

DEPARTMENT OF HEALTH
REPORT ON LYME DISEASE IN
RESPONSE TO PL 2015, R 431
AND PL 2014, R 087

JANUARY 31, 2016

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Section 1: Overview of current levels of Lyme disease in Rhode Island

Overview

Lyme disease is caused by the bacterium *Borrelia burgdorferi*, spread through the bite of infected ticks. The blacklegged tick (or deer tick, *Ixodes scapularis*) spreads the disease in the northeastern, mid-Atlantic, and north-central United States. Ticks can attach to any part of the human body but are often found in hard-to-see areas such as the groin, armpits, and scalp. In most cases, the tick must be attached for 36 to 48 hours or more before the Lyme disease bacterium can be transmitted. Most humans are infected through the bites of immature ticks called nymphs.

Lyme disease symptoms range from subclinical to life-threatening. The most common clinical marker for the disease is erythema migrans (EM), the initial “bulls eye” skin lesion that occurs in 60%-80% of patients, typically within 7 to 30 days of a tick bite, and often accompanied by non-specific symptoms: fever, malaise, headache, joint pain, and muscle pain. Late manifestations can occur days to months after the bite. These symptoms include arthritis (particularly in the knee joint), neurologic problems (such as Bell’s Palsy or neuropathy), cardiac issues, or meningitis. Early treatment with antibiotics can prevent late-stage manifestations. (<http://www.cdc.gov/lyme/>)

Lyme disease is considered highly endemic in Rhode Island. In 2014, there were 905 confirmed and probable cases of Lyme disease in Rhode Island. The rate of confirmed and probable cases in 2014 in Rhode Island was 86 cases per 100,000 people. In 2014, RI had the fourth-highest rate of Lyme disease of any state, following Maine, Vermont, and Massachusetts.

(<http://www.cdc.gov/lyme/stats/chartstable/reportedcasesstatelocality.html>)

Rhode Island surveillance system

Lyme disease surveillance activities are conducted by staff in the Center for Acute Infectious Disease Epidemiology (CAIDE), within the Division of Preparedness, Response, Infectious Disease, and Emergency Medical Services at the Rhode Island Department of Health.

The surveillance case definition of Lyme disease requires both laboratory and clinical information. Laboratory information alone is not enough for a case of Lyme disease to meet the surveillance case definition. In the decade prior to May 2013, constrained by resources, Lyme disease surveillance was passive, meaning that the Rhode Island Department of Health (RIDOH) relied solely on providers to submit case reporting forms containing clinical information for Lyme disease. The low percentage of case report forms received by the RIDOH resulted in missing clinical information for many of the cases that were reported through laboratories. As a result, most cases of Lyme disease were classified as suspect (and consequently not reported to CDC or included in Rhode Island’s annual case counts).

In May 2013, unpaid interns began working in CAIDE to help address the low reporting concerns. The additional staff allowed CAIDE to implement an improved Lyme disease surveillance system. Since May 2013, CAIDE staff now actively follow up on all lab reports of Lyme disease, including faxing out case reporting forms to providers in order to gather clinical information. Subsequently, CAIDE staff are able to reclassify suspect cases as probable or confirmed cases in greater numbers than in previous years. It has been estimated that Lyme

disease rates are underreported, both nationally and in Rhode Island (Fulton 2008, Hinkley 2014, Nelson 2015). Rhode Island's enhanced surveillance system helps to reduce the discrepancy in counts between reported cases and actual burden of disease.

Lyme disease surveillance is a high-volume and labor-intensive undertaking. The surveillance team consists of a public health nurse, a public health epidemiologist, and a small group of part-time interns. All team members work on several additional assignments as well, and can only dedicate a limited portion of their time to Lyme disease. The surveillance process is:

- 1) CAIDE receives a laboratory report of Lyme disease.
- 2) The public health nurse interprets the laboratory results, determining if the results are supportive of the surveillance case definition of Lyme disease. The nurse codes the laboratory report according to the result.
- 3) Part-time interns enter the laboratory results into RIDOH's electronic database, find contact information for the ordering provider, and fax a case report form to the provider to request additional clinical information that is necessary to meet case definition.
- 4) The team waits one month to give the provider time to respond to the request for information.
- 5) Once the physician responds, the public health epidemiologist matches the case report form with the laboratory result.
- 6) The nurse classifies the case as suspect, probable, confirmed, or not a case, based on the laboratory result and any available clinical information.
- 7) Interns enter the full case information into RIDOH's electronic database.
- 8) The nurse checks the data entry in the electronic database and notifies the epidemiologist of completed cases.
- 9) The epidemiologist performs quality assurance (for timeliness, completion and accuracy measures) on the data entered and submits the case report electronically to the Centers for Disease Control and Prevention (CDC).

This in-depth process is followed for each laboratory report of Lyme disease CAIDE receives. The volume of reports is significant. In 2014, interns faxed 1,226 case report forms to providers to obtain additional clinical information. This number does not include the laboratory reports that the nurse determined were not supportive of the case definition, or the case report forms that physicians filled out independently. In 2014, 1,509 reports of Lyme disease were entered into RIDOH's electronic database; 905 of these were probable and confirmed cases of Lyme disease and were submitted to the CDC.

Lyme disease surveillance requires a large commitment of time and effort from CAIDE's surveillance team. While the team is comprised of multiple members, no member is able to devote his or her full time to Lyme disease surveillance. The public health nurse and epidemiologist are each responsible for tracking and surveillance of approximately 15 other reportable diseases; Lyme disease can only take 25% of their time each week. In addition, the CDC provides very little funding to support Lyme disease surveillance (25% of a nurse, new in 2015; 20% of a clerical staff member to assist with data entry; and 40% of a disease intervention specialist to support provider follow-up, position vacant as of October 2015, in need of additional funding to support the remaining percentage). As a result, the labor-intensive surveillance system

is highly dependent on interns. Interns are short-term staff, and thus the continuity of the system is interrupted each time an intern leaves.

In 2014, CAIDE maintained its active surveillance system, but the process had many starts and stops as part-time interns arrived and departed. There was also a learning curve when each new intern started after each intern completed training on Lyme disease surveillance. The reliance on temporary staff resulted in a short-term backlog of lab reports and data entry in 2014.

