the annual mean temperature, have the most significant effect among all predictive models for the geographical distribution of the four major RFGB species.

The predicted high-risk regions are considerably larger than in previous reports. Identification, surveillance, and diagnosis of RFGB infections should be prioritised in high-risk areas, especially within low-income regions. Tank T, et al. *The Lancet*. [doi.org/10.1016/S2666-5247\(23\)00396-8](https://doi.org/10.1016/S2666-5247(23)00396-8).

Repellent activity of essential oils to the Lone Star tick, *Amblyomma americanum*

The Lone Star tick, *Amblyomma americanum* is important to human health because of a variety of pathogenic organisms transmitted to humans during feeding events, which underscores the need to identify novel approaches to prevent tick bites. Thus, the goal of this study was to test

natural and synthetic molecules for repellent activity against ticks in spatial, contact and human fingertip bioassays.

The efficacy of essential oils and naturally derived compounds as repellents to *Am. americanum* nymphs was compared in three different bioassays: contact, spatial and fingertip repellent bioassays.

Concentration response curves after contact exposure to 1R-trans-chrysanthemic acid (TCA) indicated a 5.6 $\mu\text{g}/\text{cm}^2$ concentration required to repel 50% of ticks (RC_{50}), which was five- and sevenfold more active than DEET and nootkatone, respectively. For contact repellency, the rank order of repellency at 50 $\mu\text{g}/\text{cm}^2$ for natural oils was clove > geranium > oregano > cedarwood > thyme > amyris > patchouli > citronella > juniper berry > peppermint > cassia. For spatial bioassays, TCA was approximately twofold more active than DEET and nootkatone at 50 $\mu\text{g}/\text{cm}^2$ but was not significantly different at 10 $\mu\text{g}/\text{cm}^2$. In spatial assays, thyme and cassia were the most active compounds tested with 100% and 80% ticks repelled within 15 min of exposure respectively and was approximately twofold more effective than DEET at the same concentration. To translate these non-host assays to efficacy when used on the human host, we quantified repellency using a finger-climbing assay. TCA, nootkatone and DEET were equally effective in the fingertip assay, and patchouli oil was the only natural oil that significantly repelled ticks.

The differences in repellent potency based on the assay type suggests that the ability to discover active tick repellents suitable for development may be more complicated than with other arthropod species; furthermore, the field delivery mechanism must be considered early in development to ensure translation to field efficacy. TCA, which is naturally derived, is a promising candidate for a tick repellent that has comparable repellency to commercialized tick repellents. Mauf AL, et al. *Parasites & Vectors*, Vol 17, Article: 202 (2024).

Emerging Trends in Information-Seeking Behavior for Alpha-Gal Syndrome: Infodemiology Study Using Time Series and Content Analysis

The study aimed to (1) describe the volume and patterns of information-seeking related to alpha-gal, (2) explore correlations between alpha-gal and lone star ticks, and (3) identify specific areas of interest that individuals are searching for in relation to alpha-gal.

Google Trends Supercharged-Glimpse, a new extension of Google Trends, provides estimates of the absolute volume of searches and related search queries. This extension was used to assess trends in searches for alpha-gal and lone star ticks (*lone star tick*, *alpha gal*, and *meat allergy*, as well as *food allergy* for comparison) in the United States. Time series analyses were used to examine search volume trends over time, and Spearman correlation matrices and choropleth maps were used to explore geographic and temporal correlations between alpha-gal and lone star tick searches. Content analysis was performed on related search queries to identify themes and subcategories that are of interest to information seekers.

Time series analysis revealed a rapidly increasing trend in search volumes for alpha-gal beginning in 2015. After adjusting for long-term trends, seasonal trends, and media coverage, from 2015 to 2022, the predicted adjusted average annual percent change in search volume for alpha-gal was 33.78%. The estimated overall change in average search volume was 627%. In comparison, the average annual percent change was 9.23% for lone star tick, 7.34% for meat allergy, and 2.45% for food allergy during this time. Geographic analysis showed strong significant correlations between alpha-gal and lone star tick searches especially in recent years ($\rho=0.80$; $P<.001$), with primary overlap and highest search rates found in the southeastern region of the United States. Content analysis identified 10 themes of primary interest: diet, diagnosis or testing, treatment, medications or contraindications of medications, symptoms, tick related, specific sources of information and locations, general education information, alternative words for alpha-gal, and unrelated or other.

The study provides insights into the changing information-seeking patterns for alpha-gal, indicating growing awareness and interest. Alpha-gal search volume is increasing at a rapid rate. Understanding specific questions and concerns can help health care providers and public health educators to tailor communication strategies. The Google Trends Supercharged-Glimpse tool offers enhanced features for analyzing information-seeking behavior and can be valuable for infodemiology research. Further research is needed to explore the evolving prevalence and impact of alpha-gal syndrome. Romeiser JL, et al. *J Med Internet Res* 2024;26:e49928, doi.org/10.2196/49928.

