Lyme disease
Consultation on draft scope – deadline for comments 5.00pm on 14 April 2016
email: Lymedisease@nice.org.uk

Please note:
Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly or arrive after the deadline. Developing NICE guidance: how to get involved has a list of possible areas for comment on the draft scope.

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<tr>
<th>Stakeholder organisation (if you are responding as an individual rather than a registered stakeholder please state name here):</th>
<th>Lyme Disease UK</th>
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<td>Name of commentator (if you are responding as an individual rather than a registered stakeholder please leave blank):</td>
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The guideline committee will make final decisions about the presentations, infections, diagnostic tests and time frames under consideration. As part of the consultation, we would welcome stakeholder’s thoughts on the following:

1) Is the time period of ‘< than 6 months since tick bite or first symptoms or signs’ an acceptable interpretation for ‘early Lyme borreliosis’?
2) Is the time period of ‘> 6 months since tick bite or first symptoms or signs’ or an acceptable interpretation for ‘late Lyme borreliosis’?
3) The use of the British Infection Association¹ position paper classification to determine the range of clinical presentations that will be considered.
4) The inclusion of the following strains of Lyme Borreliosis for consideration as part of our review of the evidence:
   - B. burgdorferi (and the subtype B. burgdorferi sensu stricto),
   - B. garinii,
   - B. afzelii
5) The appropriate diagnostic tests for consideration

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<th>Line number</th>
<th>Comments</th>
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<td>Example</td>
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<td>The draft scope currently excludes people who have already been diagnosed. We feel this group should be included because…</td>
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Consultation on draft scope – deadline for comments **5.00pm on 14 April 2016**
email: Lymedisease@nice.org.uk
Lyme Disease UK is a patient support network with nearly 4000 members and bears witness daily to thousands of patients who are suffering on an inhumane scale. Many have been ridiculed by medical professionals in various disciplines, dismissed, belittled, neglected and left with increasingly frightening and painful symptoms for which no help or guidance is offered. Many people have lost their jobs, their homes, their life savings and their relationships and are now living in isolation and poverty. Others are left with no other option but to fundraise or in order to seek private Lyme disease and co-infection treatment (often overseas) or fund it themselves in an attempt to reverse the decline in their health and save their lives. The NHS guidance currently in use is failing these patients.

The general overview is that EM rashes are frequently being ignored by GPs and that people aren’t being asked about potential tick exposure. Furthermore, it often appears that people are not being offered Lyme disease testing despite presenting with numerous symptoms consistent with the disease. Some people even report hostility from doctors if they request a test and many are told that Lyme disease is either very rare or that it does not exist in this country and that they should not be researching the disease online. There have been accounts of patients, who were previously told that their Lyme disease tests were negative, discovering that they were in fact positive when they requested a copy of the laboratory report, sometimes months or years later. It also appears that people are all too readily being turned away or misdiagnosed with CFS, fibromyalgia and mental health issues without tick-borne infections even being considered. As Cameron et al point out in the ILADS guidelines, a survey involving Lyme disease patients, conducted by Johnson et al, reveals that ‘71.6% rated their health as fair or poor. This rate is higher than that seen in other chronic diseases including congestive heart failure, fibromyalgia, post-stroke and post-myocardial infarction status, diabetes and multiple sclerosis’.

It is important to note from shared patient experience that many people who have sought ongoing private treatment for Lyme disease are seeing improvements in their health after being essentially abandoned by the NHS.

References:
All known pathogenic strains of Borrelia should be covered in the scope and not just Borrelia afzelii, Borrelia garinii and Borrelia burgdorferi. One in five patients is thought to be infected abroad and so could potentially be affected by different species which should also be covered by UK testing and come under the term ‘Lyme disease’.

Borrelia valaisiana has been found in UK ticks according to the BIA position statement on Lyme borreliosis, although it states that Borrelia valaisiana is not regarded as pathogenic. However, in this study, Borrelia valaisiana was suspected of causing infection (Saito et al, 2007).

In this study, after culturing ‘live Borrelia bissettii-like strain from residents of North America,’ the results support the fact that B. bissettii is responsible for human Lyme borreliosis worldwide along with B. burgdorferi s.s. The involvement of new spirochaete species in Lyme borreliosis changes the understanding and recognition of clinical manifestations of this disease (Rudenko et al, 2016).