Annual analyses of Lyme disease data are publicly available on RIDOH's website. This legislative report contains data from 2013 and 2014. Enhanced surveillance began in 2013 so these most recent data more accurately represent the burden of Lyme disease in Rhode Island.

Rhode Island Lyme disease data

Rates of Lyme disease represent the calculated number of cases of Lyme disease per 100,000 people in Rhode Island. This metric was calculated using data from the 2010 US Census. Rates provide a more accurate picture of a disease within a certain population rather than counting individual cases. *Counts* of Lyme disease are the actual number of cases reported to CAIDE.

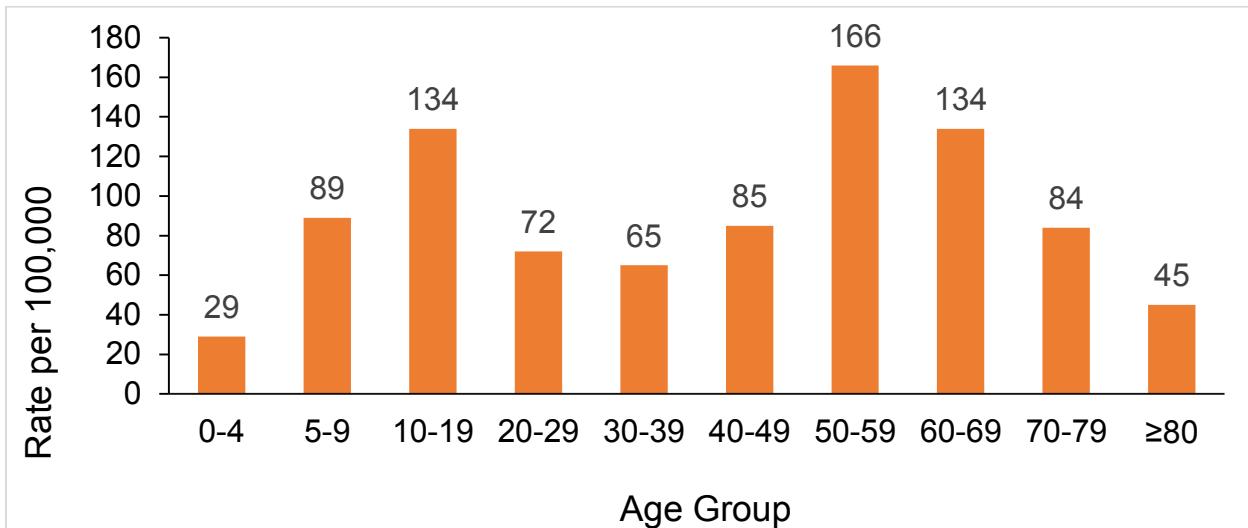
In 2014, Rhode Island had 905 cases of Lyme disease, with an incidence rate of 86 confirmed and probable cases per 100,000 Rhode Islanders. In 2013, there were 724 cases of Lyme disease in Rhode Island, and there was an incidence rate of 68.8 confirmed and probable cases per 100,000 Rhode Islanders. This rate is comparable to neighboring states.

Massachusetts also reported 86 confirmed and probable cases per 100,000 people, and Connecticut reported 65.6 confirmed and probable cases per 100,000 people. Although underreporting of Lyme disease remains a challenge, the enhanced surveillance system started in 2013 is designed to reduce the discrepancy between reported cases and actual burden of disease in Rhode Island. This problem is mirrored nationally

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5623a1.htm>

Lyme disease data by age

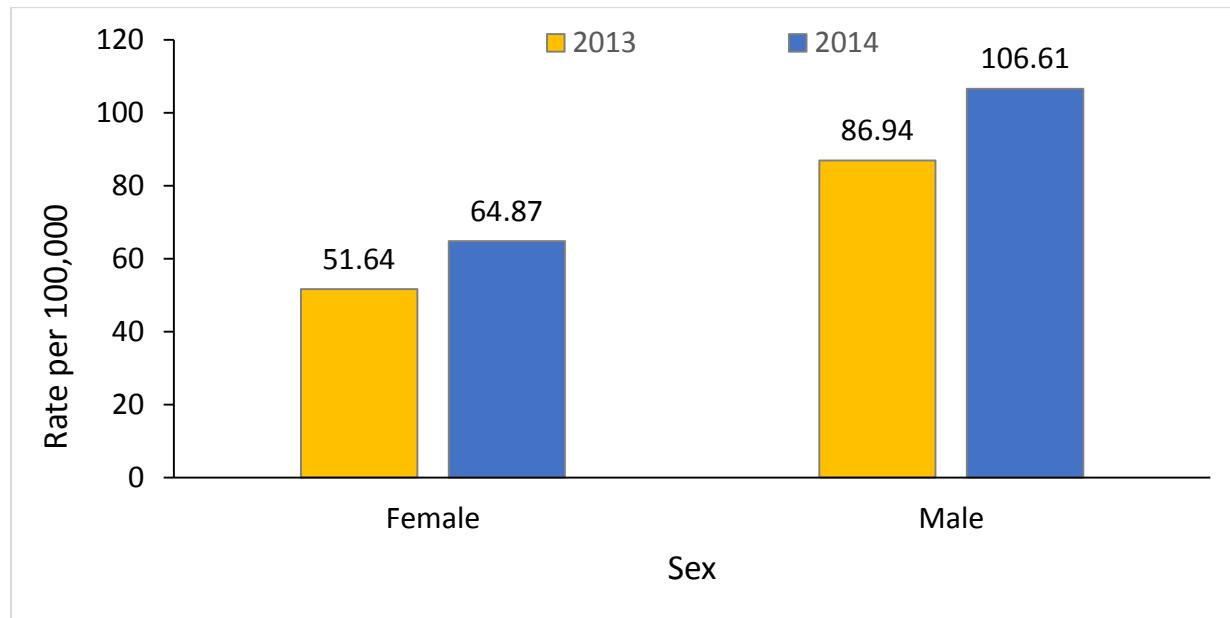
Figure 1: Rate of Lyme Disease by Age Group, Rhode Island, 2014



Adults ages 50-59 had the highest rate of Lyme disease in Rhode Island in 2014 (166 cases per 100,000 people). Rhode Islanders ages 60-69 and ages 10-19 had the next highest rates of Lyme disease (each with 134 cases per 100,000 people).

