

Lyme Disease PSP completed 2012										Original uncertainty	Comment on original uncertainty	Systematic reviews in preparation	Systematic reviews that need updating or extending	Ongoing controlled trials	Which outcomes?		
Indicative Uncertainty	Why is there uncertainty?	What is person's age?	Which types of treatments? 1	Which types of treatments? 2	Which types of treatments? 3	Which types of treatments? 4	Which types of treatments? 5	Which types of treatments? 6	Which types of treatments? 7								
Acupuncture, QiGong, graded exercise, or other alternative therapies for Lyme disease	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Complementary therapies	Physical therapies						Research into the treatment of Lyme arthritis - should this be the same as for rheumatoid arthritis - are any additional therapies recommended other than drug treatment? eg acupuncture, CBT, graded exercise, QiGong, etc					Change in symptoms; adverse effects or complications; and cost	
Alicin for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How can we incorporate extremely beneficial natural antibiotics into NHS funded treatment? I have been taking Alicin from Alicin International and it has killed all forms of the Lyme bacteria and potentially Babesia as a co-infection. No need for switching between different antibiotics and no nasty side effects as it is a natural product. More research is definitely required into natural antibiotics and their extremely beneficial effects.					Eradication of infection; improvement of symptoms	
Altered blood pH for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Can chronic Lyme disease be treated by slightly altering blood pH so the blood is slightly more alkaline than acidic					Eradication of infection; improvement of symptoms	
Alternating different antibiotics for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Is there any evidence that shows a patient recovers more quickly and more lastingly on intravenous treatment? Is there any evidence that shows a patient recovers more quickly and more lastingly on combinations of antibiotics? Is there any evidence that shows a patient recovers more quickly and more lastingly on any one regime of taking treatment, for instance by pulsing their treatment, or alternating different types of antibiotics?					Eradication of infection	
Antibiotic gels for the prevention of Lyme disease in patients with tick bites	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Is there a way of preventing catching Lyme's, e.g. vaccine or gel?			Prevention of Borrelia infection and prevention of borreliosis through application of a gel, within three days, on the site of the tick bite (EUCTR2011-00012-0246)	Prevention of Lyme disease symptoms; adverse effects or complications; and cost		
Antibiotic treatment based on clinical suspicion for Lyme disease after a negative serological test	Uncertainties identified from clinicians' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: should doctors attempt to treat people with symptoms of Lyme disease when the lab test is negative, as a therapeutic trial, particularly when there is a typical history, symptoms and signs?					Eradication of infection; improvement of symptoms	
Antibiotic treatment based on clinical suspicion versus waiting for serology results in possible Lyme disease	Uncertainties identified from clinicians' questions	No relevant systematic reviews identified	Any age	Drug	Service delivery						This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: should you treat immediately on clinical suspicion alone or await the result of blood tests Should you proceed with treatment before serology results come back?					Prevention of Lyme disease symptoms; Change in symptoms; eradication of infection; adverse effects or complications; and cost	
Antihistamines for dermatomal itching associated with Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: When symptoms continue, and further antibiotic treatment is refused, is there any problem with long term (for years) anti-histamine treatment in the over 65s for symptoms such as dermatomal itching?					Improvement of symptoms	
Appropriateness of US guidelines for early Lyme disease in treating UK and European cases	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Mixed or complex	Drug						This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What is the most effective treatment for UK/European late stage Lyme neuroborreliosis? Can the results of treating early stage disease and the American form of the disease be confidently extrapolated to UK/Europe?					Eradication of infection	
Are continuing symptoms of Lyme disease following conventional recommended treatment due to continued infection, or an immune response or other process?	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Diagnostic							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: ? Are continuing symptoms following antibiotic treatment indication of an immune system involvement (auto immune disease)? ? How much of the symptoms and disability in chronic/late stage Lyme neuroborreliosis is due to the direct response to infection/ inflammation and how much is due to auto-immune dysfunction and can this be tested for? ? Does Lyme disease trigger auto-immune disease? ? Is chronic Lyme disease a real condition, or are the tests just indicating past infection?					Change in symptoms; adverse effects or complications; acceptability to patient and clinician; and costs	