Borrelia miyamotoi also needs to be taken into consideration and incorporated into testing as it has been found in the UK (Hansford et al) and it is known to cause disease (Molloy et al, 2015).

The brief for the scope should include a review of the literature on other pathogenic strains of Borrelia, especially as there has been a number of new research papers since the BIA position statement was issued in 2011.

References:
Co-infections in Lyme disease patients appear to be common and should always be considered as part of the clinical picture, particularly in immunocompromised patients. ‘Ticks transmit more pathogens than any other arthropod, and one single species can transmit a large variety of bacteria and parasites’ (Moutalier et al, 2016).

This study states, ‘in the past, reports of pathology due to Babesia, Anaplasma, Ehrlichia, and Bartonella species have focused on the fulminant acute forms of infection that are relatively easy to diagnose and often fatal in immunocompromised patients. More recently, these organisms have been associated with chronic persistent infection in animal models and humans. The presence of coinfecting organisms has been shown to enhance the symptoms and exacerbate the severity of Lyme disease. Thus recognition of chronic coinfections supports the concept of unresolved illness due to persistent infection with the Lyme spirochete’ (Stricker and Johnson, 2011). In a patient survey conducted by the charity Caudwell LymeCo, preliminary results show that over 30% Lyme disease patients who participated also appear to have Babesia and over 15% have Bartonella henselae.

According to another survey done by Lyme Research UK in 2011, co-infections were also common in patients with Lyme disease. Out of 189 people diagnosed with Lyme borreliosis, 19 were diagnosed with Bartonella henselae, 7 with Bartonella quintana, 15 with Ehrlichia, 8 with Mycoplasma and 15 with Babesia (based specifically on positive tests with clinical assessment). Over 50% of this main group were not tested for each of these co-infections and therefore the possibility of even higher infection rates, is considerable.

The scope should consider the evidence relating to co-infections, as they could be a potential cause of comorbidity or complex conditions, rendering poorer treatment outcomes for Lyme disease patients. Considering and testing for other potential tick-borne infections should be included in the Lyme disease guidelines, particularly when there are indications of more varied or persistent symptoms or when standard Lyme disease treatment has failed.

Even if the management of other tick-borne infections is not included in the guidelines, there should be some reference to the possible complications they may cause in Lyme disease patients so that healthcare workers and the public are at least aware of their existence.

The patient experience appears to be that co-infections do not normally form part of the NHS diagnostic process, even if Lyme disease is detected, however, the ILADS guidelines state that ‘the possibility of co-infections should not be casually dismissed’ (Cameron et al, 2014).

### References:

| 4 | 2 | 51 |

Lyme disease can mimic many other conditions, including chronic fatigue syndrome (CFS). Why is CFS being singled out in this draft scope as a managed condition when there is no 100% accurate serological test for either Lyme disease or CFS and therefore the two cannot be easily separated? If the two are separated, this may lead to CFS patients being unable to have their diagnosis reconsidered even if they might have Lyme disease. Furthermore, the way in which CFS is managed could potentially be harmful to an undiagnosed Lyme disease patient.

Even if the risk of Lyme disease is properly investigated before diagnosing CFS (which does not always appear to be happening based on shared patient experience), weaknesses of current tests mean that some might nevertheless, actually have Lyme disease. Additionally, CFS patients who do not have Lyme disease may be at extra risk if they do happen to catch the disease because of the similarity in symptoms and the possibility that the infection may be dismissed as an 'exacerbation of existing CFS'. Discriminating against CFS patients who, if anything, may have a greater need to be further investigated for Lyme disease, could put these patients at risk.

Preliminary results from a patient survey conducted by VIRAS show that out of 44 participants, 16 people with Lyme disease have also been diagnosed with M.E.

The 2011 BIA position statement acknowledges that Lyme disease symptoms can overlap with other conditions - ‘late neurological sequelae of undertreated infection include a chronic encephalomyelitis, which can present with clinical features resembling multiple sclerosis.’