Lyme disease data by sex

Figure 2: Rate of Lyme Disease by Sex, Rhode Island, 2013 - 2014



In 2014, there were 353 cases of Lyme disease in females, and 542 cases in males (64.9 and 106.6 cases per 100,000 people, respectively). In 2013 and 2014, males had higher counts and rates of Lyme disease than females did. This difference is consistent with 10-year trends of Lyme disease data at the national level. From 2000 to 2010, males had a higher incidence of Lyme disease in all age groups except individuals over 70 years of age.

(<http://www.cdc.gov/lyme/stats/chartstable/incidencebyagesex.html>) In addition, the national trend of higher incidence of Lyme disease in males than in females was consistent from 1995 to 2006, with the gap widening over time.

(<http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5710a1.htm>).

Table 1: Case Count by Sex and Year		
	2013	2014
Female	281	353
Male	442	542
Unknown	1	10
Total	724	905

Lyme disease data by month

Lyme disease is a seasonal illness. As a tickborne illness, the annual peak of cases occurs during the months when the weather is warm, and people are more likely to spend time outside. In Rhode Island, transmission is highest from May through September. Accordingly, incidence of Lyme disease peaks in July, with an increase in number of cases reported between June and August. Nationally, cases of Lyme disease peak in July each year as well, with elevated levels of disease between June and August.

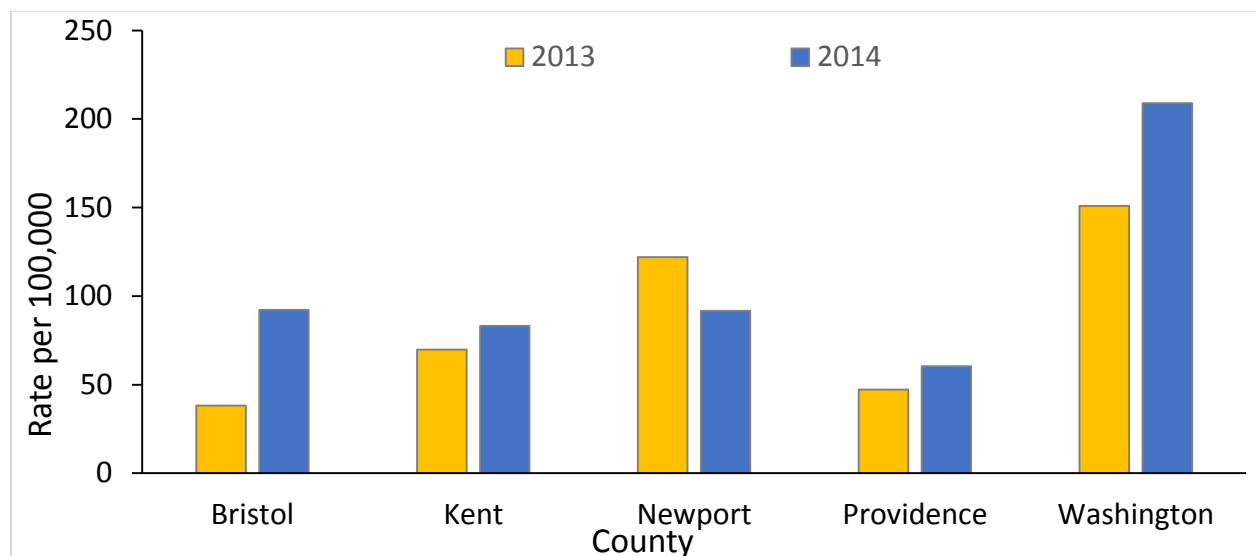
(<http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5710a1.htm>).

Table 2: Case Count by Month and Year

	2013	2014
January	25	19
February	15	20
March	34	32
April	29	31
May	41	66
June	120	160
July	187	256
August	109	122
September	60	60
October	49	65
November	38	39
December	17	35
All	724	905

Lyme disease data by geography

Figure 3: Rate of Lyme Disease by County and Year, Rhode Island, 2013 – 2014



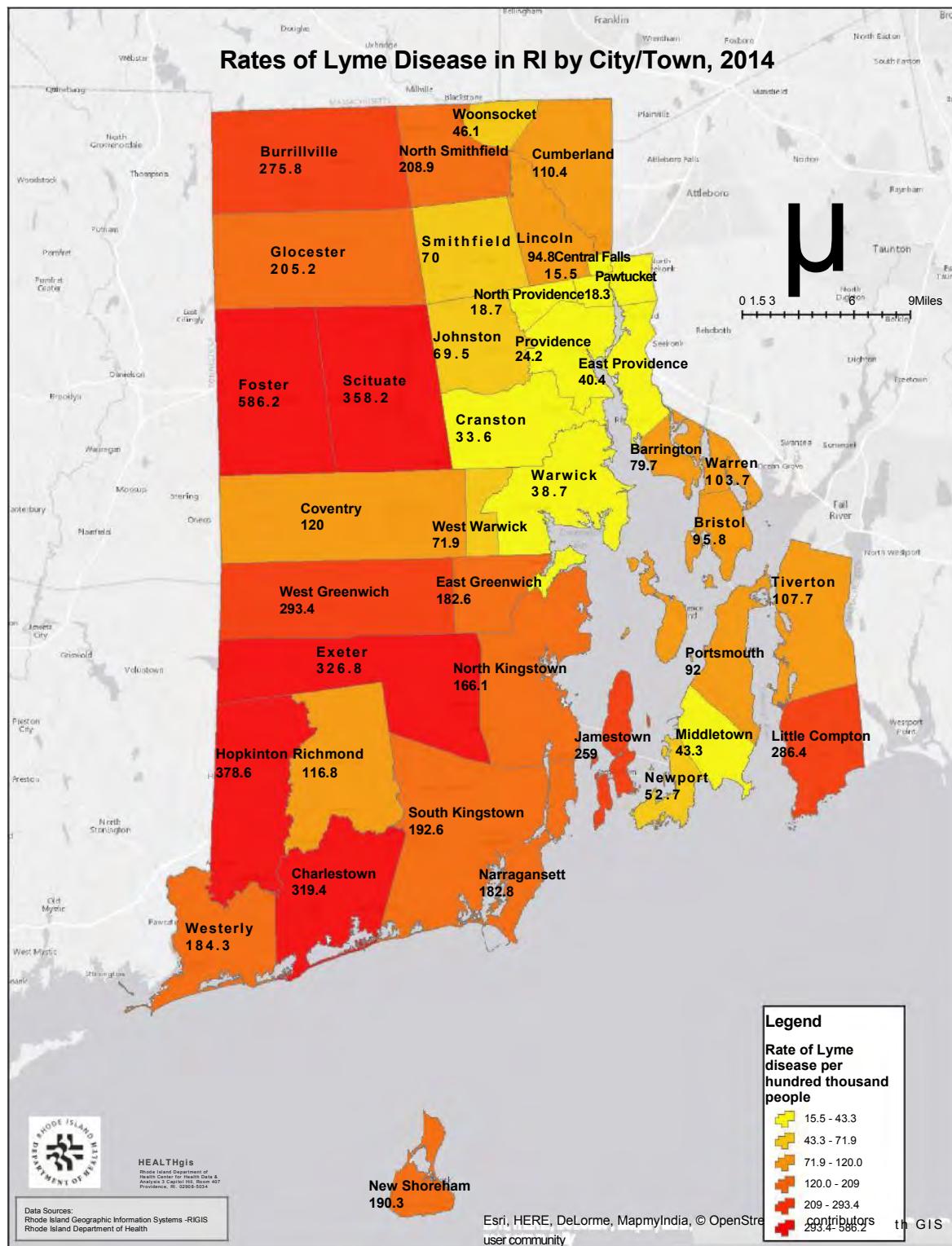
Lyme disease is clustered geographically in certain counties in Rhode Island. Washington County consistently has the majority of the burden of disease, with rates of 209 cases per 100,000 people in 2014. This is twice the rate of the two counties with the second-highest burden of disease (Bristol and Newport counties each had 92 cases per 100,000 people).