Lizards and the enzootic cycle of *Borrelia burgdorferi sensu lato*

Emerging and re-emerging pathogens often stem from zoonotic origins, cycling between humans and animals, and are frequently vectored and maintained by hematophagous arthropod vectors. The efficiency by which these disease agents are successfully transmitted between vertebrate hosts is influenced by many factors, including the host on which a vector feeds. The Lyme disease bacterium *Borrelia burgdorferi sensu lato* has adapted to survive in complex host environments, vectored by Ixodes ticks, and maintained in multiple vertebrate hosts. The versatility of Lyme borreliae in disparate host milieus is a compelling platform to investigate mechanisms dictating pathogen transmission through complex networks of vertebrates and ticks.

Squamata, one of the most diverse clade of extant reptiles, is comprised primarily of lizards, many of which are readily fed upon by Ixodes ticks. Yet, lizards are one of the least studied taxa at risk of contributing to the transmission and life cycle maintenance of Lyme borreliae. In this review, we summarize the current evidence, spanning from field surveillance to laboratory infection studies, supporting their contributions to Lyme borreliae circulation.

We also summarize the current understanding of divergent lizard immune responses that may explain the underlying molecular mechanisms to confer Lyme spirochete survival in vertebrate hosts. This review offers a critical perspective on potential enzootic cycles existing between lizard-tick-*Borrelia* interactions and highlights the importance of an eco-immunology lens for zoonotic pathogen transmission studies. Nowak TA, et al. *Molecular Microbiology*, [//doi.org/10.1111/mmi.15271](https://doi.org/10.1111/mmi.15271).

Electronic Health Record Data for Lyme Disease Surveillance, Massachusetts, USA, 2017–2018

Lyme disease surveillance based on provider and laboratory reports underestimates incidence. We developed an algorithm for automating surveillance using electronic health record data. We identified potential Lyme disease markers in electronic health record data (laboratory tests, diagnosis codes, prescriptions) from January 2017–December 2018 in 2 large practice groups in Massachusetts, USA.

We calculated their sensitivities and positive predictive values (PPV), alone and in combination, relative to medical record review. Sensitivities ranged from 57% (95% CI 47%–69%) for immunoassays to 87% (95% CI 70%–100%) for diagnosis codes. PPVs ranged from 53% (95% CI 43%–61%) for diagnosis codes to 58% (95% CI 50%–66%) for immunoassays. The combination of a diagnosis code and antibiotics within 14 days or a positive Western blot had a sensitivity of 100% (95% CI 86%–100%) and PPV of 82% (95% CI 75%–89%). This algorithm could make Lyme disease surveillance more efficient and consistent. Nagavedu K, et al. *Emerging Infectious Diseases*. 2024;30(7):1374-1379. doi:10.3201/eid3007.230942.

Human *Babesia odocoilei* and *Bartonella* spp. co-infections in the Americas

In recent years, *Babesia* and *Bartonella* species co-infections in patients with chronic, nonspecific illnesses have continued to challenge and change the collective medical understanding of “individual pathogen” vector-borne infectious disease dynamics, pathogenesis and epidemiology. The objective of this case series is to provide additional molecular documentation of *Babesia odocoilei* infection in humans in the Americas and to emphasize the potential for co-infection with a *Bartonella* species.

The development of improved and more sensitive molecular diagnostic techniques, as confirmatory methods to assess active infection, has provided increasing clarity to the healthcare community.

Using a combination of different molecular diagnostic approaches, infection with *Babesia odocoilei* was confirmed in seven people suffering chronic non-specific symptoms, of whom six were co-infected with one or more *Bartonella* species.

We conclude that infection with *Babesia odocoilei* is more frequent than previously documented and can occur in association with co-infection with *Bartonella* spp. Maggi RG, et al. *Parasites Vectors* 17, 302 (2024). <https://doi.org/10.1186/s13071-024-06385-4>.

Tick got your Pancreas? A case of Lyme induced pancreatitis

Lyme disease is a tick-borne illness caused by the spirochete *Borrelia burgdorferi*. We present a unique case of a patient who developed acute pancreatitis secondary to infection with *B. burgdorferi*. This case illustrates a rare manifestation of Lyme disease previously documented in only a few case reports. We discuss the recognition, management and clinical course of the

patient following diagnosis. Cherala R & Frageau ML. *Brown Hospital, Medicine*,2024;3(3). doi:10.56305/001c.117603.

