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Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease

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This evidence-based clinical practice guideline for the prevention, diagnosis, and treatment of Lyme disease was developed by a multidisciplinary panel representing the Infectious Diseases Society of North American (IDSA), the American Academy of Neurology (AAN), and the American College of Rheumatology (ACR). The scope of this guideline includes prevention of Lyme disease,

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and the diagnosis and treatment of Lyme disease presenting as erythema migrans, Lyme disease complicated by neurologic, cardiac, and rheumatologic manifestations, Eurasian manifestations of Lyme disease, and Lyme disease complicated by coinfection with other tick-borne pathogens. This guideline does not include comprehensive recommendations for babesiosis and tick-borne rickettsial infections, which are published in separate guidelines. The target audience for this guideline includes primary care physicians and specialists caring for this condition such as infectious diseases specialists, emergency physicians, internists, pediatricians, family physicians, neurologists, rheumatologists, cardiologists, and dermatologists in North America.

Summarized below are the 2020 recommendations for the prevention, diagnosis, and treatment of Lyme disease. The panel followed a systematic process used in the development of other Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR) clinical practice guidelines, which included a standardized methodology for rating the certainty of the evidence and strength of recommendation using the GRADE approach (Grading of Recommendations Assessment, Development, and Evaluation) (see Figure 1). A detailed description of background, methods, evidence summary and rationale that support each recommendation, and knowledge gaps can be found online in the full text (http://onlinelibrary.wiley.com/doi/10.1002/art.41562/abstract).

I. Which measures should be used to prevent tick bites and tick-borne infections?

A. Personal protective measures

Recommendation:

1. Individuals at risk of exposure should implement personal protective measures to reduce the risk of tick exposure and infection with tick-borne pathogens *(good practice statement).*

B. Repellents to prevent tick bites

Recommendation:

1. For the prevention of tick bites, we recommend N, N-Diethyl-meta-toluamide (DEET), picaridin, ethyl-3-(N-n-butyl-N- acetyl) aminopropionate (IR3535), oil of lemon eucalyptus (OLE), p-methane-3,8-diol (PMD), 2-undecanone, or permethrin *(strong recommendation, moderate-quality evidence)*.

C. Removal of attached ticks

Recommendations:

1. We recommend promptly removing attached ticks by mechanical means using a clean fine-tipped tweezer (or a comparable device) inserted between the tick body and the skin *(good practice statement)*.
2. We recommend against burning an attached tick (with a match or other heat device) or applying noxious chemicals or petroleum products to coax its detachment *(good practice statement)*.

II. Which diagnostic tests should be used following a tick bite?

A. Diagnostic tick testing

Recommendations:

1. We recommend submitting the removed tick for species identification *(good practice statement)*.

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are identical except for minor stylistic and spelling differences in keeping with each journal's style. The full guideline is available at http://onlinelibrary.wiley.com/doi/10.1002/art.41562/abstract.

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Conflict of interest information appears at the end of the text.

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[Correction added on 11 December, 2020 after first online publication: a paragraph was inserted on page 1, prior to the existing first paragraph.]