Table 3: Case Count and Rate of Disease by County and Year

	2013 Case count	2013 Rate of disease	2014 Case count	2014 Rate of disease
Bristol	19	38.1	46	92.2
Kent	116	69.8	138	83.1
Newport	101	122	76	91.7
Providence	296	47.2	379	60.5
Washington	192	151	266	209

Cases of Lyme disease are clustered in certain cities, particularly those located in more rural parts of the state. Although Washington County sees the highest rate of Lyme disease, they do not carry the entire burden of disease. Rural towns within Providence County, such as Foster and Scituate, have extremely high rates of disease (586.2 cases per 100,000 people and 358.2 cases per 100,000 people, respectively). When allocating resources, it is important to be aware of Lyme disease case counts and rates by municipality.

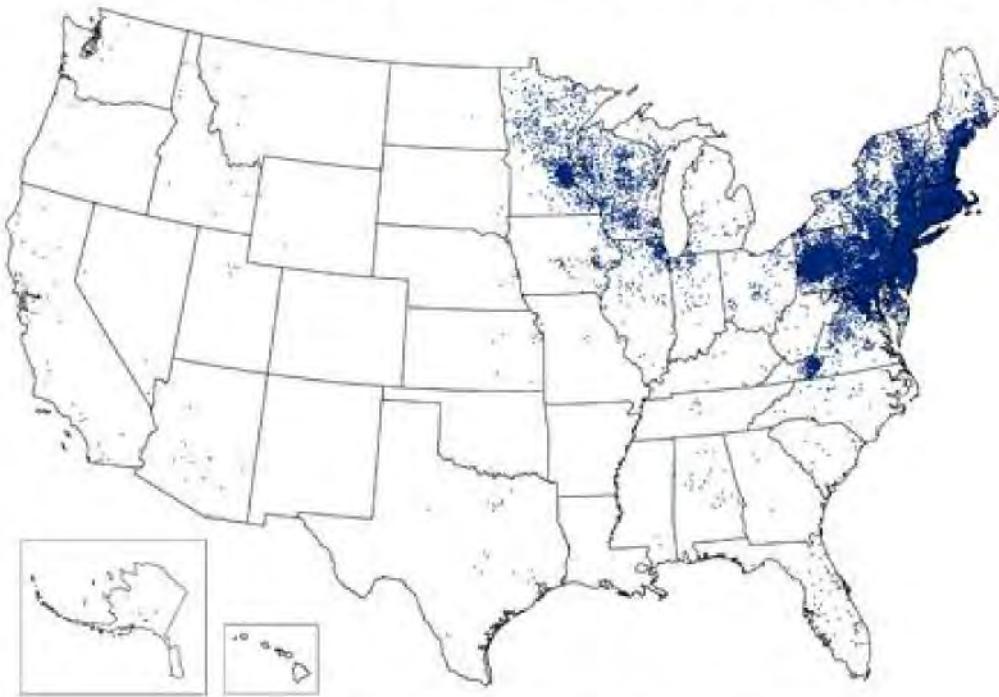
Lyme Disease Case Counts and Rates by City, 2013 - 2014, Rhode Island				
	2013		2014	
Municipality	Case Count	Rate per 100,000	Case Count	Rate per 100,000
Barrington	8	49.0	13	79.7
Bristol	7	30.5	22	95.8
Burrillville	34	213.1	45	282.0
Central Falls	<5	10.3	<5	15.5
Charlestown	17	217.2	26	332.2
Coventry	38	108.5	43	122.8
Cranston	17	21.1	27	33.6
Cumberland	33	98.5	37	110.4
East Greenwich	18	136.9	23	175.0
East Providence	15	31.9	20	42.5
Exeter	8	124.5	22	342.4
Foster	33	716.5	27	586.2
Glocester	14	143.6	20	205.2
Hopkinton	13	158.8	30	366.4
Jamestown	12	222.0	14	259.0
Johnston	12	41.7	20	69.5
Lincoln	18	85.3	23	109.0
Little Compton	20	572.7	10	286.4
Middletown	8	49.5	7	43.3
Narragansett	15	94.5	30	189.1
New Shoreham	31	2949.6	<5	190.3
Newport	13	52.7	13	52.7
North Kingstown	30	113.3	44	166.1
North Providence	6	18.7	6	18.7
North Smithfield	27	225.6	25	208.9
Pawtucket	7	9.8	12	16.9
Portsmouth	25	143.8	16	92.0
Providence	25	14.0	44	24.7
Richmond	6	77.8	10	129.7
Scituate	34	329.2	37	358.2
Smithfield	7	32.7	15	70.0
South Kingstown	47	153.4	60	195.8
Tiverton	23	145.8	16	101.4
Warren	<5	37.7	11	103.7
Warwick	29	35.1	32	38.7
West Greenwich	21	342.3	19	309.7
West Warwick	10	34.3	21	71.9
Westerly	25	109.7	42	184.3
Woonsocket	12	29.1	18	43.7