ILADS guidelines state, ‘in addition to the possible presence of co-infections, many other illnesses and conditions have clinical features which may overlap with those of Lyme disease; some examples are: infections due to Epstein–Barr virus or syphilis; autoimmune diseases such as rheumatoid arthritis, multiple sclerosis and vasculitis; metabolic and endocrine disorders such as diabetes, hypo- or hyperthyroidism and adrenal dysfunction; degenerative neurologic diseases such as Parkinson’s disease and amyotrophic lateral sclerosis and neurologic conditions such as peripheral neuropathy and dysautonomia; musculoskeletal diseases including fibromyalgia and osteoarthritis, psychiatric disorders, especially depression and anxiety and other conditions such as chronic fatigue syndrome and sleep apnea’ (Cameron et al, 2014).

Singling out CFS as an area that will not be covered may affect the literature review in terms of excluding investigations into the possibility that some CFS patients may have Lyme disease.

A recent patient survey by Caudwell LymeCo involving around 500 patients revealed that over 34% of patients who have a Lyme disease diagnosis obtained privately have only been given a CFS diagnosis by the NHS.

References
1. VIRAS patient survey 2016
http://counsellingme.com/VIRAS/IsabelSymptomCheckerSurvey.PDF
http://www.tandfonline.com/doi/full/10.1586/14787210.2014.940900
http://lymediseaseuk.com/2016/03/21/caudwell-lymeco-surveys-results-sneak-peek/
Transmission of the disease between people should not be excluded from the scope when there are so many important issues in this area. The CDC states, in this fact sheet that, ‘untreated, Lyme disease can be dangerous to your unborn child.’

The scope should include points relating to the following questions: Can Lyme disease be transmitted via blood transfusions or organ donations? Can Lyme disease be transmitted sexually or via breast milk?

Furthermore, is it ethical for people not to know how infectious they are, in particular women planning pregnancy? There is no definitive test that can prove that Lyme disease has been eradicated and yet there are many studies that show that Lyme disease can be a chronic, persistent infection. There is a great deal of uncertainty in the patient community in terms of how safe it is to become pregnant or to have unprotected sex.

Transmission via other biting insects and vectors such as horse-flies and mosquitoes should also be explored in the interests of public health and safety.

There have been a number of new research publications in these areas since the BIA position statement published in 2011 and therefore a review of the evidence would be highly beneficial both in terms of educating the medical profession and the public.

References:
1. Centers for Disease Control and Prevention Fact Sheet
2. List of 700 Articles Citing Chronic Infection Associated with Tick-Borne Disease Compiled By Dr Robert Bransfield
Prevention should be included in the key areas that will be covered, including the issue of whether prophylactic treatment following a known tick bite is helpful in certain cases, especially as the BIA position statement, published 2011, mentions that antimicrobial prophylaxis 'may be used in immunocompromised individuals following a tick bite.'

The ILADS guidelines recommend that ‘clinicians should promptly offer antibiotic prophylaxis for known Ixodes tick bites in which there is evidence of tick feeding, regardless of the degree of tick engorgement or the infection rate in the local tick population’ (Cameron et al, 2014).

It would be worth doing a literature review on the effectiveness of prophylaxis treatment and the economic costs and savings associated.

People with Lyme disease, may present without a rash (or known tick bite) and without prior basic knowledge of their risk of tick exposure. If a doctor asks them if they have been exposed to ticks and they are not even aware of their own risk (i.e. that ticks have been found in urban parks and gardens and not just geographical hotspots around the country), they may state that the chance of tick exposure is low. This could result in the patient not being tested for Lyme disease. Prevention, in terms of patient knowledge, is therefore not entirely distinct from diagnostic pathways.

Education about risks and knowledge of protection should be made available to healthcare workers and the public to reduce people’s chances of contracting Lyme disease. Leaflets and notices educating people about the disease should be visible in clinics and distributed widely in communities. According to this study, ‘encouraging a thorough check for ticks and promptly removal of ticks are the key public health strategies to reduce the risk of LB and other tick-borne diseases’ (Dehnert et al, 2012).

The ILADS guidelines recommend that when patients have been diagnosed with Lyme disease, ‘during the initial visit, clinicians should educate patients regarding the prevention of future tick bites’ (Cameron et al, 2014).