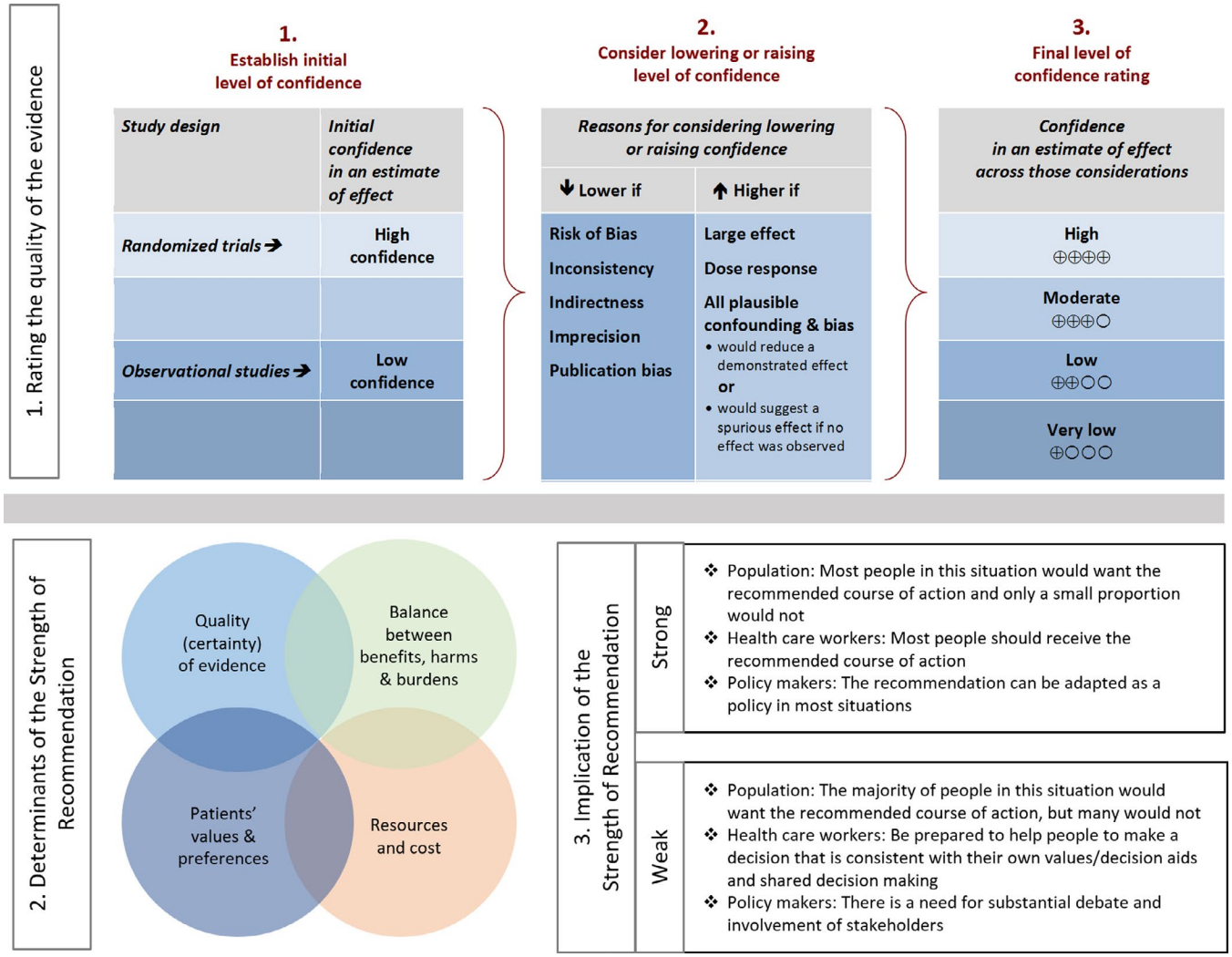

Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology (unrestricted use of the figure granted by the US GRADE Network) (1,2).

2. We recommend against testing a removed *Ixodes* tick for *B. burgdorferi (strong recommendation, moderate-quality evidence)*. **Comment:** The presence or absence of *B. burgdorferi* in an *Ixodes* tick removed from a person does not reliably predict the likelihood of clinical infection.

B. Diagnostic testing of asymptomatic patients following tick bites

Recommendation:

1. We recommend against testing asymptomatic patients for exposure to *B. burgdorferi* following an *Ixodes* spp. tick bite *(strong recommendation, moderate-quality evidence).*

III. Who should receive antibiotic prophylaxis to prevent Lyme disease following presentation with a tick bite?

Recommendation:

1. We recommend that prophylactic antibiotic therapy be given only to adults and children within 72 hours of removal of an identified high-risk tick bite, but not for bites that are equivocal risk or low risk *(strong recommendation, high-quality evidence)*. **Comment**: If a tick bite cannot be classified with a high level of certainty as a high-risk bite, a wait-and-watch approach is recommended. A tick bite is considered to be high-risk only if it meets the following 3 criteria: the tick bite was from (a) an identified *Ixodes* spp. vector species, (b) it occurred in a highly endemic area, and (c) the tick was attached for ≥36 hours.