Under-reporting of Lyme disease

Like many diseases, Lyme disease is likely underreported to healthcare providers and to the CDC. Recent studies estimate that the true number of individuals in the United States infected with Lyme disease each year is approximately 300,000 (Hinkley 2014 and Nelson 2015). This estimation is approximately 10 times the number of cases that are reported annually to CDC. Lyme disease is heavily clustered in the northeastern United States. Rhode Island is among the 15 states that report 96% of all nationally reported cases of Lyme disease. Although the studies mentioned did not take place in Rhode Island, one can extrapolate that the true burden of Lyme disease in Rhode Island is even greater than the currently reported significant numbers of disease.

Reported Cases of Lyme Disease -- United States, 2014



Section 2: Response of the medical community in treating the disease

As part of a general review of Lyme disease risks and responses in Rhode Island requested by the Rhode Island General Assembly, the Rhode Island Department of Health (RIDOH) conducted a survey of the state's primary care physicians to assess their knowledge, attitudes, and practices regarding diagnosis, treatment, and reporting of Lyme disease cases.

Methods

A list of currently licensed physicians was obtained from the Center for Professional Licensure of RIDOH, from which were extracted the email addresses of family practitioners, internists, and pediatricians licensed to practice medicine in Rhode Island. These professionals were invited to participate in an online survey of Lyme disease knowledge, attitudes, and practices patterned after surveys conducted in Connecticut and in Massachusetts for similar purposes. Potential respondents were sent two reminders at about weekly intervals following the initial invitation to participate. Survey responses were aggregated and percentages computed to describe the respondents' Lyme disease knowledge, attitudes, and practices.

Representativeness of Results

Of about 1600 actively licensed physicians engaged in these medical specialties, 211 responded in a two-month period (November 2015 through January 2016), yielding a response-rate of 13%. These physician respondents claimed to have seen between 1338 and 3425 cases of Lyme disease "in the past 12 months," with overlap possible (double-counting due to at least some referrals among respondents). Of these 1338-3425 cases, between 518 and 1359—midpoint = 939—were *reputedly* reported to RIDOH, per responses to the question, "Of those patients you have seen in the past 12 months with acute Lyme disease, approximately what percent did you report to the Rhode Island Department of Health?"

In calendar year 2014 (the latest year for which case reporting is completed and verified), RIDOH received 1174 reports of Lyme disease ("suspect," "probable," and "confirmed"), of which the 939 case reports estimated for 2015 from survey responses represent 80%. From this perspective, assuming that the number of Lyme disease cases reported to RIDOH is relatively stable from year to year, survey respondents appear to account for a large majority of Lyme disease cases reported to the state in the preceding 12 months.

This observation was checked by aggregating case reports for 2014 by physician reporter, and asking the question, "If we start with those physicians who report the most cases, and work down the list by number of cases reported, how many physicians do we need to produce 80% of the case reports?" The estimate is 336. We also asked, "If we start with those physicians who report the most cases, and work down the list by number of cases reported, what percentage of cases is reported by the first 211 physicians on the list?" The answer is 70%.

In sum, the independent analysis supports the notion that these survey respondents account for a large majority of Lyme disease case reports made to RIDOH in the preceding 12 months.

Results

Respondents

- 91% of the respondents had practiced medicine for 10 or more years
- More than half (56%) had been in practice for 20 or more years
- 87% of respondents reported seeing 20 or more outpatients per week

- 84% reported practicing in a non-hospital-based practice
- 75% reported spending 20% or more of their time practicing primary care
- 86% did not consider themselves to be "experts" in Lyme disease
- Only 13% had not seen at least one Lyme disease patient in the past year.

Case Reporting

- 44% of respondents who had seen at least one case of Lyme disease in the past year reported *none* of the diagnosed cases to RIDOH, even though Lyme disease has long been, by statute, a reportable disease in Rhode Island.
- Of reasons offered for not reporting, three were cited by 25% or more of the respondents:
 - The lab sends serologic results to RIDOH, so I don't have to report. (38%)
 - I didn't know I had to report all Lyme disease cases to RIDOH. (56%)
 - I don't have time to report. (25%)

Patient Education

- Only 58% of respondents report that any form of Lyme disease patient education is conducted (by physicians or others) in their practices.

Knowledge of the Local Problem

- 81% of respondents thought that Lyme disease is endemic in Rhode Island.
- 10% of respondents thought Lyme disease is not endemic in Rhode Island.
- 9% of respondents did not know if Lyme disease is endemic in Rhode Island.

Knowledge of Disease Transmission

- 78% of respondents knew how long a tick had to be attached to transmit disease.
- Of the remaining respondents, almost all (19%) underestimated the amount of time a tick had to be attached to transmit disease

Knowledge of Symptoms

- Generally, respondents demonstrated close familiarity with the signs and symptoms of Lyme disease.

Use and Interpretation of Serologic Tests A physician's preferences for ordering serologic tests for Lyme disease varied by the type(s) of symptoms a patient had.