References:

It is important to note that the presentation of Lyme disease can vary significantly in terms of symptoms and clinical signs. Therefore, Lyme disease testing should be routinely included as part of the differential diagnostic process for any nonspecific symptoms which could have an infectious cause and for which another cause has not been found. However, there also needs to be awareness amongst medical professionals that there is currently no 100% accurate test available for the disease and so it cannot be ruled out based purely on serology unless a more accurate test is brought to market in the UK. Doctors need to be made aware of the shortcomings of current testing methods so that they can accurately inform patients and consider making a clinical diagnosis if applicable.
The question of how doctors can make an accurate clinical diagnosis of Lyme disease should be included in the scope as well as an exploration into how often this actually occurs in reality, especially in the absence of a 100% reliable test.

Are doctors really comfortable making a clinical diagnosis of Lyme disease, particularly in the absence of an EM rash? This study states ‘modern medical practice expects to rely on evidence. Most physicians would not consider diagnosing Lyme disease without serological proof’ (Perronne, 2014) and this appears to reflect the general patient experience.

If an EM rash is present, are doctors sufficiently aware that it is diagnostic of Lyme disease without the need for serology? Patient experience would suggest that GPs often misdiagnose EM rashes. Should effects and signs of damage consistent with Lyme disease be included as part of the clinical picture?

Patients who have received a clinical diagnosis of Lyme disease from qualified medical professionals either in the UK or abroad (often with accompanying positive overseas test results) are also having the diagnosis of Lyme disease frequently dismissed. As a result, they are being denied treatment in this country. Simply running the arguably flawed UK two-tiered testing should not be used as a way to override a clinical diagnosis of Lyme disease obtained privately from a qualified doctor or positive overseas test results. UK doctors should also be allowed to use their own clinical judgement when assessing patients with signs and symptoms of Lyme disease, especially if they have a private clinical diagnosis and/or a positive test result from an overseas laboratory. According to the ILADS panel, ‘guidelines should not constrain the treating clinician from exercising clinical judgment in the absence of strong and compelling evidence to the contrary’ (Cameron et al, 2014).

The result of the confusion surrounding diagnosis is that many Lyme disease patients are not treated at all. Preliminary results from a patient survey conducted by Caudwell LymeCo reveal that 52% of the participating Lyme disease patients were prescribed no antibiotics whatsoever on the NHS for this condition.

References:
There is currently no 100% accurate test available in the UK to rule out Lyme disease. The sensitivity and specificity of the two-tiered testing used in the UK should be examined as well as alternative test kits and testing methods used abroad (including culturing the bacteria as this test is available in America). In addition, the accreditation of UK and international laboratories offering Lyme disease testing should be explored to clear up issues surrounding the validity and acceptability of the tests currently available. There is a lot of confusion amongst patients surrounding the acceptability of foreign tests and a review into this subject is very important, especially if more accurate testing methods could be available abroad and brought to the UK.

This study states that ‘the two-tier algorithm recommended by the Centers for Disease Control and Prevention utilizes a screening enzyme-linked immunosorbent assay (ELISA) or immunofluorescence assay followed by a confirmatory Western blot. Although this approach has a high test specificity, the sensitivity of the two-tier approach in Lyme disease patients tested at least 4 to 6 weeks after infection is only 44% to 56%, which is inadequate for a clinical diagnostic test and, by comparison, far below the 99.5% sensitivity of diagnostic HIV testing’ (Stricker and Johnson, 2011).

The BIA position statement mentions that ‘B. garinii appears to be the most prevalent pathogenic genospecies in most endemic areas of the country.’ However, it appears that tests currently used in the UK do not include antigens to Borrelia garinii and therefore Lyme disease cases are most likely being missed.

The evidence relating to these issues needs reviewing so that up to date recommendations can be made about the overall reliability of the different types of serological testing, particularly when it comes to different species of pathogenic Borrelia.

The merits of other types of testing to assess cardiac, neurological and endocrinological issues, for example, should also be considered and the evidence should be reviewed to assess whether these investigations may aid doctors in making a clinical diagnosis of Lyme disease when serological test results fail to confirm the infection. In these guidelines it states that, ‘in the great majority of patients, chronic Lyme disease is a disease affecting predominantly the nervous system. Thus, careful evaluation may include neuropsychiatric testing, SPECT and MRI brain scans’(Burrascano 2008). The usefulness of general blood test results indicating infection or immunosuppression in a Lyme disease diagnosis should also be explored as well as the use of a carefully designed symptom questionnaire, like the one used by Dr R. Horowitz.