Are there long-term consequences for Lyme disease if treatment is delayed?	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Diagnostic							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Can I give blood? Can I donate my organs? Is there any evidence of placental transmission from infected mother to foetus? Can Borrelia be transmitted from breast milk to a feeding baby? Can Lyme disease be transmitted between individuals? Bodily fluids, blood transfusions, sexually and pregnancy?					Change in symptoms; adverse effects or complications; acceptability to patient and clinician; and costs	
Artesunate for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How effective is artesunate in treating Lyme? Can it also be used to treat other co-infections?					Change in symptoms; eradication of infection; adverse effects or complications; and cost	
Can Lyme disease be transmitted via other means?	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Diagnostic							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How common is relapse of infection following the standard evidence-based 28 days of oral doxycycline treatment is late stage LD more prone to relapse than LD treated at an early stage? Is treatment failure related to gender differences in infecting Borrelia strains or any particular risk groups? Does the presence of a coinfection adversely affect outcome in Lyme borreliosis? Can Lyme disease be transmitted via other means: person to person sexually, transplacentally or by breast feeding, through organ donation, through blood transfusion?					Transmission	
Clinical course of action when a patient undergoing treatment for Lyme disease experiences a second tick bite	Uncertainties identified from clinicians' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How long do you treat for if further tick bite during initial 2-week course of antibiotics?					Eradication of infection; adverse effects or complications; and cost	
Combined treatment with macrolides and hydroxychloroquine for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Are macrolides with hydroxychloroquine a valid combination of treatment to target both the cyst form and the spirochetal form of B burgdorferi?					Eradication of infection	
Comparison of initial antibiotic regimens for Lyme disease where both options are less than one month	Uncertainties identified from clinicians' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Optimal treatment at various stages including minimum duration I would like to know how long a course of treatment should be at each stage for optimal success-ideal length of treatment for antibiotics, best method of diagnosis/ specificity/ sensitivity of serological testing, How long antibiotic treatment needs to be continued for? How long should antibiotics be given for to treat/cure?-Duration of treatment and treatment efficacy Why is there no firm answer about the best treatment for Lyme disease? What doses of antibiotics are best depending upon the weight of the patient? How long should antibiotic treatment continue for optimum result?					Eradication of infection; adverse effects or complications; and cost	
Criteria for prophylactic treatment, and choice of antibiotic regimen, to prevent Lyme disease following a tick bite	Uncertainties identified from clinicians' questions	Relevant reliable up-to-date systematic reviews do not address continuing uncertainties about treatment effects	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: To clarify when to give prophylactic antibiotic treatment following a known tick bite. Which antibiotic to prescribe and duration of therapy. Should we just treat every tick bite with antibiotics if history of tick bite is better to justify treat? are prophylactic antibiotics warranted after a bite in a Lyme area. how should post treatment symptoms be tackled Should you give prophylactic antibiotics for tick bites? Should prophylactic antibiotics be given for tick-bites? If I remove a large (engorged) tic from my Child / Adolescent should they be given prophylactic antibiotics?					Warshafsky S, Lee DH, Francis LK, Nowakowski J, Nadelson RB, Wormser GP. Efficacy of antibiotic prophylaxis for the prevention of Lyme disease: an updated systematic review and meta-analysis. J Antimicrob Chemother. 2010 Jun;66(6):1127-44. (15 1090)doi:10.1093/acq/kq079	Prevention of Lyme disease symptoms; adverse effects or complications; and cost
Detoxification therapy for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How important is detoxification whilst taking medication for Lyme/co-infections and what are the best detoxification products/medications to take.					Eradication of infection; improvement of symptoms	
Dietary interventions during recovery from Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Diet							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What is the role of diet in the recovery process from Lyme Disease? What is the recommended diet for patients with Lyme Disease? Number of cases in the UK, how effectively it can be treated, how long it takes to treat, change of diet and sleep a nutrition as well as ability of sleep and exercise					Change in symptoms; adverse effects or complications; and cost	
