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# Comparing Short Versus Long Term Antibiotics for Reducing Persistent Lyme Symptoms

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## Abstract

- Lyme disease is the most common tick borne illness in the United States with over 300,000 cases annually.
- Two main organizations called the Infectious Disease Society of America and the International Lyme and Associated Diseases Society differ on their opinions in the treatment duration of Lyme disease.
- A review of the literature explored studies that compared the effectiveness of short term versus long term antibiotics in the treatment of Lyme. Determining the most effective treatment method duration for reducing the long term risk of persistent symptoms of Lyme will be important for the improvement of the delivery of care for patients.

## Introduction

- Lyme disease is caused by spirochetes called *Borrelia burgdorferi* sensu lato that is transmitted to humans by ticks. The transmission happens through injection of tick saliva during feeding. Infection in humans activate innate and adaptive immune responses that kill spirochetes.
- Virulence factors that can cause persistent infection including downregulation of immunogenic surface proteins, alteration of antigenic properties of lipoproteins and binding to components of extracellular matrix
- Horowitz (2013) described that *Borrelia* has 3 major forms: cell wall, cystic, and intracellular which can protect itself from the body's immune system depending on the internal environment it's in.
- Bratton (2008) reported Lyme *Borrelia* spirochetes are susceptible to tetracyclines, penicillins, macrolides, and 2<sup>nd</sup> and 3<sup>rd</sup> cephalosporins.
- IDSA recommends treatment with antibiotics 14-21 days and ILADS recommends using treatment regimens of minimum of 4-6 weeks.
- Borgermans (2014) found when Lyme is treated early, the outcomes are good. 20% of people display recurrent symptoms after antibiotic treatment.

## Statement of the Problem

- Cameron (2014) found that 34% of patients were ill an average of 6.2 years after standard antibiotic treatment. A meta-analysis of 504 patients treated for Lyme disease found this group had more fatigue, musculoskeletal pain and neurocognitive difficulties.
- IDSA and ILADS, have different sets of guidelines for treating Lyme disease. IDSA does not recognize the efficiency of long-term antibiotics. ILADS recognizes that the standard course of antibiotics are needed but that additional longer treatment may be needed to further eliminate symptoms.

## Research Question

- In patients diagnosed with Lyme *Borrelia burgdorferi*, is short versus long term antibiotics better for reducing persistent Lyme symptoms?