This study explains that ‘the complexity of Lyme disease requires high quality diagnostic methods, yet serology is the only diagnostic tool widely used’ (Perronne, 2014).

The use of more expensive tests or a greater number of tests to increase diagnostic accuracy needs to be weighed up against the cost of missing or misdiagnosing Lyme disease in a patient who then may be unable to work and who may require a higher usage of NHS services for continuing health problems. Preliminary results from a recent patient survey conducted by Caudwell LymeCo show that nearly 50% Lyme disease patients who participated are too ill to work.

The accuracy of the tests also needs to be stated clearly so that GPs and other treating physicians can better evaluate the likelihood of Lyme disease. Many patients have found that GPs are unaware of the questionable performance of the tests currently used and therefore, the chance to make a Lyme disease diagnosis in the early stages is frequently missed.

Physicians need to be aware that the current tests perform differently when different species of Borrelia are involved, or in specific groups of individuals such as immunocompromised patients.
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<td>The 2011 BIA position statement mentions that ‘some patients with previously untreated infection can develop features of late-stage disease, months or years later.’ This disease cannot be easily divided into two 6 month phases as proposed in the draft scope and it isn’t useful to do this, especially if people are unaware of when they were bitten or if their symptoms have a delayed onset. At present, there is no 100% accurate serological test to define any of these phases of the illness. A new, more precise list of patient categories and clinical scenarios needs to be composed by the committee and used to form the basis of evidence reviews.</td>
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<td>Possible terms include:</td>
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<td>• <strong>Acute Lyme disease</strong> - recently infected, seronegative due to lack of antibody production (usually less than 6 weeks).</td>
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<td>• <strong>Secondary/2nd stage Lyme disease</strong> - seropositive unless treated in acute stage with antibiotics. Disseminated infection but no lasting damage if treated adequately.</td>
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<td>• <strong>Tertiary/3rd stage Lyme disease</strong> - disseminated infection with permanent damage or complications.</td>
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<td>• <strong>Latent Lyme disease</strong> - seropositive but no current symptoms (as demonstrated by studies showing that a percentage of forestry workers have antibodies to Borrelia whilst being asymptomatic). It is unknown whether these people will go on to become symptomatic following stress on their immune system of any kind.</td>
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<td>• <strong>Refractory Lyme disease</strong> - standard treatment given but symptoms persist. With clearly defined terminology which covers a wide range of scenarios, suitable evidence reviews can take place. Terms like ‘chronic Lyme disease’ and even ‘early’ and ‘late’ Lyme disease cannot be properly defined in medical contexts and are open to interpretation which leads to overall confusion both for physicians and patients.</td>
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The term ‘definitive treatment’ should be replaced with ‘standard treatment’ as there is no proof that the treatment currently being offered for Lyme disease by the NHS is effective in the majority of cases. In fact this study showed that ‘over 63% of the Lyme disease cases had at least one diagnosis associated with PTLDS’ (post treatment Lyme disease symptoms) following early standard treatment (Adrion et al, 2015). Patients would argue that a continuation of symptoms does not mean that the treatment was ‘definitive’ or successful.

This information is available on Lymedisease.org’s website: ‘The International Lyme and Associated Diseases Society (ILADS), recently published new treatment guidelines. These guidelines contained a rigorous assessment of the evidence and found treatment failure rates ranging from 16% to 39% for early treatment. Estimates for patients with chronic Lyme disease are much higher, ranging from 26% to 50%. (Johnson 2004)’

Whether ongoing symptoms are due to a continuing infection or due to a past infection is uncertain, but with many studies showing Borrelia’s ability to persist, ongoing infection cannot be ruled out and therefore treatment cannot be described as ‘definitive’.