New *Borrelia burgdorferi* populations quickly become similar to established populations

Population dynamics of the Lyme disease bacterium, *Borrelia burgdorferi*, during rapid range expansion in New York State

Recent changes in climate and human land-use have resulted in alterations of the geographic range of many species, including human pathogens. Geographic range expansion and population growth of human pathogens increase human disease risk. Relatively little empirical work has investigated the impact of range changes on within-population variability, a contributor to both colonization success and adaptive potential, during the precise time in which populations are colonized. This is likely due to the difficulties of collecting appropriate natural samples during the dynamic phase of migration and colonization. We systematically collected blacklegged ticks (*Ixodes scapularis*) across New York State (NY), USA, between 2006 and 2019, a time period coinciding with a rapid range expansion of ticks and their associated pathogens including *Borrelia burgdorferi*, the etiological agent of Lyme disease. These samples provide a unique opportunity to investigate the population dynamics of human pathogens as they expand into novel territory. We observed that founder effects were short-lived, as gene flow from long-established populations brought almost all *B. burgdorferi* lineages to newly colonized populations within just a few years of colonization. By 7 years post-colonization, *B. burgdorferi* lineage frequency distributions were indistinguishable from long-established sites, indicating that local *B. burgdorferi* populations experience similar selective pressures despite geographic separation. The *B. burgdorferi* lineage dynamics elucidate the processes underlying the range expansion and demonstrate that migration into, and selection within, newly colonized sites operate on different time scales.

International Section

Unknown genetic variant, rs1061632 associated with enhanced LB susceptibility

Genome-wide analyses in Lyme borreliosis: identification of a genetic variant associated with disease susceptibility and its immunological implications

Genetic variation underly inter-individual variation in host immune responses to infectious diseases, and may affect susceptibility or the course of signs and symptoms.

We performed genome-wide association studies in a prospective cohort of 1138 patients with physician-confirmed Lyme borreliosis (LB), the most common tick-borne disease in the Northern

hemisphere caused by the bacterium *Borrelia burgdorferi* sensu lato. Genome-wide variants in LB patients—divided into a discovery and validation cohort—were compared to two healthy cohorts. Additionally, ex vivo monocyte-derived cytokine responses of peripheral blood mononuclear cells to several stimuli including *Borrelia burgdorferi* were performed in both LB patient and healthy control samples, as were stimulation experiments using mechanistic/mammalian target of rapamycin (mTOR) inhibitors. In addition, for LB patients, anti-*Borrelia* antibody responses were measured. Finally, in a subset of LB patients, gene expression was analysed using RNA-sequencing data from the ex vivo stimulation experiments.

We identified a previously unknown genetic variant, rs1061632, that was associated with enhanced LB susceptibility. This polymorphism was an eQTL for *KCTD20* and *ETV7* genes, and its major risk allele was associated with upregulation of the mTOR pathway and cytokine responses, and lower anti-*Borrelia* antibody production. In addition, we replicated the recently reported SCGB1D2 locus that was suggested to have a protective effect on *B. burgdorferi* infection, and associated this locus with higher *Borrelia burgdorferi* antibody indexes and lower IL-10 responses.

Susceptibility for LB was associated with higher anti-inflammatory responses and reduced anti-*Borrelia* antibody production, which in turn may negatively impact bacterial clearance. These findings provide important insights into the immunogenetic susceptibility for LB and may guide future studies on development of preventive or therapeutic measures. Vrijmoeth HD, et al. *BMC Infect Dis.* 2024; 24: 337. doi: [10.1186/s12879-024-09217-z](https://doi.org/10.1186/s12879-024-09217-z).

Phase 3 VALOR Lyme Disease Trial: Valneva and Pfizer Announce Primary Vaccination Series Completion

Pfizer and Valneva announced on July 17th, 2024, that participants of the Phase 3 trial “Vaccine Against Lyme for Outdoor Recreationists” (VALOR) have completed the three-dose primary vaccination series of Lyme disease vaccine candidate VLA15. A booster will be administered approximately one year after primary vaccination series completion. The participants will be monitored for Lyme disease until the end of Lyme season in 2025.

VLA15 is the most advanced vaccine along the clinical development pipeline, and no safety concerns have been observed in adult populations to date by an independent Data Safety Monitoring Board. A second Phase 3 trial assessing VLA15’s safety profile in pediatric populations (5-17 years) is ongoing.