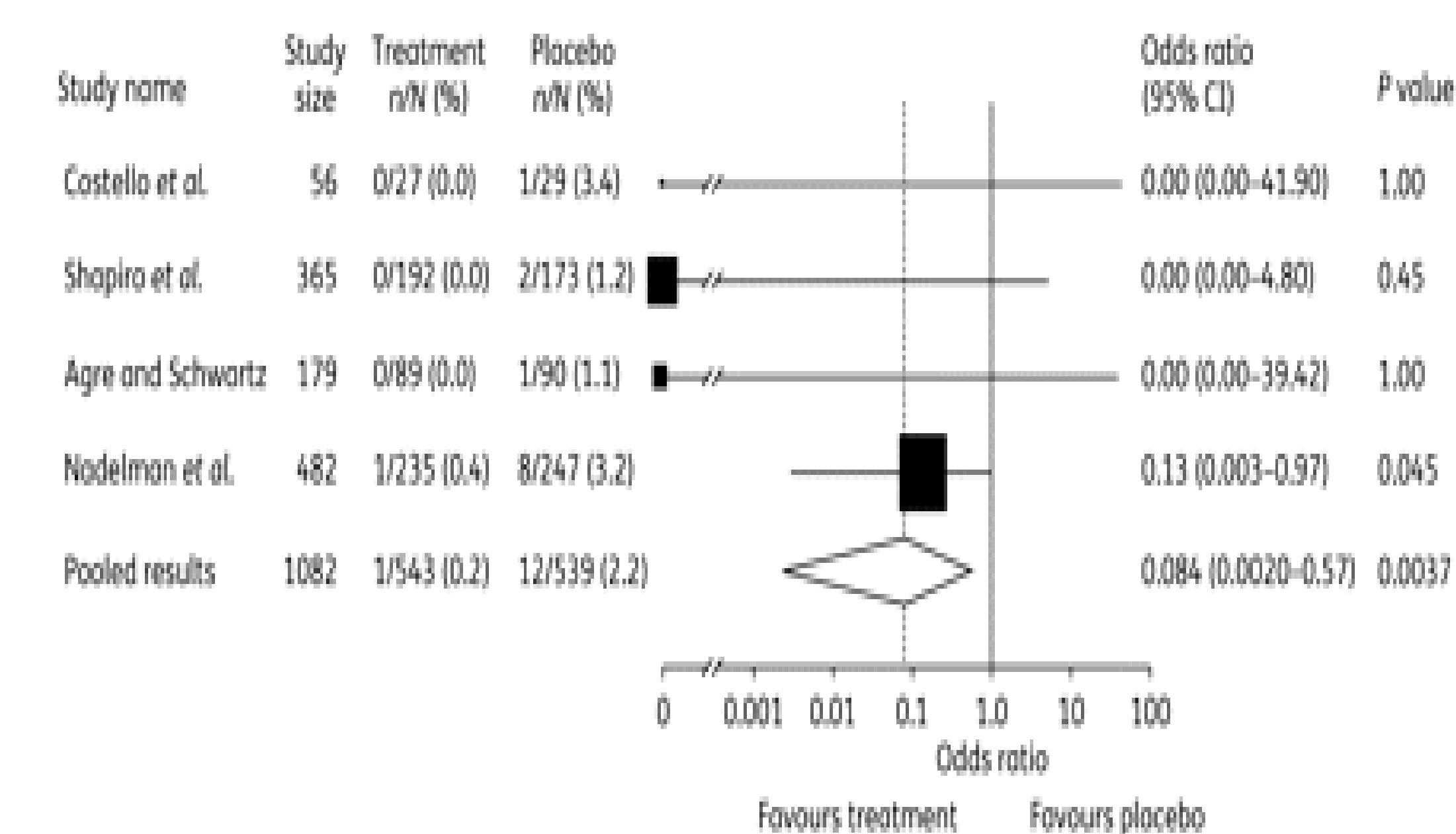
## Literature Review

The search of the literature found the main points:

- Stanek (2012) estimates it takes anywhere from 17-36 hours for *Borrelia* to be transferred.
- Ixodes nymphs are most active from early summer to early autumn. Adults will not become active until autumn. Adults remain active through winter months except when temperature drop less than 37.4 degrees F.
- Preboth (2001) found IDSA recommends antibiotic treatment for 10-21 days for erythema migrans rash.
- Cameron (2014) found ILADS recommends a minimum of a 20 day course of antibiotics for Ixodes tick bite. When erythema migrans is present, treatment with antibiotics for a minimum of 4-6 weeks is recommended. Patients with persistent symptoms are treated with additional 4-6 weeks of antibiotics.
- Warshafsky (2010) found that those who received antibiotic prophylaxis by single dose or antibiotic <10 day duration, within 72 hours of Ixodes tick bite accompanied by erythema migrans as the presenting symptom were less likely to acquire Lyme disease than those given placebo with a RRR of 91%.
- Kowalski (2010) reported patients with early localized or early disseminated Lyme disease treated for <10 days with antibiotics have long-term outcomes similar to those of patients treated with longer courses of antibiotics.
- Fallon (2008) found that patients with Lyme encephalopathy treated with additional 10 weeks of IV ceftriaxone had greater improvement in cognition, physical functioning, pain and fatigue at 12 weeks after treatment, but at the 24<sup>th</sup> week improvement in cognition was not sustained. The study did find clinical significance in the most severely affected patients on physical function and pain.
- Delong (2012) found that when patients with confirmed Lyme disease received one standard course of antibiotic therapy for 21 days, who continued to have symptoms within 6 months of disease and received an additional 4 week course of IV ceftriaxone were found to have improved function and pain levels.
- Krupp (2003) reported that when patients received 28 days of IV ceftriaxone, after being treated with the standard course of 21 days of antibiotics, within 6 months of treatment they were found to have improvements in fatigue but not cognitive function (95% CI, P<.001).
- Horowitz (2013) reports that 75% of patients with acute Lyme disease will have resolution of symptoms in < 2 months if all 3 forms of Lyme *Borrelia* are treated with different regimens of antibiotics. Close to 25% of patients may need a longer course >2 months of antibiotic treatment if symptoms persist.