- 82% of respondents would order a Lyme test if "patient thinks s/he was bitten by a tick over a month ago and now presents with flu-like symptoms,"
- 49% of respondents would order a test if "patient presents with a typical erythema migrans rash"
- 29% of respondents would order a test if "patient reports being bitten by a tick 3 weeks ago, but is unsure of the tick species and presents with no symptoms."
- 50% of respondents think that serologic tests for Lyme disease can distinguish between active and past infection
- 42% of respondents think that serologic tests for Lyme disease cannot distinguish between active and past infection
- 8% of respondents did not know if serologic tests for Lyme disease can distinguish between active and past infection

- 10% of respondents think that serologic tests for Lyme disease can be used to track treatment effectiveness
- 78% of respondents do not think that serologic tests for Lyme disease can be used to track treatment effectiveness
- 12% of respondents did not know if serologic tests for Lyme disease can be used to track treatment effectiveness

Initial Use of Antibiotics

In response to the question "Describe how you would usually treat an asymptomatic patient with a tick bite (unknown type of tick), and who had no laboratory testing performed to date,"

- 30% of respondents selected "Do not prescribe antibiotic at this time."
- 57% of respondents selected "Prescribe antibiotic prophylaxis to patient to prevent Lyme disease from developing."
- 5% of respondents selected "Prescribe full treatment regimen of antibiotics to patient to treat Lyme disease."

Prescribing preferences differed in response to the question, "Describe how you would treat a patient with erythema migrans, but who had no laboratory testing performed to date."

- 94% of respondents selected "(Typically) prescribe an antibiotic for Lyme disease."
- 3% of respondents selected "Do not prescribe antibiotic at this time."

In response to the question "How often do you prescribe antibiotics to patients for possible Lyme disease in response to their concerns, even though they are asymptomatic and have no history of a tick bite?"

- 68% of respondents said never
- 22% of respondents said rarely
- 7% of respondents said sometimes
- 2% of respondents said often
- 1% of respondents said always

Discussion

Survey results suggest several areas in which clarification may be of benefit to primary care physicians:

- Natural history of Lyme disease transmission
- Burden of Lyme disease in Rhode Island (endemicity, incidence, prevalence)
- Use and interpretation of serologic tests
- Antibiotic prescribing in the absence of signs and symptoms
- Patient education in the primary care setting
- Case reporting

Public health can play an effective role in clarifying these issues for physicians and other healthcare providers, but its role must be active and continuous, because as the survey reveals, most primary care physicians actually see between zero and one Lyme disease case per year, even in a state where the disease is common and quite burdensome. Thus, for many physicians, addressing a tick bite, or the (vague) signs and symptoms of acute Lyme disease is not a frequent occurrence, and therefore, few can be expected to become proficient on the basis of practice alone.

Section 3: Analysis of best practices in the treatment of Lyme disease

Analysis of Best Practices in the Treatment of Lyme Disease

The treatment of Lyme disease (*Borrelia burgdorferi*) depends on both the stage of disease and the organ system involved. *B. burgdorferi* has a predilection for the skin, joints, nervous tissue, and heart. The choice of which antibiotic, duration of antibiotic, or whether antibiotics are needed at all first requires an accurate diagnosis of stage of disease. The diagnosis relies on the patient's clinical history, a physical exam of the patient, and the results of serology lab tests.

The three clinical stages of Lyme disease are early localized, early disseminated, and late-stage Lyme. The International Lyme and Associated Diseases Society (ILADS), as well as other Lyme-literate physicians recommend that the length of therapy is four to six weeks of either oral or intravenous (IV) medication depending on the symptom presentation⁶. The following table outlines the clinical guidelines for treatment of Lyme disease by the Infectious Disease Society of America (IDSA) and the Centers for Disease Control and Prevention (CDC)⁷.

Symptom	Oral or IV antibiotic	Antibiotic options	Duration
Erythema migrans (bulls-eye rash)	Oral	Doxycycline Amoxicillin Cefuroxime	14 days (range, 10-21 days)
Early disseminated			
Meningitis	IV	Ceftriaxone	14 days (range, 10-28 days)
-Cranial nerve palsy (Bells palsy)	Oral or IV	Doxycycline (oral) Ceftriaxone (IV)	14 days (range, 14-21 days)
Cardiac disease	Oral or IV	Doxycycline oral Ceftriaxone IV	14 (14 – 21)
Late stage			
Arthritis without neurologic involvement	Oral	Doxycycline	28 days
Recurrent arthritis after one course of antibiotics	Oral or IV	Doxycycline oral Ceftriaxone IV	28 days (range, 14-28 days)
Antibiotic refractory arthritis after two courses of antibiotics	Symptomatic	N/A	N/A
Central/peripheral neurologic disease	IV	Ceftriaxone	14 days (range, 14-28 days)
-Acrodermatitis chronica atrophicans	Oral	Doxycycline	21 days (range, 14-28 days)
Post-treatment Lyme disease syndrome (chronic Lyme)	Antibiotic therapy has not proven to be useful; not recommended for patients with chronic (6+ months) subjective symptoms after administration of recommended treatment regimens for Lyme disease		

Diagnosis of Chronic Lyme/Post-Treatment Lyme Disease Syndrome

The most significant difference in treatment guidelines is regarding post-treatment Lyme disease syndrome (PTLDS), more commonly referred to as chronic Lyme. The debate is due to the ambiguity of this diagnosis and whether or not an active infection persists. This diagnosis is considered to be ambiguous because the persistent symptoms are non-specific and subjective, and there are not usually objective findings when the doctor performs a physical exam.

The three chronic symptoms most commonly reported by patients are fatigue, pain, and cognitive difficulties. Each of these symptoms are also reported by patients who have never been infected with Lyme disease. In the United States, 20%-30% of adults report chronic fatigue; 11% of adults report chronic pain; and 2%-3% of adults report cognitive difficulties^{8, 9, 10}. In addition, there is no standardized clinical test that can measure the severity of any of these non-specific symptoms. Because these symptoms are subjective symptoms and prevalent among all adults, a diagnosis of chronic Lyme/PTLDS can be difficult to distinguish from other conditions.

The IDSA/CDC guidelines state that a diagnosis of PTLDS should require a prior diagnosis of Lyme disease that is based on objective, clinical evidence (erythema migrans, positive serology as per CDC guidelines, or positive *Borrelia* PCR on synovial fluid). More specifically, the IDSA/CDC guidelines define PTLDS as the persistence of symptoms for longer than six months after treatment of Lyme disease that was diagnosed as a result of Erythema migrans or positive serology results.

ILADS guidelines do not require a positive serology or presence of Erythema migrans to diagnose PTLDS. Therefore, anyone with one of the three generalized, subjective symptoms could potentially be diagnosed with chronic Lyme/PTLDS.