For those who have been treated, the patient experience often seems to be that people are told categorically by GPs that they cannot possibly still have Lyme disease following a standard course of antibiotics from the NHS. The ILADS guidelines state that, ‘there is no compelling evidence to support routinely withholding antibiotic retreatment from ill patients. While antibiotics are not always effective, the importance of providing patients with the opportunity to receive an adequate trial of antibiotic therapy is heightened by the lack of other effective treatment approaches. Palliative care may be helpful in addressing some symptoms in some cases, but it is important to bear in mind that palliative interventions also carry risks. Additionally, clinicians must not assume that palliative interventions would provide adequate treatment in the face of an underlying persistent infection. Therefore, in the panel’s judgment, antibiotic retreatment will prove to be appropriate for the majority of patients who remain ill’ (Cameron et al, 2014).

References:
   http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0116767
2. Lymedisease.org: Chronic Lyme Disease
   https://www.lymedisease.org/lyme-basics/lyme-disease/chronic-lyme/
   http://www.tandfonline.com/doi/full/10.1586/14787210.2014.940900
An extra point should be added here (point 4.6) to include groups of patients who are immunocompromised, who have co-morbidities, who are pregnant, and who have other concurrent tick-borne infections. The BIA position statement from 2011 refers to immunocompromised patients on page 334. Children may also present differently clinically and require different treatment and this should be reflected in the guidelines.

This article from Lymedisease.org highlights this point: ‘Children with Lyme disease have special issues. Since they can’t always explain what feels wrong, they may just come across as cranky and irritable. They suffer when their bodies hurt, when their illness disrupts their sleep at night, when they struggle in school, when they don’t even feel like playing. They may feel confused, lost and betrayed by parents and teachers who fail to recognize that they are sick and need help. Children with Lyme often have trouble in the classroom, because the disease can contribute to learning disabilities and behavioral problems.’

References:

An extra point for ‘Main Outcomes’ needs to be included (point 8) and the evidence should be reviewed on issues of chronic complex sequelae and comorbidity which may relate to Lyme disease such as heart problems, gallbladder and thyroid disease, to name a few. Many Lyme disease patients appear to suffer from the conditions mentioned above and so searching for and assessing the literature on these issues and potential connections, may lead to a greater understanding and improvements in Lyme disease patient outcomes.

The draft scope mentions that early symptoms of Lyme disease ‘are similar to those for flu.’ However, it is also important to note that Lyme disease can mimic many other conditions and present in numerous different ways, including neuropsychiatric manifestations. Fallon and Nields, in this study state that, ‘up to 40% of patients with Lyme disease develop neurologic involvement of either the peripheral or central nervous system. Dissemination to the CNS can occur within the first few weeks after skin infection’ and that ‘early signs include meningitis, encephalitis, cranial neuritis, and radiculoneuropathies.’

This quote reflects what appears to happen frequently in the patient community: ‘Time and again, Fallon, an expert in hypochondria, had seen frustrated doctors dismiss medically ill patients as psychiatric cases due to their own inability to diagnose the disease. With Lyme, the mistake was especially damaging since a delay in treatment could turn a curable, acute infection into a chronic, treatment-resistant disease’ (Weintraub, 2008).

It is important to include in the scope and guidelines that initial symptoms of Lyme disease are not always concurrent with a dismissable flu-like illness. Doctors must be made aware of the wide variety of ways in which Lyme disease may present and not assume symptoms are restricted to those of flu in the initial stages, especially as without a known tick bite or EM rash, it is often hard to distinguish between an acute early infection and a disseminated infection.

References:
The sentence ‘Lyme disease is frequently self-limiting and resolves spontaneously’ should be removed or rephrased. It is not representative of the general patient experience and it does not take into consideration existing and emerging evidence that Lyme disease can be a persistent infection. Furthermore, in the absence of 100% reliable tests, it cannot be proven that Lyme disease has been eradicated from a patient’s body.

This is highlighted in this study: ‘Clinicians have no diagnostic tests to check for the persistence of live borreliae. *B. burgdorferi*, having a complex genetic structure, is a highly adaptable organism capable of evading immune response through different processes’ (Perronne, 2014).

The ILADS guidelines state that ‘ongoing symptoms at the completion of active therapy were associated with an increased risk of long-term failure in some trials and therefore clinicians should not assume that time alone will resolve symptoms’ (Cameron et al, 2014).

