Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of a vaccine for Lyme disease was compared with no vaccination.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised 15- to 70-year-old persons at risk of Lyme disease. A hypothetical cohort of 20,000 people was created using Monte Carlo simulations with 10,000 assigned to each strategy.

Setting
The setting was primary care. The economic study was set across the USA.

Dates to which data relate
Vaccine efficacy data were taken from a study published in 1998. The input parameters for the model were derived from publications dating from 1992 to 2000. The prices were taken from studies published between 1992 and 1999.

Source of effectiveness data
The estimates for the final outcomes were derived from a synthesis of published studies.

Modelling
A Markov decision analysis model was used to compare the clinical effectiveness, in terms of cases of Lyme disease avoided, and the cost-effectiveness of vaccine versus no vaccine strategies. The Markov model had 1-year cycles and a time horizon of 10 years.

Outcomes assessed in the review
The following input parameters were used in the model:

the incidence of Lyme disease as a national average and in endemic areas;

vaccine efficacy in the first and second years;

the efficacy of oral antibiotics for early infection, for isolated facial palsy and first-degree atrioventricular (AV) block, and for arthritis;
the efficacy of intravenous (IV) antibiotics for arthritis;

the probability of presenting with early Lyme disease;

the probability of neurologic sequelae of isolated facial palsy and meningitis, encephalopathy, radiculopathy or cranial neuritis;

the probability of cardiac sequelae of first-degree AV block and high-grade AV block;

the probability of arthritis sequelae;

the probability of minor and major adverse reactions to oral doxycycline; and

the probability of minor and major adverse reactions to IV ceftriaxone.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
The authors referenced 12 publications.

Methods of combining primary studies
The estimates were not combined but were reported as point estimates and a range.

Investigation of differences between primary studies
Not reported.

Results of the review
The incidence of Lyme disease was the driver of the cost-effectiveness of vaccination.

The average national incidence was estimated to have a probability of 0.000067 (6.7 cases per 100,000) with a range of 0.000 to 0.005.

The incidence in endemic regions was 0.01 (range: 0.005 - 0.10).

Vaccine efficacy was 49 (range: 50 - 95) in the first year and 76 (range: 50 - 95) in the second year.

The efficacy of oral antibiotics was 0.95 (range: 0.80 - 0.99) for early infection, isolated facial palsy and first degree AV block, and 0.70 (range: 0.60 - 0.90) for arthritis.
The efficacy of IV antibiotics was 0.90 (range: 0.80 - 0.99) in general and 0.50 (range: 0.40 - 0.60) for arthritis.

The probability of presenting with early Lyme disease was 0.85 (range: 0.60 - 0.95).

The probability of neurologic sequelae was 0.17 (range: 0.05 - 0.20) in general, 0.05 (no range given) for isolated facial palsy, and 0.12 (no range given) for meningitis, encephalopathy, radiculopathy or cranial neuritis.

The probability of cardiac sequelae was 0.06 (range: 0.02 - 0.10) in general, 0.04 (no range) for first-degree AV block, and 0.02 (no range) for high-grade AV block.

The probability of arthritis sequelae was 0.60 (range: 0.50 - 0.75).

The probability of adverse reactions to oral doxycycline was 0.04 (range: 0.00 - 0.10) for minor reactions and 0.0001 (range: 0.00 - 0.01) for major reactions.

The probability of adverse reactions to IV ceftriaxone was 0.06 (range: 0.00 - 0.10) for minor reactions and 0.0005 (range: 0.000 - 0.001) for major reactions.

**Measure of benefits used in the economic analysis**
The outcome measure used in the economic analysis was the number of cases of Lyme disease averted.

**Direct costs**
The cost boundary appears to have been that of the health service, although this was not explicitly stated. The direct costs included were for one vaccine booster plus administration, initial vaccination, doxycycline (for 14, 21 and 28 days), amoxicillin (for 14, 21 and 28 days), 3 weeks' ceftriaxone, 3 weeks' penicillin G, minor and major oral antibiotic reaction, minor and major IV antibiotic reaction, neurologic sequelae, cardiac sequelae and rheumatologic sequelae.

The price data were drawn from published studies and then adjusted to 1999 prices using the medical care services component of the Consumer Price Index. The study did not describe how the base-case costs were determined. A range of prices for each factor, established from the literature and expert opinion, was also presented. The future costs were discounted at a rate of 3% per annum.