Cause of Persistent Symptoms

In addition to the debate regarding diagnosis of chronic Lyme/PTLDS, the cause of persistent symptoms is also debated.

ILADS supports the theory that persistent symptoms are caused by ongoing infection of the spirochete that causes Lyme disease (*Borrelia burgdorferi*) despite antibiotic treatment. This theory is largely based on the premise that the spirochetes which infect tissues as extracellular bacteria, are not present in a patient's blood stream, and are not killed by antibiotics.

Though the research on Lyme disease, particularly chronic Lyme/PTLDS is limited, the available research does not support the theory of ongoing infection beyond a recommended course of antibiotics as outlined above. Studies have been conducted in both animals and humans, and there have been some studies that have found positive DNA PCR evidence of *B. burgdorferi* in tissues of animals and humans after they have completed antibiotics; however, none of the samples from the studies have resulted in eventual reproduction of a live spirochete. This suggests that the DNA PCR evidence represents dead spirochetes.

One study in particular tested for spirochete DNA at one month, two months, three months, and six months after finishing antibiotics. At each interval, there was a declining level of spirochete DNA, and there was no spirochete DNA at the six-month mark¹¹.

Two studies in the United States investigated humans for the presence of spirochetes in skin tissue after they had completed treatment for Lyme based and had had a bulls-eye rash. The first study had 18 cultures from 13 patients. Before antibiotic treatment, all of the patients' skin biopsies tested positive for the presence of the spirochete. After the patients completed

antibiotic treatment, all of the skin biopsy cultures tested negative for the presence of the spirochete¹². In the second study, all 13 patients' skin biopsy cultures tested negative for the presence of the spirochete after the patients had finished taking antibiotics¹³.

A third study in the United States studied 12 patients who had chronic Lyme symptoms that persisted after they finished taking antibiotics. Blood samples from all 12 patients were cultured on routine and special media. None of the blood samples reproduced a living spirochete. In addition, 128 cerebral-spinal fluid (CSF) specimens were obtained at different intervals. None of the CSF specimens tested positive for the presence of the spirochete¹⁴.

Due to the results of these four separate studies, the IDSA and the CDC do not support the theory of persistent infection in patients with chronic symptoms following Lyme treatment.

Treatment of Post-Treatment Lyme Disease Syndrome

Given the difference of professional opinion on the cause of chronic symptoms, there is also a difference in professional opinion on how to treat chronic Lyme/PTLDS.

Clinicians who follow ILADS guidelines will often choose to retreat patients with additional courses of antibiotics, four to six weeks at a time, with re-evaluation at the end of each course to determine the patient's response to treatment⁶. Though not supported by randomized trials, the ILADS reports observational/anecdotal success in certain, individual patients who were re-treated on different occasions.

There have only been four randomized controlled trials (RCTs) conducted in the United States that compared patients who had chronic symptoms and had taken antibiotics long term with patients who had chronic symptoms who had a placebo. ILADS clinicians do not support the outcomes of these trials because statistically, the studies had a small number of participants so ILADS believes the validity of these results is limited. However, the authors of these studies conclude that the small numbers of study participants was due to the small number of patients who met objective inclusion criteria, showing most people with chronic symptoms do not have evidence of past Lyme infection.

In the first two RCTs, there were two groups of participants. One group was patients with a positive Lyme serology and the second group had a negative Lyme serology. All participants in both groups reported ongoing symptoms after documented treatment for Lyme disease. Half of the patients received additional antibiotics, and the other half received a placebo. All participants were followed for 90 days. The study measured any improvement in the individual patient's quality of life. There was no difference observed in either group¹⁵.

The third RCT looked at fatigue and subjective cognition improvement in patients who had documented Lyme disease, had been treated by existing guidelines, and had ongoing symptoms. Half of the patients received one month of an IV antibiotic, and the other half received a placebo. All patients were followed for a total of six months. For patients who received the IV antibiotic, there was a documented decrease in fatigue but no difference in cognitive difficulties. However, patients who received the IV antibiotics had a significant higher incidence in adverse events (sepsis, anaphylaxis) in their treatment arm as compared to patients who received the placebo¹⁶.

The fourth RCT study looked for cognitive and memory improvement by administering neuropsychological tests so that there was an objective measure for improvement rather than subjective reporting by participants. There were three groups: Lyme patients who received IV

antibiotics, Lyme patients who received IV placebos, and non-Lyme matched control patients. All patients were followed for a total of six months. There was no change in memory impairment among all three groups. Initially, the Lyme patients who received IV antibiotics had a higher rate of improved cognition at the three-month point, but this was not sustained through to the six-month point. Patients who received IV antibiotics had a higher rate of adverse events (26%) compared to patients who received IV placebos¹⁷ (7%).

Given these findings, IDSA/CDC clinicians do not routinely offer re-treatment if they can confirm a patient has already received an appropriate course of antibiotics and confirm a new infection of Lyme disease has not occurred.

Section 4: Identifying any gaps in coverage or insurance protocols that affect access to comprehensive and adequate treatment

Access to treatment, insured individuals

In Rhode Island, access to the recommended antibiotic therapies for people who have health insurance coverage appears to be, for the most part, adequate. Health insurance coverage for Lyme disease treatment is available in all states, including Rhode Island. Specifically, health insurance companies are generally willing to cover the standard antibiotic treatment of administering antibiotics for 30 days. However, patients who report symptoms after the 30-day course of antibiotic treatment may find that their health insurance plan is reluctant or unwilling to pay for additional treatment. The decision to not cover additional treatment is typically made for proposed regimens that go beyond treatment(s) recommended by the Infectious Disease Society of America (IDSA), the Centers for Disease Control and Prevention (CDC), and other nationally-recognized groups. Businesses with group health plans that are self-insured are not mandated to provide this coverage.

Access to treatment, uninsured individuals

As with other pharmaceutical therapies, access to antibiotic therapies for Lyme disease for uninsured individuals is more challenging. Doxycycline is much more expensive than amoxicillin. In January 2016, the RIDOH conducted an informal survey of several Rhode Island retail pharmacies and determined that they all offer pharmaceutical cost assistance programs such as RIRX and HelpRX. Some individual pharmacies also offer cost assistance services specific to their pharmacy. Even with these programs, the discounted cost of doxycycline ranges from \$150 to \$217 for a 30-day supply. Amoxicillin is much less expensive with discounted prices ranging from \$4 to \$15 for a 30-day supply. (Note: Price ranges given are accurate as of January 28, 2016.)