IV. What is the preferred antibiotic regimen for the chemoprophylaxis of Lyme disease following a high-risk tick bite?

Recommendation:

1. For high-risk *Ixodes* spp. bites in all age groups, we recommend the administration of a single dose of oral doxycycline within 72 hours of tick removal over observation *(strong recommendation, moderate-quality evidence)*. **Comment:** Doxycycline is given as a single oral dose, 200 mg for adults and 4.4 mg/kg (up to a maximum dose of 200 mg) for children.

V. What is the preferred diagnostic testing strategy for erythema migrans?

Recommendations:

1. In patients with potential tick exposure in a Lyme disease endemic area who have 1 or more skin lesions compatible with erythema migrans, we recommend clinical diagnosis rather than laboratory testing *(strong recommendation, moderate-quality evidence)*.
2. In patients with 1 or more skin lesions suggestive of, but atypical for erythema migrans, we suggest antibody testing performed on an acute-phase serum sample (followed by a convalescent-phase serum sample if the initial result is negative) rather than currently available direct detection methods such as polymerase chain reaction (PCR) or culture performed on blood or skin samples *(weak recommendation, low-quality evidence)*. **Comment:** If needed, the convalescent-phase serum sample should be collected at least 2–3 weeks after collection of the acute-phase serum sample.

VI. What are the preferred antibiotic regimens for the treatment of erythema migrans?

Recommendation:

1. For patients with erythema migrans, we recommend using oral antibiotic therapy with doxycycline, amoxicillin, or cefuroxime axetil *(strong recommendation; moderate-quality evidence)*. **Comment:** For patients unable to take both doxycycline and beta-lactam antibiotics, the preferred second-line agent is azithromycin.

VII. How long should a patient with erythema migrans be treated?

Recommendation:

1. We recommend that patients with erythema migrans be treated with either a 10-day course of doxycycline or a 14-day course of amoxicillin or cefuroxime axetil rather than longer treatment courses *(strong recommendation, moderate-quality evidence)*. **Comment:** If azithromycin is used, the indicated duration is 5–10 days, with a 7-day course preferred in the United States, as this duration of therapy was used in the largest clinical trial performed in the United States (3).

VIII. Should patients with the southern tick–associated rash illness (STARI) be treated with antibiotics?

Recommendation:

1. In patients who develop an erythema migrans–like skin lesion following the bite of the lone star tick (*Amblyomma americanum*), an illness referred to as STARI, we make no recommendation for or against the use of antibiotics *(no recommendation; knowledge gap)*. **Comment:** In certain geographic regions both STARI and Lyme disease are endemic (4). Distinguishing single erythema migrans due to Lyme disease from STARI may not be possible clinically unless the responsible tick has been identified (5). When STARI cannot be distinguished from Lyme disease–associated erythema migrans in areas endemic for both conditions, antibiotic therapy directed toward Lyme disease is indicated.

IX. What is the preferred diagnostic testing strategy for Lyme neuroborreliosis?

Recommendations:

1. When assessing patients for possible Lyme neuroborreliosis involving either the peripheral nervous system (PNS) or central nervous system (CNS), we recommend serum antibody testing rather than PCR or culture of either cerebrospinal fluid (CSF) or serum *(strong recommendation, moderate-quality evidence)*.

2. If CSF testing is performed in patients with suspected Lyme neuroborreliosis involving the CNS, we (a) recommend obtaining simultaneous samples of CSF and serum for determination of the CSF:serum antibody index, carried out by a laboratory using validated methodology, (b) recommend against CSF serology without measurement of the CSF:serum antibody index, and (c) recommend against routine PCR or culture of CSF or serum *(strong recommendation, moderate-quality evidence)*.