**Statistical analysis of costs**
The costs were treated as point estimates in the base-case. The range of estimated values was explored in the sensitivity analysis.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was performed to explore variability in the data collected. A one-way sensitivity analysis was conducted on all inputs into the model, using the ranges described in the 'Results of the Review' section, and on all the costs described in the 'Direct Costs' section. A two-way sensitivity analysis was carried out with the incidence of Lyme disease and key variables.

**Estimated benefits used in the economic analysis**
The number of cases averted, that is the incremental effectiveness of the vaccine strategy compared with the no-vaccine strategy given an incidence of Lyme disease at the national average of 0.00067, was 0.00048 for both yearly and 3-yearly boosters.

The number of cases averted, given an incidence of Lyme disease in an endemic area of 0.01, was 0.0717 for both yearly and 3-yearly boosters.

These results were derived from a 10-year analysis of the two strategies.

**Cost results**
Over the 10-year analysis, given an incidence of Lyme disease at the national average of 0.00067, the average cost per patient was $781.20 for a yearly vaccine booster and $397.70 for a 3-yearly vaccine booster. Given an incidence of Lyme disease in an endemic area of 0.01, the average costs per patient were $808.80 (yearly booster) and $425.50 (3-yearly booster), respectively.

With the no-vaccine strategy, the average cost per patient was $0.60 given an incidence of Lyme disease at the national average, and $95.90 given an incidence of Lyme disease in an endemic area.

**Synthesis of costs and benefits**
At a national incidence of 0.067%, the incremental cost-effectiveness (i.e. the incremental cost per case averted by vaccination) was close to $1,600,000 with a yearly booster and $830,000 with a 3-yearly booster. In an endemic region in which the incidence of Lyme disease was 1%, the incremental cost-effectiveness was nearly $9,900 with a yearly booster and $4,500 with a 3-yearly booster.

From the one-way sensitivity analysis, it was shown that the cost-effectiveness of vaccination against Lyme disease increases as the duration of vaccine protection and efficacy of the vaccine increase, but the cost-effectiveness decreases as the vaccine cost increases.

In the two-way sensitivity analysis, the threshold for dominance of the vaccine strategy was affected by several variables. More specifically, the cost of ceftriaxone treatment, the cost of rheumatologic sequelae, the efficacy of the antibiotics, the probability of arthritis sequelae, and the probability of presenting with erythema migrans.

**Authors' conclusions**
Vaccination against Lyme disease is only cost-effective for people who live in areas where the disease is endemic and who are frequently exposed to the vector, ticks. The vaccine may only be cost-effective when the individual risk exceeds 1%.

**CRD COMMENTARY - Selection of comparators**
Although no explicit justification was given for the comparator used, it would appear to have represented current practice in the authors' setting. You should decide if the comparator represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken. The effectiveness estimates were combined to form a range of values for entering into the model.

**Validity of estimate of measure of benefit**
The benefit measure used in the economic evaluation was the number of cases of Lyme disease averted. This was derived directly from the model.
Validity of estimate of costs
The authors did not state the cost perspective. The costs included for various sequelae were not described, so it was not possible to determine whether all the relevant costs were included. The model input parameters were taken from published sources. The range of values from the literature formed the range over which the sensitivity analyses were conducted. The price estimates were established from the literature and from expert opinion. Sensitivity analyses were conducted using the ranges obtained from these sources. Appropriate adjustments were made for the price year. The costs were discounted.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. Although the issue of generalisability to other settings was not directly addressed, the range of Lyme disease incidence considered facilitates the application of the findings from this study to other settings.

The authors do not appear to have presented their results selectively and they acknowledged several limitations to the study. The analysis assumed that no serious adverse effects were associated with the vaccine. However, there have only been two years of reported follow-up. By not including the indirect costs, the cost-effectiveness of the vaccine was underestimated. The authors suggested that vaccination might also decrease the overdiagnosis and overtreatment of Lyme disease, thereby reducing the societal cost of these factors.

Implications of the study
The authors noted that their findings are consistent with those of the American Committee on Immunization Practices, which recommend vaccination only for those people who are exposed to ticks frequently, or for a prolonged time, and who live in an area where Lyme disease is endemic. Preventive measures should also be continued to avoid other tick-borne illnesses.

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Other publications of related interest


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