<https://www.pfizer.com/news/press-release/press-release-detail/phase-3-valor-lyme-disease-trial-valneva-and-pfizer>

Article references and further information:

1. ClinicalTrials.gov. An Efficacy, Safety, Tolerability, Immunogenicity, and Lot-Consistency Clinical Trial of a 6-Valent OspA-Based Lyme Disease Vaccine (VLA15) (VALOR). July 2022. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT05477524>. Accessed April 2024.
2. Bézay N, Hochreiter R, et al. Safety and immunogenicity of a novel multivalent OspA-based vaccine candidate against Lyme borreliosis: a randomised, phase 1 study in healthy adults. *Lancet Infect Dis.* 2023 Oct;23(10):1186-1196. doi: [10.1016/S1473-3099\(23\)00210-4](https://doi.org/10.1016/S1473-3099(23)00210-4).

3. Valneva and Pfizer Report Further Positive Phase 2 Data for Lyme Disease Vaccine Candidate. February 2022. Available at: [Valneva and Pfizer Report Further Positive Phase 2 Data for Lyme Disease Vaccine Candidate | Pfizer](#)
4. Valneva and Pfizer Announce Collaboration to Co-Develop and Commercialize Lyme Disease Vaccine, VLA15. April 2020. Available at: [Valneva and Pfizer Announce Collaboration to Co-Develop and Commercialize Lyme Disease Vaccine, VLA15 | Pfizer](#). Accessed April 2024.
5. Valneva and Pfizer Enter into Equity Subscription Agreement and Update Terms of Collaboration Agreement for Lyme Disease Vaccine Candidate VLA15. June 2022. Available at: [Valneva and Pfizer Enter into an Equity Subscription Agreement and Update Terms of Collaboration Agreement for Lyme Disease Vaccine Candidate VLA15 | Pfizer](#) Accessed April 2023.
6. Stanek, et al. Lyme Borreliosis. 2012. The Lancet 379:461–473.
7. Burn L, et al. Incidence of Lyme Borreliosis in Europe from National Surveillance Systems (2005–2020). 2023. Vector Borne and Zoonotic Diseases. 23(4):156–171.
8. Kugeler KJ, et al. Estimating the frequency of Lyme disease diagnoses—United States, 2010–2018. 2021. Emergency Infectious Disease. 27(2).
9. Centers for Disease Control and Prevention. Lyme disease. Signs and Symptoms. Available from: https://www.cdc.gov/lyme/signs_symptoms/index.html. Accessed September 2022.
10. Steere AC, Strle F, Wormser GP, et al. Lyme borreliosis. Nature Reviews Disease Primers. 2016;2:16090.
11. Centers for Disease Control and Prevention. Understanding Lyme and Other Tickborne Diseases. May 2022. Available from: <https://www.cdc.gov/ncezid/dvbd/media/lyme-tickborne-diseases-increasing.html>. Accessed April 2024.



TIC-NC is grateful for the financial contributions of Insect Shield International, LLC.



About Insect Shield Technology:

Insect Shield’s EPA-registered technology converts clothing and gear into effective and convenient insect protection. The repellency is long-lasting and appropriate for use by the entire family with no restrictions for use.

Quick Facts:

- Repellency is in the clothing and gear – not on your skin
- Lasts through 70 launderings
- EPA-registered
- No restrictions for use
- Appropriate for the entire family
- No need to re-apply
- Repels mosquitoes, ticks, ants, flies, chigger and midges including those that can cause Lyme disease, malaria and other dangerous insect-borne diseases

www.insectshield.com

Get your own clothes treated: **Insect Shield Your Own Clothes**
<https://www.insectshield.com/IS-Your-Own-Clothes-P338.aspx>



Tick-Borne Infections Council of North Carolina is a non-profit 501(c)3 organization formed to improve the recognition, treatment, control, and understanding of tick-borne diseases in North Carolina. We are all-volunteer and appreciate donations.

Board

Fran McCullough, President, Hillsborough
Kim Brownley, PhD, Vice-president and Treasurer, Mebane
Liz Crabill, Secretary
McGregor Bell, Director, Durham
Marcia E. Herman-Giddens, PA, DrPH, Scientific Advisor & Director, Pittsboro
Amy J. Stinnett, MPA, Director, Durham

Disclaimer

TIC-NC's newsletter content, including text, graphics, images and information is for general informational purposes only. The contents are not intended to be a substitute for professional medical advice, diagnosis or treatment.

Any contact information is provided for you to learn about tick borne illnesses and related issues. Our organization is not responsible for the content of other material or for actions as a result of opinions or information expressed which may appear from time to time.

It is the responsibility of you as an individual to evaluate the usefulness, completeness or accuracy of any information you read and to seek the services of a competent medical professional of your choosing if you need medical care.

This organization is not a representative, program, affiliate of any other organization, unless specifically stated. Contact us at info@tic-nc.org or 919-542-5573

You have received this newsletter because you are on our membership list. If you want to be taken off at any time, just reply with 'unsubscribe' in the subject box.