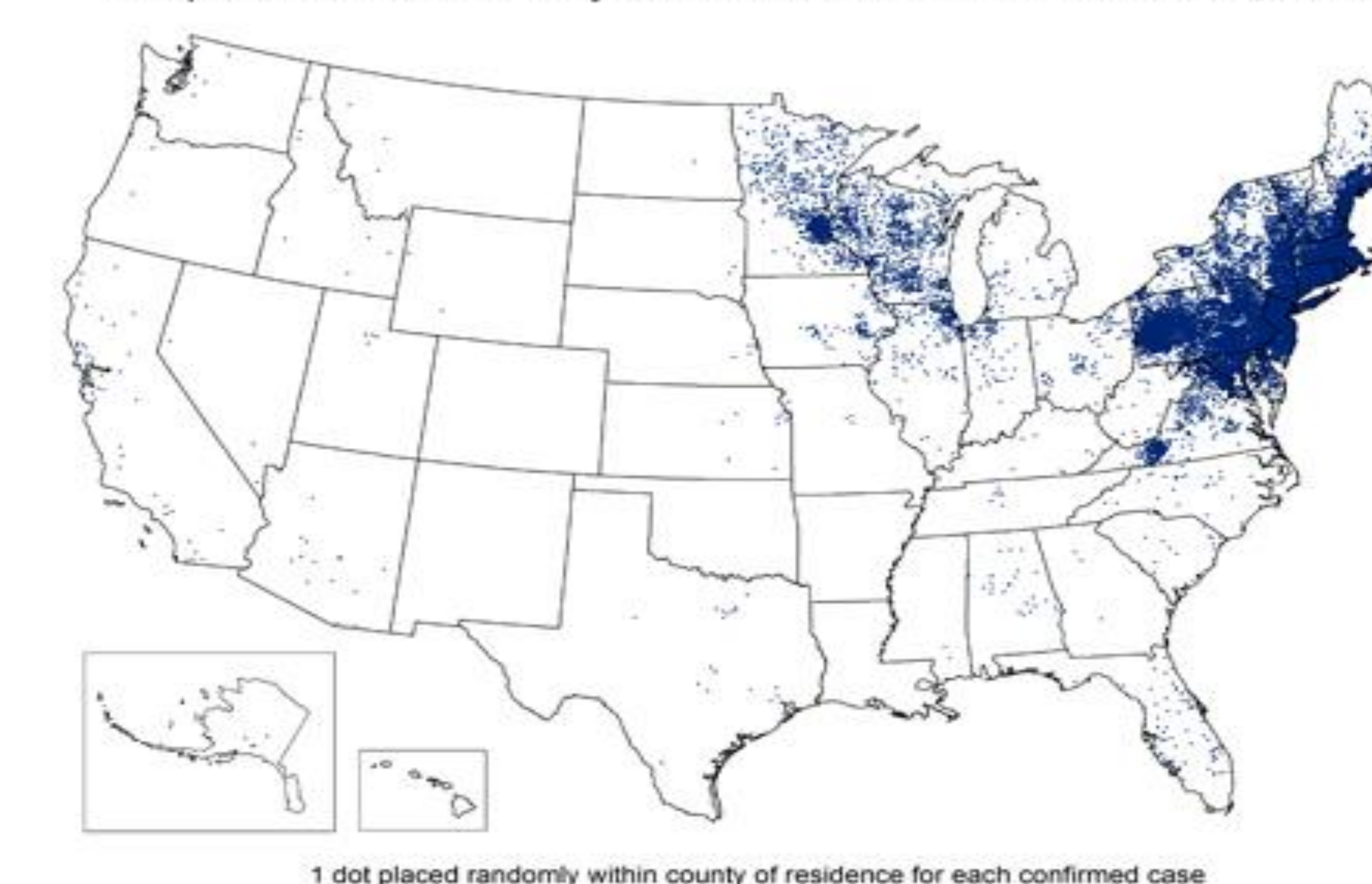
## Discussion

- Both short term and long term treatment regimens can be beneficial for reducing the persistent symptoms of Lyme disease.
- Short term course of antibiotics are beneficial if treatment is performed early enough in the course of the disease.
- Patients with persistent symptoms, would benefit from long term antibiotic treatments to help with symptoms of fatigue, pain, cognition and function.
- No one duration of antibiotic treatment has been demonstrated superior from the current research.
- 25-34% of patients will have ongoing Lyme symptoms after initial course of antibiotic treatment.
- All of the research found the use of a single antibiotic treatment regimen of either short term or long term had some benefit in symptoms.
- More research is needed for the use of combined antibiotic treatments and durations.



Forest plot of odds ratios of antibiotic treatment versus placebo for prophylaxis of Lyme disease. Black squares with horizontal bars indicate odds ratios and 95% confidence intervals (CIs) for individual studies. The size of each square is proportional to the size of the trial. The pooled odds ratio is represented by the white diamond; the width of the diamond represents the pooled 95% CI. The ratio  $n/N$  is defined as the number ( $n$ ) of Lyme disease cases that developed among the total number ( $N$ ) of study patients allocated to treatment or placebo.

Reported Cases of Lyme Disease -- United States, 2014



Reported cases of Lyme disease in the United States in 2014. Most cases reported are in the northeastern states and the Great Lakes Region. One dot is placed randomly within the county of residence for each reported case. From the Center for Disease Control and Prevention.

## Applicability to Clinical Practice

- Most clinicians in the United States use the IDSA guidelines for treatment of Lyme disease of 14-21 days.
- Improvements are seen in the majority of patients when treated early.
- Be aware of ongoing symptoms of Lyme disease which can include: fatigue, arthralgias, myalgias, headaches, sleep insomnia and numbness or tingling in the extremities.
- Testing for Lyme disease with the current diagnostic tests has low specificity and sensitivity. A clinical diagnosis is usually needed.
- Lyme disease treatments should be clinical and patient based.
- Horowitz questionnaire is a great tool to use for initial screening to help with clinical diagnosis of Lyme disease.

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