Dietary supplements, herbal medicines, or other alternative medications for Lyme disease when taken in combination with conventional treatment.	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug	Complementary therapies						Are there any alternative therapies/ herbal medications that are effective against Lyme/Co-infections and can they be utilised in conjunction with conventional medicine?					Change in symptoms; eradication of infection; adverse effects or complications; and cost	
Effect of antibiotic treatment on the results of serological tests for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Current ELISA/MS test: Clear guidance needed when this may not show a positive result eg too soon or too long after a bite and whether a recent course of antibiotics affects the result. If on antibiotics at the time of tick bites, does this prevent Lyme disease? If clear guidance is needed on the reliability of the blood tests?					Accuracy of serological tests for Borrelia sp	
Effect of time from infection to commencement of treatment on Lyme disease outcomes	Uncertainties identified from clinicians' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Are there longterm consequences if treatment is delayed?					Prevention of Lyme disease symptoms; Change in symptoms; eradication of infection; adverse effects or complications; and cost	
Exercise interventions during recovery from Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Exercise							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What effect does different types of exercise have on the recovery process from Lyme disease? When suffering from fatigue during Lyme disease is exercise harmful or beneficial? How much exercise and what type is best to aid health improvements when on treatment? Exercise: is it good or bad? what sort of exercise should be prescribed for Lyme sufferers, who are often exhausted and who sleep for long periods each day at certain phases of the illness? Exercise ? is it good or bad for Lyme sufferers? What type of exercise should they try? How safe is it? what sort of exercise is best for Lyme sufferers? If exercise is as simple as walking or yoga) could be proved to help, Lyme sufferers might be kept more mobile for later in life which will be good for them and good for their carers/the health service too. Number of cases in the UK, how effectively it can be treated, how long it takes to treat, change of diet and sleep a nutrition as well as ability of sleep and exercise					Change in symptoms; adverse effects or complications; and cost	
Fixed courses of antibiotics versus continuing until all symptoms are resolved in Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							Should antibiotic treatment continue until after all symptoms have disappeared, cdt7 is in normal range etc or should it be stopped earlier and the immune system supported so that it can get on top of the remaining infection?					Eradication of infection; change of symptoms; adverse effects or complications; and cost	

Heavy metal chelation for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug	Complementary therapies															What is the efficacy of heavy metal chelation as treatment for someone with chronic Lyme who has not improved after long courses of antibiotics?	This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What is the efficacy of heavy metal chelation as treatment for someone with chronic Lyme who has not improved after long courses of antibiotics?							Change in symptoms; adverse effects or complications; and cost																		
Home versus hospital-based intravenous antibiotic treatment for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug	Service delivery															This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How cost-effective/safe is home IV antibiotic treatment for Lyme borreliosis vs Hospital based treatment?											Eradication of infection															
Homeopathy for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug	Complementary therapies															This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Have you looked into this? What homeopathic and alternative treatments (not chemical based) can help with killing Lyme Disease? I was diagnosed using a Quantum QNCS/SD's diagnostic system and cured by homeopathy. Have you looked into this?										Change in symptoms; eradication of infection; adverse effects or complications; and cost																
How common is relapse and treatment failure in Lyme disease?	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Diagnostic																This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Which single test performs best in diagnosing or ruling out active Lyme disease? Could a combination of tests be used to improve diagnostic sensitivity? Why does the US IGeneX test appear to be successful on UK patients? Would using more bands in the immunoblot increase sensitivity? Should antigens from UK strains of Borrelia be used, as at the Inverness lab? Do the UK tests detect borreliosis due to species and strains present in the UK? Have the tests kept pace with new discoveries of pathogenic species of Borrelia in Europe? Is there a test which can differentiate persistent active infection versus autoimmune response? Do older people have a weaker immune response and should patient age be taken into account when interpreting the serology tests? In very long standing infection do the antibody levels decline and should this be taken into account when interpreting the blood test