X. For which neurologic presentations should patients be tested for Lyme disease?

Recommendations:

1. In patients presenting with 1 or more of the following acute disorders: meningitis, painful radiculoneuritis, mononeuropathy multiplex including confluent mononeuropathy multiplex, acute cranial neuropathies (particularly VII, VIII, less commonly III, V, VI, and others), or in patients with evidence of spinal cord (or rarely brain) inflammation, the former particularly in association with painful radiculitis involving related spinal cord segments, and with epidemiologically plausible exposure to ticks infected with *B. burgdorferi*, we recommend testing for Lyme disease *(strong recommendation, moderate-quality evidence)*.
2. In patients with typical amyotrophic lateral sclerosis, relapsing-remitting multiple sclerosis, Parkinson's disease, dementia or cognitive decline, or new-onset seizures, we recommend against routine testing for Lyme disease *(strong recommendation, low-quality evidence)*.
3. In patients with neurologic syndromes other than those listed in [1] or [2], in the absence of a history of other clinical or epidemiologic support for the diagnosis of Lyme disease, we recommend against screening for Lyme disease *(strong recommendation, low-quality evidence)*.
4. In patients presenting with nonspecific magnetic resonance imaging white matter abnormalities confined to the brain in the absence of a history of other clinical or epidemiologic support for the diagnosis of Lyme disease, we suggest against testing for Lyme disease *(weak recommendation, low-quality evidence)*.

XI. Should adult patients with psychiatric illnesses be tested for Lyme disease?

Recommendation:

1. In patients with psychiatric illness, we recommend against routine testing for Lyme disease *(strong recommendation, low-quality evidence)*.

XII. Should children with developmental, behavioral, or psychiatric disorders be tested for Lyme disease?

Recommendation:

1. In children presenting with developmental, behavioral, or psychiatric disorders, we suggest against routinely testing for Lyme disease *(weak recommendation, low-quality evidence)*.

XIII. What are the preferred antibiotic regimens for the treatment of acute neurologic manifestations of Lyme disease without parenchymal involvement of the brain or spinal cord?

Recommendation:

1. In patients with Lyme disease–associated meningitis, cranial neuropathy, radiculoneuropathy, or with other PNS manifestations, we recommend using intravenous (IV) ceftriaxone, cefotaxime, penicillin G, or oral doxycycline over other antimicrobials *(strong recommendation, moderate-quality evidence)*. **Comment:** Decisions about the choice of antibiotic among these, including the route of administration, should primarily be made based on individual factors such as side effect profile, ease of administration, ability to tolerate oral medication, concerns about compliance unrelated to effectiveness. Treatment route may be changed from IV to oral during treatment. The preferred antibiotic duration is 14–21 days.

XIV. Should patients with Lyme disease–related parenchymal involvement of the brain or spinal cord be treated with oral or intravenous antibiotics?

Recommendation:

1. In patients with Lyme disease–associated parenchymal involvement of the brain or spinal cord, we recommend using IV over oral antibiotics *(strong recommendation, moderate-quality evidence)*.

XV. Should patients with Lyme disease and facial nerve palsy receive corticosteroids in addition to antimicrobial therapy?

Recommendation:

1. In patients with Lyme disease–associated facial nerve palsy, we make no recommendation on the use of corti-

costeroids in addition to antibiotics (no recommendation; knowledge gap). **Comment:** In patients age 16 or older presenting with acute facial nerve palsy but without other objective clinical or serologic evidence of Lyme disease, corticosteroid treatment should be administered within 72 hours in accordance with current facial nerve palsy guideline recommendations (6).

XVI. Should all patients with early Lyme disease receive an electrocardiogram (ECG) to screen for Lyme carditis?

Recommendation:

1. We suggest performing an ECG only in patients with signs or symptoms consistent with Lyme carditis *(weak recommendation, low-quality evidence)*. **Comment:** Symptoms and signs of cardiac involvement in Lyme disease include dyspnea, edema, palpitations, lightheadedness, chest pain, and syncope.

XVII. Which patients with Lyme carditis require hospitalization?

Recommendation:

1. In patients with or at risk for severe cardiac complications of Lyme disease including those with significant PR prolongation (PR >300 milliseconds), other arrhythmias, or clinical manifestations of myopericarditis, we recommend hospital admission with continuous ECG monitoring *(strong recommendation, very low-quality evidence).* **Comment:** Clinical manifestations of Lyme carditis include exercise intolerance, palpitations, presyncope, syncope, pericarditic pain, evidence of pericardial effusion, elevated biomarkers (such as troponin), edema, and shortness of breath.

