Funded by the National Institute for Health Research

UK Lyme Disease Priority Setting Partnership
Deciding the Final Priorities

How the shortlist was created

The full list of 967 questions submitted by both clinicians and patients during the 2011 survey was sorted and duplicates merged. After eliminating those questions which were outside the scope of the project the list was consolidated into a set of 81 representative questions.

An independent information specialist examined the scientific literature, and the questions were categorised as follows:

1. 69 questions **not currently answered** by a systematic review and needing further research;
2. 5 questions currently the subject of **a study or trial,** so no research indicated on these at the moment;
3. 7 questions **already answered** and not in need of further research.

The 69 currently unanswered questions in group 1 included separate questions on the best treatment at different stages of the disease - early Lyme disease, neurological Lyme disease, Lyme carditis, late Lyme disease etc. It had been necessary to separate these for the purposes of a literature search but it was clear that if they were left as individual questions, they would be likely to nearly fill the top 10 without leaving room for other questions.

The 69 questions were therefore further consolidated into a set of 39 questions which provided a manageable number for the final on-line priority survey in which people were asked to vote for their own top 10. Fewer people responded to this final survey than had submitted uncertainties in the first survey. This may have been because some questions were technical and required some knowledge of Lyme disease or perhaps because the final survey was open for a considerably shorter time and was publicised in very few LMC (Local Medical Committee) newsletters.

Submission of questions: 253 submissions, 34% of them from clinicians
Final survey of priorities: 103 responses, 24% of them from clinicians

Priority Survey Results and the top 10

The James Lind Alliance process generally aims to take the top 25 from the national survey to a final round-the-table discussion to determine the top 10.

The priority survey gave a fairly clear top 25 - all those questions which were in the top 10 for patients were in the top 25, but one question that was in the top 10 for clinicians fell just outside the top 25. This question was therefore included, bringing the shortlist to 26.

Present at the final meeting were 5 patients and 4 doctors: one doctor was ill and unable to make it on the day. There was, in the end, agreement by everyone present on the overall top 10 priorities.

The discussion was managed by facilitators from the James Lind Alliance and observed by representatives of the Department of Health and the Health Protection Agency.

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The 39 questions which were included in the priority survey are shown below with their original numbering. Those that did not make it through to the shortlist of 26 are shown in small print in grey. The top 10 are shown with a star.

Treatment

★ 1. 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 drug(s), dose, duration.

2. Is there a difference in efficacy between different initial durations of antibiotics a) where both are less than a month, e.g. 14 versus 28 days of treatment or similar; b) where one is much longer e.g. 14 days versus 100 days?

★ 3. What are the outcomes of cases where long term treatment has been used?

★ 4. Should antibiotic treatment be continued until all symptoms have resolved?

5. Do biofilms or different morphological forms (eg cyst form) of *B burgdorferi* exist in vivo and do they affect treatment regimen?

6. Are there clinically relevant differences in antibiotic susceptibility of different genospecies and strains of *B burgdorferi* sl?

7. Is treatment other than antibiotics effective in Lyme disease? (eg artesunate, DMARDs (methotrexate) or immunosuppressive drugs such as those used for rheumatoid arthritis)?

8. Are there alternative medications or therapies that might be useful in Lyme disease? E.g. the Marshall Protocol, supplements, herbal medications, acupuncture, QiCong, heavy metal chelation)?

9. Are there any particular dietary factors or exercise regimes or supportive treatments that would aid recovery from Lyme disease?

10. What is the best way to handle staying at, or returning to, work during and after treatment?

11. When should prophylactic treatment be given, and what regimen should be used? (ie preventative treatment after a tick bite)

12. If there is a further tick bite during treatment for diagnosed Lyme disease, how long should treatment be continued?

13. If there is clinical suspicion (other than EM) should treatment be started without waiting for blood test results?

14. Can response to treatment help to confirm the diagnosis?

★ 15. Are there long-term consequences if treatment is delayed?

★ 16. What is the optimal course of action if symptoms persist after initial treatment (continue current treatment or change drug or dose)?

★ 17. What is the optimal course of action if symptoms relapse after a treatment course is finished?

★ 18. How common is relapse and treatment failure and is it related to disease stage, gender, co-infections or any other factor?

★ 19. What is the optimal course of action if treatment fails i.e. if symptoms continue after the agreed course(s) of antibiotics?

20. Are corticosteroids and immunosuppressive drugs harmful in Lyme disease if used for symptomatic relief or because of a misdiagnosis?

4. 16 & 19 combined

21. What is the effect of raised body temperature on Lyme disease? Either during a course of antibiotics or independently?
22. Are there effective treatments for any of the psychiatric symptoms associated with Lyme disease?
23. What is an effective treatment for the neuropathic pain experienced in Lyme disease?

Diagnosis

24. Which single test and what combination of tests performs best in diagnosing or ruling out active Lyme disease, and should stage of the disease and patient age be taken into account when interpreting the tests?
25. Could repeated tests be used to chart disease development and treatment success or failure?
26. Are there inter-laboratory variations in the performance of the different tests for Lyme disease within the UK?
27. How effective are the current UK tests in detecting infections due to the genospecies and strains of *B burgdorferi* sl in the UK?
28. Can any of the tests identify LD in 'the dormant cyst stage'?
29. Would it be clinically advantageous and economically feasible to use a direct microbiological test in cases where diagnosis is in doubt? (eg culture, microscopy, PCR etc)
30. Under what circumstances do antibiotics, steroids and immunosuppressive drugs affect blood test results?
31. What key questions (clinical and epidemiological) should be considered to help make a diagnosis of Lyme disease in children and adults in the UK; would a weighting table be useful?
32. Are continuing symptoms following conventional recommended treatment due to continued infection, or an immune response or other process?
33. Does Post Lyme Syndrome exist, and what is its definition?
34. What is the role of SPECT scans in the differential diagnosis?
35. Are other types of test of use (CD 57 test, or testing for anti-GAD antibodies)
36. Is a Quantum QXCI/SCIO machine of use for diagnosis of Lyme disease?
37. Can Lyme disease be transmitted by vectors other than ticks?
38. Can Lyme be transmitted via other means: person to person sexually, transplacentally or by breast feeding; through organ donation; through blood transfusion?
39. Should family members be tested if they travelled with a confirmed case?

24 & 27 combined

Those questions that have been combined, although initially considered different, were during workshop discussion considered to be so interlinked as to be difficult to separate for the purposes of research.

The complete process, with the number of questions at each stage, is shown below.