result? Is it possible to have very late stage Lyme disease and yet have negative standard blood tests? Are antibodies produced to different antigens as Lyme disease develops in a person and should the likely stage of the disease (ie early or late) determine the criteria used (ie which bands and how many) for interpreting a Western blot test result? When there are positive IgM antibodies several months into the infection, why are the antibodies not said to be related to the infection? How are genuine seronegative cases identified? Which blood test is any accurate enough to identify if the infection has been adequately treated? Is there a test which can differentiate persistent active infection versus autoimmune response? Why is there a 2 tier form of testing when the manufacturers of the test say that a negative result should not rule out a diagnosis of Lyme disease. Why not use western blot concurrently? How common is relapse and treatment failure in Lyme disease and is it related to disease stage, gender, coinfections or any other factor?																										Relapse
How effective are the current UK tests in detecting Lyme disease infections due to the genospecies and strains of B burgdorferi in the UK?	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Diagnostic																This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: 3 weeks treatment as effective as 3 years? What are the long term outcomes of antibiotic treatment of 2 weeks, versus several months or years? Does the long generation time of B burgdorferi mean that a longer course of treatment is likely to be necessary than most for other infections: are there any studies of patients who have recovered on long term antibiotics? Is there evidence that the Lyme Disease Paediatricians/Clinicians who treat their patients for a number of months/years can have successful outcomes with patients for whom shorter courses of treatment have previously failed? How effective are the current UK tests in detecting Lyme disease infections due to the genospecies and strains of B burgdorferi in the UK and which single test and what combination of tests performs best in diagnosing or ruling out active Lyme disease. Should stage of the disease and patient age be taken into account when interpreting these tests?																										Diagnostic
Immunosuppressive drugs for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Are continuing symptoms following antibiotic treatment indication of an immune system involvement (auto immune disease) and if so, how are would immune suppressive drugs be of use?														Change in symptoms; eradication of infection; adverse effects or complications; and cost												
Interventions for facial palsy associated with Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What is the best treatment for facial palsy due to Lyme disease? In a patient with probable Lyme Disease & recent onset Bell's palsy - do antibiotics need to be continued until the Bell's palsy has resolved?												Improvement of symptoms														
Interventions for failure of the initial course of antibiotics for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: If symptoms continue after initial treatment, should treatment be continued for a longer time, at a higher dose or with a different antibiotic?													Eradication of infection; Change in symptoms; adverse effects or complications; and cost													
Interventions for neuropathic pain in Lyme disease	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Mixed or complex	Exercise	Drug	Psychological therapy	Physical therapies	Complementary therapies											This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Are there effective treatment options for neuropathic pain and discomfort caused by Lyme disease? eg pregabalin, gabapentin, antidepressants?													Change in symptoms; adverse effects or complications; and cost													
Interventions for psychiatric symptoms associated with Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Psychological therapy																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What research is being carried out about the effects of Borrelia burgdorferi on the brain and mental functions? (the fog-like sense that results from Lyme disease, the deterioration in memory that results, etc.)												Change in symptoms; adverse effects or complications; and cost														
Interventions for relapse in Lyme disease following completion of treatment regimen	Uncertainties identified from clinicians' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Is there any reason not to give longer courses of antibiotics to people who have Lyme disease where they clearly respond well but then relapse immediately on stopping antibiotics? Is it feasible that a patient will benefit from a second course of antibiotics after the first course has been successful, but the patient relapses shortly after completing the treatment?															Eradication of infection; Change in symptoms; adverse effects or complications; and cost											
Interventions to aid staying at or returning to work during or following Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Adult	Mixed or complex	Exercise	Psychological therapy	Complementary therapies	Physical therapies												This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Work - should Lyme disease patients try to work or would they be better concentrating on trying to recover without the stresses and strains that work inevitably brings?													Change in symptoms; return to work; adverse effects or complications; and cost													