Other cost-assistance programs available to Rhode Islanders include the Rhode Island Pharmacy Assistance for the Elderly (RIPAE) Program, discount programs offered by the manufacturers of the antibiotics, and community health centers who are able to get pharmaceuticals at discounted costs as a provision of Section 340B of the US Public Health Service Act. Prices of antibiotics vary significantly, and patients should be advised to search for the best price for the pharmaceuticals they need.

Section 5: Department's current and long-term goals and strategies to address the high incidence of disease in the state

Lyme Disease Prevention Campaign Overview

In 2014, RIDOH launched the *One Bite* Lyme prevention campaign, educating Rhode Islanders about preventing tick bites, and what to do if exposed to ticks. RIDOH continued the campaign in 2015 using funds from the Department's Climate Change program. The following activities are part of the 2015 campaign:

Advertising with the PawSox

- Director threw out first pitch at June 27 game
- Director did interview about Lyme on PawSox live radio
- RIDOH staff available at June 27 game to answer questions and distribute educational materials
- Outfield Billboard: ***Strike Out Lyme Disease***
- Print ads (*Pawsox Patter* game program; subscriber/fan home mailings)
- Radio ads (30-second spots with key prevention messages aired during live Pawsox radio broadcasts of games, April-September)
- Video ad (30-second video displayed on ballpark jumbo-tron during each game)
- Billboard message display featuring campaign slogan/messaging shown during each game
- Monthly social media posts from PawSox facebook and twitter accounts during game season

Email promotions

- Health Connections (monthly e-newsletter to licensed providers)
- Email blast from Director to schools and summer camps to promote free Lyme educational materials

DEM partnership

- Education materials distributed by DEM interns at resources tables during Great Outdoor Pursuit events

Media buy

- Block Island ferry poster ads, July and August
- *Hey Rhody* summer guide, spring and summer
- Rhode Island Family Guide

Other opportunities

- Director interviewed on PODER-1110 Latino radio
- Educational column in America News Latino print newspaper
- Banner on RIDOH's home page with link to prevention information
- Social media posts
- Seasonal press release with prevention messages and information on how to remove a tick, Lyme symptoms

Anticipated 2016 Prevention and Surveillance Activities

The RIDOH will continue building on its current efforts, including:

- Surveillance of Lyme Disease in Rhode Island
- Distribution of current clinical guidance and protocols to healthcare providers via monthly e-newsletters
- Utilizing RIDOH's social media channels to provide seasonally-appropriate information about Lyme disease prevention
- As resources permit, provide Lyme disease educational materials to schools, summer camps, and other state agencies
- As grant funding is available, renew media buys

More research is needed regarding Lyme disease, particularly in the diagnosis and treatment of chronic Lyme/PTLDS. Lyme disease is still a relatively new disease since its identification in the late 1970s, and many questions remain unanswered. Currently, several active studies are evaluating new Lyme disease blood tests that will help diagnose the disease at an earlier point in time compared to current antibody serology. We know that those who are diagnosed early in disease stage have better treatment outcomes, so these tests could be very beneficial if proven to be accurate. In addition, some researchers are looking at potential biomarkers that would help distinguish who will have persistent symptoms (chronic Lyme/PTLDS) versus those who have full symptom resolution. Research also needs to be done on prevention strategies, as prevention efforts are critical to the fight against Lyme disease and other tick-borne illnesses.

Glossary of terms

Case Definition for Surveillance

Rhode Island uses the 2011 CDC case definition of Lyme disease for surveillance purposes. The definition in its entirety can be found at

<https://www.cdc.gov/nndss/conditions/lyme-disease/case-definition/2011/>

CSTE Position Statement 10-ID-06

Background

This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis.

Clinical Description

A systemic, tick-borne disease with early and late manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The most common clinical marker for the disease is *erythema migrans* (EM), the initial “bulls eye” skin lesion that occurs in 60%-80% of patients. For most patients, the rash is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. For purposes of surveillance, late manifestations include any of the following when an alternate explanation is not found:

Musculoskeletal system. Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints. Muscles or joint aches without objective swelling do not meet the criteria.

Nervous system. Any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis. Headache, fatigue, prickling sensations, or mildly stiff neck alone are not criteria for neurologic involvement.

Cardiovascular system. Acute onset of second-degree or third-degree heart blockage that resolves in days to weeks and is sometimes associated with myocarditis.

Laboratory Criteria for Diagnosis

For the purposes of surveillance, the definition of a qualified laboratory assay is

- Positive Culture for *B. burgdorferi*, OR
- Two-tier testing interpreted using established criteria¹, where:
 - Positive IgM is sufficient only when ≤30 days from symptom onset
 - Positive IgG is sufficient at any point during illness
- Single-tier IgG immunoblot seropositivity using established criteria.¹⁻⁴
- CSF antibody positive for *B. burgdorferi* by Enzyme Immunoassay (EIA) or Immunofluorescence Assay (IFA), when the titer is higher than it was in serum

Exposure: having been (less than or equal to 30 days before onset of EM) in wooded, brushy, or grassy areas (potential tick habitats) in a county in which Lyme disease is endemic. A history of tick bite is not required.

Endemicity: A county in which Lyme disease is endemic is one in which at least two confirmed cases have been acquired in the county or in which established populations of a known tick vector are infected with *B. burgdorferi*. (All five counties in Rhode Island are areas where Lyme Disease is endemic).

Suspected case

- A case of EM where there is no known exposure (as defined above) and no laboratory evidence of infection (as defined above), **OR**
- A case with laboratory evidence of infection but no clinical information available (e.g., a laboratory report).

Probable case

Any other case of physician-diagnosed Lyme disease that has laboratory evidence of infection (as defined above).

Confirmed case

- A case of EM with a known exposure (as defined above), **OR**
- A case of EM with laboratory evidence of infection (as defined above) and without a known exposure **OR**
- A case with at least one late manifestation that has laboratory evidence of infection.

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