References:

As there is no test that can rule out an active Lyme disease infection, the term ‘post-infectious Lyme disease’ should not be used, especially when there is evidence that the infection can persist. This study states, ‘extensive evidence now shows that persistent symptoms of Lyme disease are due to chronic infection with the Lyme spirochete in conjunction with other tick-borne coinfections’ (Stricker and Johnson, 2011). It would be more effective to review evidence and consider alternative terminology for ongoing symptoms consistent with Lyme disease.

References:

The evidence on how to define relapse should be reviewed as the ILADS guidelines state: ‘given that prior *B. burgdorferi* infections do not provide durable immunoprotection, clinicians should consider the possibility that the patient was re-infected and seek information to confirm or dispel that this occurred. In the absence of clear evidence of re-infection, clinicians and patients will need to consider the relative risks and benefits of assuming that relapsing symptoms such as EM lesions or flu-like symptoms in the summer are indicative of ongoing infection and not re-infection’ (Cameron et al, 2014).

References:
The statement ‘early treatment is almost always successful’ requires an evidence review. This is not reflective of the overwhelming number of people in the patient community who report ongoing health problems despite standard treatment for Lyme disease. Follow ups often do not occur, especially if patients move on to seek private Lyme disease treatment after feeling let down by the NHS, as is often the case based on anecdotal evidence from patients. The ILADS guidelines observe that ‘the optimum duration of post-treatment observation for EM has not been determined, in part, because while disease relapse is known to occur, the duration of the latent period is variable and can be prolonged’ (Cameron et al, 2014).

This study shows that following early treatment, 63% patients treated for Lyme disease still had symptoms which were then attributed to ‘post-treatment Lyme disease symptoms (PTLDS)’ (Adrion et al, 2015). In our opinion, this does not reflect ‘successful’ treatment. Furthermore, clinicians have no diagnostic tests to check for the persistence of live borreliae. B. burgdorferi, having a complex genetic structure, is a highly adaptable organism capable of evading immune response (Perronne, 2014).

The ILADS guidelines also state that ‘the harms associated with restricting treatment of an EM rash to 20 or fewer days of oral azithromycin, cefuroxime, doxycycline and penoxymethylpenicillin/amoxicillin outweigh the benefits. In assessing the risk–benefit profile, the panel determined that the failure rates for antibiotic treatment of 20 or fewer days were unacceptably high and that for those who failed treatment, the magnitude of the potential harm created by delaying definitive treatment, which includes the increased risk of developing a chronic and more difficult to treat form of the disease, was too great’ (Cameron et al, 2014).

References:
   http://www.tandfonline.com/doi/full/10.1586/14787210.2014.940900
   http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0116767

It is important to include the fact that ticks can be found in a variety of environments including urban parks (Jennett et al, 2013). Anecdotal evidence in the patient community also demonstrates that people have been bitten in urban gardens.

References:
   http://www.bristol.ac.uk/biology/people/richard-l-wall/pub/32548259

Anecdotal evidence from patients suggests that many doctors fail to recognise the EM rash. Many people with EM rash appear to be diagnosed with cellulitis, a bite allergy or ringworm instead and therefore the window for early treatment is frequently missed.

This study highlights this issue by stating ‘this lesion may go unrecognized, or be mistaken for an “insect bite” or an “allergic rash.” Mini-erythema migrans are less likely to be diagnosed’ (Perronne, 2014).

References:
When there is currently no test available to distinguish past infection from ongoing infection or new infection, the evidence and tests that the term ‘relapse’ is based on, should be reviewed.

Additionally, anecdotal evidence exists to suggest that patients who still have a positive test following ‘standard’ treatment for Lyme disease are told it is likely to be a false positive, even when clinical signs would suggest an ongoing infection.

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### Checklist for submitting comments

- Use this form and submit it as a Word document (not a PDF).
- Include page and line number (not section number) of the text each comment is about.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 response from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Underline and highlight any confidential information or other material that you do not wish to be made public.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Spell out any abbreviations you use
- For copyright reasons, do not include attachments such as research articles, letters or leaflets. We return comments forms that have attachments without reading them. The stakeholder may resubmit the form without attachments.

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Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory Committees.