XVIII. What pacing modality should be used if needed for the management of Lyme carditis?

Recommendation:

1. For patients with symptomatic bradycardia due to Lyme carditis that cannot be managed medically, we recommend temporary pacing modalities rather than implanting a permanent pacemaker *(strong recommendation, moderate-quality evidence)*.

XIX. What are the preferred antibiotic regimens for the treatment of Lyme carditis?

Recommendations:

1. In outpatients with Lyme carditis, we suggest oral antibiotics over IV antibiotics *(weak recommendation, very low-quality evidence)*.
2. In the hospitalized patient with Lyme carditis, we suggest initially using IV ceftriaxone over oral antibiotics until there is evidence of clinical improvement, then switching to oral antibiotics to complete treatment *(weak recommendation, very low-quality evidence)*.
3. For the treatment of Lyme carditis, we suggest 14–21 days of total antibiotic therapy over longer durations of treatment *(weak recommendation, very low-quality evidence)*. **Comment:** Oral antibiotic choices for Lyme carditis are doxycycline, amoxicillin, cefuroxime axetil, and azithromycin.

XX. Should patients being evaluated for acute myocarditis/pericarditis or chronic cardiomyopathy of unknown cause be tested for Lyme disease?

Recommendations:

1. In patients with acute myocarditis/pericarditis of unknown cause in an appropriate epidemiologic setting, we recommend testing for Lyme disease *(strong recommendation, low-quality evidence).*
2. In patients with chronic cardiomyopathy of unknown cause, we suggest against routine testing for Lyme disease *(weak recommendation, low-quality evidence)*.

XXI. What is the preferred diagnostic testing strategy for Lyme arthritis?

Recommendations:

1. When assessing possible Lyme arthritis, we recommend serum antibody testing over PCR or culture of blood or synovial fluid/ tissue *(strong recommendation, moderate-quality evidence)*.
2. In seropositive patients for whom the diagnosis of Lyme arthritis is being considered but treatment decisions require more definitive information, we recommend PCR applied to synovial fluid or tissue rather than *Borrelia* culture of those samples *(strong recommendation, moderate-quality evidence).*

XXII. What are the preferred antibiotic regimens for the initial treatment of Lyme arthritis?

Recommendation:

1. For patients with Lyme arthritis, we recommend using oral antibiotic therapy for 28 days *(strong recommendation, moderate-quality evidence)*.

XXIII. What are the approaches to patients in whom Lyme arthritis has not completely resolved?

Recommendations:

1. In patients with Lyme arthritis with partial response (mild residual joint swelling) after a first course of oral antibiotic, we make no recommendation for a second course of antibiotic versus observation *(no recommendation, knowledge gap)*. **Comment:** Consideration should be given to exclusion of other causes of joint swelling than Lyme arthritis, medication adherence, duration of arthritis prior to initial treatment, degree of synovial proliferation versus joint swelling, patient preferences, and cost. A second course of oral antibiotics for up to 1 month may be a reasonable alternative for patients in whom synovial proliferation is modest compared to joint swelling and for those who prefer repeating a course of oral antibiotics before considering IV therapy.
2. In patients with Lyme arthritis with no or minimal response (moderate to severe joint swelling with minimal reduction of the joint effusion) to an initial course of oral antibiotic, we suggest a 2–4-week course of IV ceftriaxone over a second course of oral antibiotics *(weak recommendation, low-quality evidence)*.

XXIV. How should post-antibiotic (previously termed antibiotic-refractory) Lyme arthritis be treated?

Recommendation:

1. In patients who have failed 1 course of oral antibiotics and 1 course of IV antibiotics, we suggest a referral to a rheumatologist or other trained specialist for consideration of the use of disease-modifying antirheumatic drugs, biologic agents, intraarticular steroids, or arthroscopic synovectomy *(weak recommendation, very low-quality evidence)*. **Comment:** Antibiotic therapy for longer than 8 weeks is not expected to provide additional benefit to patients with persistent arthritis if that treatment has included 1 course of IV therapy.

XXV. Should patients with persistent symptoms following standard treatment of Lyme disease receive additional antibiotics?