Interventions when Lyme disease symptoms are failing to respond during treatment	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: - If symptoms continue after initial treatment, should treatment be continued for a longer time, at a higher dose or with a different antibiotic? Although I completed the treatment and was discharged from hospital, some brightlight after the last IV injection I began to notice that my intellectual function in particular, seemed to be deteriorating. The return of other symptoms, including facial twitching, mild headaches and lethargy, led me to ask my GP to request a further consultation with the neurologist, prior to the scheduled review. The latter declined to see me before a four month period had elapsed, however and indicated to both me and my GP that in his opinion, the treatment was over. I understand that this is because the treatment I have received is in line with NICE guidelines, but if this is so, what can be done for people whose symptoms continue?																									Eradication of infection; Change in symptoms; adverse effects or complications; and cost	
Intravenous ceftriaxone for late Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: How effective is intravenous Ceftriaxone on late stage Lyme and does its effectiveness increase in combination with other drugs and if so, which ones and for how long?													A double-blind, randomised, placebo-controlled trial of prolonged antibiotic treatment after intravenous ceftriaxone in patients with (possible) persistent Lyme disease (NTR2466).	Eradication of infection												
Intravenous versus oral antibiotic treatment for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug																This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Comparison of intravenous v. oral antibiotic regimens for the eradication of borrelia infection. Is there any evidence that shows a patient recovers more quickly and more lastingly on intravenous treatment? Is there any evidence that shows a patient recovers more quickly and more lastingly on combinations of antibiotics? Is there any evidence that shows a patient recovers more quickly and more lastingly on any one regime of taking treatment, for instance by pulsing their treatment, or alternating different types of antibiotic?																							Eradication of infection; adverse effects or complications; and cost			



Steroids for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What are the effects of steroids and immune-suppressive drugs on Lyme disease?					Eradication of infection; improvement of symptoms
Tetracycline versus doxycycline for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Is there evidence that tetracycline might be more effective than doxycycline? Is there any proven treat for ongoing arthralgia post Lyme which was treated late but appropriately. Can the organism be identified in synovial fluid.					Eradication of infection
The Marshall Protocol for Lyme disease	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: I have read about the Marshall Protocol for treating chronic Lyme disease. MarshallProtocol.com It is American and seems to use a different approach, but successfully - should we be looking into this in UK?					Improvement of symptoms; eradication of infection
Treatment with a single antibiotic versus a combination of antibiotics for Lyme disease	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Is there any evidence that shows a patient recovers more quickly and more lastingly on combinations of antibiotics? I would like to know what combination of antibiotics gives the greatest chance of success. Comparative studies of different treatment regimes long versus short course antibiotics, combination therapy? Are a combination of antibiotics more effective on some patients? And it seems from our experience of our toddler worsening with her initial treatment that NHS guidelines aren't adequate? Are a combination of antibiotics more effective in treating Lyme disease? Does a pulsed regimen of antibiotics have any advantage over a continuous course. Are metronidazole/trimethoprim effective antibiotics for the treatment of Lyme disease and how should they be used? Is it advisable to use a higher dose of doxycycline (>200mg/day) to ensure high enough concentration in the CSF? should the dose of antibiotic depend on the patient's weight? UK DUES identifier: 413671, 413662, 413663, 413664, 413665, 413671, 413670.				Eradication of infection; adverse effects or complications; and cost	