Recommendation:

1. For patients who have persistent or recurring nonspecific symptoms such as fatigue, pain, or cognitive impairment following recommended treatment for Lyme disease, but who lack objective evidence of reinfection or treatment failure, we recommend against additional antibiotic therapy *(strong recommendation, moderate-quality evidence)*. **Comment:** Evidence of persistent infection or treatment failure would include objective signs of disease activity, such as arthritis, meningitis, or neuropathy.

XXVI. What is the preferred antibiotic regimen for the treatment of borrelial lymphocytoma?

Recommendation:

1. In patients with borrelial lymphocytoma, we suggest oral antibiotic therapy for 14 days *(weak recommendation, low-quality evidence)*.

XXVII. What is the preferred antibiotic regimen for the treatment of acrodermatitis chronica atrophicans?

Recommendation:

1. In patients with acrodermatitis chronica atrophicans, we suggest oral antibiotic therapy for 21–28 days over shorter durations *(weak recommendation, low-quality evidence)*.

XXVIII. Under what circumstances should a patient with Lyme disease be evaluated for coinfection with *A. phagocytophilum* or *B. microti*?

Recommendation:

1. In patients with Lyme disease who have a high-grade fever or characteristic laboratory abnormalities, clinicians should assess for possible coinfection with *Anaplasma phagocytophilum* and/or *B. microti* infection in geographic regions where these infections are endemic *(good practice statement)*. **Comment:** Coinfection should be investigated in patients who have a persistent fever for >1 day while on antibiotic treatment for Lyme disease. If fever persists despite treatment with doxycycline, *B. microti* infection is an important consideration.

Characteristic laboratory abnormalities found in both anaplasmosis and babesiosis include thrombocytopenia, leukopenia, neutropenia, and/or anemia. Evidence of hemolysis, such as elevated indirect bilirubin level, anemia, and elevated lactate dehydrogenase, is particularly suggestive of babesiosis.

Supplementary data. Supplementary materials (in addition to the full guideline) are available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.41562/abstract. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Conflict of interest statement. See the Methodology section in the full guideline (on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.41562/abstract) for approach to conflict of interest (COI) by the IDSA/AAN/ACR COI review group. The following list is a reflection of what has been reported to the IDSA/AAN/ACR COI review group. To provide thorough transparency, the IDSA/AAN/ACR requires full disclosure of all relationships, regardless of relevancy to the guideline topic. The assessment of disclosed relationships for possible COI is based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. Dr. Lantos has received research funding from the National Cytomegalovirus Foundation and from the NIH and educational funding from Duke University; and has served as a consultant and reviewed trial protocol for Frederick O'Connor Medical Consultants, LLC. Dr. Bockenstedt has received research funding from the NIH and the Gordon and Llura Gund Foundation; has received remuneration from L2 Diagnostics for investigator-initiated NIH-sponsored research; and was awarded an endowed professorship as the Harold W. Jockers Professor of Medicine at Yale University. Dr. Falck-Ytter serves as director of the Evidence Foundation and the GRADE Network; conducts GRADE workshops with the Evidence Foundation; has served as the chair of the Guidelines Committee for the American Gastroenterological Association; and has received research funding from the Cleveland VA Medical Research and Education Foundation. Dr. Aguero-Rosenfeld serves as a council member for the New York City chapter of the American Society of Microbiology (ASM) and as a Board member of the American Lyme Disease Foundation; has provided legal testimony and consultation regarding Lyme disease and tick-borne diseases; and has received research grants from the NIH, BioFire, New York State Department of Health, and ViraMed. 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Dr. Belani reviews non-continuing medical education (CME) lectures for and received honoraria and travel reimbursement from Horizon Therapeutics; and has received research funding from the NIH and the Children's Hospitals and Clinics of Minnesota. Dr. Bowie has provided expert testimony to the Canadian Senate Subcommittee on Bill C-442: An Act Respecting a National Lyme Disease Strategy on behalf of the Association of Medical Microbiology and Infectious Disease Canada; and has received research funding from GlaxoSmithKline, Pfizer Canada, the Canadian Institutes of Health Research, and Vancouver Coastal Health Research Institute. 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All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Lantos had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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