What are the outcomes of cases in Lyme disease where long term treatment has been used?	Uncertainties identified from carers' questions	Existing relevant systematic reviews are not up-to-date	Any age	Diagnostic							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What is the best treatment for o early localised Lyme disease in children and adults? o early disseminated Lyme disease (inc cardiac) in children and adults? o late Lyme disease in children and adults, without neurological involvement? o late Lyme neuroborreliosis in children and adults? o very late diagnosed Lyme disease (ie more than 3 years of infection) Is a combination of antibiotics more effective in treating Lyme disease? Does a pulsed regimen of antibiotics have any advantage over a continuous course. Are metronidazole/trimethoprim effective antibiotics for the treatment of Lyme disease and how should they be used? Is it advisable to use a higher dose of doxycycline (>200mg/day) to ensure high enough concentration in the CSF? should the dose of antibiotic depend on the patient's weight? UK DUES identifier: 413671, 413662, 413663, 413664, 413665, 413671, 413670.	Cadavid D, Auwaerter P, Aucoti J, Rumbaugh J. Treatment for the neurological complications of Lyme disease. Cochrane Database of Systematic Reviews. (10.1002/14651858.CD006878)	Loewen PS, Marra CA, Marra F. Systematic Review of the Treatment of Early Lyme Disease. Drugs. 1999 Feb;57(2):157-73.	Antibiotic Treatment of Multiple Erythema Migrans NCT01163994 Study of Lyme Neuroborreliosis NCT01630206 Doxycycline and Ceftriaxone in Suspected Early Lyme Neuroborreliosis NCT00942006	Change in symptoms; adverse effects or complications, acceptability to patient and clinician; and costs	
What is the best treatment for children and adults presenting with a) early Lyme disease without neurological involvement and not including erythema migrans and b) late Lyme disease of any manifestation?	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: What is the optimal course of action if symptoms persist after initial treatment: should antibiotic treatment be continued until all symptoms have resolved or should a different dose or different antibiotic be used and what is the course of action if treatment appears to fail completely? In the treatment of early Lyme Disease in patients with systemic symptoms - eg fatigue, myalgia - how quickly would patients be expected to start responding to antibiotics? After what period of time should a doctor consider changing antibiotics or adding in a second antibiotic in a patient who is not responding? Is the current regime of short term anti-biotic treatment sufficient and if not, in what circumstances should alternatives be used? what is the optimal treatment strategy for antibody positive patients with chronic symptoms What is the optimum dose of which antibiotic and for how long in the case of chronic Lyme disease UK DUES identifier: 413670 What is the best treatment for children and adults presenting with a) early Lyme disease without neurological involvement and not including erythema migrans and b) late Lyme disease of any manifestation? To include consideration of drugs), dose, duration?				Change in symptoms; adverse effects or complications, acceptability to patient and clinician; and costs	
What is the optimal course of action for Lyme disease if symptoms relapse after a treatment course is finished?	Uncertainties identified from patients' questions	No relevant systematic reviews identified	Any age	Drug							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Would a "weighting table" be useful in aiding diagnosis (eg scoring symptoms, signs, tick exposure, test results, etc. similar to a risk calculator. What is the frequency of different presentations in the UK? Is there any combination of symptoms and signs that indicate Lyme disease? Clinical differential diagnosis: How best can Lyme disease be differentiated from rheumatoid arthritis, CFS/ME, Multiple sclerosis, Bionmyalgia, auto-immune diseases and psychiatric conditions.				Change in symptoms; adverse effects or complications, acceptability to patient and clinician; and costs	
What is the optimal course of action if symptoms persist in Lyme disease after initial treatment?	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Drug							This is one of the Lyme Disease Ranked top ten priorities. This is an indicative uncertainty, and the following questions were submitted to the survey and the Steering group felt the above uncertainty captured all of the following submissions: Is it feasible that a patient will benefit from a second course of antibiotics after the first course has been successful, but the patient relapses shortly after completing the treatment? Is there any reason not to give longer courses of antibiotics to people who have Lyme disease where they clearly respond well but then relapse immediately on stopping antibiotics? What is the optimal length & combination of treatment in late/relapsing Lyme? UK DUES identifier: 413680 What is the optimal course of action if symptoms persist in Lyme disease after initial treatment: should antibiotic treatment be continued until all symptoms have resolved or should a different dose or different antibiotic be used and what is the course of action if treatment appears to fail completely?				Change in symptoms; adverse effects or complications, acceptability to patient and clinician; and costs	
What key questions (clinical and epidemiological) should be considered to help make a diagnosis of Lyme disease in children and adults in the UK?	Uncertainties identified from carers' questions	No relevant systematic reviews identified	Any age	Diagnostic							This is one of the Lyme Disease Ranked top ten priorities. What key questions (clinical and epidemiological) should be considered to help make a diagnosis of Lyme disease in children and adults in the UK and would a weighting table be useful?				Diagnostic; change in symptoms; adverse effects or complications, acceptability to patient and clinician; and costs	